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Perception and regulation of emotions elicited by chemosensory signals in socially anxious individuals

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Dirk Adolph

aus Soest

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Zusammenfassung

In fünf Studien sollte der Zusammenhang zwischen der Verarbeitung und der volitionalen Regulation emotionaler Reaktionen mit sozialer Ängstlichkeit untersucht werden. Dabei wurden emotionale Reaktionen auf nicht-soziale (Ekel) und soziale (Angst, Aggression/ Dominanz) emotionale chemosensorische Signale erhoben.

In Studie I wurde zunächst untersucht, ob sozial ängstliche Personen im Vergleich zu nicht ängstlichen Personen eine Hyperreaktivität auf chemosensorische Angstsignale zeigen. Dazu wurde bei 16 nicht ängstlichen und 16 ängstlichen Personen während der Wahrnehmung von chemosensorischen Angstsignalen, Sport-Stimuli und reiner Wattepad-Kontroll-Stimuli der Startle-Reflex ausgelöst. Hierbei zeigten sich größere Startle-Reaktionen auf die Präsentation chemosensorischer Angstsignale im Vergleich zu den Kontrollstimuli. Dieser Effekt war bei sozial ängstlichen Personen ausgeprägter, als bei nicht Ängstlichen. Zudem zeigten die sozial Ängstlichen im direkten Vergleich zu den nicht ängstlichen Personen höhere Startle-Reaktionen auf chemosensorischer Angstsignale.

In den Studien II und III wurde die Spezifität dieser Hyperreaktivität sozial ängstlicher Personen untersucht. Zudem wurde die Fähigkeit zur volitionalen Emotionsregulation auf chemosensorische Angstsignale erfasst. In beiden Studien wurden jeweils 20 sozial ängstliche und nicht ängstliche Personen instruiert, ihre Emotionen in Reaktion auf ängstliche Gesichtsausdrücke im Kontext chemosensorischer Angstsignale (Studie II) oder in Reaktion auf nicht-soziale Ekel assoziierte Bilder und Gerüche (Studie III) zu verstärken oder abzuschwächen. Das Ausmaß der emotionalen Reaktionen wurde wiederum mit dem Startle-Reflex, aber auch mittels Selbstbewertungen erfasst. Es zeigte sich, dass die Probanden ihre Emotionen, nachdem sie sie abgeschwächt hatten, als weniger negativ und weniger emotional erregend einschätzten. In Studie II zeigte sich zudem, dass sozial ängstliche Personen stärkere Startle-Reaktionen auf der Wahrnehmung ängstlicher Gesichter im Kontext chemosensorischer Angstsignale zeigten als nicht ängstliche Personen. Beide Personengruppen zeigten sich gleich effektiv in ihrer Fähigkeit zur Emotionsregulation. In Studie III lösten Ekel assoziierte Gerüche stärkere Startle-Reaktionen aus als ebensolche Bilder. Geruchlich ausgelöste Emotionen konnten zudem schlechter reguliert werden als visuell ausgelöste. Die Ergebnisse aus den Studien II und III unterstreichen die einzigartige Rolle geruchlicher Reize bei der Auslösung emotionaler Reaktionen, und belegen darüber hinaus, dass die Effektivität volitionaler Emotionsregulation begrenzt ist. Sie zeigen zudem eine spezifische Hyperreaktivität sozial Ängstlicher auf soziale chemosensorische Stimuli.

In Studie IV wurde die Modulation früher (N1, N170) und später (P3, LPP) Ereignis korrelierter Potentiale (EKP) während volitionaler Emotionsregulation untersucht. Hierzu wurden die Probanden (je 18 ängstliche und nicht ängstliche Personen) instruiert, kognitive Strategien zu nutzten, um Ihre durch die Wahrnehmung ängstliche Gesichter im Kontext chemosensorischer Angstsignal, Sportstimuli, und reiner Wattepad-Kontroll-Stimuli ausgelösten Emotionen zu regulieren. Die Ergebnisse zeigen erstmals, dass auch die frühe perzeptuelle Verarbeitung von Zielreizen (N1) durch Emotionsregulation verstärkt und abgeschwächt werden kann. Nicht ängstliche Personen zeigten im Gegensatz zu ängstlichen Personen zudem Emotionsregulationseffekte in späten perzeptuellen Verarbeitungsprozessen (LPP) von ängstlichen Gesichtern im Kontext von Wattepad-Reizen. Die beobachtete verstärkte Verarbeitung der emotionalen Gesichter (N170, P3) bei sozial ängstlichen Personen ist vermutlich verantwortlich für diesen Effekt. Die zusätzliche Präsentation chemosensorischer Angst- und Sportstimuli als Kontextreize führte zu einer vertieften frühen perzeptuellen (N1, N170) und einer abgeschwächten späten evaluativen (P3, LPP) Verarbeitung der emotionalen Gesichter. Zudem zeigten sich keine Emotionsregulationseffekte, wenn die Gesichter im Kontext der chemosensorischen Angst- und Sportstimuli präsentiert wurden. Diese Resultate legen den Schluss nahe, dass die chemosenosrischen Kontextinformationen neuronale Ressourcen von der Verarbeitung der Gesichtsreize abgezogen und somit ihre volitionale Regulation erschwert haben.

In Studie V wurde erstmals untersucht, ob neben chemosensorischen Angstsignalen auch Aggressions-/ Dominanzsignale chemosensorisch zwischen Menschen kommuniziert werden können, und ob durch ihre Wahrnehmung physiologische Reaktionen ausgelöst werden. Dafür wurde bei 18 Personen die Elektrodermale Reaktion (EDR) auf die Wahrnehmung von chemosensorischen Aggressions-/ Dominanzsignalen und chemosensorischen Sportstimuli erfasst. Die Ergebnisse belegen eine verstärkte EDR in Reaktion auf die Aggressions-/ Dominanzsignale im Vergleich zu den Sport-Kontroll Reizen. Eine Regressionsanalyse zeigte zudem einen positiven linearen Zusammenhang zwischen höheren EDR auf Aggressions-/ Dominanzsignale mit höheren Werten auf einer Skala zur Erfassung sozialer Ängstlichkeit.

Zusammengefasst unterstreichen die vorliegenden Ergebnisse die Bedeutung chemosensorischer Reize für die Emotionswahrnehmung. Eine stärkere Vermeidungsmotivation wird demnach sowohl durch chemosensorische Angstsignale im Vergleich zu chemosensorischen Kontrollreizen ausgelöst (Studie I), als auch durch Ekel-

assoziierte Gerüche im Vergleich zu ebensolchen Bildern (Studie III). In Studie III zeigte sich zudem, dass die geruchlich gegenüber den visuell ausgelösten Emotionen (Ekel) schlechter reguliert werden können. Korrespondierend hierzu fanden sich keine Emotionsregulationseffekte auf späte evaluative EKP (LPP) in Reaktion auf ängstliche Gesichter im Kontext chemosensorischer Signale (Studie IV).

Die vorliegenden Ergebnisse zeigen erstmals eine Hyperreaktivität sozial ängstlicher Personen im Vergleich zu nicht Ängstlichen auf chemosensorische Angstsignale und ängstliche Gesichter im Kontext solcher Signale (Studien I, II, IV). Diese Hyperreaktivität ist spezifisch für soziale Chemosignale, da sie nicht in Reaktion auf Ekel-assoziierte Gerüche beobachtet wurde (Studie III). Die Ergebnisse von Studie V zeigen erstmals, dass auch chemosensorische Aggressions-/ Dominanzsignale zwischen Menschen kommuniziert werden können, und dass soziale Ängstlichkeit auch mit einer erhöhten Reaktivität auf diese Reize einhergeht. Die Erkenntnisse der vorliegenden Studien ergänzen somit bestehende Forschungsergebnisse, welche eine Hyperreaktivität sozial Ängstlicher in Reaktion auf visuelle und akustische soziale Reize zeigen konnten, und legen eine multimodale Hyperreaktivität sozial ängstlicher Personen nahe. In der Summe erweitern die vorliegenden Studien das vorhandene Wissen in den Bereichen der chemosensorischen Kommunikation, der Emotionsregulation und der sozialen Ängstlichkeit.

Abstract

In five studies it was aimed to explore the relationship between the processing and the voluntary regulation of emotions elicited by chemosensory signals and social anxiety. Therefore, emotional responses to non social (disgust) and social (anxiety, aggression/dominance) emotional chemosensory signals were assessed.

In study I, it was assessed whether socially anxious individuals exhibit a hyperreactivity towards chemosensory anxiety signals as compared to non-anxious individuals. Therefore, 16 non anxious and 16 socially anxious individuals perceived chemosensory anxiety signals, chemosensory sport stimuli, and cotton pad control stimuli while the startle response was elicited. The startle response was larger in the context of the chemosensory anxiety signals than in the context of control stimuli. This modulation was more pronounced in the socially anxious group, and socially anxious participants showed larger startle responses to the chemosensory anxiety stimuli than non-anxious individuals.

Within study II, and III, the specificity of this hyperreactivity in socially anxious individuals towards social emotional stimuli was investigated. Furthermore, emotion regulation was assessed. Within both studies, 20 socially anxious individuals and 20 non anxious individuals regulated their emotions in response to fearful facial expressions presented in the context of chemosensory anxiety signals (study II) or to disgusting pictures and odors (study III) while the startle reflex was assessed. Results demonstrate that participants described themselves to feel less negative, and less aroused, while down regulating their emotions as compared to the instruction to enhance their emotions in both studies. In study II, anxious participants showed larger startle responses towards faces in the context of chemosensory anxiety signals than non anxious participants, but both groups showed effective emotion regulation. In study III, disgusting odors elicited larger startle responses than pictures and emotion regulation towards them was less effective. The results highlight the unique role of chemosensory stimuli in emotion processing, and suggest that the effectiveness of cognitive emotion regulation is limited. Furthermore they demonstrate a specific hyperreactivity in socially anxious individuals towards social chemosensory signals.

Study IV examines early (N1, N170) and late (P3, LPP) event-related potential modulation during the voluntary regulation of emotions elicited by fearful facial expressions in the context of chemosensory anxiety signals. Therefore, 18 socially anxious and 18 non anxious participants used cognitive regulation strategies in response to fearful facial

expressions presented either in the context of chemosensory signals (anxiety, sport) or control stimuli (cotton pad). Results demonstrate that the early perceptual processing of target stimuli (N1) is modulated by the instruction to enhance or decrease emotions. Furthermore, anxious, but not non anxious participants showed emotion regulation effects on the late positive potential (LPP) in response to faces presented without a chemosensory context. An enhanced processing of the facial stimuli (N170, LPP) in anxious participants may account for this effect. Overall, the chemosensory context stimuli enhanced early perceptual processing (N1, N170), but diminished late evaluative (P3, LPP) processing of the faces. Correspondingly, no emotion regulation effects on the LPP were found when the faces were presented with contextual chemosensory stimuli. It is assumed that the chemosensory context information has distracted neuronal resources from the elaborative processing of the facial expressions, leading to reduced late ERPs towards the faces, and thus to impaired emotion regulation.

Study V investigated, whether chemosensory signals of aggression/ dominance are also communicated between humans, and whether they elicit physiological changes in the perceiver. Therefore chemosensory stimuli of aggression/ dominance were presented to 18 participants while the skin conductance response (SCR) was measured. Results reveal that the SCR was larger in response to chemosensory signals collected during the aggression/ dominance condition as compared to those collected during the sport control condition. Furthermore, regression analyses showed, that higher scores on trait social anxiety were related to larger SCRs towards the chemosensory signals of competition.

Taken together results highlight the unique role of chemosensory cues in emotion processing. Chemosensory anxiety signals elicited larger withdrawal motivation than control stimuli (study I). Additionally, disgusting odors elicited larger startle responses than disgusting pictures and emotions elicited by them were also less effectively regulated by the participants (study III). Furthermore, when fearful facial expressions were presented in the context of chemosensory anxiety signals, emotion regulation was not effective in terms of late positive potentials (study IV). Concerning social anxiety, the current results demonstrate for the first time a hyperreactivity (more intense early stimulus processing, larger withdrawal related motor behavior) of socially anxious individuals towards social chemosensory signals of anxiety, and fearful facial expression presented in the context of these stimuli, as compared to non anxious individuals (study I, II, IV). This hyperreactivity was specific for social emotional signals and did not manifest in response to non social disgusting odors (study III). Furthermore, it could be shown that also social signals of aggression/ dominance are

communicated chemosensorily between humans and that socially anxious individuals are also more sensitive towards these stimuli. These findings parallel research showing a hyperreactivity of socially anxious individuals towards visual social signals of threat. In sum, the current studies extend existing knowledge in the fields of chemosensory communication of emotions, emotion regulation and social anxiety.

1 Theoretical and empirical background

1.1 Introduction

The studies presented here investigate the perception and regulation of emotions elicited by chemosensory signals. It is thereby aimed to explore the effects of chemosensory signals of emotional states on the emotional responding in socially anxious individuals.

Emotions have evolved throughout evolution to promote the individuals survival and adaptation to changing environmental demands. They occur in response to internal or external stimuli that are meaningful to the individuals' survival or well being. Emotions are also important elements of everyday social interaction, and the ability to communicate emotions is important for both the encoder, and the decoder. For example the communication of anxiety provides important information of environmental dangers to the perceiver. Emotions are thereby communicated via diverse communication channels, including vision and chemoreception. In this sense, the experience, communication and perception of emotions is adaptive. However, in several situational contexts, the expression of emotions may be inadequate. Moreover, while in most cases emotions like anxiety helps to protect the organisms from a wide variety of threats, anxiety disorders arise from a dysregulation of normal defensive responses. This may lead to states of heightened anxiety, sustained negative or inappropriate affect, chronic worry, and avoidance. Thus, the voluntary or automatic control of emotional responses - that is emotion regulation - is thought to play a major role in everyday social interaction, and is of special importance for the maintenance of mental health.

Within this framework the introduction section of the present thesis provides a brief overview over emotion theories, the communication of emotions via visual and chemosensory channels, as well as over brain systems involved in the processing of these signals. The theoretical and biological basis of emotion regulation is introduced, and the processing of emotional signals in social anxiety is described.

1.2 Defining emotions

Despite the fact that there is still debate concerning the definition of the term "emotion", there is also some agreement among what is considered an emotion (Hamm, Schupp, & Weike, 2002; Janke, Debus, & Schmidt-Daffy, 2008). Emotions have evolved throughout evolution to promote the individuals survival and adaptation to changing environmental demands (Frijda,

1994; Levenson, 1994, 1999; Smith & Lazarus, 1990; for an overview see Keltner & Gross, 1999). They provide the motivation to react to environmental stimuli with incentive character (Davidson, Jackson, & Kalin, 2000).

In general, two distinct theoretical approaches in defining emotions have been proposed. Regarding the categorical theories of emotion, researchers have stated that throughout evolution a finite set of "basic emotions" have evolved. Each of these emotions is thereby thought to be unique in its adaptive function and physiological expression (Darwin, 1872). Modern theorists have mainly described six basic emotional states: Happiness, anger, fear, disgust, sadness, and surprise. Each of these emotions is thereby expressed by a distinct facial expression, which can be universally recognized largely independent of cultural influences (Ekman & Friesen, 1971). Within the framework of dimensional theories, emotions are proposed to be action dispositions founded in two motivational systems, organizing behavior along a basic appetitive-aversive dimension (Dickinson & Dearing, 1979; Konorski, 1967; Lang, Bradley, & Cuthbert, 1990; based on the "Lust-Unlust" dimension defined by Wundt, 1896). An appetitive motivational system activates approach behavior when consummation, procreation or nurturance is the subjects' goal, while the aversive motivational system activates defensive behaviors in order to protect the organism from threat (Bradley, Codispoti, Cuthbert, & Lang, 2001; Lang, et al., 1990). Motivational engagement of the individual is thereby determined by the hedonic value (emotional valence) and the amount of emotional arousal elicited by the emotional stimulus (Bradley, et al., 2001; Russell, 1979; Watson & Tellegen, 1985). While positively valenced stimuli initiate approach motivation, negatively valenced stimuli activate defensive motivation. The amount of emotional arousal mediated by the stimulus determines the intensity with which the respective system is activated.

1.3 Measuring emotions

To accomplish their adaptive function emotions provide a bodily milieu that is ideal for effective responses (Levenson, 1999). Thus, emotions are whole body phenomena accompanied by changes in subjective experience, behavior, and central (see reviews in Phan, Wager, Taylor, & Liberzon, 2002; Phan, Wager, Taylor, & Liberzon, 2004) as well as peripheral physiology (Ekman, 1992; Izard, 1993; Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). Emotions can disrupt ongoing behavior and shift attention towards the emotion

eliciting stimulus (Anderson, 2005; Anderson & Phelps, 2001; Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Öhman, Flykt, & Esteves, 2001), activate associated memory networks (LeDoux, 1993), and rapidly initiates somatic reactions, like facial expressiveness (Dimberg, Thunberg, & Grunedal, 2002; Phelps, 2004), muscular tension (Azevedo, Volchan, Imbiriba, Rodrigues, Oliveira, Oliveira et al., 2005), autonomic nervous system (Bradley, et al., 2001; Ekman, Levenson, & Friesen, 1983), as well as endocrine activity (Fredrikson, Sundin, & Frankenhaeuser, 1985; Zorawski, Cook, Kuhn, & LaBar, 2005) (for a review of this topic see Levenson, 1999). Taken together, methodological approaches to measure emotions should address these three manifestation levels: subjective experience, behavior, and central and peripheral physiology.

To assess the subjective experience of emotion the Self Assessment Manikin (Bradley & Lang, 1994), a language free rating scale has been developed. It is mainly based on the three dimensions “Lust”, “Spannung” and “Beruhigung”, defined by (Wundt, 1896), and consist of the three scales “valence”, “arousal, and “dominance”. These three dimensions have consistently been shown to underlie affective judgments of diverse categories of emotional stimuli (Bradley, et al., 2001; Russell, 1979; Watson & Tellegen, 1985). Interestingly, it could be demonstrated that judgments on the valence and arousal scale systematically vary with physiological responses to the same stimulus. In brief, the heart rate response, as well as the startle reflex varies with the pleasure of the presented stimulus, while the skin conductance response, a measure of sympathetic nervous system activity, systematically varies with arousal ratings. Thus the SAM can be used as a rough measure of emotional motivation of the individual towards the currently perceived emotional stimulus. It is therefore well suited to assess the subjective experience of emotions according to the biphasic theory of emotions.

To assess withdrawal related action tendencies associated with emotion, the startle response has been widely used. The startle reflex is a protective whole body reflex initiated after the perception of a sudden intense stimulus, such as a loud noise. It is thought to be a defensive reflex, indicating withdrawal from the stimulus source. It involves contractions of various muscle groups, and subsequently leads to changes in physiology, including blood pressure, heart rate, and breathing (see Dawson, Schell, & Böhmelt, 1999). The startle reflex as a measure of defensive motivation has been investigated intensively. In one of the first experiments, it has been observed that in rats the whole body startle reaction is potentiated when it is elicited during the application of a conditioned stimulus (CS, light) previously paired with an aversive unconditioned stimulus (UCS, footshock) (Brown, Kalish, & Farber,

1951). The neuronal pathway included in fear potentiated startle has now been described in detail. In terms of acoustically induced startle, the acoustic stimulus reaches the ear, and is then transmitted via the cochlear nucleus to the brain stem (N. reticularis pontis caudalis). On level of the brainstem, affect modulation is largely mediated by a cortical-subcortical network focusing on the amygdala. Afterwards a motor response is initiated via motor neurons (Davis, 1992a). In humans, one of the earliest components of the startle response is the eye-blink reflex. It has been extensively studied using the picture viewing paradigm. As mentioned before emotions are thought to be part of two basic motivational systems where the appetitive system activates approach behavior in response to appetitive stimuli and the defensive system activates defense behavior in response to potentially harmful stimuli in order to protect the organism from threat. These two systems modulate reflex responses that are compatible or incompatible with the required behavior. Thus, in humans it could be observed that the eyeblink startle reflex elicited by a loud noise varies with emotional valence of the stimulus perceived simultaneously. For example, in comparison to neutral stimuli the startle response is potentiated when viewing slides with negative content, and reduced when viewing positive pictures (Bradley, et al., 2001; Lang, et al., 1990; Vrana, Spence, & Lang, 1988).

The involvement of the autonomic nervous system in the perception of emotional stimuli has been widely investigated using electrodermal activity. The electrodermal system has been closely linked with psychological concepts of emotion, arousal and attention (Dawson, Schell, & Filion, 2007). Major constituents of this system are the eccrine sweat glands which are involved in thermoregulation of the body, as well as in grasping behavior. Those glands occurring on the palmar and plantar surface are largely involved in grasping and have been demonstrated to be more responsive to psychologically significant stimuli than to thermal stimuli. This phenomenon has been named “psychological sweating” (Dawson, et al., 2007). It is controlled by the autonomic nervous system, and thus activity of the electrodermal system reflects activity of the autonomic nervous system. Activation of the electrodermal system has been linked to the orienting response towards motivationally meaningful stimuli (Barry, 1990). Accordingly, several lines of research have repeatedly shown that the skin conductance response (SCR) varies with emotional arousal elicited by the emotional stimulus (for an example see Bradley, et al., 2001). Therefore the SCR has been argued to be an ideal first candidate to assess the motivational relevance of stimuli.

Finally, using electroencephalography it is possible to assess the electrical activity produced by the firing of neurons within cortical areas of the brain. Moreover, event related

brain potentials provide the possibility to assess the processing of emotional stimuli in a highly time sensitive manner. In general, it has been suggested that early ERP components, like the N100, are affected by stimulus characteristics like stimulus intensity, and selective attention paid to the stimulus (Hillyard, Vogel, & Luck, 1998; Krauel, Pause, Sojka, Schott, & Ferstl, 1998). The face specific N170 component has been argued to reflect the structural encoding of facial features and configurations (Bentin, Allison, Puce, Perez, & McCarthy, 1996), and may also vary with emotional content of the stimulus, indicating that emotional stimuli are more deeply processed (Batty & Taylor, 2003; Mühlberger, Wieser, Herrmann, Weyers, Troger, & Pauli, 2009). However, late components, like the P3 reflects motivation-driven elaborated processing of (subjective) stimulus meaning (Duncan-Johnson & Donchin), and has been linked to the facilitated perceptual processing of motivationally relevant arousing stimuli (Late Positive Potential, LPP, Cuthbert, et al., 2000; Schupp, Cuthbert, Bradley, Cacioppo, Ito, & Lang, 2000; Schupp, Junghofer, Weike, & Hamm, 2003; Schupp, Ohman, Junghofer, Weike, Stockburger, & Hamm, 2004).

1.4 Neuronal processes in emotion generation

Early studies on the neural basis of emotion has focused on the limbic system as a mediator of emotion including the hippocampus, the anterior thalamus, cingulate gyrus, hypothalamus, the basal ganglia, as well as the orbitofrontal cortex and the amygdala (Maclean, 1949; MacLean, 1952). More recently, researchers have focused on the concept of fear and fear learning to uncover the neuronal basis of emotions (LeDoux, 1995). The expression of fear is considered to be largely conserved across human cultures and at least throughout most mammalian species. Fear learning is considered to be a highly adaptive response to aversive events that ensure survival in changing and novel environments (LeDoux, 1995). Several studies have described the neuronal circuits involved in fear conditioning from stimulus perception to emotional responses. Thereby, both animal and human studies have consistently shown that the amygdala is involved in the acquisition, and the expression of conditioned fear responses (Davis, 1992b; LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; LeDoux, Cicchetti, Xagoraris, & Romanski, 1990). In detail, emotional information reaches the lateral nucleus of the amygdala via sensory thalamus. This region of the amygdala receives input from sensory association cortex, thalamus, perirhinal cortex, and hippocampus. The lateral nucleus then projects the integrated stimulus information to the central nucleus of the amygdala from which projections initiate defensive behaviors (via central grey), autonomic nervous system

responses (via lateral hypothalamus, and medulla), and stress responses involving pituitary adrenal axis activation (via bed nucleus of the stria terminalis, paraventricular hypothalamus) (see Figure 1.1, review in LeDoux, 1995). One important finding was that information about a stimulus or a conditioned stimulus can reach the amygdala through two separate pathways. On the one hand, a subcortical pathway projects from the thalamus directly to the amygdala, providing fast but coarse stimulus information to enable rapid responses on the basis of limited stimulus information (LeDoux, 1995). On the other hand, emotional information also projects through a cortical pathway projecting from the sensory thalamus via sensory cortical areas to the amygdala.

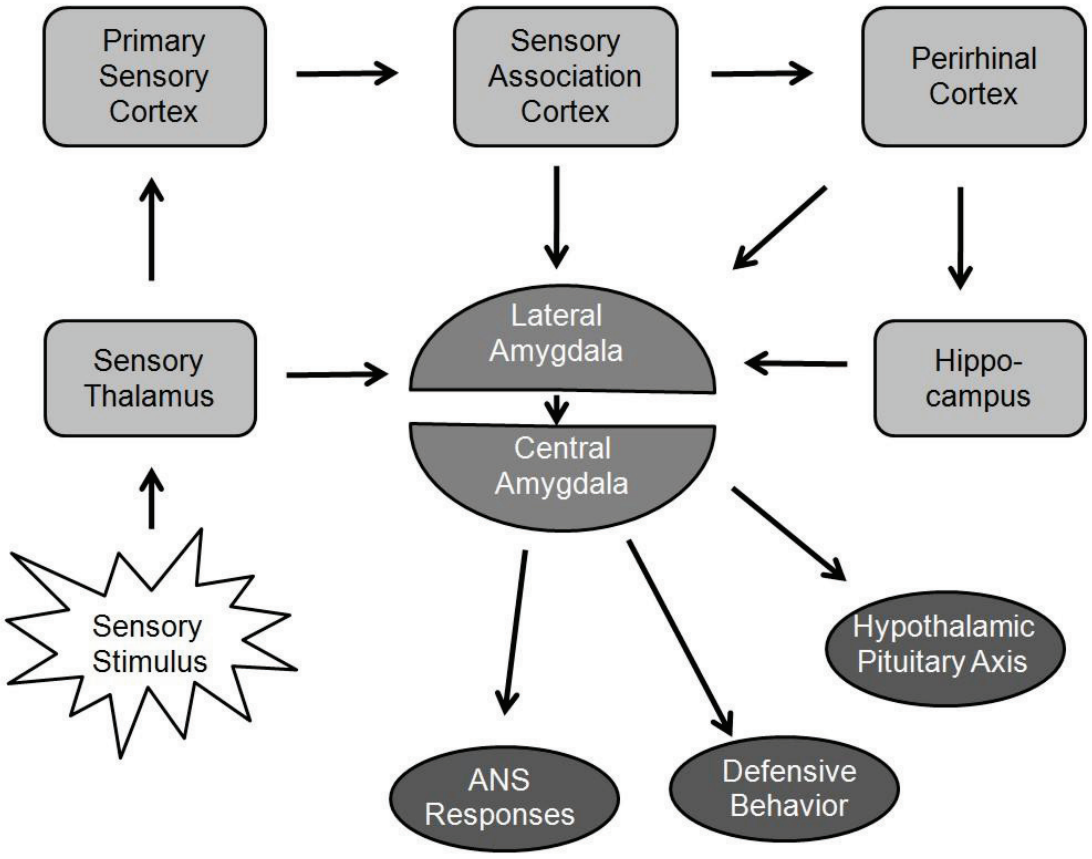

Figure 1.1. The fear conditioning pathway: Emotional information reaches amygdala via sensory thalamus. The lateral nucleus of the amygdala receives input from several cortical areas and projects the integrated information to the central nucleus of the amygdala from which projections initiate defensive behaviors (via central grey), autonomic nervous system responses (via lateral hypothalamus, and medulla), and stress responses involving pituitary adrenal axis activation (via bed nucleus of the stria terminalis, paraventricular hypothalamus)

The rapid and automatic fear processing and the immediate responses to environmental threat, mediated via subcortical projections, are thought to be highly adaptive (Mineka & Öhman, 2002; Öhman & Mineka, 2001). However, the cortical projections reach the amygdala more slowly, but provide more detailed information about the stimulus, as well as the context in which the stimulus has to be evaluated to enable more flexible emotional responses (Phillips & LeDoux, 1992). The existence of a subcortical pathway in fear conditioning indicates that on the one hand emotion processing, and emotional responsiveness does not necessarily rely on conscious stimulus processing (LeDoux, 1995). Indeed, it has been repeatedly shown that unconsciously perceived emotional stimuli can initiate a variety of emotional responses. For example, although conscious stimulus evaluation is disrupted using a backward masking procedure, amygdala activation can still be observed in response fear relevant angry (Morris, Öhman, & Dolan, 1998) and fearful (Whalen, Rauch, Etcoff, McInerney, Lee, & Jenike, 1998) facial expressions. In addition, in a series of experiments it has been shown that responses of the autonomic nervous system (for example responses of the electrodermal system) to previously conditioned fear relevant stimuli can be observed in the absence of conscious stimulus perception (Öhman & Soares, 1994; Soares & Öhman, 1993). In the same vein, facial expressiveness has been observed in response to unconsciously perceived emotional expressions (Dimberg, Thunberg, & Elmehed, 2000).

However, on the other hand, it has been suggested that the subjective experience of emotions does rely on conscious emotion evaluation (LeDoux, 1994), and that the amygdala is not necessarily for the conscious experience of emotions (Anderson & Phelps, 2002). This issue is reflected in the appraisal theories of emotion, and is described for example in the modal model of emotion (Gross & Thompson, 2007). Appraisal theories of emotion state that the emotional response of an individual towards a significant emotional situation (internal or external) catching the persons' attention, is tightly linked to the persons' appraisal of that situation. That is, the persons' assessment of, for example, the situations familiarity, valence, and reinforcing relevance (Ellsworth & Scherer, 2003). (see Figure 1.2).

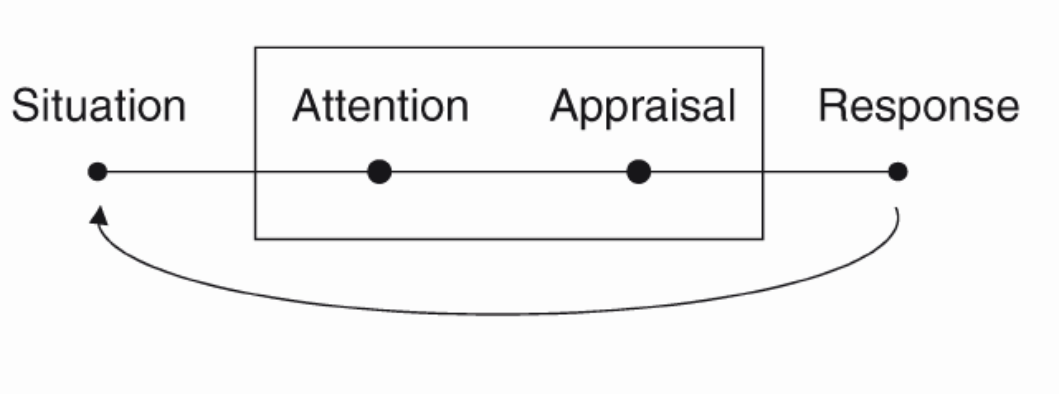

Figure 1.2. The modal model of emotion: According to the modal model of emotion an emotional response is the outcome of a person-situation transaction that compels attention, has a particular meaning to the individual and produces a flexible multisystem response. The emotional response generated by the appraisal, involve changes in experiential, behavioral, and neurobiological response systems. The emotional response in turn may recursively change the situation giving rise to another person-situation interaction (Aspects of this model are further discussed later) (adapted from Gross & Thompson, 2007).

In line with this, it is has been argued that there is considerable interaction between brain regions involved in emotional and cognitive neuronal processing (LeDoux, 1994; LeDoux, 2000; Phelps, 2006). Thus, besides the amygdala, also higher order brain areas are implicated in the processing of emotional stimuli and in the regulation of emotional responses. The orbitofrontal cortex has been shown to be strongly involved in the valence coding of emotional stimuli (Anderson, Christoff, Stappen, Panitz, Ghahremani, Glover et al., 2003), in the coding of reward value of primary reinforcing stimuli, and in stimulus-reinforcement association learning (Kringelbach & Rolls, 2004). The orbitofrontal cortex is also implicated in complex decision making processes. Several studies have shown that patients with lesions to the orbitofrontal cortex are performing worse in decision making tasks and are impaired in the flexible adaptation of strategies after the switching of reward contingencies (Bechara, Damasio, & Damasio, 2000; Fellows & Farah, 2005).

Besides from lesion studies, evidence from neuroimaging studies suggests that medial prefrontal cortical (MPFC) areas may serve a general role in emotional processing because MPFC activity is frequently observed in brain imaging studies on emotion processing and its activation is not emotion specific (Phan, et al., 2002; Phan, et al., 2004). For example, emotional films, pictures, emotion recall as wells as positive and negative emotion, the mixture of these emotions all separately engage the MPFC (Reiman, Lane, Ahern, Schwartz, Davidson, Friston et al., 1997). Moreover, the MPFC was observed to be active during the

feeling of self generated emotions (Damasio, Grabowski, Bechara, Damasio, Ponto, Parvizi et al., 2000; Ochsner & Gross, 2007; Reiman, et al., 1997). It has been argued that the MPFC is involved in the cognitive aspects of emotion processing like attention to emotion, appraisal/identification of emotion, and awareness of emotions (Drevets & Raichle, 1998; Phan, et al., 2004). The MPFC has dense and direct interconnections to the amygdala (Price, 2003), and thus is especially well suited to be involved in the top-down regulation of emotional responses (Ochsner & Gross, 2007).

Neuroimaging studies also consistently find activations of anterior cingulate cortex (ACC), and insula when emotional stimuli are perceived or when participants are engaged in emotion related tasks (Phan, et al., 2002; Phan, et al., 2004). For example, emotional recall or imagery and emotional tasks with cognitive demand recruit activity in the anterior cingulate and insula. In the somatic markers theory it is proposed that the insula might integrate emotionally relevant information between somatic internal feelings and external stimuli (Damasio, Everitt, & Bishop, 1996). The insula is interconnected with the amygdala and may, via these projections, provide interoceptive information based on internal somatic sensations evoked by emotional stimuli to the amygdala. Accordingly, it has been proposed that the insula might constitute an "alarm center for internally sensed dangers or homeostatic changes" (Phan, et al., 2004, p. 264) and as such is involved in the evaluation of interoceptive emotional meaning (Reiman, et al., 1997). Finally, the insula is also involved in the decoding of social emotions (Britton, Phan, Taylor, Welsh, Berridge, & Liberzon, 2006) and empathic feelings (Jabbi, Swart, & Keysers, 2007). The ACC is thought to participate in attention guided regulation of both cognitive (dorsal ACC), and emotional neuronal processing (ventral/ rostral ACC) (Bush, Luu, & Posner, 2000). The ACC has close connections to prefrontal cortical regions, including the medial prefrontal cortex, and thus has been proposed to interact with the MPFC to regulate tasks with cognitive and affective components during an emotional response (Phan, et al., 2004). Furthermore, it seems to be involved also in the processing of social emotional information (Britton, Phan, et al., 2006; Britton, Taylor, Sudheimer, & Liberzon, 2006).

Taken together, Ochsner and Gross (2007) stated that the generation of emotional phenomena including emotional responding and/ or emotional experience, can either be mediated by bottom-up or top-down processes. Bottom-up processes mainly consist of emotional learning of stimulus-response associations (i.e. classical conditioning) and associations between actions and their outcomes (i.e., operant conditioning). Top-down

emotion generation on the other hand is seen as the product of an individuals' appraisal of the situation, according to his goal, wants and needs (Ellsworth & Scherer, 2003), and enables the individual to actively control the appraisal process (Ochsner & Gross, 2007). Thus, it is proposed that emotion processing integrates bottom-up systems that encode the affective properties of stimuli, and generate fast and adaptive emotional reactions (like the amygdala) and control systems that enable effective and controlled top-down stimulus appraisals (prefrontal Cortex, ACC) (Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner, Ray, Cooper, Robertson, Chopra, Gabrieli et al., 2004) (see Figure 1.3).

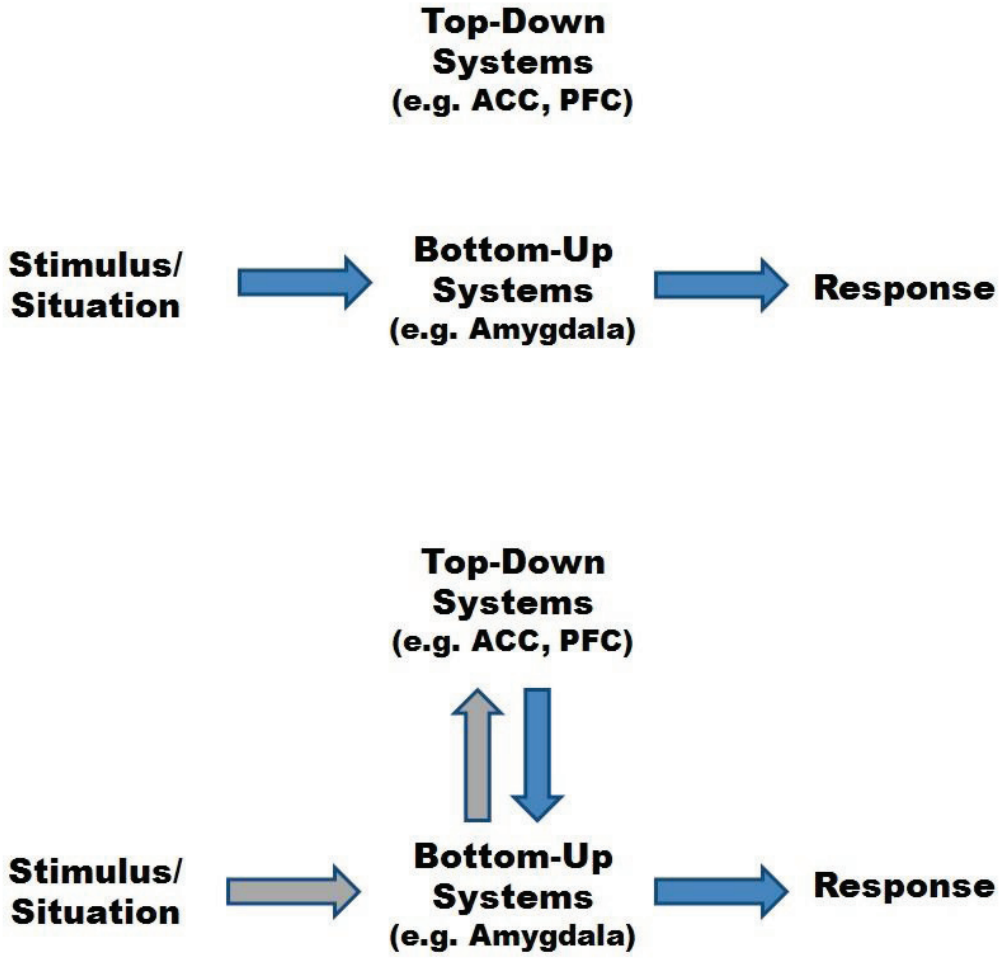

Figure 1.3. Bottom-Up (upper part) and Top-Down (lower part) emotion generation: During bottom-up emotion generation an emotional response is generated directly after the perception of a stimulus with intrinsic or previously learned affective value. In top-down emotion generation, an otherwise neutral stimulus (grey arrows) is appraised as emotionally evocative (for example threatening) and initiates an emotional response (blue arrows) (adapted from Ochsner and Gross, 2007)

1.5 Social communication of emotions

According to Darwin (Darwin, 1872), the expression of emotions has evolved through evolution and constitute a highly adaptive signaling system promoting the survival of the species. The expression of emotion also serves communicative functions, and organizes social interaction between conspecifics in providing the reaction of an individual and its corresponding behavior intentions to other group members (Scherer, 2001). Moreover, social emotional signals provide an important channel for the communication of potential environmental dangers via fearful facial expressions, and the rapid perception of these stimuli is discussed to serve to enhance awareness and behavioral responses toward emotionally relevant stimuli (Vuilleumier, 2002). Consequently, changes in emotional expressiveness are considered a central component of the emotional response (Scherer, 2001). Most research in the communication of emotions between humans has focused on the expression of emotion through emotional facial expressions. According to its' adaptive function the ability to reliably decode emotions from facial displays and to encode emotional facial expressions is largely independent of cultural context (Ekman, 1994; Ekman & Friesen, 1971). There is evidence that even young babies can express emotions in response to emotional stimuli in facial expression (Rosenstein & Oster, 1988; Stenberg, Campos, & Emde, 1983). Emotional reactions to emotional facial expressions have been observed even in 5 month old babies (Balaban, 1995), suggesting successful encoding of emotional information from facial expressions. Moreover, according to the preparedness theory (Seligman, 1970; Seligman, 1971), it has been demonstrated that fear conditioning is more resistant to extinction with fear relevant facial expressions than neutral or happy facial expressions (Dimberg, 1986) and even possible with unconsciously perceived faces (Esteves, Parra, Dimberg, & Öhman, 1994). This suggests that fear relevant facial expressions are evolutionary significant stimuli, and thus are preferentially associated with defensive responses (Öhman & Mineka, 2001). Accordingly, the perception of emotional facial expressions initiates a variety of emotional responses. For example, threatening facial expressions have been shown to rapidly capture attention (Öhman, Lundqvist, & Esteves, 2001), and initiate approach and avoidance motivation, as measured behaviorally (Adams, Ambady, Macrae, & Kleck, 2006), or in terms of the affect modulated startle reflex (Hess, Sabourin, & Kleck, 2007; Springer, Rosas, McGetrick, & Bowers, 2007). The perception of fear relevant facial expressions elicit physiological responses in the perceiver, for example changes in electrodermal activity or heart rate (Dimberg, Fredrikson, & Lundquist, 1986; Merckelbach, Van Hout, Van den Hout, & Mersch, 1989; Vrana & Gross, 2004), and facial mimicry (Dimberg, 1982), suggesting emotional contagion in response to

emotional facial expressions (Hess & Blairy, 2001; Lundqvist & Dimberg, 1995; Schneider, Gur, Gur, & Muenz, 1994).

1.6 Neuronal processing of social signals of fear

As mentioned above the processing of fear is mediated subcortically and fear related stimuli are processed fast and automatic (Öhman & Mineka, 2001). In line with this, studies using event related brain potentials (ERPs) could show that fearful facial expressions are analyzed more rapidly than other facial expression and can affect cortical processing at very short latencies (Adolphs, 2008; Eimer & Holmes, 2007). On a neuronal level, the perception of social fear signals recruit brain regions involved in the perception of social stimuli, as well as emotion related brain areas. As for non-social fear related stimuli, the amygdala seems to be crucial for the recognition of fear from facial expressions (Adolphs, Tranel, Damasio, & Damasio, 1994; Adolphs, Tranel, Damasio, & Damasio, 1995). Thereby as compared to happy expressions the amygdala has been shown to habituate less rapidly during the perception of fearful expressions, (Wright, Fischer, Whalen, McInerney, Shin, & Rauch, 2001), is responsive even to the presentation of fearful eye-whites only (Whalen, Kagan, Cook, Davis, Kim, Polis et al., 2004), or when the faces are presented unconsciously (Whalen, et al., 1998). Finally, in a direct comparison, the amygdala is activated more during the perception of fearful than angry facial expressions (Whalen, Shin, McInerney, Fischer, Wright, & Rauch, 2001). Besides the amygdala, the perception of facial expressions recruits further brain regions which are associated with the processing of emotional and social signals. The fusiform gyrus (Kanwisher, 2000; Yovel & Kanwisher, 2004), is especially involved in the representation of static features of faces and thus involved in the encoding of identity. Recent evidence suggest that fearful as compared to neutral expression modulate the response of the fusiform gyrus indicating a more sophisticated analysis of fearful as compared to neutral information (Vuilleumier, Armony, Driver, & Dolan, 2001). Fearful facial expressions also activate areas in the frontal cortex, including lateral prefrontal cortex (Kesler-West, Andersen, Smith, Avison, Davis, Kryscio et al., 2001) and the orbitofrontal cortex (Vuilleumier, et al., 2001).

Taken together, the perception of fear related social signals and the perception of non-social fear relevant stimuli involve largely overlapping brain regions. Moreover, the

perception of threatening facial expression, as well as non-social fear relevant stimuli elicits rapid orienting, as well as emotional reactions when being perceived.

1.7 Chemosensory communication of stress in animals

The ability of chemosensory perception has developed early in evolution and is shared by many organisms, including bacteria. Moreover, throughout the animal kingdom many species have developed the ability to communicate via chemosensory signals, and this form of communication has been argued to be highly adaptive (Wyatt, 2003). Indeed, chemical communication has many advantages above other forms of communication. Chemosensory signals can be produced at considerable low costs for the organism, are easily transmitted over physical barriers and long distances, and are also perceptible by darkness or in noisy environments. Within may species, including mammals, chemosensory signals have been shown to influence and mediate a variety of social behaviors, including mate choice, kin recognition, and the constitution and maintenance of social hierarchies (Brennan & Zufall, 2006; Wyatt, 2003). For example, evidence suggests that aggression/ dominance is communicated chemosensorily between animals. In rodents, territory owner scent marks their habitat to advertise their identity and competitive ability or dominance over their territory (Hurst, 1993). Responses to those scent marks vary in dependence of the perceivers own competitive ability (Gosling, Atkinson, Dunn, & Collins, 1996), and are usually avoided to prevent possible conflicts (Jones & Nowell, 1973). Those chemosensory cues also initiate attention and orientation towards a possible aggressor (Hurst, 1993) and subsequent withdrawal behavior. Moreover, also inter-male aggressive behavior may be related to the recognition of chemosensory cues from the opponent prior to an encounter (Mackintosh & Grant, 1966; Tollman & King, 1956), and male mice produce an androgen-dependent pheromone that elicits aggressive behavior in other males (Mugford & Nowell, 1970). Finally, oestrous female mice use scent marks as a reliable signal of high quality mates and show more sexually related behavior when interacting with dominant territory owners(Rich & Hurst, 1998).

Another especially important form of chemosensory communication constitutes the communication of alarm signals between conspecifics. Alarm signals are discussed to be the most widespread form of chemosensory communication and have evolved independently in all major taxa (Wyatt, 2003). The existence of an alarm signal has been first described in the

minnow by von Frisch who observed flight behavior in response to the presentation of wounded conspecifics (von Frisch, 1941). Since von Frisch, the communication of alarm states/ stress is best described in rodents. It could be demonstrated that mice can distinguish the scent of stressed conspecifics from those of unstressed conspecifics (Valenta & Rigby, 1968). Moreover, it has been repeatedly shown that the presentation of chemosensory signals of stressed mice initiate avoidance of and withdrawal behavior in perceiving mice towards the odor source (Inagaki, Kiyokawa, Kikusui, Takeuchi, & Mori, 2008; Kiyokawa, Shimozuru, Kikusui, Takeuchi, & Mori, 2006; Müller-Velten, 1966; Rottman & Snowdon, 1972; Zalaquett & Thiessen, 1991). Thereby the intensity of defensive behaviors in reaction to the alarm signal seems to be related to the intensity of the stressor applied to the odor producing rats (Mackay-Sim & Laing, 1981). Moreover, the perception of chemosensory signals of stressed conspecifics has also been observed to initiate a number of stress-related physiological adaptations. Perceiving animals show stress induced analgesia (Fanselow, 1985; Moynihan, Karp, Cohen, & Ader, 2000), hyperthermia (Kikusui, Takigami, Takeuchi, & Mori, 2001; Kiyokawa, Kikusui, Takeuchi, & Mori, 2005), and changes in cellular and humoral immune responses (Cocke, Moynihan, Cohen, Grota, & Ader, 1993; Moynihan, et al., 2000). The production of chemosensory alarm signals seems to depend on the activity of the hypothalamus-pituitary-adrenal-axis (Abel, 1994), and the amount of glucocorticoid produced by the stressed rat is positively related to the intensity of defensive behaviors in the perceiving rat (Mackay-Sim & Laing, 1981). Finally, it is suggested that the Grueneberg ganglion, a recently discovered olfactory sub system which was found also in human embryos, mediate the detection of chemosensory alarm signals in mice (Brechbuhl, Klaey, & Broillet, 2008). However, in animals, the vomeronasal organ (Doving & Trotier, 1998), trace amin associated receptors (Liberles & Buck, 2006), as well as the olfactory system, are also discussed to serve this function. Taken together, the results from animal research suggest that the chemosensory signals produced by stressed animal convey an alarm signal, initiating a number of behavioral and physiological adaptations in the perceiving animal. And these adaptations are best described as a stress response themselves.

1.8 Chemosensory communication of anxiety in humans

Although it has been argued that humans are a rather microsmatic species (Smith & Bhatnagar, 2004), relying more on vision and audition, it has been impressively demonstrated that olfactory capabilities of humans are comparable to other mammals (Porter, Craven, Khan,

Chang, Kang, Judkewitz et al., 2007). Like in other species, chemosensory signals also influence human social behavior (Jacob, Zelano, Hayreh, & McClintock, 2002). In line with this, chemosensory signals have been shown to be involved in mate choice and reproduction (Jacob, McClintock, Zelano, & Ober, 2002; McClintock, 1971; Preti, Wysocki, Barnhart, Sondheimer, & Leyden, 2003; Wedekind & Füri, 1997), and on a neuronal level, humans can distinguish self from non-self body odors (Pause, Krauel, Sojka, & Ferstl, 1998). Axillary secretions, consisting of secretions from the sebaceous, eccrine, apoeccrine, and apocrine glands (Heckmann, Teichmann, Pause, & Plewig, 2003), are thereby thought to form one source of chemosensory signals in humans (Jacob, McClintock, et al., 2002)

Moreover, a growing body of evidence suggests that like many non-human species, also alarm states, like fear or anxiety are communicated chemosensorily between humans. Initial evidence from behavioral studies suggests that human axillary secretions donated during an anxiety condition (i.e. the viewing of a frightening movie) can be discriminated above chance from axillary secretions donated in a neutral or funny situation. However, results also indicate that the perceiving individuals were not able to reliably classify the samples as chemosensory anxiety cues (Ackerl, Atzmueller, & Grammer, 2002; Chen & Haviland-Jones, 2000). On a behavioral level, it has been shown that the perception of chemosensory anxiety signals has an influence on cognitive performance. Recipients made slower, but more accurate decisions in a word association test, indicating that anxiety signals enhance cautiousness in decision making (Chen, Katdare, & Lucas, 2006). Recent results replicated the findings of enhanced response latencies during the perception of chemosensory anxiety signals, but also reported higher risk taking behavior in a gambling task (Haegler, Zernecke, Kleemann, Albrecht, Pollatos, Brückmann et al., 2010). Chemosensory signals of anxiety have also been reported to have an influence on the visual perception of emotional signals. It could be shown that the perceptual acuity of visual safety cues (happy facial expressions) is diminished in the context of chemosensory anxiety signals (Pause, Ohrt, Prehn, & Ferstl, 2004), while the perceptual acuity of fear from ambiguous facial expression (morphs between happy and fearful facial expressions) is enhanced (Zhou & Chen, 2009).

Most importantly, it could be shown in the animal model that the perception of chemosensory alarm signals directly induces withdrawal behavior, like avoidance of or flight from the odors source. In line with this, it has been demonstrated that the perception of chemosensory anxiety signals enhances the startle-reflex in humans (Prehn, Ohrt, Sojka, Ferstl, & Pause, 2006). Interestingly most of the participants were unable to discriminate the

chemosensory stimuli from room air. Thus, the results suggest, that chemosensory signals pre-attentively prime defensive behaviors in humans. Startle potentiation during the perception of alarm signals was also recently observed in rats (Inagaki, et al., 2008). Research in rodents has documented hat a key structure involved in the potentiation of the startle reflex is the amygdala (Davis, 1992a). Thus, in line with the findings on startle potentiation, a recent brain imaging study found that the amygdala is indeed involved in the processing of chemosensory signals collected from humans in a highly stressful condition (Mujica-Parodi, Strey, Frederick, Savoy, Cox, Botanov et al., 2009). A recent ERP study showed intensified neural investment of chemosensory anxiety signals as compared to sport control stimuli (Pause, Lübke, Laudien, & Ferstl, 2010). The medial prefrontal cortex, a region strongly involved in the processing of emotionally relevant stimuli (Phan, et al., 2002; Phan, et al., 2004), was identified as the source of this effect. Furthermore, the perception of chemosensory anxiety signals does recruit a neuronal network (fusiform gyrus, insula, precuneus, cingulate cortex) implicated in the processing of social emotional information and in the regulation of empathic feelings, and it was found that also attention networks (thalamus, dorsomedial prefrontal cortex) are more effectively triggered by chemosensory anxiety than control stimuli (Prehn-Kristensen, Wiesner, Bergmann, Wolff, Jansen, Mehdorn et al., 2009).

Taken together, converging evidence suggest that chemosensory anxiety stimuli constitute fear relevant signals, which are processed within the amygdala, a brain region involved in the processing of fear relevant stimuli (Adolphs, 2008), and initiate behavioral avoidance in the perceiver. Moreover, recent evidence suggests that chemosensory anxiety signals may be contagious and recruit empathy related neural networks. This finding parallels data from research in rodents, which has shown that the stress-response of the signal producing animal is conveyed to the perceiving animal through chemosensory channels.

1.9 Emotion regulation

One of the earliest works on emotion regulation was done by the workgroup of Richard Lazarus. They initially stated that "[…] the same stimulus may be either a stressor or not, depending upon the nature of the cognitive appraisal the person makes regarding the significance for him" (Speisman, Lazarus, Mordkoff, & Davison, 1964, p. 364). Based on this early work on emotion regulation there is now a growing body of evidence showing that

voluntary emotion regulation can influence subjective emotion experience, as well as behavioral, and physiological emotional responses.

Emotion regulation has been defined as "[…] the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotional reactions, especially their intensive and temporal features, to accomplish one's goals" (Thompson, 1994, p. 27-28). Gross and Thompson (2007) stated, that emotion regulation can be automatic, or controlled, conscious or unconscious, and regulatory strategies can either be intrinsic (self regulation) or extrinsic (regulation in others). Based on the modal model of emotion (as proposed by Gross & Thompson, 2007), emotions are thought to be processes that unfold over time. Thus these authors state, that emotion regulation involves changes in "emotion dynamics", that is the latency, rise time, magnitude, duration, and offset of emotional responses. Finally, emotion regulation may dampen, intensify, or simply maintain emotion, depending on an individual's goals (Gross & Thompson, 2007). Emotion self regulation can be accomplished using different emotion regulation strategies. These emotion regulation strategies can be classified according to their occurrence in the emotion generation process (see Figure 1.4). Those occurring early during this process (that is before the emotional response has been generated) are called antecedent focused. Those occurring later in this process are called response focused (Gross, 2002; Gross & Thompson, 2007).

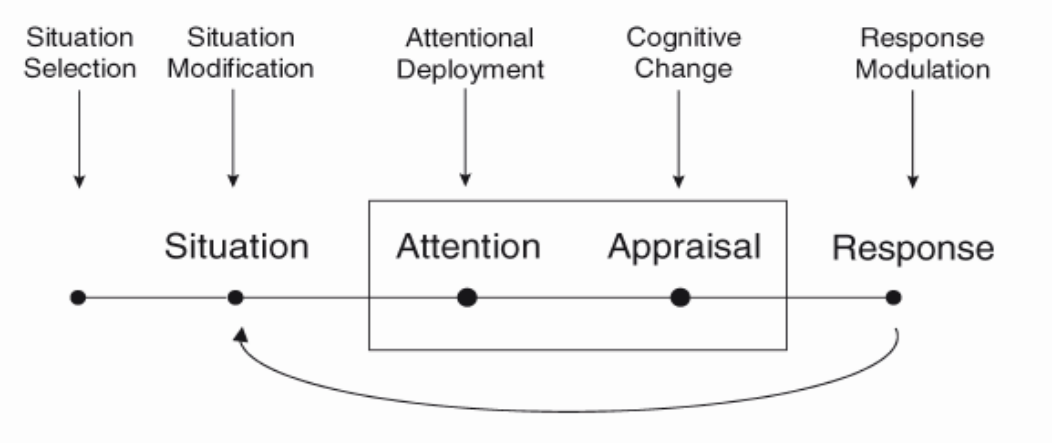

Figure 1.4. The process model of emotion regulation: The five emotion regulation strategies either focus on antecedents of the emotional response or on the response itself. Situation selection and situation modification refer to the individuals' ability to change or avoid emotion eliciting situations, attention deployment refers to the fact that an individual may distract attention from, or draws attention to specific features of the situation to modify his emotion. Cognitive change refers to the reappraisal (re-thinking the meaning) of the emotion eliciting situation. In contrast to other emotion regulatory processes, response modulation occurs after response tendencies have been initiated. It refers to influencing physiological, experiential, or behavioral responding as directly as possible, for example in trying to suppress them. (adopted from Gross & Thompson, 2007)

One widely investigated emotion regulation strategy is cognitive change, often also referred to as cognitive reappraisal. It has been shown that reappraisal (antecedent focused emotion regulation) is highly effective in down-regulating subjective emotional experience, and physiological emotional responses (Driscoll, Tranel, & Anderson, 2009; Jackson, Malmstadt, Larson, & Davidson, 2000). This is not surprising. It was suggested that an emotion can be generated either via bottom up, or via top-down processes, each of it involving different brain areas (Ochsner & Gross, 2007). Furthermore, cortical and subcortical brain regions involved in the emotion generation process are widely interconnected (Price, 2003; Swanson, 2003) and interact during emotion processing (LeDoux, 1994; LeDoux, 2000; Ochsner & Gross, 2007; Phelps, 2006)und Gross 2007). Thus it has been suggested that the impact of top-down regulatory control mechanisms on bottom-up emotion generation circuits form the neuronal basis of emotion regulation through cognitive reappraisal (Figure 1.5 outlines this view), and more generally that the emotion generation process can be influenced by top-down regulatory control.

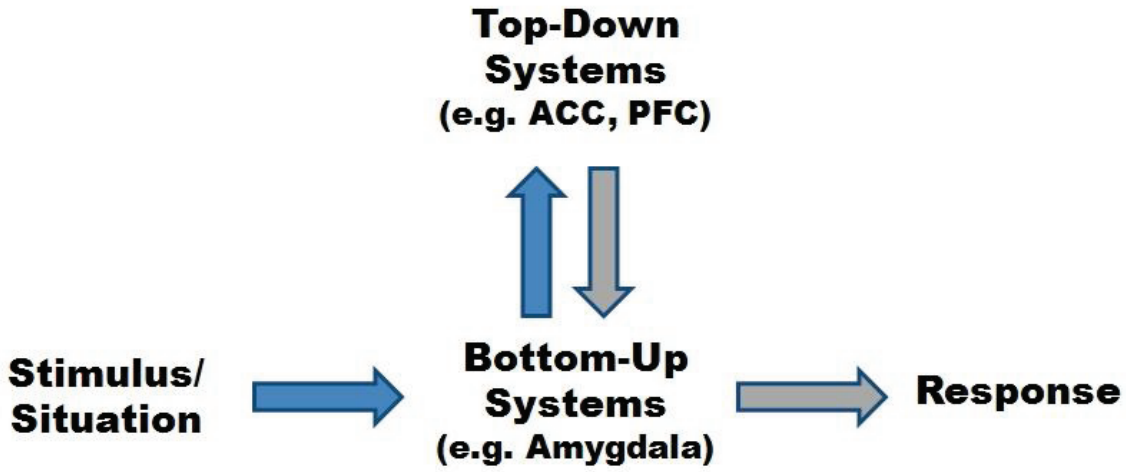

Figure 1.5. Emotional responses may be generated directly via bottom-up processes, including for example the amygdala. However, regulatory control of top-down appraisal systems including for example prefrontal cortical areas (PFC) and ACC may modulate these systems and change the emotional response. Thus, if a threatening stimulus is encountered and information about it is processed to bottom-up systems (blue horizontal arrow), this information is transmitted to top-down regulatory areas (blue vertical arrow). However, when the perceiving person actively generates a neutral interpretation/ appraisal of the stimulus, top-down regulatory systems are involved in response generation and emotional responses are modified (grey arrows). (adopted from Ochsner & Gross, 2007)

Indeed several brain imaging studies have found that enhanced activation in medial and lateral prefrontal cortical areas and the ACC is inversely correlated with reduced activity in subcortical brain areas involved in automatic emotion-generation like the amygdala (Goldin, McRae, Ramel, & Gross, 2008; Ochsner, et al., 2002; Ochsner, et al., 2004; Urry, van Reekum, Johnstone, Kalin, Thurow, Schaefer et al., 2006), and also in those structures, involved in flexible, goal directed emotion processing, like the orbitofrontal cortex (Ochsner, et al., 2002).

From a clinical point of view, the down regulation of emotional responses via cognitive reappraisal is of special interest, because many psychological disorders include disturbances in regulatory processes like sustained negative, or inappropriate affect, chronic worry, and avoidance (Cole, Michel, & Teti, 1994). Thus researchers have widely investigated the effect of cognitive reappraisal on emotional responses. Several studies have found effects of reappraisal on a wide variety of emotional responses, including self-report and physiological responses. One of the earliest works on voluntary emotion regulation investigated the impact of appraisals on film-induced negative affect (Lazarus & Alfert, 1964; Speisman, et al., 1964). The authors presented to the participants a disgusting film showing a medical surgery, and varied the accompanying soundtrack. Some participants heard a soundtrack designed to minimize the negative emotional impact of the film (denying the pain, focusing on the joyful aspects), others heard no soundtrack. They found that the soundtrack based instruction to appraise the film as non-threatening reduced subjective, as well as physiological stress reactions, as measured by skin conductance and heart rate. Using instructions to actively generate an unemotional appraisal in response to the negative emotion eliciting stimulus (according to Gross, 1998), reappraisal on subjective experience, heart rate and skin conductance changes found by Lazarus and colleagues could be replicated (Driscoll, et al., 2009). Based on this work, recent studies have focused on the effects of reappraisal on the startle reflex, a measure of defensive motivation. They consistently found, that the instructions to actively generate an unemotional appraisal of the negative emotion eliciting stimulus decreases, while the instruction to enhance the emotion increases the amplitude of the startle response (Dillon & LaBar, 2005; Driscoll, et al., 2009; Jackson, et al., 2000; Lissek, Orme, McDowell, Johnson, Luckenbaugh, Baas et al., 2007). Several studies have demonstrated emotion regulation effects also on brain electrical activity using ERPs (Hajcak & Nieuwenhuis, 2006; Moser, Hajcak, Bukay, & Simons, 2006; Moser, Krompinger, Dietz, & Simons, 2009). The late positive potential (LPP), linked to the facilitated perceptual processing of motivationally relevant arousing stimuli (Cuthbert, et al., 2000; Schupp, et al.,

2000; Schupp, et al., 2003; Schupp, et al., 2004), was thereby shown to decrease during the instruction to down regulate and to increase during the instruction to enhance emotions elicited by unpleasant pictures. Taken together, it has been consistently shown that cognitive reappraisal, that is the active process of interpreting the emotion eliciting event in a non emotional way, can reduce subjective experience of negative emotions, as well as decrease physiological responses related to negative emotional reactivity. Furthermore, cognitive emotion regulation also influences the activity of emotional brain areas implicated in fear responding, like the amygdala.

As mentioned before, many anxiety (Amstadter, 2008) and mood disorders (Mayberg, 1997) have shown to be accompanied by emotion regulation deficits, or elevated negative affect. Furthermore, abnormally enhanced physiological responding (Hoehn-Saric & McLeod, 2000) and related heightened activity in emotion related brain areas like the amygdala have also been observed regularly in anxiety disorders, including social anxiety disorder (for a review of this topic see Etkin & Wager, 2007).

1.10 Processing of social emotional stimuli in social anxiety

Social anxiety disorder (SAD) is one of the most prevalent anxiety disorders, with prevalence rates varying between 4-8%. Individuals with SAD have an enhanced risk of developing one or more further anxiety disorders, depression, or substance abuse (Consbruch & Stangier, 2007). According to the Diagnostic and Statistic Manual of mental disorders (DSM-IV) people suffering from SAD show enhanced fear in one or more social situations. In generalized anxiety disorder, this enhanced fear is evident in mostly all social situations. Moreover, the confrontation with the feared situation is accompanied by an intense fear response, sometimes as intense as a panic attack.

So far, it has been argued that bodily symptoms associated with a hyperreactivity of the autonomic nervous system (e.g. sweating, dizziness, elevated heart rate) in response to social situations play an important role in the acquisition and maintenance of social fear. For example, the experience of elevated fear and unpleasant or embarrassing (e.g., flushing) physiological responses lead to avoidance behavior, and thus further supports the maintenance of the disorder (overview in Gerlach, 2002). Thus, many studies so far have investigated the psychophysiological, as well as brain responses to social stimuli in social anxiety. Most studies have consistently shown hat social anxiety is accompanied by a hyperreactivity in

response to social situations like public speaking, or the anticipation of such situations (Davidson, Marshall, Tomarken, & Henriques, 2000). Moreover, it has been argued that social anxiety is characterized by a more general abnormal processing of social threat information, involving processing biases in attention, interpretation and memory (Hirsch & Clark, 2004). In line with this, a growing body of evidence suggest, that socially anxious individuals do also show abnormal processing of single social, fear relevant cues including threatening (i.e. fearful, angry) facial expressions. For example, several studies have shown a hyperreactivity in emotion processing brain areas. It has been demonstrated that patients with social phobia respond to angry and fearful facial expressions with increased activity of the insula, and the amygdala (Phan, Fitzgerald, Nathan, & Tancer, 2006; Straube, Kolassa, Glauer, Mentzel, & Miltner, 2004; Straube, Mentzel, & Miltner, 2005). Just recently, in a direct comparison, it was shown that social phobia might be especially related to an enhanced reactivity of the amygdala to fearful facial expressions (Blair, Shaywitz, Smith, Rhodes, Geraci, Jones et al., 2008). Furthermore, as compared to normal controls, social phobics exhibit elevated activation of the amygdala even in response to neutral facial expressions (Birbaumer, Grodd, Diedrich, Klose, Erb, Lotze et al., 1998), and to neutral faces previously paired with an aversive stimulus (UCS) (Schneider, Weiss, Kessler, Muller-Gartner, Posse, Salloum et al., 1999). Also, activation of the extrastriate visual cortex was enhanced in phobics perceiving threatening facial expressions indicating an enhanced allocation of attentional resources of phobics to these stimuli (Straube, et al., 2005). In line with this, using ERPs previous studies have shown enhanced automatic guidance of motivated attention and an enhanced late evaluated processing (Mühlberger, et al., 2009) as well as an enhanced early structural encoding (Kolassa & Miltner, 2006) of fearful and angry facial expressions in social anxiety. Enhanced vigilance for threatening faces in social phobia was also shown in behavioral studies (Mogg, Philippot, & Bradley, 2004).

Finally, also inconsistent, evidence suggests enhanced reactivity of the autonomic nervous system towards threatening facial expressions in people high in social speaking fear. It could be shown that high anxious individuals showed increased skin conductance activity when exposed to social stimuli as compared to low fearful individuals (Dimberg, et al., 1986; Vrana & Gross, 2004). Moreover, trait social anxiety, as assessed by questionnaire, was shown to predict enhanced startle reactivity in response to emotional stimuli, including facial expressions (Cornwell, Johnson, Berardi, & Grillon, 2006; Schulz, Alpers, & Hofmann, 2008).

Taken together, evidence from different studies suggests that threatening facial expressions, including both angry and fearful expressions are fear relevant stimuli for socially anxious individuals. They preferentially capture attention, are evaluated more intensely, and when perceived elicit enhanced activity in emotion generating brain areas, as well as an enhanced physiological responding.

1.11 Aim of the studies

Taken together, the aim of the present studies was to explore the effects of chemosensory signals of anxiety on emotional responding in socially anxious individuals. In detail, the first aim was to assess whether socially anxious individuals' exhibit elevated emotional responding towards chemosensory signals of anxiety. Furthermore, in a second step, it was aimed to investigate whether socially anxious individuals show any deficits in the regulation of fearful facial expressions in the context of chemosensory anxiety signals. Finally, it was investigated whether also another socially relevant emotion, aggression/ dominance is communicated chemosensorily, and whether socially anxious individuals exhibit elevated emotional responding towards these chemosensory signals too.

The first studies' aim was to find out whether socially anxious individuals are more sensitive towards chemosensory signals of anxiety than non anxious individuals. It has been shown that anxiety can be transmitted chemosensorily between humans, and that the startle reflex elicited during the perception of these signals is enhanced in comparison to a control stimulus (Prehn, et al., 2006). Thus it can be concluded that chemosensory signals of anxiety are potent signals of threat that induce withdrawal motivation in humans. Another line of evidence suggests that social anxiety is related to enhanced emotional reactions towards visual social signals of threat (e.g. Dimberg, et al., 1986; Phan, et al., 2006), including enhanced startle reactivity (Cornwell, et al., 2006; Schulz, et al., 2008). Taken together, for the first study it was assumed that socially anxious individuals show enhanced withdrawal related motor behavior towards chemosensory anxiety signals, as compared to non-anxious individuals. Having established a relationship between social anxiety and a hyperreactivity towards chemosensory anxiety signals, it was aimed to extend on these findings in study II and address the question whether socially anxious individuals are impaired regulating socially transmitted emotions.

Thus, within study II, it was aimed to extend on the assumed hyperreactivity towards chemosensory signals of anxiety in socially anxious individuals found in study I, and assess whether socially anxious individuals are impaired in regulating their emotions towards social stimuli. Therefore, emotion regulation in response to fearful facial expressions presented in the context of either chemosensory anxiety signals, or a chemosensory sport (control) stimulus was assessed. So far, cross modal influences on information processing between chemosensory and visual social signals have been previously shown (Pause, et al., 2004; Zhou & Chen, 2009), and a simultaneous communication of warning signals via different sensory

channels has been argued to be adaptive in terms of survival of the species (Wyatt, 2003). Moreover, fearful facial expressions engage neuronal resources in emotion related brain areas like the amygdala (Adolphs, 2008), indicating that fearful faces are indeed potent fear relevant signals to humans. Chemosensory anxiety signals enhance the startle-reflex (Prehn, et al., 2006), and the processing of these signals also engages emotion related brain areas (Mujica-Parodi, et al., 2009; Prehn-Kristensen, et al., 2009). In terms of emotion regulation, it was argued that anxiety disorders are accompanied by emotion regulation deficits (Amstadter, 2008), but previous studies did not find impaired emotion regulation towards negative emotional facial expressions in social phobics (Goldin, Manber, Hakimi, Canli, & Gross, 2009). Within the second study it was aimed to probe this finding. In assessing withdrawal related motor behavior in terms of the startle reflex in high socially anxious individuals it was aimed to assess whether these individuals show impaired emotion regulation in response to a combination of visual and chemosensory social signals of anxiety.

In study III, the specificity of the previous findings was addressed. It was aimed to assess whether socially anxious individuals show a hyperreactivity and impaired emotion regulation towards negative emotional stimuli in general. Therefore, emotional reactivity and emotion regulation towards non social negative odors and pictures was assessed. Study III focuses on disgusting stimuli because odors and pictures were assessed in a direct comparison, and it has been argued that reaction to malodors are almost ever classified as ‘‘disgust’’ (Alaoui-Ismaïli, Robin, Rada, Dittmar, & Vernet-Maury, 1997; Ehrlichman & Bastone, 1992). However, disgust is a primary emotion (Ekman & Friesen, 1971) which has been thought to have evolved throughout evolution to protect the organism from contamination (Rozin & Fallon, 1987). Disgusting stimuli have been shown to be extremely potent elicitors of emotion, recruiting brain areas involved in emotion processing (Schafer, Schienle, & Vaitl, 2005) and reliably potentiates the startle-reflex (Yartz & Hawk, 2002). Thus, in study III, emotional reactivity was again assessed with the startle reflex.

To date, only one study assessed emotion regulation towards non social emotional stimuli in socially anxious individuals. In that study, it has been shown that individuals suffering from social anxiety disorder were not impaired in regulating their emotions (Goldin, et al., 2009) and did not differ from healthy controls in their amygdala response towards non-social threat cues (Goldin, et al., 2009). On the other hand, it has been stated that anxiety disorders, including social anxiety, are accompanied by emotion regulation deficits (Amstadter, 2008). Moreover, this study did only address brain responses leaving open the

question of whether also withdrawal related motor behavior can be effectively regulated by socially anxious individuals. However, based on this previous report, it was assumed that non anxious and socially anxious individuals show equal emotional engagement towards the non social emotional stimuli and do not differ from non anxious individuals in their emotion regulating abilities towards these stimuli (Goldin, et al., 2009).

In study I, II, and III, emotional engagement was assessed using the startle reflex. Contrary to this, in study IV, ERPs were recorded to assess the time course of stimulus processing during the regulation of emotions elicited by fearful facial expressions presented in the context of chemosensory anxiety signals. Like in the previous studies, a group of socially anxious participants was compared to a group of non anxious participants. Because the late positive potential is related to evaluative processing of emotionally relevant stimuli, and can be significantly enhanced or reduced using emotion regulation (Moser, et al., 2009), it was also analyzed in the present study. However, it has yet to be determined whether also early, more exogenous driven steps of stimulus processing related for example to the structural encoding of the stimulus, are influenced by emotion regulation. However, this question is especially important in terms of social anxiety, as it has been shown that larger N170 amplitudes, linked to the structural encoding of facial expressions, are enhanced in socially anxious individuals as compared to non anxious individuals, especially when viewing emotionally relevant, including fearful facial expressions (e.g. Mühlberger, et al., 2009). Moreover, also the late evaluative processing of fearful facial expressions is enhanced in socially anxious individuals (Mühlberger, et al., 2009). Thus also concerning ERPs social anxiety is accompanied with a hyperreactivity towards social signals of fear, at an early, and late processing stage. Taken together, it is assumed that in terms of ERPs socially anxious participants show enhanced processing of the social stimuli. In addition, it is asked whether this enhanced perceptual processing relates to impairments in the regulation of late evaluative processing.

In study V, it was aimed to address the question whether also other emotions may be communicated between humans, and how socially anxious individuals process such signals. Evidence from the animal literature shows, that for example in rodent societies, the chemosensory communication of aggression/ dominance serves important social functions. In humans, evidence from a recent study suggests that chemosensory cues associated with trait dominance may also be communicated between humans (Havlicek, Roberts, & Flegr, 2005). In addition, previous work has shown that humans also communicate their emotional states

chemosensorily (Mujica-Parodi, et al., 2009; Pause, Lubke, Laudien, & Ferstl, 2010; Prehn-Kristensen, et al., 2009; Prehn, et al., 2006; Zhou & Chen, 2009). So far, human research into dominance/ aggression has focused largely on the signalling characteristics of facial displays of anger, showing that angry facial expressions preferentially capture attention (Ohman, et al., 2001), and elicit autonomic changes related to emotional arousal (Merckelbach, et al., 1989). Orienting and arousal responses towards emotionally meaningful stimuli can be effectively assessed with the skin conductance response (Barry, 1990; Bradley, et al., 2001). Thus, in the fifth study it was aimed to test whether state dominance/ aggression is also communicated chemosensorily between humans in terms of the skin conductance response. Moreover, numerous studies have shown that social anxiety is related to an enhanced processing of social threat cues, including angry facial expressions (see above). Thus, in assessing social anxiety by questionnaire it was aimed to assess initial evidence for a relationship between heightened physiological responding in social anxiety and the perception of chemosensory signals of aggression/ dominance.

2 Methods

2.1 Recruitment of the participants

To enhance the validity of the current studies several exclusion criteria were introduced. As they are also listed in the original research articles, this paragraph will take the advantage to highlight several especially important issues and present them in greater detail. Within all studies, participants with irregular menstrual cycles, mental and bodily illnesses, especially those of the respiratory tract, were excluded (all studies). Furthermore, to ensure that the participants were able to perceive the chemosensory stimuli, participants suffering from general hyposmia (studies I, II, IV, and V) were excluded. Moreover, participants were also excluded if they did not perceive the stimuli used in the respective studies as sufficiently negative or fear inducing (study II and III). Due to the fact that participants were selected based on questionnaire data, those participants scoring too high on social desirability were excluded. Finally, only those participants scoring reliably above the mean of the standard sample on trait social anxiety were scored as high socially anxious.

2.1.1 Questionnaires

As recruitment of high socially anxious individuals in study I-IV was based on questionnaire, it was aimed to reduce the probability that participants filled in the questionnaires based on social desirability. Therefore in all studies, participants scoring too high on social desirability (as assessed with the Lying Scale of the Eysenck Personality Inventory, Eggert & Ratschinski, 1983) were excluded. In order to assess a group of participants scoring reliably high on social anxiety, only those participants scoring 1.5 standard deviations above the mean of a standardized questionnaires were scored as high socially anxious (assessed with the Social Interaction Anxiety Schedule, SIAS, Stangier, Heidenreich, Berardi, Golbs, & Hoyer, 1999). Finally, participants scoring higher than 0.5 SD and lower that 1.5 SD above mean were excluded in order to assess clearly separated groups. Results of this procedure indicate that in all studies socially anxious participants mean SIAS scores were reliably (> 3SD) above the mean of the non-anxious control group reported by Stangier and co-workers (Stangier, et al., 1999). A considerable amount of participants scored well above the suggest cut-off score in that study (Stangier, et al., 1999).

2.1.2 Stimulus Ratings

To be sure to induce negative affect and withdrawal motivation within the emotion regulation paradigm, in study II, and III, those participants were excluded who did not feel unpleasant while perceiving the stimuli. In detail, in study II, it was important to assure that the presented facial expressions were perceived as threatening. Therefore the amount of basic emotions induced by the faces was assessed with visual analogue scales (range 0-10 cm). Participants were excluded if they evaluated a stimulus as positive (not fear-inducing). In study III, all participants rating more than three pictures as neutral, or more than one picture as positive were excluded. This was assessed with the Self Assessment Manikin (SAM, Bradley & Lang, 1994). In terms of the odors, participants rating more than two odors as neutral or more than one as positive were also excluded. Finally, if participants were included although they rated their emotions towards the stimuli as positive, trials containing these stimuli were excluded from analysis.

2.1.3 Olfactory hyposmia screening

In order to ensure that the participants were generally able to perceive the chemosensory stimuli in study I, III, IV, and V, all participants were screened for general hyposmia, and those participants failing the screening were excluded. Therefore all participants had to identify a bottle containing phenyl ethyl alcohol (PEA, 99%, Fluka, Germany, 1:100 (*v/v*) diluted in 1,2-propanediol) from a series of three bottles (two consecutive trials).

2.2 Stimuli

2.2.1 Chemosensory stimuli: body odors

For study I (N=49, 28 males) and II (N=20, all males), chemosensory stimuli were sampled from students of European descent, all exhibiting a body mass index within the normal range, and all reporting to have a regular sleep-wake-cycle. All described themselves as healthy, especially with respect to hormonal, neurological, immunological, and cardiological diseases, and diseases of the axillae. They were within the normal range for trait anxiety. Within study I, 28 male, and 21 female (all of them had a regular menstrual cycle), and within study II 20 male individuals donated sweat from both axillae within two donation situations using cotton pads (Ebelin Maxi Pads, dm-drugstore, Germany) following a well established sampling

protocol (Pause, et al., 2004). During an interview session, the donors gave written informed consent to procedures and were instructed to refrain from eating garlic, onions, asparagus or spicy food, not to use deodorants and to wash their armpits exclusively with an unperfumed medical soap (Eubos®, Dr. Hobein GmbH, Germany) within 24 hours prior to donation. The anxiety condition consisted of waiting for an important oral examination at the university in order to assess an academic degree, while the sport control condition consisted of ergometer training. During the donation conditions, the donors' emotional experience was assessed using the SAM (valence, arousal, and dominance), and the intensities of the six basic emotions (Ekman & Friesen, 1971). During the anxiety condition, the donors felt more anxious, and less happy (basic emotions), and more unpleasant (SAM valence), as compared to the sport control condition. To control for physiological arousal, the donors' heart rate was sampled during the interview session (baseline) and in the test conditions. During the sport control condition the heart rate did not differ from the anxiety condition.

In study V, a total of 6 male members of a badminton club donated axillary sweat while winning an important badminton match in order to enhance the individual position within the clubs' position table (aggression/ dominance condition) and during a sport control condition (jogging). All exclusion criteria and behavioral instructions were essentially the same as in the previously described sampling procedures. Saliva samples were collected to determine testosterone and cortisol levels (SaliCaps, IBL, Germany) during both sampling conditions. To control for physiological arousal and physical activity, the donors' heart rate was sampled in the aggression/ dominance condition. During the sport control condition this heart rate was held constant. Results indicate that the testosterone increase was higher during the aggression/ dominance, as compared to the sport control condition, and, as a trend, the donors described their mood to be more positive during the aggression/ dominance, as compared to the sport control condition.

For all studies, the sweat samples were pooled with distinction to the respective donation conditions and stored at −20°C. For the experiment, the homogenized samples were divided into small portions and delivered to the participants via an olfactometer.

2.2.2 Chemosensory stimuli: disgusting odors

Five negative disgust related odors (isovaleric acid, ethanethiole, isobutyraldehyde, pyridine, 3-methyl-indole) served as chemosensory stimuli. These odors were chosen because they

have been shown to be experienced as unpleasant/ disgusting in several previous studies (Masaoka, Yoshimura, Inoue, Kawamura, & Homma, 2007; Royet, Zald, Versace, Costes, Lavenne, Koenig et al., 2000; Villemure, Slotnick, & Bushnell, 2003; Wicker, Keysers, Plailly, Royet, Gallese, & Rizzolatti, 2003; Zald & Pardo, 1997). Each odor was diluted in solvent using three dilution steps following a half-logarithmic serial dilution (see Table 2.1). To adjust the amount of perceived disgust elicited by the five odors across participants', each participant was asked to indicate for each odor the concentration (out of three) that was clearly unpleasant and disgusting, but still tolerable for her. These individually adjusted concentrations were later used in the main experiment. Participants then rated the chosen concentrations as high in intensity and unpleasantness, but low in pleasantness and familiarity.

Table 2.1 Concentrations of Odor stimuli used in study III

Odor	Solvent	Concentrations (v/v)		
		high	Medium	low
Ethanethiole (97%)	Diethyl Phtalate(99%)	1:30000	1:100000	1:300000
Isobutyraldehyde(99%)	Diethyl Phtalate(99%)	1:30	1:100	1:300
Isovaleric Acid(99%)	Diethyl Phtalate(99%)	1:30	1:100	1:300
Pyridine(97%)	1,2-Prapanediol(99%)	1:30	1:100	1:300
3-Methyl-Indole(98%)	1,2-Prapanediol(99%)	1:100	1:300	1:1000

Note: all odors and solvent provided by Sigma Aldrich, Germany, except of 1,2-Prapandiol, provided by Merck, Germany

2.2.3 Presentation of the chemosensory stimuli

In study II, III, IV the chemosensory stimuli were presented with a constant-flow (50 ml/s), five channel olfactometer, having a mean stimulus-onset latency of 0.9s, and a mean stimulus rise time of 0.5s. Stimuli are delivered to the participant using a modified oxygen mask (Figure 2.1). For study I, and V the chemosensory stimuli were presented with a constant flow

(100 ml/s), six channel olfactometer (OM6b, Burghart, Germany) was used to stimulate both nostrils simultaneously. Both air streams were controlled by separate mass flow controllers (see also Kobal, 2003). In the olfactometer, the glass tubes containing the stimuli were stored in a warm-water chamber, and the chemosensory stimuli were delivered through a teflon tube. The temperature of the gas flow at the exit of the olfactometer was 37 °C and the relative humidity above 80% (Figure 2.1).

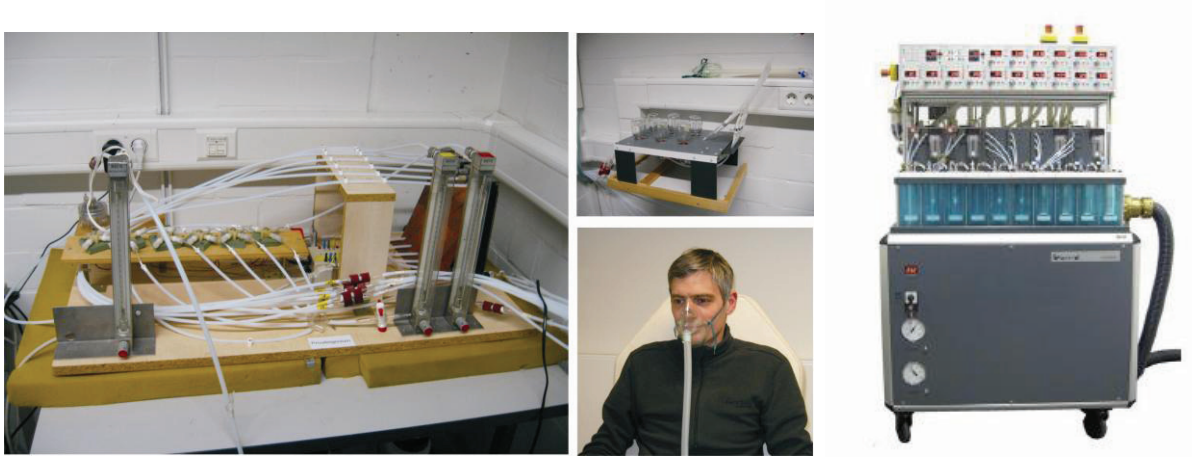

Figure 2.1. Olfactometer used in study II, III, and IV: control unit with magnet valves and flow meters (left side), glass tubes containing the stimuli during the experiment (middle column, upper picture) and modified oxygen mask for stimulus delivery (middle column, lower picture). Olfactometer used in study I, and V. Warm-water chambers containing the stimuli are shown in blue (right side).

2.2.4 Visual Stimuli

For studies II and IV, emotional facial expressions were depicted from the Karolinska Directed Emotional Faces set of emotional facial expressions (KDEF, Lundqvist, Flykt, & Öhman, 1997). The KDEF consist of emotional facial expressions, posed by 70 (35 male) well-instructed Caucasian individuals displaying six different self generated emotions (happy, angry, afraid, disgusted, sad, surprised), and a neutral expression, and were photographed from five different angles. Actors were between 20 and 30 years of age and wore no beards, jewelry, glasses or makeup. Within a pilot-study each of 64 participants (41 female, mean age 31.2 years, SD = 13.5, range 18-65 years) had to choose for each of the six basic emotions (Ekman & Friesen, 1971) those five male and female actors from this set which most convincingly portrayed the respective emotion. Out of these ratings a list ranking all actors for each of the six basic emotions was assessed. For the purpose of the present study II, 14 pictures of the best seven male actors showing anxious facial expressions both with an averted

gaze to the left and to the right were chosen (see Figure 2.2). Within study IV, 60 pictures of the best 30 male actors displaying the same expression and visual angles were chosen. Fearful expressions with an averted gaze were chosen, because they point to threat in the environment. They have been shown to display avoidance motivation more reliably and to be perceived as more emotionally intense as compared to fearful faces with direct gaze (Adams & Kleck, 2005).

Figure 2.2. Fearful facial expressions from the KDEF set of emotional facial expressions used in study II.

For study III, seven negative disgust-related color pictures (1111, 1205, 1274, 3150, 3250, 9300, 9340) were chosen from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 2005). These pictures were chosen to be relatively uniform in color and luminance, as well as easy to decode. They exhibit a variety of previously determined categories of disgust related items (see Schienle, Walter, Stark, & Vaitl, 2002), including death/ mutilation, hygiene, oral rejection (including disgusting insects), and rotten food/ garbage (Figure 2.3).

Figure 2.3. Disgusting pictures from the IAPS set used in study III.

2.3 Dependent Variables

2.3.1 Emotion self-ratings

Within all five studies the participants were asked to give ratings of their current emotional state using the Self Assessment Manikin (SAM, Bradley & Lang, 1994). The SAM directly assesses the valence, arousal, and dominance in response to an object or event on three pictographically nine-point scales (see Figure 2.4). For the valence scale, SAM ranges from a positive, happy to a negative, unhappy figure, and for the arousal scale from an excited, to a relaxed figure. The dominance scale ranges from a large figure indicating maximum control in the situation, to a small figure indicating no control in that situation. For the purpose of the current studies, the participants were asked to indicate on the scales how the currently felt. They could place the cross either over any of the five figures in each scale, or between any two figures.

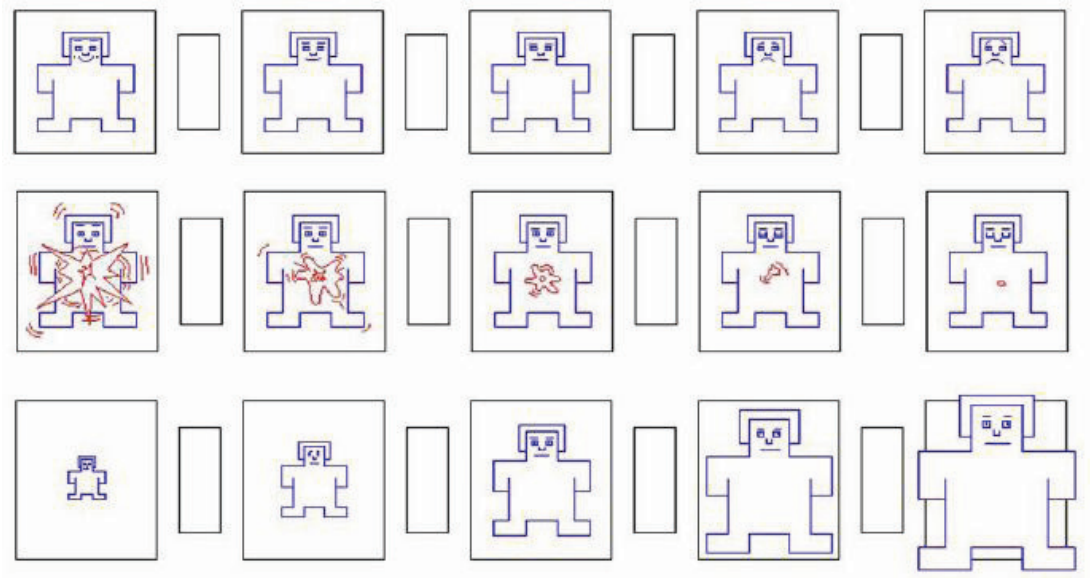

Figure 2.4. The SAM scales: SAM valence scale (upper row), SAM arousal scale (middle row), and SAM dominance scale (lower row).

2.3.2 Startle Reflex

The startle reflex can be used as a measure of defensive motivation in response to the perception of threatening stimuli. It is typically measured from the Orbicularis Oculi muscle between two electrodes (see Figure 2.5). The raw signal is then integrated and the intensity of the startle response can be determined in terms of peak amplitude (Berg & Balaban, 1999). In terms of the present studies, the startle reflex is assessed using two Ag/AgCl electrodes

attached beneath the right eye according to the guidelines published by Fridlund & Cacioppo (1986). It is used to assess differences in withdrawal motivation towards chemosensory anxiety cues between high and non socially anxious individuals (study I). In terms of emotion regulation (study II and III) smaller startle magnitudes in response to the instruction to down-regulate the emotion would indicate successful regulation of the emotion, leading to less withdrawal motivation towards the emotional stimulus.

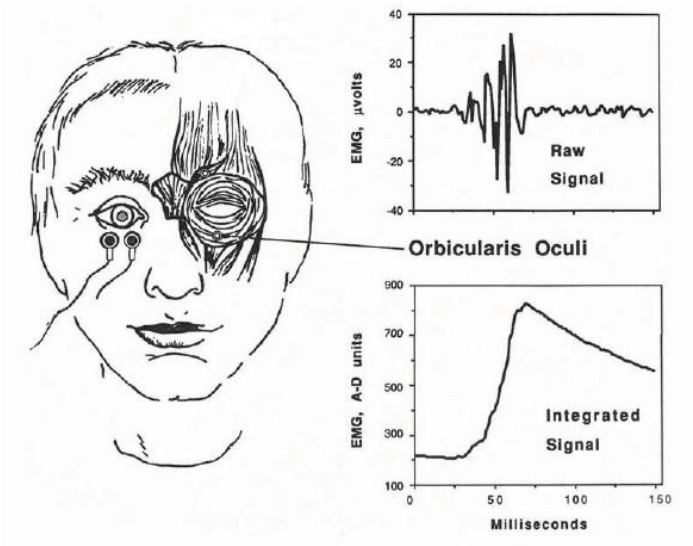

Figure 2.5. Measurement of the startle-reflex: Recording of the startle reflex can be accomplished using two electrodes placed over the Orbicularis Oculi muscle (left side). Raw electromyographical activity in response to the startle eliciting stimulus can then be recorded, and further processed (right side) (taken from Lang, et al., 1990)

2.3.3 Skin Conductance Response

The electrodermal system has been closely linked with psychological concepts of emotion, arousal and attention (Dawson, et al., 2007) towards emotionally evocative stimuli. If confronted with a significant stimulus, the skin conductance response (SCR) can be measured by passing a small current through a pair of surface electrodes placed over the thenar and hypothenar eminences of the palm. When the voltage is then held constant, it is possible to assess the skin conductance directly, by measuring the resultant current between the two electrodes. An example of the resulting curve is displayed in Figure 2.6 (right side). Several parameters can be derived from the skin conductance response with the most common being the peak amplitude of the SCR. The SCR amplitude can typically measured in a time window between two to six seconds after the onset of the eliciting stimulus (Dawson, et al., 2007). In

study V, the SCR data were recorded in response to chemosensory signals of aggression/ dominance using two Ag/AgCl electrodes (4 mm inner diameter) placed on the thenar and hypothenar of the non-dominant hand (according to Boucsein, 1988).

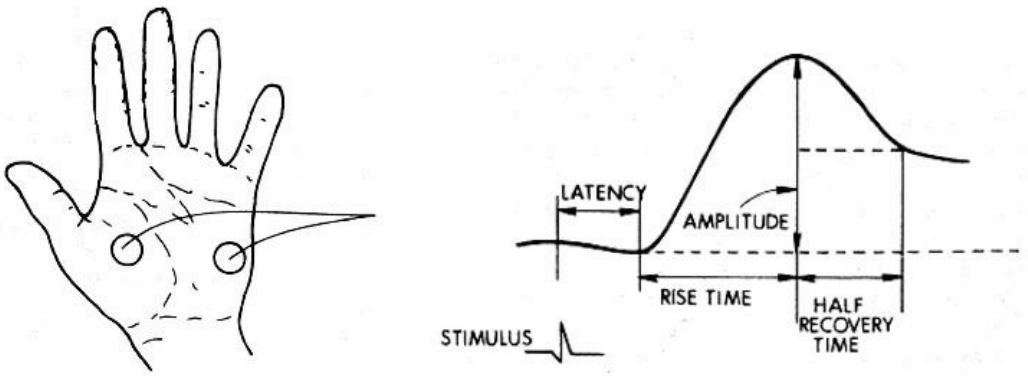

Figure 2.6. Assessment via two electrodes placed over the thenar and hypothenar eminences of the palm (left side) and quantification of the skin conductance response (right side) (taken from Dawson, et al., 2007).

2.3.4 Event related brain potentials

In Experiment IV, the EEG was recorded in reference to the average across all electrodes with Ag/AgCl electrodes (inner diameter 6 mm) from 25 scalp locations (AF7,FP1, FPz, FP2, AF8, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, PO7, O1, Oz, O2, PO8) and the earlobes using an electrode cap (see Figure 2.7) in accordance with the international 10/20 system. In addition, two electrodes were placed near the right eye (3 cm above, inside the vertical pupil axis and 1.5 cm below, outside the vertical pupil axis) for the recording of vertical and horizontal eye movements.

In order to assess stimulus processing under the conditions of emotion regulation in a time sensitive manner (study IV), early components (N1, N170) assessing exogenous characteristics of stimulus processing, and late ERP components (LPP/ P3) covering endogenous characteristics of stimulus processing were recorded. Within the present study, the N1 component was quantified as the peak amplitude at frontopolar, frontal and central electrode sites within a time window between 70 and 140 ms after stimulus onset. The N170 component was analyzed as peak amplitude over parietal and occipital electrode sites (130-180 ms after stimulus onset), while the P3 and the LPP were extracted from all electrodes (P3

peak amplitude time window: 300 to 500 ms, LPP mean activity time window: 400 to 600 ms).

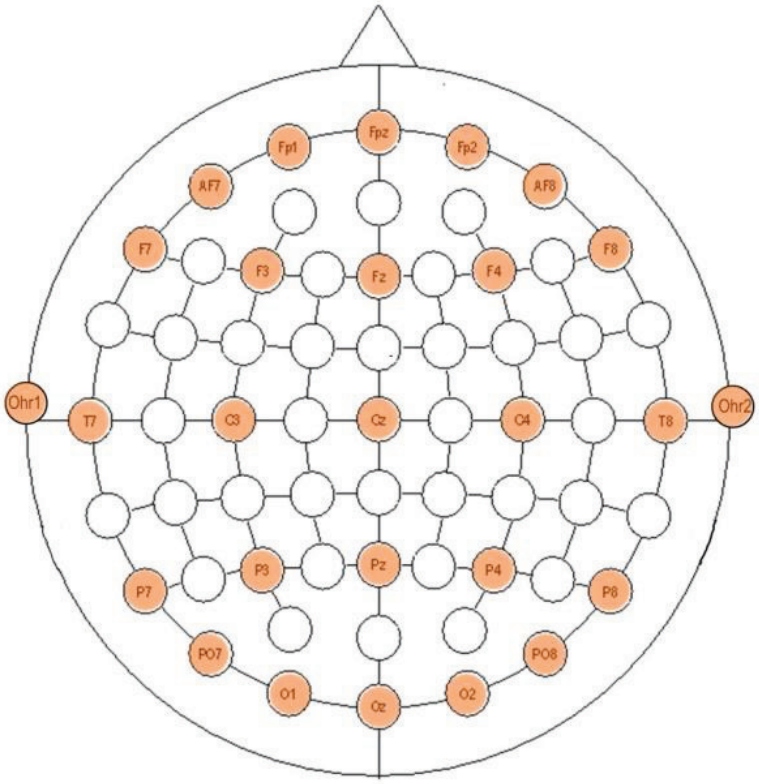

Figure 2.7. EEG setup used in study IV: Electrode positions used are shown in orange.

3 Overview over the studies

Study I: Pause, B. M., Adolph, D., Prehn-Kristensen, A. & Ferstl, R. (2009). Startle response potentiation to chemosensory anxiety signals in socially anxious individuals, International Journal of Psychophysiology, 74, 88–92

In study I it was aimed to extend on previous findings of startle reflex potentiation during the perception of chemosensory anxiety signals, in assessing whether high socially anxious individuals exhibit a hyperreactivity towards these signals, as compared to non anxious participants.

16 non anxious individuals (8 female) were matched to 16 high socially anxious individuals according to age, gender and their depression scores (Beck Depression Inventory, BDI, German Version,Hautzinger, Bailer, Worall, & Keller, 1995). In addition to gender, self-reported depressive symptoms, and age, the two groups did not differ in social agreeableness (agreeableness scale of the NEO-FFI, Borkenau, 1993). The startle procedure took place in two separate sessions. During each, the chemosensory stimuli (chemosensory anxiety signal, chemosensory sport, cotton pad control) were presented for 3s in pseudo-randomized order within two blocks of 27 trials each. During each trial, startle probes were presented during odor presentation, and the inter stimulus intervals. In addition to the startle probe procedure, participants rated the chemosensory stimuli for intensity, pleasantness, unpleasantness, and familiarity, and their subjective emotional responses to the chemosensory stimuli on the valence, arousal, and dominance scale of the SAM (Bradley & Lang, 1994).

Results indicate that only one participant was able to distinguish both chemosensory stimuli from cotton pad. Accordingly, participants rated their emotional responses to the chemosensory stimuli as neutral and the stimuli as hardly perceivable. Startle responses were stronger in the context of the chemosensory stimuli donated in the anxiety condition than in the context of sweat donated in the sport control condition. This effect was independent of sex of the perceiver, and sex of the donor. However, this modulation was more pronounced in the socially anxious group. Moreover, socially anxious participants showed stronger startle responses to the chemosensory anxiety stimuli than non anxious individuals.

The present study confirms the hypothesis that humans communicate emotional states via chemoreception. Chemosensory anxiety signals prime defensive motivation independent of the sex of the sender or the sex of the perceiver. The priming of defensive behavior towards chemosensory stress signals is also present in animals (Inagaki, et al., 2008). Thus in both

animals and humans the adaptations to the perception of chemosensory stress consist of the initiation of withdrawal behavior. Most participants were unable to differentiate the chemosensory stimuli from pure cotton pad. Therefore, the observed effect is assumed to be independent of attention. Finally, the observation that socially anxious individuals exhibit larger withdrawal behavior towards the chemosensory anxiety signals is in line with the assumption of processing biases in social anxiety towards social threat information (Hirsch & Clark, 2004), and the fact that enhanced reactivity towards threatening (fearful, angry) emotional facial expressions in social anxiety has been repeatedly demonstrated (Blair, et al., 2008; Phan, et al., 2006; Straube, et al., 2005). Moreover, the hyperreactivity towards social stimuli in social anxiety does also include enhanced startle reactivity (Cornwell, et al., 2006; Schulz, et al., 2008). Thus it is concluded that the previously observed hyperreactivity in response to threatening emotional facial expressions in socially anxious individuals is also evident in response to chemosensory anxiety signals.

Study II and III: Adolph, D., Dedekind, A., Meyer, S., Schaub, D., & Pause, B.M. (submitted). Emotion regulation with non-social and social chemosensory stimuli – Disgusting odors and chemosensory anxiety signals. Psychological Science

Within study II, and III, the specificity of a processing bias in socially anxious individuals towards social emotional stimuli was addressed. Within study II emotion regulation was assessed towards emotions elicited by fearful facial expressions in the context of chemosensory anxiety signals or chemosensory sport control stimuli. In study III, it was aimed to explore whether socially anxious individuals in comparison to non anxious participants show a more general hyperreactivity towards and are impaired in regulating their emotions in response to negative non social disgusting odors and scenes.

Within both studies, 20 high socially anxious individuals (as assessed with the SIAS) and 20 non anxious individuals were recruited. Socially anxious participants scored higher but within the medium range for trait anxiety (assessed with the State Trait Anxiety Inventory, STAI Laux, Schaffner, Glanzmann, & Spielberger, 1981) and depressive feelings (assessed with the Depression Scale, DS, von Zerssen & Koeller, 1976), than the non anxious participants who scored low on both questionnaires. Both groups scored within the medium range in the frequency of everyday-life use of reappraisal (assessed with the Emotion Regulation Questionnaire, ERQ, Abler & Kessler, 2009). In both studies, the two groups did

not differ for these questionnaires and for age. In study II, the two groups also did not differ for self-reported empathic feeling (German version of the Interpersonal Reactivity Index Paulus, 2009), while in study III they did not differ for disgust sensitivity (as assessed with the Fragebogen zur Erfassung der Ekelempfindlichkeit, FEE, Schienle, et al., 2002). To adjust the amount of perceived disgust elicited by the five odors across participants', in study III, each participant was asked to indicate for each odor the concentration (out of three) that was clearly unpleasant and disgusting, but still tolerable for her. These individually adjusted concentrations were later used in the main experiment. In study II, the participants rated their emotional response to the fearful facial expressions as moderately negative and arousing, while they rated their emotions towards the disgusting scenes and the disgusting odors as equally intensely negative, and arousing (study III). In both studies, the stimuli were presented in four counterbalanced blocks. In study II, a fearful face in the context of either the chemosensory anxiety or sport control stimulus, while in study III, an odor or a picture was presented twice, before and after one of two visual regulation instructions. Participants were instructed to inhale during the complete time of the odor and picture presentations. During the inter trial interval emotion regulation outcome was measured with valence and arousal ratings (SAM). Startle probes were presented either before the participants were instructed to regulate their emotions (baseline: during the first stimulus presentation), or during emotion regulation (early emotion regulation interval: during the second stimulus presentation, late emotion regulation interval: briefly after stimulus offset).

Results indicate that in both studies, participants rated their emotional experience as neutral, and as significantly less negative after down-regulating their emotions than after enhancing their emotions. Similarly, after down-regulation they rated their experienced arousal as neutral, and as significantly less arousing than after enhancing their emotions. Thus on a subjective level, emotion regulation was successful in both studies and for socially anxious, and non anxious individuals.

In study II, according to the startle results, all participants were able to effectively regulate their emotions towards the facial expression (startle responses: down-regulate < enhance). However, as expected socially anxious individuals showed larger startle responses towards the faces presented in the context of chemosensory anxiety cues than the non anxious individuals. This effect was most pronounced briefly after stimulus offset, indicating a prolonged withdrawal related adaption to the chemosensory anxiety signals in socially anxious individuals. Thus, while emotion regulation towards social cues in socially anxious

participants has been demonstrated on a behavioral level before (Goldin, et al., 2009), the present results extend on these findings and show that also withdrawal related motor responses towards socially relevant stimuli can be regulated effectively. The finding that anxious participants showed a heightened startle response towards the faces in the context of the chemosensory anxiety signal replicates previous work showing a hyperreactivity of socially anxious individuals towards facial (for example, Blair, et al., 2008), and chemosensory signals of anxiety (study I of the present thesis).

In study III, the startle-reflex was larger in response to the disgusting odors than to the disgusting pictures (independent of social anxiety). Moreover, while participants showed clear emotion regulation effects in response to the disgusting scenes, especially during the early emotion regulation interval (startle responses: down-regulate < enhance), emotion regulation towards the odors was not effective during the early emotion regulation interval (startle responses during early emotion regulation interval: down regulate = enhance, late interval: down regulate < enhance). However there were neither differences in reactivity towards the negative scenes or odors, nor differences concerning emotion regulation between socially anxious and non anxious participants in study III.

Contrary to disgusting pictures, for odors emotion regulation was not effective until odor offset. These data parallel finding of increased withdrawal related behavior towards odors in comparison to pictures. As mentioned before, the fear related modulation of the startle reflex is thought to be dependent of the amygdala (Davis, 1992a), which is thus most likely the source of the heightened startle responses towards the odors in study III. This assumption is also in line with previous research, which could demonstrate that as compared to other visual or auditory stimuli negative odors are superior in modulating neuronal responses within the amygdala (Royet, et al., 2000).

However, taken together, in terms of social anxiety, the results from study II and III argue against a general hyperreactivity in socially anxious individuals. Withdrawal related motor behavior was more pronounced in socially anxious individuals for socially communicated negative emotions rather than for negative emotions in general. Moreover, contrary to the suggestion that people suffering from anxiety disorders show problems with emotion regulation (Campbell-Sills, Barlow, Brown, & Hofmann, 2006), socially anxious individuals did not show any difference in emotion regulation as compared to non anxious individuals. Interestingly, no differences were found in the self-reported frequency of use of reappraisal in everyday live between socially anxious and non anxious individuals in both

studies. In everyday life, especially sub clinically anxious individuals (as in the present study) who do not show frequent avoidance behavior are frequently confronted with their feared situations. Thus anxious individuals may have simply developed more effective regulation strategies and thus are able to overcome their hyperreactivity towards the social cues in the present study. Indeed, in comparison to healthy controls, it has been shown that social phobics show less activation in emotion regulation related brain areas during the reappraisal of emotions elicited by threatening facial expressions but comparable reduction of negative self-reported emotion (Goldin, et al., 2008).

Study IV: Adolph, D., Meister, L., & Pause, B.M. (submitted). Regulation of emotions elicited by fearful faces in the context of chemosensory anxiety signals. Social Cognitive and Affective Neuroscience

Study IV examines early (N1, N170) and late (P3, LPP) event-related potential modulation during the voluntary regulation of emotions elicited by fearful facial expressions presented either in the context of chemosensory anxiety, or sport control signals, or without a chemosensory context (that is in the context of pure cotton pad). Thirty six female students were classified as either non anxious or socially anxious based on their trait social anxiety scores (SIAS, Stangier, et al., 1999). Socially anxious individuals scored higher (but within normal range) for trait anxiety (STAI, Laux, et al., 1981) and depressive feelings (DS, von Zerssen & Koeller, 1976), than non anxious participants. Both groups did not differ and scored within the medium range for the frequency of everyday-life use of reappraisal (ERQ, Abler & Kessler, 2009), and for empathy (German version of the Interpersonal reactivity index, Paulus, 2009). The two groups did not differ for age. Stimuli were presented in three counterbalanced blocks (enhance, down-regulate, watch) of 60 trials each. During each trial the same facial expression was presented prior to and after a visual instruction to start emotion regulation. During the second presentation, the face was paired with one of the three context stimuli (N=20 trials of chemosensory anxiety, chemosensory sport, or cotton pad during each block). During the inter trial interval, participants rated their current emotional state for valence and arousal (SAM, Bradley & Lang, 1994). Results concerning the ratings indicate that subjective emotion regulation was successful in non anxious individual both for perceived emotional valence, and arousal (down-regulate < watch < enhance). However, socially anxious individuals did not show a reduction in negative emotional engagement during the down-regulation trials (down-regulate = watch < enhance). In terms of ERPs,

emotion regulation was first analyzed in response to anxious expressions presented without a chemosensory context stimulus (cotton pad condition). Overall, regardless of emotion regulation instruction the chemosensory context stimuli (chemosensory anxiety, chemosensory sport) enhanced early perceptual processing (N1, N170), but diminished late evaluative (P3, LPP) processing of the fearful facial expressions, in comparison to the cotton pad condition. In line with the enhanced late evaluative processing of faces in the context of chemosensory signals, no emotion regulation effects on the LPP were found when the faces were presented with contextual chemosensory stimuli (chemosensory anxiety, chemosensory sport). This result corresponds with the preferential processing of contextual chemosensory information, as indexed by reduced elaborative processing (LPP) of faces presented in the context of the chemosensory stimuli as compared to faces presented with cotton pad. Just recently it could be shown that the perception of chemosensory information (sport/ anxiety), elicits large P3 amplitudes (Pause, et al., 2010). This suggests the allocation of considerable neuronal resources during the processing of these stimuli. Thus the additional chemosensory context stimulus might have distracted neuronal resources from the elaborative processing of the concurrently presented facial expressions, leading to diminished late evaluative processing of the facial expressions.

Non anxious, but not socially anxious participants showed emotion regulation effects on the late positive potential (LPP) in response to faces presented without a chemosensory context. An enhanced early structural encoding (N170) and late evaluative processing (LPP) of the facial stimuli in socially anxious participants as compared to non anxious individuals may be responsible for this effect. Moreover, socially anxious individuals showed larger LPPs than non anxious individuals in response to fearful facial expressions presented in the context of chemosensory anxiety signals. However, results for both socially anxious and non anxious individuals show that the early perceptual processing of target stimuli is modulated by the instruction to enhance and decrease emotions. Within the N1 latency range ERPs were larger during enhancing, as compared to down-regulating the emotions. The N1 component is especially sensitive to selective attention (Hillyard, et al., 1998). Recent results indicate that selective attention during an emotion regulation task was controlled by the participants depending on their regulatory task (van Reekum, Johnstone, Urry, Thurow, Schaefer, Alexander et al., 2007). Thus it is assumed, that in study IV the participants may have automatically allocated different amounts of attention to the stimuli, in dependence of their regulatory task.

Taken together study IV again shows deviant processing of social emotional stimuli in socially anxious individuals. This was evident in enhanced early structural encoding of fearful facial expressions, as well as enhanced late evaluative processing of these faces presented in the context of chemosensory anxiety signals. These findings are in line with an enhanced automatic guidance of motivated attention to fearful faces in social anxiety, and an enhanced elaborative processing of fearful facial expressions in socially anxious individuals, as compared to non anxious participants (Mühlberger, et al., 2009). Thus converging evidence from previous and the current study suggest a general negativity bias in response to threatening (angry, fearful) faces and chemosensory signals of anxiety in socially anxious participants, which may also explain the observed emotion regulation deficits.

Study V: Adolph, D., Schlösser, S., Hawighorst, M., & Pause, B.M. (2010). Chemosensory signals of competition increase the skin conductance response in humans, Physiology & Behavior, 101, 666-671.

Study V investigates, whether chemosensory signals of aggression/ dominance are also communicated between humans, and whether they elicit physiological changes, assessed by means of the skin conductance response in the perceiver. Furthermore it was aimed to assess whether the responding to such stimuli is related to trait social anxiety.

Participants were 18 students (9 males). Males and females did not differ for age. The participants scored low on self-reported depressive feelings (BDI Hautzinger, et al., 1995), and within the medium range for trait aggression (Freiburger Aggressions Fragebogen, FAF Hampel & Selg, 1998), and social anxiety (SIAS Stangier, et al., 1999). Male and female participants did not differ in any of these questionnaires. The chemosensory stimuli (chemosensory signals of aggression/ dominance, chemosensory sport stimuli) were presented for 0.5s within an olfactory oddball paradigm, consisting of two blocks of 100 pseudo-randomized trials each (25 deviant stimuli in a train of 75 standard stimuli, during the two blocks, the competition and the sport control stimuli, served either as the standard or the deviant stimulus). A short break was introduced after the first 100 trials.

The chemosensory stimuli were rated as mildly intense and mildly unpleasant, as well as low in pleasantness, and familiarity. The participants described their emotional reactions to the stimuli as neutral. The chemosensory stimuli of aggression/ dominance elicited larger SCRs than chemosensory sport stimuli. Moreover, regression analysis revealed that trait

social anxiety, but not depression, or trait aggression was related to participants' electrodermal responding towards the chemosensory aggression/ dominance stimulus.

The skin conductance response indicates activity of the sympathetic nervous system, and is associated with arousal and orienting towards emotionally meaningful stimuli in comparison to neutral ones (Bradley, et al., 2001; Dawson, et al., 2007). Thus the current results are in line with previous studies demonstrating that angry facial expressions preferentially capture attention (Ohman, et al., 2001) and elicit larger skin conductance responses than neutral facial expressions (Merckelbach, et al., 1989). In line with animal studies (Rich & Hurst, 1998), the present results indicate that chemosensory signals of aggression/ dominance are potent signals of threat to conspecifics and thus preferentially initiate the automatic allocation of attention and orienting. The positive association between trait social anxiety and skin conductance responding towards chemosensory signals of aggression/ dominance is consistent with studies showing that high socially anxious individuals show deviant perceptual processing of angry facial expressions (Kolassa & Miltner, 2006; Moser, Huppert, Duval, & Simons, 2008), and increased neuronal activity of the amygdala towards these stimuli (Straube, et al., 2004).

Taken together study V provides evidence for the first time that chemosensory signals of aggression/ dominance are transmitted between humans and preferentially capture attention. Moreover, correlation analysis indicates that trait social anxiety might be accompanied by an enhanced vigilance towards these signals.

4 General Discussion

In five studies it was aimed to explore the relationship between the processing and the voluntary regulation of emotions elicited by chemosensory signals and social anxiety. Therefore, emotional responses to non-social (disgust) and social (anxiety, aggression/dominance) emotional chemosensory signals were assessed. Moreover, in assessing emotional reactions towards social and non social emotional stimuli it was aimed to explore the specificity of an assumed hyperreactivity towards social emotional stimuli in social anxiety. Results indicate that chemosensory anxiety signals and chemosensory signals of dominance/ aggression elicit larger emotional responses than sport control stimuli. Furthermore, disgusting non social odors elicit stronger withdrawal motivation than comparable pictures, and emotion regulation of the odors is less effective. Finally high socially anxious individuals show an enhanced reactivity towards social, but not non social emotional stimuli as compared to non anxious individuals, and are not generally impaired in emotion regulation.

In general, it was found that chemosensory signals of anxiety elicit larger withdrawal related motor behavior than sport control stimuli (startle reflex in study I). Larger withdrawal related motor behavior in response to chemosensory signals of anxiety has been demonstrated before (Prehn, et al., 2006), suggesting that withdrawal motivation is reliably induced through chemosensory anxiety signals. Moreover, the findings further support the assumption that chemosensory signals of anxiety can be communicated chemosensorily between humans (Chen, et al., 2006; Mujica-Parodi, et al., 2009; Pause, et al., 2004; Prehn-Kristensen, et al., 2009; Zhou & Chen, 2009). In study V, chemosensory signals of aggression/ dominance elicited larger arousal related orienting responses than sport control stimuli (skin conductance response in study V). This provides evidence for the first time that chemosensory signals of aggression/ dominance are also transmitted between humans and elicit autonomous nervous system adaptation in the perceiver. A strong influence of chemosensory signals on the social interaction with species members has been suggested in both non human animals and humans (Stockhorst & Pietrowsky, 2004). Accordingly, human chemosensory signals have been shown to be involved in mate choice and reproduction (Jacob, McClintock, et al., 2002; McClintock, 1971; Preti, et al., 2003; Wedekind & Füri, 1997), and to serve discriminative functions in social interactions (e.g. mother-infant recognition Kaitz, Good, Rokem, & Eidelman, 1987). The results from study I and V extend on these findings and strongly suggest that chemosensory signals also serve to communicate specific emotional states like

anxiety or aggression/ dominance between humans. These results further underline the importance of chemosensory signals for human social interaction. Interestingly, it has been demonstrated that diverse emotional states are transmitted visually between humans (e.g. happiness, anger, disgust, sadness, surprise, anxiety, Ekman & Friesen, 1971), and evidence from the present studies demonstrate that two of these emotions are also transmitted chemosensorily between humans. As the communication of emotions in general is thought to be highly adaptive, and advantageous (Chemosensory signals can be transmitted over physical barriers and long distances, and are also perceptible by darkness), on the basis of the present results it can be speculated that also other emotional states are transmitted chemosensorily between humans.

Results show that socially anxious, as compared to non anxious individuals, exhibit enhanced withdrawal motivation (assessed with the startle reflex) towards human chemosensory signals of anxiety alone (study I), and towards fearful facial expressions, presented in the context of chemosensory anxiety signals (study II). This enhanced reactivity was specific for chemosensory anxiety signals, as it was not observed for fearful faces in the context of chemosensory sport stimuli (study II). In addition to the findings concerning startle responses, socially anxious individuals as compared to non anxious individuals show an enhanced early structural encoding (N170) and late evaluative processing (LPP) of the fearful expressions without chemosensory context, and an enhanced late evaluative processing when the faces are presented in the context of chemosensory anxiety signals (study IV). Furthermore, the results provide initial evidence that higher scores on trait social anxiety (but not self reported depression or trait aggression) are related to enhanced arousal driven orienting towards chemosensory signals of aggression/ dominance (study V). Finally, no enhanced withdrawal motivation in socially anxious individuals was observed in response to disgusting non social odors and pictures (study III).

Taken together, the results from the present studies are in line with the general assumption that social anxiety is accompanied with a processing bias towards social threat information (Hirsch & Clark, 2004). Data from the current and from previous studies strongly suggest that social anxiety is accompanied by deviant processing of social emotional stimuli at virtually all levels of stimulus processing. Using facial expressions as evocative stimuli several studies have demonstrated enhanced automatic guidance of motivated attention, structural encoding and enhanced elaborative processing (Kolassa & Miltner, 2006; Moser, et al., 2008; Mühlberger, et al., 2009), enhanced amygdala activation, (Blair, et al., 2008; Phan,

et al., 2006; Stein, Goldin, Sareen, Zorrilla, & Brown, 2002; Straube, et al., 2004), and enhanced physiological emotional responding (Merckelbach, et al., 1989) towards fearful and angry emotional facial expressions. The current findings extend the existing literature and shows that socially anxious individuals not only show a processing bias towards visual social signals of threat, but also in response to emotional chemosensory signals of anxiety. Moreover, initial evidence suggests that social anxiety might also be accompanied by an enhanced vigilance towards chemosensory signals of aggression/ dominance. Socially anxious participants did not show enhanced withdrawal related motivation towards non-social disgusting odors or pictures. This suggests a specific processing bias in social anxiety towards social threat information which may be generalized to multiple social communication channels. This view is also supported by findings of increased activation of emotion processing brain areas in social phobics towards threatening (angry) prosody (Quadflieg, Mohr, Mentzel, Miltner, & Straube, 2008).

Taken together, findings from the literature and the current results suggest a specific multichannel sensitivity of socially anxious individuals towards threat related social information. These findings have important implications. Etiological models suggest that information-processing biases play a central role for the development and maintenance of the disorder (Clark & Wells, 1995). In specific, it has been argued that socially anxious individuals fail to habituate during social encounters and exhibit continued presence of subjective distress, which may lead to subsequent avoidance, being implicated in the maintenance of the disorder (Beidel, Turner, & Dancu, 1985). The observed processing biases towards social threat stimuli may mediate this failure in habituation to the social situation. Thus, therapeutic interventions may profit from incorporating chemosensory, visual, and acoustic threat signals into therapeutic treatments.

Non anxious and socially anxious individuals did not show any differences in the regulation of withdrawal related motor behavior towards the fearful facial expressions (regardless of chemosensory context). This is in line with previous findings on emotion regulation towards non social threatening scenes using the startle reflex (for example Jackson, et al., 2000; Lissek, et al., 2007). Results are also in line with a recent study showing that patients suffering from social phobia are not impaired in regulating their subjective emotional experience towards threatening facial expressions. Thus, the present results extend on these findings and show that also withdrawal related motor behavior towards socially relevant stimuli can be regulated effectively. However, results from the ERP study show emotion regulation effects on the late evaluative processing of the fearful facial expressions (without a

chemosensory context) only in non anxious individuals. Socially anxious participants showed larger LPPs during the watch, and during the down regulate condition as compared to non anxious participants. This indicates a ceiling effect of engagement of neuronal resources in socially anxious individuals towards fearful faces which consequently could not be altered using cognitive regulation strategies. Together these results indicate a dissociation of the impact of emotion regulation on early visual stimulus processing stages and on the initiation of behavioral action tendencies. Thus, socially anxious individuals, although impaired in voluntarily regulating motivated attention towards fear relevant stimuli are not impaired in the later regulation of withdrawal related action tendencies. Interestingly, in a recent emotion regulation study, it could be demonstrated that social phobics were not impaired in regulating their subjective emotional experience towards social threat stimuli, but recruit significantly more neuronal resources in brain areas associated with emotion regulation than non anxious controls to accomplish this goal (Goldin, et al., 2009). In a study using fMRI and ERP it was suggested that the enhanced LPP in response to visual emotional stimuli represents brain activity in a circuit of visual cortical structures, reflecting a perceptual sensitivity to the motivational relevance of visual stimuli (Sabatinelli, Lang, Keil, & Bradley, 2007). Thus, taken together, previous and the current data suggest that socially anxious individuals may overcome this initial hypersensitivity towards social threat cues through the allocation of more neuronal resources in emotion regulation brain areas.

There were no effects on the late evaluative processing of fearful facial expressions presented in the context of chemosensory stimuli. A recent study demonstrated that the perception of chemosensory information (sport/ anxiety), although not consciously perceived, elicits large P3 amplitudes (Pause, et al., 2010), suggesting that the processing of these information depend on the allocation of neuronal resources. Thus the additional chemosensory context information in the present study might have distracted neuronal resources from the elaborative processing of the concurrently presented facial expressions, leading to reduced late ERPs towards the faces. Interestingly, results indicate that also the regulation of non-social disgusting odors was impaired. In addition, overall disgusting odors elicited larger startle responses than the pictures. This suggests that odors are not only more potent emotion elicitors, but emotions elicited by them might also be less effectively regulated. This effect might result from a preferential representation of chemosensory information in emotionally relevant brain areas. The amygdala has been suggested to be a part of the primary olfactory cortex. It holds dense and direct interconnections to other olfactory brain areas like the olfactory bulb, entorhinal cortex, and olfactory tubercle (Carmichael,

Clugnet, & Price, 1994). Thus the amygdala is more closely involved into odor processing than into any other sensory modality. Moreover, olfactory stimuli might activate the amygdala more directly, because as compared to other modalities olfactory stimuli can bypass thalamic gating (Price, 1985). The amygdala is interconnected with the orbitofrontal cortex, which is responsible for the coding of the hedonic value of emotional stimuli (e.g. Anderson, et al., 2003), and both structures are preferentially activated by odors as compared to pictures (Royet, et al., 2000). Because these areas have been shown to be the major target of cognitive linguistic emotion regulation strategies via prefrontal cortex areas (Ochsner, et al., 2002), a preferential activation of these areas in response to odors as compared to pictures might result in less effective top-down regulatory control. Presumably, a preferential processing of chemosensory information also account for the lack of findings concerning emotion regulation towards fearful facial expressions in the context of chemosensory signals. More generally, it has been demonstrated that the perception of body odors from a stranger engages distinct brain regions associated with threat detection, namely the amygdala and the insula (Lundström, Boyle, Zatorre, & Jones-Gotman, 2008). Moreover, processing of chemosensory signals of stress and anxiety also engages the amygdala (Mujica-Parodi, et al., 2009), but furthermore also recruit significant neuronal resources in medial frontal areas (Pause, et al., 2010), a brain region which is thought to be directly engaged in emotion regulation (Ochsner & Gross, 2007).

However, the amygdala may also be the source for the present results of preferential processing of chemosensory emotional information. Study I and III assessed emotional reactivity with the startle reflex, and the amygdala is considered to be responsible for the enhancement of the startle response towards fear relevant stimuli (Davis, 1992a). Moreover, study V assessed emotional reactions with the skin conductance response. Interestingly, it has been suggested that on the basis of the central nervous system the amygdala is also involved in the excitatory control of the skin conductance response (Dawson, et al., 2007). Thus, taken together it is suggested that the amygdala is most likely also the source of the present effects. This view is also supported by recent findings of amygdala activity in response to chemosensory signals of stress in humans (Mujica-Parodi, et al., 2009), and the aforementioned results concerning a preferential involvement of the amygdala in the processing of emotional odors as compared to other modalities (Royet, et al., 2000).

Finally, an important limitation for the generalization of the present results may be the fact that only non-clinically anxious individuals were investigated. This raises the question

whether the reported effects do also hold for patients suffering from social phobia. However, a recent review suggests that processing biases towards social threat stimuli are comparable between social phobics and sub-clinically anxious individuals (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007). In addition, for studies II, III, and IV for reasons of homogeneity only female perceivers were recruited. Related, for studies II and IV axillary sweat was collected from male donors only. However, in study I and V of the present thesis it was demonstrated that the effects of the chemosensory stimuli were independent of the sex of the donor and the sex of the perceiver. Thus it is assumed that the observed effects of studies II, III, and IV hold for male and female perceivers.

5 References

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6 Original Research Articles

This cumulative Dissertation is based on the following original research reports, which have been published in or are submitted to international peer-reviewed journals.

Article #1

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Article #2

Adolph, D., Dedekind, A., Meyer, S., Schaub, D., & Pause, B.M. (submitted). Emotion regulation with non-social and social chemosensory stimuli – Disgusting odors and chemosensory anxiety signals. *Psychological Science*

Article #3

Adolph, D., Meister, L., & Pause, B.M. (submitted). Regulation of emotions elicited by fearful faces in the context of chemosensory anxiety signals. *Social Cognitive and Affective Neuroscience*

Article #4

Adolph, D., Schlösser, S., Hawighorst, M., & Pause, B.M. (2010). Chemosensory signals of competition increase the skin conductance response in humans, *Physiology & Behavior*, 101, 666-671.

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Startle response potentiation to chemosensory anxiety signals in socially anxious individuals

Bettina M. Pause [a,*], Dirk Adolph [a], Alexander Prehn-Kristensen [b], Roman Ferstl [c]

[a] Department of Experimental Psychology, University of Duesseldorf, Duesseldorf, FRG
[b] Center of Integrative Psychiatry, University of Kiel, Kiel, FRG
[c] Department of Psychology, University of Kiel, Kiel, FRG

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ABSTRACT

The present study aimed to investigate whether withdrawal related behavior is activated in the context of chemosensory anxiety signals. Moreover, it was examined whether chemosensory perception of social stress is modulated by the degree of social anxiety. Axillary sweat was collected from students, awaiting an oral examination at the university (anxiety condition) and from the same students in a sport control condition. The chemosensory stimuli were presented to 32 participants (16 socially anxious) via an olfactometer during inhalation (duration = 3 s). 102 dB white noise bursts served as startle probes. During a single session only male or female axillary sweat was presented, therefore, all participants were tested in two separate sessions. Even though the chemosensory stimuli were perceived at the perceptual threshold level, participants could identify (forced choice) the emotion of the donors in the anxiety condition. In the context of chemosensory anxiety signals the acoustic startle reflex was significantly augmented as compared to startle responses obtained in the context of sport sweat ($p = 0.002$). This effect was more pronounced in socially anxious than in non-anxious participants. It is concluded that human motor systems automatically adapt to chemosensory stress signals. This adaptation is neither dependent on the gender of the odor donor nor on the gender of the perceiver, but is intensified in socially anxious participants.

1. Introduction

Chemosensory alarm signals are supposed to have evolved independently within all major taxa (Wyatt, 2003). Across species, the chemosensory-mediated alarm response entails avoidance of the odor source and withdrawal behavior (von Frisch, 1941; Ressler et al., 1968; Müller-Velten, 1966; Suh et al., 2004), which can vary from increased motor activity and alertness (Zalaquett and Thiessen, 1991) to freezing (Mackay-Sim and Laing, 1981). Physiological reactions to these signals within the receiver resemble stress-related adaptations, such as an increase of the core body temperature (Kikusui et al., 2001), an increase of endogenous opioids (Fanselow, 1985) and an impaired immunological function (Moynihan et al., 2000). Different sensory systems seem to contribute to the processing of chemosensory alarm signals in rodents. Trace-amine-associated receptors expressed in the olfactory epithelium of mice are capable to detect stress-related social chemosignals (Liberles and Buck, 2006). In addition, olfactory receptors mediate an innate fright response to predator odors in mice (Kobayakawa et al., 2007). Moreover, sensory receptors outside the olfactory epithelium, like the vomeronasal organ (Kiyokawa et al., 2007) or the grueneberg ganglion cells (Brechbühl et al., 2008) were demonstrated to process chemosensory alarm signals.

In humans, chemosensory anxiety signals are processed in brain areas involved in the regulation of empathic feelings (insula, precuneus, cingulate cortex) and in the perception of social anxiety signals (fusiform cortex; Prehn-Kristensen et al., 2009). The brain's adaptation has been discussed to resemble a contagion of the feeling of anxiety between the signal sender and the signal perceiver. Hereby, full recognition of the odor quality is not required for the physiological adaptations to occur. Likewise, in a chemical context of anxiety, perceptual and behavioral performances are adjusted without the recruitment of attentional resources: In the context of chemosensory stress signals the cognitive performance of perceivers in a word-association task is enhanced, most likely due to a more effortful allocation of attentional resources in potentially harmful situations (Chen et al., 2006). Moreover, the perceptual acuity for social safety cues (happy facial expressions) is reduced in female participants exposed to chemosensory anxiety signals (Pause et al., 2004). Similarly, ambiguous facial expressions are evaluated as anxiety-like, when presented in the context of chemosensory anxiety signals (Zhou and Chen, 2009). So far, one study indicated that chemosensory anxiety signals activate withdrawal related motor systems in humans by measuring the eye blink startle reflex (Prehn et al., 2006). Just recently, a similar phenomenon has been demonstrated in rats (Inagaki et al., 2008).

* Corresponding author. Department of Experimental Psychology, University of Duesseldorf, Universitaetsstraße 1, 40225 Duesseldorf, FRG. Tel.: +49 211 81 14384; fax: +49 211 81 12019.
E-mail address: bettina.pause@uni-duesseldorf.de (B.M. Pause).

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It was the aim of the present study to validate the effect of chemosensory anxiety signals on the startle reflex. As socially anxious individuals demonstrate preferential processing of social threat (Bar-Haim et al., 2007; Hirsch and Clark, 2004), in the present study a group of non-clinical socially anxious participants was compared to non-anxious control participants. The socially anxious participants were matched to the control participants according to their depression scores, since anxiety and depression often co-occur (Mineka et al., 1998) and the startle response is differentially modulated in anxious and depressed individuals (Kaviani et al., 2004; Larson et al., 2007). Additionally, in comparison to the study by Prehn et al. (2006), the present study was based on a larger sample size (32 participants instead of 7 participants) and effects of gender (of the odor donors and participants) were analyzed. Axillary sweat served as the anxiety signal and was collected on cotton pads from 49 students (28 males) while awaiting an oral examination to obtain a university degree (anxiety condition). The chemosensory control stimuli were collected from the same participants during an ergometer training (sport condition). In detail, the sweat donors and the sampling procedure are described elsewhere (Prehn-Kristensen et al., 2009).

2. Methods

2.1. Participants

The participants were assigned to two groups according to their self-reported degree of social anxiety (Social Interaction Anxiety Scale, SIAS, Stangier et al., 1999). Participants scoring 22 or higher were defined as socially anxious, those scoring 16 and lower were defined as non-anxious and participants scoring between 17 and 21 were excluded from participation. 16 (8 males) out of 32 non-anxious participants were matched to 16 (8 males) socially anxious participants according to their depression scores (Beck Depression Inventory, BDI, German Version, Hautzinger et al., 1995). Accordingly, the SIAS scores of the two groups were significantly different (non-anxious participants: $M=12.25$, $SD=2.75$, socially anxious participants: $M=29.31$, $SD=6.07$, $t\ (30)=10.24$, $p<0.001$, $d=3.24$), and the depression scores did not differ between groups (non-anxious participants: $M=4.94$, $SD=3.49$, socially anxious participants: $M=5.31$, $SD=3.20$; $t\ (30)=0.32$, $p=0.754$).

In order to differentiate social anxiety from social interest, the agreeableness scale of the Big Five personality inventory was applied (NEO-FFI; Borkenau and Ostendorf, 1993). The two groups did not differ in their tendency to be compassionate and cooperative towards others (non-anxious participants: $M=2.59$, $SD=0.40$, socially anxious participants: $M=2.45$, $SD=0.38$; $t\ (30)=1.02$, $p=0.317$). Furthermore, the groups did not differ in age (non-anxious participants: $M=24.00$, $SD=4.71$, socially anxious participants: $M=22.94$, $SD=2.05$; $t\ (30)=1.61$, $p=0.123$).

All participants reported to be non-smokers and of European origin. None of them suffered from any mental (according to the Structured Clinical Interview for DSM-IV, SKID, German Version, Wittchen et al., 1997) or physical (self-report) diseases, especially not from diseases of the upper respiratory tract or the auditory system. None of them reported to be on long-term or acute medication. All female participants had a regular menstrual cycle ($+/-3$ days). All participants gave written, informed consent and were paid for their participation. The study was approved by the ethical committee of the Medical Faculty of the University of Kiel.

2.2. Presentation of the chemosensory stimuli

The sweat samples were pooled with distinction to the respective donation conditions and the donor's sex and stored at -20 °C. For the startle experiment the homogenized samples were divided into small portions (0.4 g) and renewed after each experiment. The chemosensory stimuli were presented in accordance with the method described by Kobal (2003). A constant flow (100 ml/s), six channel olfactometer (OM6b, Burghart, Germany) was used, and both nostrils were stimulated simultaneously. Both air streams were controlled by separate mass flow controllers. In the olfactometer, the glass tubes containing the stimuli (0.4 g) were stored in a warm-water chamber, and the chemosensory stimuli were delivered to the participants through a teflon tube, the temperature of the gas flow at the exit of the olfactometer was 37 °C and the relative humidity above 80%.

2.3. Startle probe

The startle-eliciting stimulus was a 102 dB (A) white noise burst (duration = 50 ms, rise-time <1 ms), presented through earplugs (ER3-14A, Etymotic Research, Inc., IL, USA).

2.4. Olfactory hyposmia screening

In order to assess general hyposmia, all participants had to identify a bottle containing phenyl ethyl alcohol (PEA, 99%, Fluka, Germany, 1:200 (*v/v*) diluted in 1,2-propanediol) from a series of three bottles (two consecutive trials). The remaining two bottles contained the same volume of solvent. No subject had to be excluded due to general hyposmia.

2.5. Stimulus detection, stimulus and self-ratings

To determine subjects' stimulus detection performance, the chemosensory stimuli were administered via the olfactometer (duration = 3 s). The participants were asked to select the most intense stimulus from a series of three stimuli (three-alternative forced choice, including one worn cotton pad, either from the anxiety or from the sport condition, and two blank odors consisting of clean cotton pad). This procedure was carried out twice for each stimulus condition. Participants who failed once to detect the chemosensory stimulus (from the anxiety or the sport condition) were defined as non-detectors.

Ratings of the chemosensory stimuli for intensity, pleasantness, unpleasantness, and familiarity were carried out using visual analogue scales (presented on a computer screen, range 0–500: 0 = no smell, 500 = strongest smell). In addition, the participants were asked to identify the emotional state of the sweat donors. The six basic emotions were written on a computer screen and the participants indicated their guess by mouse click (forced choice).

To determine participants' subjective emotional responses to the chemosensory stimuli, the SAM scale (Bradley and Lang, 1994) was applied (valence: -4–$+4$, arousal: 1–9, dominance: 1–9), and the participants had to evaluate whether the chemosensory stimuli evoked a specific emotion (6 basic emotions, forced choice).

2.6. Procedure

All participants were tested individually in two separate sessions. During both sessions, the participants completed an identical experimental protocol with the exception that either chemosensory stimuli donated by male or female persons were presented. The order of these sessions was balanced across participants.

In the beginning of the sessions, the olfactory hyposmia screening and the stimulus detection test were carried out, furthermore the self-ratings and the ratings of the stimulus intensity, pleasantness, unpleasantness and familiarity were registered. Thereafter, the eye blink response was recorded in the context of chemosensory stimuli donated during the anxiety or the sport control condition, or in the context of pure cotton pad. The chemosensory stimuli were presented in pseudo-randomized order within two blocks of 27 trials each, thus, each stimulus was presented 18 times in total. Both blocks started with a habituation phase lasting 30 s, including the presentation of 9

startle probes. At the beginning of each trial a visual countdown instructed the participants to prepare for inhalation (duration = 3.6 s). During the subsequent inhalation phase (duration = 3 s) the chemosensory stimuli were presented (the odor valve was activated 0.6 s before the inhalation phase started). The participants' breathing cycle was recorded with a breathing belt. During each trial, two startle probes were presented (First: randomly between seconds 2 and 3 after the beginning of the inhalation phase during odor presentation. Second: randomly between 9 and 10 s after the end of the inhalation phase during the inter-stimulus interval (ISI). The second probes served to prevent classical conditioning between the tone and the odor, thus the startle responses to the second probes during the ISI were not analyzed.). Startle probes were embedded in a background white noise of 70 dB (A). The trial duration was 20 s. One second after the inhalation phase ended, the participants were asked to identify the emotional state of the donors within a period of 4 s.

2.7. Data recording

The eye blink component of the startle reflex was recorded bipolarly from the orbicularis oculi muscle beneath the left eye (according to Berg and Balaban, 1999), using two Ag/AgCl electrodes (6 mm inner diameter). A ground electrode was placed on the forehead. The physiological data were recorded, amplified and filtered with Acquire software (version 4.2, NeuroScan Inc., Virginia, USA), sampled at 2000 Hz, and filtered on-line using a 50 Hz notch filter. In addition, the raw EMG was high- (30 Hz, 24 dB/octave) and low-pass filtered (500 Hz, 24 dB/octave; Blumenthal et al., 2005).

2.8. Data reduction

Out of all startle responses 5.3% had to be rejected, because they were neither recorded during an increase in inhalation nor briefly after the inhalation maximum (200 ms). The remaining trials were baseline corrected (0–20 ms after startle probe onset; Berg and Balaban, 1999), and rectified. The eye blink reaction was calculated as the area under the curve in the 30–90 ms time window after startle probe onset (Blumenthal et al., 2005). Exclusively those trials including amplitudes which exceeded the largest amplitude within the baseline interval for the factor two were defined as startle responses (Grillon and Davis, 1995), non-responses (2.6% of all trials) were scored as zero. In order to minimize the probability that differences between conditions could be due to single outlier values, 3.3% of the standardized startle responses were excluded, which differed more than two standard deviations from the condition average (Blumenthal et al., 2005). After trial selection, the minimum number of trials per condition and participant was 5, with no participant having to be excluded due to the selection criteria. Finally, the startle responses were *z*-standardized within each participant.

2.9. Data analysis

For the analyses of the startle response data a 4-way ANOVA with the within subject factors Social Anxiety (matched groups dependent-samples design according to Kirk (1995): non-anxious, socially anxious participants), Sex of the Donor (male, female), Chemosensory Condition (anxiety condition, sport condition, cotton pad), and the between subject factor Sex of the Perceiver (male, female) were performed (SPSS 12.0). For significant effects Cohen's effect-size *f* (ANOVA) or Cohen's *d* (*t*-test) was calculated. Huyn–Feldt corrections of degrees of freedom were applied, and corrected *p*-values are reported. An alpha level of 5% was used for all statistical tests.

Binomial and Fisher tests were used to analyze the detection rates, and Pearson's chi-square test was calculated to analyze the ratings of the participants' emotional states which were ascribed to be stimulus evoked.

Table 1
Participants' ratings of the emotional state of the sweat donors (number of evaluations).

	Anxiety sweat		Sport sweat		Cotton pad	
	Mean	SD	Mean	SD	Mean	SD
Surprise	5.5	2.5	5.7	2.8	5.7	2.2
Disgust	4.6	2.2	4.8	2.3	4.2	2.2
Sadness	5.4	3.9	5.6	2.1	5.5	2.8
Anger	5.0	2.1	5.0	2.5	5.3	2.7
Anxiety	8.0	3.1	6.3	2.7	5.0	2.5
Joy	7.4	3.7	8.5	4.3	10.1	6.3

Note: each stimulus was evaluated 36 times by each participant.

3. Results

3.1. Stimulus detection

On average, 28.1% of the participants could olfactorily detect the chemosensory stimuli donated in the sport control condition and 26.6% of them could detect the chemosensory stimuli donated in the anxiety condition. Only one subject was able to detect both chemosensory stimuli. There were no significant detection differences with respect to the donation conditions, sex of the donor, or the degree of social anxiety (binomial test, $p>0.10$), or between male and female participants (Fisher test, $p>0.10$).

3.2. Stimulus ratings

In accordance with the low detection rates, the magnitude of all odor features was described as low (intensity: $M=119.65$, $SD=68.16$; pleasantness: $M=136.72$, $SD=71.43$; unpleasantness: $M=112.15$, $SD=76.23$; familiarity: $M=97.40$, $SD=62.27$). The odor evaluations did not vary with either of the experimental conditions ($p>0.10$).

Deciding which of the basic emotion fits best to the emotional state of the donors, the participants evaluated the chemosensory stimuli donated in the anxiety condition as smelling anxiety-like and the chemosensory stimuli donated during the sport condition as joy-like (Chemosensory Condition × Emotion: $F\ (10,\ 140)=3.08$, $p=0.001$, $f=0.47$; Table 1). Anxiety was ascribed significantly more often to the chemosensory samples donated in the anxiety condition than to the samples donated in the sport condition ($t\ (15)=2.73$, $p=0.016$, $d=0.68$) and than to the control cotton pads ($t\ (15)=5.12$, $p<0.001$, $d=1.29$). Joy was ascribed significantly more often to the control cotton pads than to the samples donated in the anxiety condition ($t\ (15)=2.91$, $p=0.011$, $d=0.64$).

3.3. Self-ratings

The emotional responses to the chemosensory stimuli were judged as neutral (SAM valence: $M=0.01$, $SD=0.60$; SAM arousal: $M=4.40$, $SD=0.83$; SAM dominance: $M=5.09$, $SD=0.60$). Accordingly, during stimulus administration the participants did not report experiencing a specific emotion. All statistical analyses including self-ratings were not significant ($p>0.10$).

3.4. Startle reflex

Startle responses were stronger in the context of the chemosensory stimuli donated in the anxiety condition than in the context of sweat donated in the sport control condition (Chemosensory Condition: $F\ (2,\ 28)=7.55$, $p=0.002$, $f=0.73$; single comparisons: anxiety vs. sport: $t\ (15)=3.87$, $p=0.002$, $d=0.97$; anxiety vs. cotton pad: $t\ (15)=2.03$, $p=0.06$, $d=0.51$; sport vs. cotton pad: $t\ (15)=1.84$, $p=0.09$, $d=0.46$; Fig. 1). The eye blink reactions were neither affected by the sex of the sweat donors, nor by the sex of the participants ($p>0.10$).

As the main aim of the study was to explore possible effects of social anxiety in the perceiver, *t*-tests between the emotion conditions were carried out for both groups separately (however, the interaction

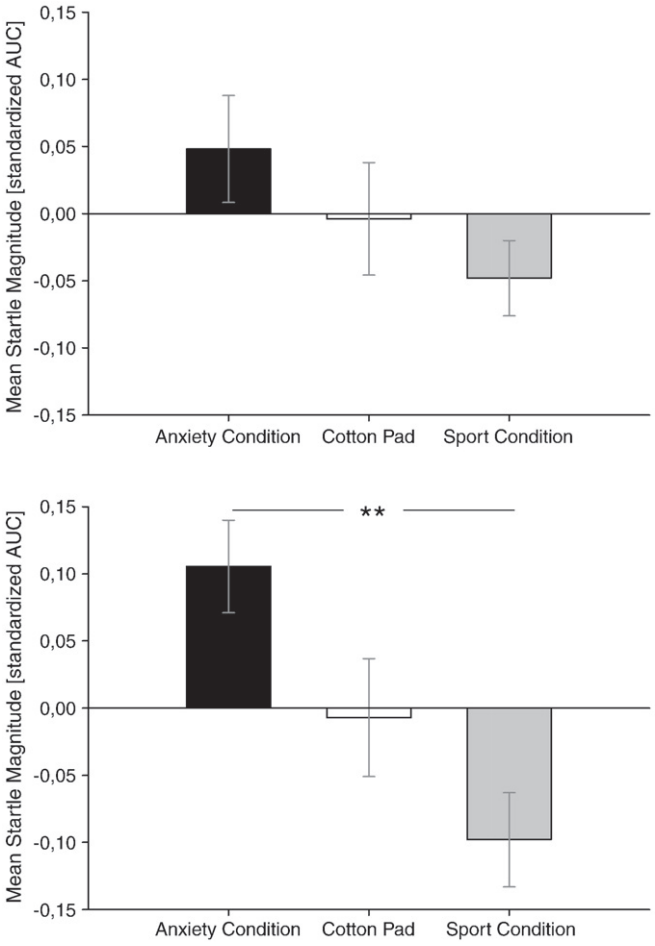

Fig. 1. Mean startle magnitudes (+/−SEM) in the context of chemosensory stimuli donated in the anxiety condition (dark bars), the sport control condition (grey bars) and in the context of pure cotton pad (white bars). Top: non-anxious participants. Bottom: highly anxious participants. Note: $^{**}p<0.01$.

of Chemosensory Condition by Group was not significant: $F\,(2, 28) = 0.56$, $p = 0.58$). According to these t-tests, the ability of chemosensory anxiety signals to increase the startle reflex is more pronounced in the socially anxious group (anxiety compared to sport: $t\ (15) = 3.60$, $p = 0.003$, $d = 0.90$), than in the non-socially anxious group (anxiety compared to sport: $t\ (15) = 1.76$, $p = 0.10$, $d = 0.44$).

In order to investigate possible effects of the session order, a second ANOVA was run, including the within subject factors Social Anxiety (non-anxious, socially anxious participants), Session number (first, second), Chemosensory Condition (anxiety condition, sport condition, cotton pad), and the between subject factor Sex of the Perceiver (male, female). The factor Sex of the Donor was excluded, because it was confounded with the session order and did not show significant effects within the first ANOVA. This ANOVA again revealed a significant odor effect (Chemosensory Condition: $F\ (2, 28) = 7.55$, $p = 0.002$, $f = 0.73$), and in addition, a significant interaction Social Anxiety × Session × Chemosensory Condition ($F\ (2, 28) = 5.49$, $p = 0.010$, $f = 0.63$). During the first session, the highly socially anxious participants showed stronger startle responses than the control participants in the context of chemosensory anxiety signals ($t\ (15) = 3.58$, $p = 0.003$, $d = 0.89$; see Table 2).

Table 2
Mean startle magnitudes of socially anxious and control participants, separated for the session order.

Session	Group	Anxiety sweat		Sport sweat		Cotton pad	
		Mean	SD	Mean	SD	Mean	SD
First	A	0.153	0.181	−0.158	0.176	0.004	0.269
	C	−0.018	0.202	−0.039	0.149	0.062	0.182
Second	A	0.058	0.192	−0.038	0.173	−0.019	0.168
	C	0.114	0.223	−0.058	0.149	−0.069	0.234

Note: A = highly socially anxious participants, C = control participants.

4. Discussion

The present study confirms the hypothesis that humans communicate emotional states via their chemosensory senses. Chemosensory anxiety signals potentiate the startle reflex, independently of the sex of the sweat donor or the sex of the perceiver, and thus have the ability to automatically prime defensive emotional systems in humans (Lang et al., 1990). The defense system is considered to be the source of negative affect in humans, in animals its activation is a direct indicator of threat related to pain or predation (Lang and Davis, 2006). It is concluded that the basic consequences of chemosensory stress perception are the same in humans and animals, namely the activation of withdrawal behavior.

In line with the first study on startle modulation in the context of chemosensory anxiety signals (Prehn et al., 2006), both genders responded equally in the context of chemosensory stimuli. Therefore, the priming of withdrawal related motor behavior through chemosensory anxiety signals seems to be of similar importance for both sexes. Moreover, the present study revealed for the first time, that the chemosensory stress signals released by women as well as by men are equally effective.

Most of the participants were not able to differentiate the body odors from pure cotton pad. Accordingly, they described the chemosensory stimuli as emotionally neutral and hardly perceivable and did not report any specific emotion evoked by the chemosensory stimuli. However, under forced choice conditions only, they were able to identify the most prominent emotional state of the sweat donors (see also: Ackerl et al., 2002; Chen and Haviland-Jones, 2000). Therefore, the potentiation of the startle reflex through chemosensory anxiety signals is considered to be mainly independent of the allocation of attentional resources. As common odors do have to carry a distinct emotional value in order to modulate the startle reflex (Ehrlichman et al., 1997; Miltner et al., 1994), it is supposed that the effects of chemosensory anxiety signals are not due to a specific odor, but to an innate readiness to avoid such social distress signals. Our results are in line with the recent demonstration of an affective startle modulation through subliminally presented emotional slides (Ruiz-Padial and Vila, 2007). Thus, both studies support the conclusion that biologically relevant signals are able to prime defensive behavior without conscious mediation. Accordingly, a meta-analysis recently summarized that biologically salient stimuli are more potent in eliciting a threat-related bias, when automatic stimulus processing is required (Bar-Haim et al., 2007).

Exploratory analyses revealed that the startle reflex modulation through chemosensory anxiety signals is more pronounced in socially anxious participants than in non-anxious participants. In addition, significant group differences were observed during the first session, with anxious participants showing stronger startle reflexes in the context of chemosensory anxiety signals than non-anxious participants. Thus, it is speculated that in highly socially anxious participants the normal adjustments to chemical signals of anxiety are intensified. It is generally agreed that social anxiety is characterized by abnormal processing of social threat information, involving processing biases in attention, interpretation and memory (Hirsch and Clark, 2004). Accordingly, socially anxious individuals show a processing advantage for angry/threatening faces during the early (N170 amplitude of the event-related potential, Kolassa and Miltner, 2006) and late elaborative stimulus processing (P3 amplitude of the event-related potential, Moser et al. 2008). As indicated by several brain imaging studies, this

processing bias seems to be related to a deviant activation pattern of emotion processing brain structures. Consistently, socially anxious individuals respond to angry, disgusted or fearful faces with increased amygdala activation (Phan et al., 2006; Stein et al., 2002; Straube et al., 2004). A hyperactivation of the amygdala during social threat perception could also account for the increased startle response in socially anxious subjects in the present study, because the central nucleus of the amygdala is considered to be the main relay during startle potentiation, responsible for the activation of the N. reticularis pontis caudalis (Lang and Davis, 2006).

Further studies on the chemosensory communication of emotions need to address the emotion specificity of the startle potentiation. In the present study the donors reported to experience anxiety while waiting for their examination and joy during ergometer training. All other emotions were reported to be experienced on a marginal level. However, as only anxiety related signals were investigated in the present study, further studies should rule out whether the startle effects are specific of anxiety related emotional states or related to the perception of social distress signals in general. Furthermore, since only non-clinical socially anxious participants were investigated, it remains to be shown how patients with social phobia process chemosensory anxiety signals. However, similar effects are to be expected, because the threat-related processing bias appears to be similar in clinically and non-clinically anxious individuals (Bar-Haim et al., 2007). Maybe, in the future, the knowledge about an intensified processing of chemosensory anxiety signals in socially anxious individuals might form the basis to develop specific chemosensory-related diagnostic tools and therapeutic treatments.

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Emotion regulation with non-social and social chemosensory stimuli – Disgusting odors and chemosensory anxiety signals

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Running Head: EMOTION REGULATION AND CHEMORECEPTION

Emotion regulation with non-social and social chemosensory stimuli – Disgusting odors and chemosensory anxiety signals

Dirk Adolph, Antje Dedekind,

Ruhr-Universitaet Bochum, Germany,

Sonja Meyer, Dominique Schaub & Bettina M. Pause

Heinrich-Heine-Universitaet Düsseldorf, Germany

Coresponding Author:

Bettina M. Pause

University of Duesseldorf, Germany

Department of Experimental Psychology

Universitaetsstraße 1

D-40225 Duesseldorf

Tel.: +49 (0) 211 - 81-14384

Fax: +49 (0) 211 - 81-12019

e-mail: bettina.pause@uni-duesseldorf.de

Abstract

The present study assessed emotion regulation in response to chemosensory stimuli. Using cognitive reappraisal high socially anxious (HSA) and non socially anxious (NSA) participants regulated their emotions in response to disgusting pictures and odors (Experiment I) or to fearful facial expressions presented in the context of chemosensory anxiety signals (Experiment II). During emotion regulation the startle reflex was elicited and emotion ratings were assessed. Participants described themselves to feel less negative, and less aroused, while down regulating their emotions in both experiments. In Experiment I, disgusting odors elicited larger startle responses than pictures and emotion regulation towards them was less effective. In Experiment II, HSA participants showed larger startle responses towards faces in the context of chemosensory anxiety than NSA participants, but both groups showed effective emotion regulation. The results highlight the unique role of olfaction in emotion perception, and suggest that the effectiveness of cognitive emotion regulation is limited.

Introduction

Emotion regulation has been defined as the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotions (Thompson, 1994). One example for such processes is the voluntary reappraisal of emotion eliciting situations (Gross, 2002). Several studies have yet demonstrated the usefulness of reappraisal in regulating negative emotional states. Self-reported emotions, as well as a number of physiological responses to threatening pictures, including heart rate and electrodermal activity (review in \Gross, 2002), brain electrical activity (Moser, Krompinger, Dietz, & Simons, 2009), neuronal responses in the amygdala (Ochsner, Bunge, Gross, & Gabrieli, 2002), and the affect modulated startle-reflex (Jackson, Malmstadt, Larson, & Davidson, 2000) can be significantly enhanced or reduced using cognitive reappraisal.

Emotion regulation research so far has focused almost exclusively on visual stimuli to elicit emotions. No study has used olfactory stimuli, although odors have been demonstrated to be very potent elicitors of emotion: Emotional odors modulate the startle reflex (Miltner, Matjak, Braun, Diekmann, & Brody, 1994), heart rate (Delplanque, Grandjean, Chrea, Coppin, Aymard, Cayeux et al., 2009), brain electroencephalographic activity (Pause, Raack, Sojka, Goder, Aldenhoff, & Ferstl, 2003) and blood flow in the amygdala (Anderson, Christoff, Stappen, Panitz, Ghahremani, Glover et al., 2003). This is not surprising, given the strong overlap between olfactory cortex and limbic brain structures. For example, the amygdala has been suggested to be a part of the primary olfactory cortex holding dense and direct interconnections to the olfactory bulb, entorhinal cortex, and olfactory tubercle (Carmichael, Clugnet, & Price, 1994), and thus the amygdala is more closely involved into olfaction than into any other sensory modality. Furthermore, olfactory information can bypass sensory thalamic gating (Price, 1985), suggesting a more direct input of olfactory information into

emotion processing areas, as compared to other sensory modalities. Therefore, effective regulatory top-down neuronal control of emotions elicited by odors seems to be less likely.

To date, also only little research has been published using social emotional stimuli in emotion regulation, although in everyday life, mostly all emotion regulation efforts are made in the presence of others (Gross, Richards, & John, 2006). To our knowledge, only one study (Goldin, Manber, Hakimi, Canli, & Gross, 2009) has shown that on a verbal report level, emotion regulation is effective in response to threatening facial expressions of emotion. However, emotions can also be communicated chemosensorily between humans. Chemosignals of anxiety alter emotion related neuronal activity (Prehn-Kristensen, Wiesner, Bergmann, Wolff, Jansen, Mehdorn et al., 2009) and enhance the startle-reflex (Prehn, Ohrt, Sojka, Ferstl, & Pause, 2006). Moreover, socially anxious as compared to non-anxious individuals show enhanced reactivity to chemosensory anxiety signals (Pause, Adolph, Prehn-Kristensen, & Ferstl, 2009).

Taken together, the aim of the present study was to assess emotion regulation in response to either non-social or social chemosensory stimuli. In Experiment I emotion regulation in response to disgusting odors and pictures, in Experiment II emotion regulation towards anxious facial expressions in the context of chemosensory anxiety signals anxiety or a control stimulus was assessed. Emotion regulation has strong clinical importance, since many psychological disorders include disturbances in regulatory processes like inappropriate affect, chronic worry, or avoidance (Cole, Michel, & Teti, 1994). Thus, in assessing a group of high, and a group of non-anxious individuals, it was aimed to assess whether socially anxious individuals show emotion regulation deficits, and if so, whether these deficits are generalized to negative stimuli or specific for threatening social stimuli.

Experiment I: non-social odors

Methods

Participants. Forty[1] non-smoking female students from the Heinrich-Heine-University of Düsseldorf reported a regular menstrual cycle, not to use any medication, and not to suffer from mental and physical diseases. All scored low on social desirability (<5 on the Lie scale of the EPI, Eggert & Ratschinski, 1983). Participants were classified as either non-socially-anxious (NSA, scores < 17, n=20) or high-socially-anxious (HSA, scores > 21, n=20) based on their trait social anxiety scores (SIAS, Stangier, Heidenreich, Berardi, Golbs, & Hoyer, 1999) (see Table 1 for questionnaire data). HSA participants scored within the normal range for trait anxiety (STAI, Laux, Schaffner, Glanzmann, & Spielberger, 1981) and depressive feelings (DS, von Zerssen & Koeller, 1976), while NSA participants scored low on both questionnaires. Both groups scored within the medium range for disgust sensitivity (FEE, Schienle, Walter, Stark, & Vaitl, 2002), and the frequency of everyday-life use of reappraisal (ERQ, Abler & Kessler, 2009). The two groups did not differ for age, p=.06 (M=23.95, SD=5.05, range 19-40). All participants were paid for participation and gave written informed consent. The study was approved by the ethics committee of the German Psychological Society (DGPs).

-Table1-

Stimuli. Five negative disgust-related odors (isovaleric acid, ethanethiole, isobutyraldehyde, pyridine, 3-methyl-indole) served as olfactory stimuli. Each odor was diluted in solvent using three dilution steps following a half-logarithmic serial dilution (supplemental Table T1). Seven negative disgust-related color pictures (1111, 1205, 1274, 3150, 3250, 9300, 9340) were chosen from the International Affective Picture System (IAPS, Lang, Bradley, &

Cuthbert, 2005). The startle-eliciting stimulus was a 104 dB/A white noise burst (50 ms, rise-time < 1 ms), presented through earplugs (ER4-14A Etymotic Research, USA).

Individual stimulus validation. To adjust the amount of perceived disgust elicited by the five odors across participants', each participant was asked to indicate for each odor the concentration (out of three) that was clearly unpleasant and disgusting, but still tolerable for her. These individually adjusted concentrations were later used in the main experiment. Participants then rated the chosen concentrations as high in intensity (M=6.67, SD=0.98) and unpleasantness (M=5.71, SD=1.10), but low in pleasantness (M=1.87, SD=0.90) and familiarity (M=3.83, SD=1.50) (scales range: 1-9).

Afterwards, participants rated the odors and pictures for valence and arousal (Self Assessment Manikin, SAM, Bradley & Lang, 1994). Participants rating more than three of the stimuli as neutral, or more than one as positive (SAM valence) were excluded (N=31). Two (Stimulus Type: Odors, Pictures) x 2 (Group: NSA, HSA participants) ANOVAs were run for SAM ratings. Both odors and pictures were perceived as equally unpleasant (M=-2.33, SD=0.47), $F(1,38)=2.83$, $p>.10$, and arousing (M=6.47, SD=0.86), $F(1,38)=2.92$, $p=.095$. There were no group effects concerning the SAM ratings, $p>.20$.

Stimulus Presentation. The picture stimuli were presented using the Presentation® software (Neurobehavioral Systems, USA). The olfactory stimuli were presented with a constant-flow (50ml/ s) 5-channel olfactometer (Prehn-Kristensen, et al., 2009) including five glass bottles with cellulose pads carrying 1ml of each odor stimulus. Stimuli were presented in four counterbalanced blocks (enhance odors/ pictures, down-regulate odors/ pictures) of 21 trials each (Figure 1). After a fixation cross was presented for 3s either an odor or a picture was presented twice: before and after one of two visual regulation instructions. Participants were instructed to inhale during the complete 2s of the odor and picture presentations. During the

inter stimulus interval (ISI, varying randomly between 15 and 16s) emotion regulation outcome was measured with valence and arousal ratings (SAM). Each scale was presented for 3.5s. Afterwards the word "RELAX" occurred randomly for 5-6s. Startle-probes were presented at three different probe positions (A=baseline, B=early emotion regulation interval: both presented randomly between 1-1.9 seconds after stimulus-onset, C=late emotion regulation interval: 2-2.9s after the beginning of the ISI). Sven startle probes were presented at each probe position, and trials including different startle-probe positions were equally distributed within blocks.

-Figure1-

Procedure. After having received detailed breathing instructions and only after they were able to breathe correctly, participants were given detailed instructions to use cognitive linguistic emotion regulation strategies (Jackson, et al., 2000) and practiced at least 10 learning trials of each experimental condition. At the beginning of the experiment all participants received 8 startle probes to induce habituation.

Data recording. The startle eyeblink was recorded electromyographically from the orbicularis oculi muscle beneath the left eye using two Ag/AgCl electrodes (inner diameter 5mm). To assess the participants' breathing cycles, respiration belts (BP-BM-10, Brain Products, Germany) were placed around the abdomen and the thorax.

The physiological data were amplified with a 22-bit amplifier (Quick-Amp, Brain Products, Germany) and recorded using the BrainVision Recorder Software (Brain Products, Germany), sampled at 2000 Hz, and filtered on-line using a 50 Hz notch filter. Off-line, the raw EMG was high- (28Hz) and low-pass filtered (500 Hz, 24 dB/octave) (van Boxtel, Boelhouwer, & Bos, 1998).

Data reduction. For startle-probes A and B together 1.73% eyeblink responses were rejected, because they were neither recorded during an increase in inhalation nor briefly (200 ms) after the inhalation maximum, 0.89% were rejected because the participants rated the stimuli as positive during the interview session, and 0.95% because the blink onset occurred during baseline. The remaining trials were rectified and smoothed (20ms moving average). The startle data were corrected for baseline (0-20 ms after startle probe onset), and the startle-response was scored as the maximum deflection within 30 to 150ms after startle probe onset. Non-responses (amplitudes $\leq$ 2*the largest amplitude within the baseline interval; 1.99% responses) were scored as zero. Outlier values differing more than two standard deviations from the condition average were excluded (1.46 % responses) (Blumenthal, Cuthbert, Filion, Hackley, Lipp, & van Boxtel, 2005). After trial selection, the minimum number of trials per condition and participant was 3. Due to excessive differences in startle amplitude the startle-responses were z-standardized within each participant and across conditions.

Data analysis. For startle responses ANOVAS with the within subjective factors, 2 (Stimulus: pictures, odors) x 2 (Regulation Instruction: enhance, down-regulate) x 3 (Probe Position: A=baseline, B=early emotion regulation, C=late emotion regulation) by 2 (Group: NSA participants, HSA participants) were performed using SPSS 18.0. For SAM ratings 2 (Stimulus type: pictures, odors) x 2 (Emotion Regulation Instruction: enhance, down-regulate) by 2 (Group: NSA participants, HSA participants) were run, and Cohen's effect-size *f* was calculated. Huyn-Feldt corrections of degrees of freedom were applied, and corrected *p*-values are reported. Subsequent nested effects (Page, Braver, & MacKinnon, 2003) and t-tests were calculated. An alpha level of 5 % was used for all statistical tests.

Results

Ratings. After down-regulating their emotion, participants rated their emotional experience as neutral (See Table 2 for descriptive statistics) and significantly less negative than after enhancing their emotion, $F(1, 38)=137.93$, $p<.001$, $f = 1.91$ (Main effect Instruction). Similarly, after down-regulation they rated their experienced arousal as neutral and significantly less arousing than after enhancing their emotion, $F(1,38)=191,38$, $p<.001$, $f= 2.24$ (Main effect Instruction). Independent of emotion regulation, the participants rated the pictures as more arousing as the odors, $F(1,38)=8.34$, $p=.006$, $f=0.47$ (Main effect Stimulus). There were no effects including social anxiety.

-Table2-

Startle-reflex. Startle responses were larger in response to probe A, $F(1,38)=6.07$, $p=.004$, $f= 0.40$ (Main effect Probe Position) as compared to probe B, $t(39)=2.78$, $p=.008$, or probe C, $t(39)=3.15$, $p=.003$. Startle responses in response to probe B and C did not differ, $p>0.20$.

Odors elicited larger startle magnitudes than pictures, $F(1,38)=5.12$, $p=.029$, $f=0.37$ (main effect Stimulus). This effect was especially pronounced during the first probe presentation (probe A), $t(39)=3.12$, $p=.003$, interaction Stimulus by Probe Position, $F(2,76)= 6.03$, $p=.004$, $f=0.40$.

Independent of stimulus modality, participants showed smaller startle magnitudes when down-regulating their emotions ($M=-0.115$, $SD=0.313$) as compared to the enhance instruction ($M=0.115$, $SD=0.313$), $F(1,38)=5.34$, $p=.026$, $f=0.37$ (main effect Instruction). Due to the largely differing physiological baseline-responses to odors and pictures (Interaction Stimulus by Probe Position), emotion regulation was also analyzed separately for odors and pictures. While down-regulating their emotions to pictures, participants showed smaller startle magnitudes as compared to enhancing their emotions in response to probe A, $t(39)=2.07$, $p=.045$, and B, $t(39)=2.80$, $p=.007$, but not to probe C, $p>.20$. In contrast, while

down-regulating their emotions to odors, participants showed smaller startle magnitudes as compared to enhancing only in response to probe C, $t(39)=2.12$, $p=.040$ (Figure 2 A). There were no effects of social anxiety.

-Figure2-

Discussion

Emotion regulation towards disgusting odors and disgusting pictures was assessed with the startle reflex and emotion ratings. Although odors and pictures were rated as similarly negative and arousing prior to the Experiment, odors elicited larger startle responses than pictures. This extends previous research, showing that as compared to other modalities odors are superior in modulating neuronal responses within the amygdala (Royet, Zald, Versace, Costes, Lavenne, Koenig et al., 2000), and demonstrates, that also motor behavior related to defensive motivation is more effectively triggered by olfactory than by comparable visual stimuli. Because the amygdala is strongly implicated in startle-reflex modulation (Davis, 1992), it is most likely the source of this effect. Moreover, as odors and pictures were rated as comparable in intensity and valence, the present data support the idea of a preferential neuronal processing of emotional olfactory information.

The participants were able to regulate their emotions towards visual stimuli. While this has been shown before (Jackson, et al., 2000), the present study shows for the first time that emotion regulation is impaired for negative odors. For pictures, regulatory effects on the startle-reflex occurred already very early, and lasted until picture-offset, while for odors, emotion regulation was not effective until odor-offset. These data parallel finding of larger startle magnitudes towards odors, suggesting that odors are not only more potent emotion elicitors, but might also be less effectively regulated in terms of cognitive linguistic strategies. This effect might result from a preferential representation of odors in emotionally relevant brain areas: Olfactory in comparison to visual information can bypass thalamic gating and thus might activate the amygdala more directly. The amygdala is strongly interconnected with the orbitofrontal cortex, responsible for the coding of the hedonic value of emotional stimuli (Anderson, et al., 2003), and both structures are preferentially activated by odors as compared to pictures (Royet, et al., 2000). Because these areas have been shown to be the major target

of cognitive linguistic emotion regulation strategies via prefrontal cortex areas (Ochsner, et al., 2002), a preferential activation of these areas in response to odors as compared to pictures might result in less effective top-down regulatory control.

Here, disgusting stimuli were presented. Disgust is an evolutionary shaped basic emotion to prevent the organism from contamination (Rozin & Fallon, 1987). Thus, the current data suggest that in terms of disgust, odors may be especially well suited to serve as potent evolutionary shaped, cheat proof warning signals: They may be more potent elicitors of disgust, inducing withdrawal behavior more effectively, and might be less prone to cognitive biases than comparable visual cues. This is especially important given the strong involvement of olfaction in mammalian food perception and nutrition (Shepherd, 2006) and is also consistent with findings on preferential odor association learning (Yeshurun, Lapid, Dudai, & Sobel, 2009).

Emotion regulation effects on the startle reflex in response to pictures were already found when participants were not yet instructed to regulate their emotions. Because the participants knew the upcoming emotion regulation instruction before the beginning of each trial (balanced block design), they most likely initiated an automatic regulation process (see Mauss, Bunge, & Gross, 2007), beginning already before trial-onset.

No differences were found between HSA and NSA individuals. In Experiment II it was aimed to investigate emotion regulation with socially relevant negative stimuli (anxious facial expressions in the context of anxiety-related chemosensory stimuli).

Experiment II: social odors

Methods

Participants. Forty[1] female non-smoking students of European descent fulfilled the same inclusion criteria as in Experiment I and did not suffer from general hyposmia. They were classified as either NSA (n=20) or HSA (n=20) (see Experiment I). Both groups significantly differ according to their self reported trait social anxiety (SIAS) (see Table 1 for questionnaire data). High socially anxious participants scored within the normal range on both trait anxiety (STAI) and self reported depressive feelings (DS), while non-socially anxious participants scored low on both questionnaires. Both groups significantly differ for self-reported depressive feelings and trait anxiety. Both scored within the medium range for empathy (German version of the Interpersonal Reactivity Index, Paulus, 2009), and the frequency of everyday-life use of reappraisal (ERQ). The two groups did not differ for age, $p>.20$ ($M=24.95$, $SD = 5.73$, range 19-45). All participants were paid for their participation and gave written informed consent to procedures. The study was approved by the ethics committee of the German Psychological Society (DGPs).

Stimuli. As chemosensory stimuli sweat from both axillae was sampled from 20 healthy male students of European descent in an anxiety condition (AC, waiting for an oral examination at the university in order to reach an academic degree) and a sport control condition (SC, ergometer training). During the AC, the donors felt more anxious, less happy (self rating using 10 cm Visual Analogue Scales), more unpleasant, more aroused, and less dominant (SAM ratings) than during the SC. The donors' physiological arousal did not differ between the two conditions (heart rate). As visual stimulus material, 14 pictures from 7 male actors (AM05, AM08, AM10, AM14, AM19, AM22) showing anxious facial expressions with averted gazes to the left and right were chosen from the Karolinska Directed Emotional Faces set (KDEF, Lundqvist, Flykt, & Öhman, 1997). (see supporting information available online)

Individual stimulus validation and odor detection. The participants rated their emotional experience towards the pictures as negative (SAM valence, M=-1.13, SD=1.01) and mildly arousing (SAM arousal M=4.79, SD=1.37). Furthermore, the most prominent emotion elicited by the pictures was anxiety (M=5.53, SD=1.66, 10 cm visual analogue scales) differing significantly from the ratings of the other basic emotions (anger, disgust, sadness, happiness $p<.01$, surprise, $p=.06$).

The participants rated the chemosensory stimuli as moderately intense (M=5.35, SD=1.68), unpleasant (M=4.64, SD=1.60), and familiar (M=4.74, SD=1.77), and low in pleasantness (M=3.19, SD=1.43). They rated their own emotional response towards the chemosensory stimuli as mildly negative and arousing (SAM valence, M=-0.64, SD=1.15, SAM Arousal M=4.63, SD=1.51).

Twenty-six (65%) of the participants were able to differentiate the chemosensory stimuli from pure cotton pad (two correct detections for each stimulus within three-alternative forced choice tests including cotton pads from either condition, and two non-used cotton pads, all administered via the olfactometer for 2s).

Stimulus presentation. Stimulus presentation was the same as in Experiment I with the exception, that two odor bottles of the olfactometer were filled with 1.2g of cotton pad (homogenized sweat samples either from the anxiety and the sport condition). As in Experiment I, the stimuli were presented in four counterbalanced blocks of 21 trials each. Within the blocks, anxious facial expressions were either presented in the context of chemosensory anxiety signals (enhance/ down-regulate face + anxiety signal) or sport stimuli (enhance/ down-regulate face + sport stimulus) (Figure 1 C).

Procedure, data recording, data reduction and data analysis. The procedure, data recording and data reduction were the same as in Experiment I with the exception that in the ANOVAs for calculating emotion regulation outcome the Stimulus factor was replaced by the factor Chemosensory Context (anxiety, sport).

Results

Ratings. After down-regulating their emotions, the participants rated their own emotional experience as neutral (descriptive statistics see Table 3) and significantly less negative as after enhancing their emotion, $F(1, 38)=57.60$, $p<.001$, $f = 1.23$ (Main effect Instruction). Similarly, after down-regulating, participants rated their experienced arousal as neutral and significantly lower, as after enhancing their emotion, $F(1,38)=68.61$, $p<.001$, $f= 1.34$ (Main effect Instruction). Independent of the emotion regulation strategy, the participants felt more negative when the faces were presented along with a chemosensory anxiety cue, as compared to a sport cue, $F(1,38)=8.07$, $p=.007$, $f=0.46$ (Main effect Stimulus).

-Table3-

Startle-reflex. The participants showed smaller startle magnitudes towards the faces in the down-regulation ($M=-0.112$, $SD=0.288$) than the enhance condition ($M=0.112$, $SD=0.288$), $F(1,38)=5.99$, $p=.019$, $f=0.40$ (Main effect Instruction).

Independent of the emotion regulation strategy, high socially anxious individuals showed larger startle magnitudes towards the pictures presented in the context of chemosensory anxiety cues than the non-anxious individuals, especially during the at probe C, $F(2,76)=3.36$, $p=.040$, $f =0.30$ (Interaction Chemosensory Context by Probe Position by Group, nested effects: Group by Chemosensory Context within probe C: $F(1,38)=4.69$, $p=.037$; Group within probe C within Chemosensory anxiety: $F(1,38)=6.60$, $p=.014$) (Figure 2

B).

Discussion

Emotion regulation was assessed in response to anxious facial expressions presented in the context of chemosensory anxiety or sport stimuli in HSA and NSA individuals. Regardless of the chemosensory context, both HSA and NSA participants were able to effectively regulate their emotions towards the faces: they exhibited smaller startle-responses, felt less negative and less aroused when down regulating, as compared to enhancing their emotions. Thus, while emotion regulation towards social cues in HSA participants has been demonstrated before (Goldin, et al., 2009), the present results show that also motor-responses towards socially relevant stimuli can be regulated effectively.

Prior to the main experiment, the anxious facial expressions were rated as fear-inducing and negative in valence. In the main experiment, when presented in the context of chemosensory anxiety signals, the faces were rated as more negative as when presented alongside chemosensory sport stimuli. Moreover, HSA participants showed a heightened startle-response towards the faces in the context of the chemosensory anxiety signal as compared to NSA participants. This extends previous work showing a hyperreactivity of HSA individuals towards facial (Blair, Shaywitz, Smith, Rhodes, Geraci, Jones et al., 2008), and chemosensory signals of anxiety (Pause, et al., 2009).

The chemosensory context had no influence on the participants' ability to regulate their emotions towards the faces. Contextual chemosensory anxiety signals have been shown to provide further situational information mainly when the facial foreground information is ambiguous (Zhou & Chen, 2009) or incongruent (Pause, Ohrt, Prehn, & Ferstl, 2004). Because in the present study, the participants perceived all faces as clearly negative and fear-inducing, the congruent chemosensory information did not add any new information and might therefore had no influence. From an evolutionary point of view this is plausible, and suggests that visual and chemosensory communication channels constitute specialized

independent communication systems, integrating under circumstances of perceptual uncertainty only.

The results of Experiment II demonstrate that salient visual foreground information can be modulated via top-down neuronal control and that contextual chemosensory anxiety cues do alter general emotional significance of this visual information rather than interacting directly with top-down control mechanisms

General Discussion

The here presented studies investigated emotion regulation in response to non-social disgusting odors (Experiment I) and anxious facial expressions presented in the context of chemosensory anxiety stimuli (Experiment II) in groups of HSA and NSA participants.

HSA participants showed heightened startle-responses towards anxiety related chemosensory signals but not non-social disgusting odors. These findings extend previous research showing a specific hypervigilance in social anxiety towards visual social cues (Moser, Huppert, Duval, & Simons, 2008), and argues against a generalized hyperreactivity towards divers negative emotional stimuli. However, consistent with previous reports (Goldin, et al., 2009) no evidence was found for impaired emotion regulation in HSA participants, neither to non-social disgusting stimuli nor to emotional social stimuli. Interestingly, no differences were found in the self-reported frequency of use of regulation strategies in everyday live between HSA and NSA participants. Because they are frequently confronted with their feared situation, HSA participants may have simply developed more effective regulation strategies and thus are able to overcome their initial hyperreactivity towards the social cues in the present study. Indeed, initial evidence suggest that social phobics show less signal change in emotion regulation related brain areas during cognitive reappraisal, but show no impairment in emotion regulation outcome (Goldin, et al., 2009).

Conclusion

The current findings support previous research showing that cognitive reappraisal is effective in the regulation of emotional states (Jackson, et al., 2000; Moser, et al., 2009; Ochsner, et al., 2002), and even possible for socially anxious individuals confronted with their feared stimulus (threatening facial expressions, Goldin, et al., 2009). In demonstrating that odors preferentially elicit withdrawal related motor behavior and are less effectively regulated, the current study also demonstrates that the effectiveness of cognitive reappraisal may be limited and highlights the unique role of olfaction in emotion perception.

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Footnotes

[1]For both Experiments, a total of 312 persons were excluded because they did not fulfill the inclusion criteria.

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Table1.

Personality profile of the NSA and HSA participants of Experiment I (left) and Experiment II (right)

	Experiment I					Experiment II				
	NSA		HSA			NSA		HSA		
	M	SD	M	SD	p	M	SD	M	SD	p
SIAS	10.90	3.99	33.95	10.91	<0.001	10.00	3.96	34.05	9.12	<.001
STAI X2	32.6	5.42	45.65	9.31	<0.001	35.60	4.50	42.05	7.95	.003
DS	4.60	3.39	9.55	4.73	<0.001	3.75	2.45	8.51	5.66	.003
ERQ_{reap}	5.21	0.92	4.77	0.87	>0.10	4.73	0.86	4.93	0.73	>.200
FEE	2.31	0.48	2.27	0.51	>0.20	-	-	-	-	-
SPF	-	-	-	-	-	30.10	5.70	29.20	5.37	>.200

Note. SIAS= Social Interactionand Anxiety Schedule, STAI= State Trait Anxiety Inventory Trait Form, DS= Depression Scale, FEE= Questionnaire for the assessment of disgust sensitivity, SPF=Saarbrücker Personality Questionnaire, ERQ_{reap} = Reappraisal subscale of the Emotion Regulation Questionnaire

Table 2.

Descriptive data of emotion regulation effects on subjective emotions elicited by pictures and odors in Experiment I

	Pictures				Odors			
	Enhance		Down-Regulate		Enhance		Down-Regulate	
	M	SD	M	SD	M	SD	M	SD
$SAM_{valence}$	-2.40	0.68	-0.33	1.01	-2.21	0.64	-0.46	0.88
$SAM_{arousal}$	6.94	1.10	4.83	1.19	6.52	1.31	4.60	1.16

Note. $SAM_{valence}$ range: -4 to 4; $SAM_{arousal}$ range: 1 to 9

Table 3.

Descriptive data of emotion regulation effects on subjective emotions elicited anxious faces in the context of chemosensory anxiety or sport-control stimuli in Experiment II

	Chemosensory Sport Control				Chemosensory Anxiety			
	Enhance		Down-Regulate		Enhance		Down-Regulate	
	M	SD	M	SD	M	SD	M	SD
$SAM_{valence}$	-1.70	0.78	-0.36	1.10	-1.80	0.72	-0.45	1.08
$SAM_{arousal}$	6.14	1.20	4.28	1.36	6.16	1.20	4.42	1.39

Note. $SAM_{valence}$ range: -4 to 4; $SAM_{arousal}$ range: 1 to 9

Figure Legends

Figure 1

In Experiment I, either disgusting pictures (A) or disgusting odors (B) were presented before and after visual sues instructing the participants to either enhance or regulate their emotions. In Experiment II (C) this procedure was the same, with the only difference that anxious facial expressions were presented twice in the context of chemosensory anxiety signals or chemosensory control stimuli. Startle probes were presented at three different probe positions during the trials.

Figure 2

(A) In Experiment I, mean startle magnitudes towards pictures were higher during the enhance condition as compared to the down-regulate condition during the startle positions A and B (left side), while emotion regulation effects towards odors emerged during startle position C only. (B) In Experiment II, HAS participants showed larger startle magnitudes than NSA participants towards the anxious facial expression presented in the context of the chemosensory anxiety signal during startle position C.

Table S1.

Concentrations of Olfactory stimuli used in Experiment I

Odor	Solvent	Concentrations (v/v)		
		high	medium	low
Ethanethiole $_{(97\%)}$	Diethyl Phtalate$_{(99\%)}$	1:30000	1:100000	1:300000
Isobutyraldehyde$_{(99\%)}$	Diethyl Phtalate$_{(99\%)}$	1:30	1:100	1:300
Isovaleric Acid$_{(99\%)}$	Diethyl Phtalate$_{(99\%)}$	1:30	1:100	1:300
Pyridine$_{(97\%)}$	1,2-Prapanediol$_{(99\%)}$	1:30	1:100	1:300
3-Methyl-Indole$_{(98\%)}$	1,2-Prapanediol$_{(99\%)}$	1:100	1:300	1:1000

Note: all odors and solvent provided by Sigma Aldrich, Germany, except of 1,2-Prapandiol, provided by Merck, Germany

Collection of chemosensory stimuli in Experiment II

Chemosensory stimuli were sampled from 20 male students of European descent. Their age ranged from 22 to 30 (M=24.90, SD=2.47). Their body mass index was within the normal range (range: 19.60 - 27.30, M=23.16, SD=1.89), and all reported to have a regular sleep-wake-cycle. All described themselves as healthy, especially with respect to hormonal, neurological, immunological, cardiological, and diseases of the axillae. They were within the normal range for trait anxiety (as assessed with the State Trait Anxiety Inventory, STAI, Laux, Schaffner, Glanzmann, & Spielberger, 1981) (M=36.85, SD=7.04). All donated sweat from both axillae for 90 minutes within two donation situations using cotton pads (Ebelin Maxi Pads, dm-drugstore, Germany) following a well established sampling protocol (Pause, Adolph, Prehn-Kristensen, & Ferstl, 2009; Pause, Ohrt, Prehn, & Ferstl, 2004; Prehn-Kristensen, Wiesner, Bergmann, Wolff, Jansen, Mehdorn et al., 2009; Prehn, Ohrt, Sojka, Ferstl, & Pause, 2006). During an interview session, the donors gave written informed consent to procedures and were instructed to refrain from eating garlic, onions, asparagus or spicy food, not to use deodorants and to wash their armpits exclusively with an unperfumed medical

soap (Eubos®, Dr. Hobein GmbH, Germany) within 24 hours prior to donation. The anxiety condition consisted of waiting for an important oral examination at the university in order to assess an academic degree (subjective importance, M=8.29, SD=0.87, scale range 0-10), while the sport control condition consisted of ergometer training. During the donation conditions, the donors' emotional experience was assessed using the Self Assessment Manikin (SAM, Bradley & Lang, 1994) (valence: -4 – 4, arousal: 1-9, dominance: 1-9), and the intensities of the six basic emotions (Ekman & Friesen, 1971) (using 10 cm visual analogue scales). During the anxiety condition, the donors felt more anxious, and less happy, as compared to the sport control condition. There were no differences in ratings of disgust, sadness, surprise, or anger between the donation conditions. In accordance with the anxiety ratings, the donors reported to feel more unpleasant during the anxiety condition. They also felt more aroused, and less dominant during the anxiety condition (see Table S2). To control for physiological arousal, the donors' heart rate was sampled during the interview session (baseline) and in the test conditions. During the sport control condition the heart rate did not differ from the anxiety condition, p=.792 (anxiety condition: M=91.25, SD=22.07 beats per minute, sport control condition, M=90.95, SD=19.61 beats per minute). However, both heart rates were higher than during baseline recording (M=68.80, SD=11.22), both p<.001. The sport control condition took place on average 6 (SD = 4.13) days after the anxiety condition, while the time of day was held constant (M = 83.75, SD = 85.65 minutes difference between the beginning of the two donation situations).

The sweat samples were pooled with distinction to the respective donation conditions and stored at −20°C. For the experiment, the homogenized samples were divided into small portions (1.2 g each).

Table S2.

Self reported feelings of the intensities of basic emotions and SAM ratings of the sweat donors in Experiment II.

	Anxiety Condition		Sport-Control Condition		Significance
	M	SD	M	SD	p
Anxiety	6.68	1.69	0.46	0.58	<0.001
Happiness	3.89	2.37	7.09	2.26	<0.001
Anger	1.74	1.42	1.18	1.54	>0.200
Disgust	0.90	1.28	0.66	1.23	>0.450
Sadness	1.78	1.91	1.05	1.06	>0.125
Surprise	3.04	2.18	2.65	2.45	>0.450
$SAM_{valence}$	-0.05	1.76	2.20	1.28	<0.001
$SAM_{arousal}$	7.35	0.88	3.85	1.60	<0.001
$SAM_{dominance}$	4.50	1.70	6.70	1.31	0.001

Note: Basic Emotions range: 0 to 10cm visual analogue scale, $SAM_{valence}$ range -4 to 4, $SAM_{arousal}$ and $SAM_{dominance}$ range: 1 to 9.

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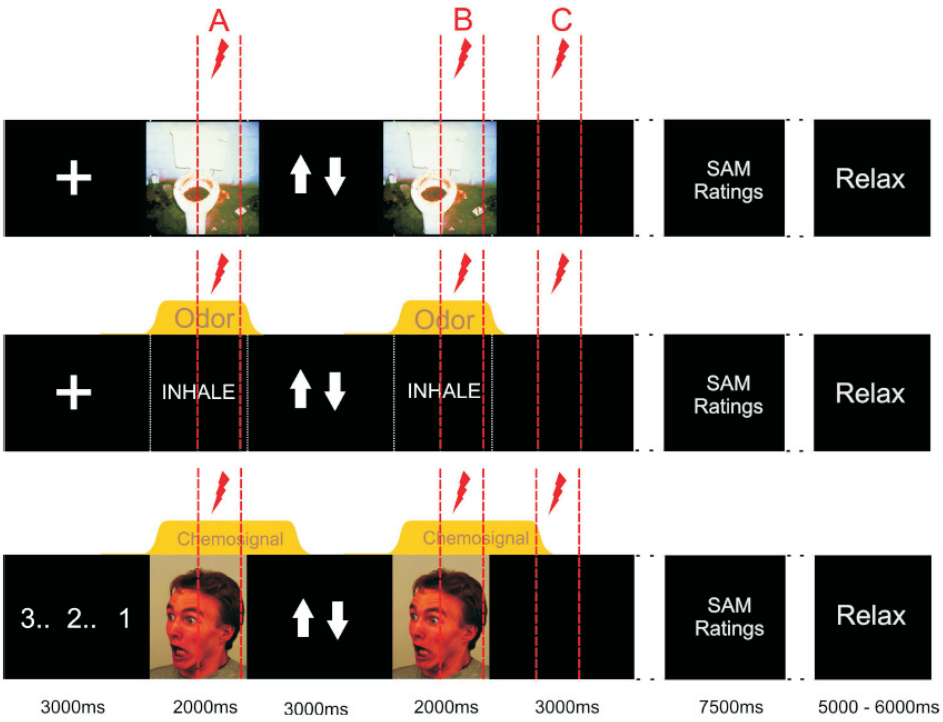

Figure 1. In Experiment I, either disgusting pictures (A) or disgusting odors (B) were presented before and after visual sues instructing the participants to either enhance or regulate their emotions. In Experiment II (C) this procedure was the same, with the only difference that anxious facial expressions were presented twice in the context of chemosensory anxiety signals or chemosensory control stimuli. Startle probes were presented at three different probe positions during the trials.

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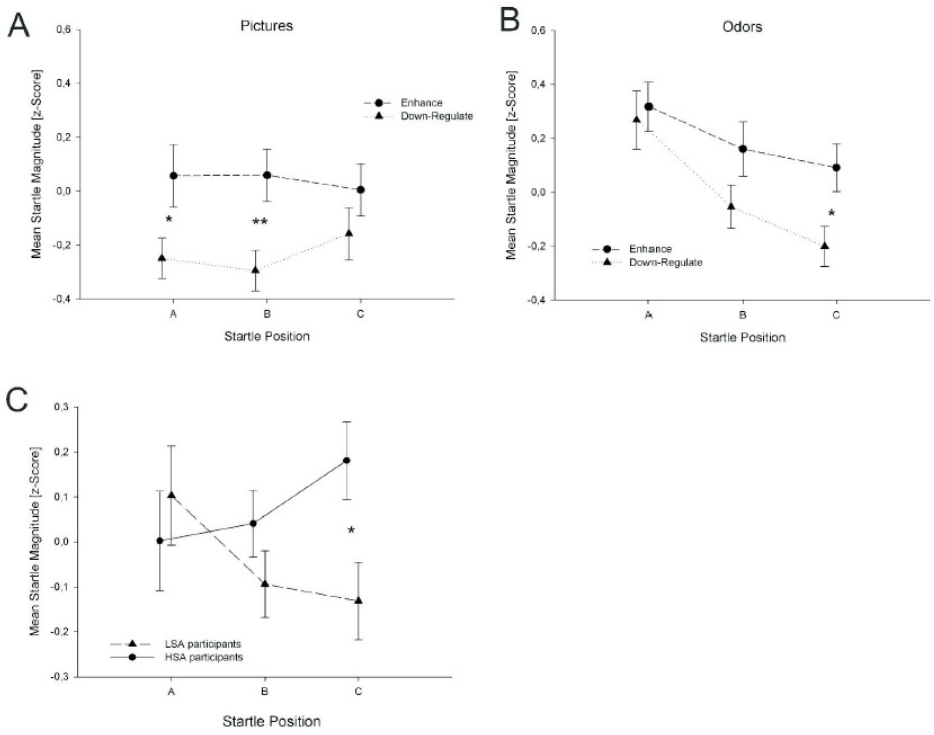

Figure 2. (A) In Experiment I, mean startle magnitudes towards pictures were higher during the enhance condition as compared to the down-regulate condition during the startle positions A and B (left side), while emotion regulation effects towards odors emerged during startle position C only. (B) In Experiment II, HAS participants showed larger startle magnitudes than NSA participants towards the anxious facial expression presented in the context of the chemosensory anxiety signal during startle position C.

238x189mm (600 x 600 DPI)

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Regulation of emotions elicited by fearful faces in the context of chemosensory anxiety signals

Dirk Adolph,

Ruhr-Universitaet Bochum,

Lukas Meister & Bettina M. Pause

Heinrich-Heine-Universitaet Duesseldorf, Germany

Corresponding Author:

Bettina M. Pause

Heinrich-Heine-University Duesseldorf, Germany

Department of Experimental Psychology

Universitaetsstraße 1

D-40225 Duesseldorf

Tel.: +49 (0) 211 - 81-14384

Fax: +49 (0) 211 - 81-12019

e-mail: bettina.pause@uni-duesseldorf.de

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Abstract

The present study examines early (N1, N170) and late (P3, LPP) event-related potential modulation during the voluntary regulation of emotions. High socially anxious (HSA) and non socially anxious (NSA) participants used cognitive regulation strategies in response to fearful facial expressions presented either in the context of chemosensory signals (anxiety, sport) or control stimuli (cotton pad control). Results show for the first time, that the early perceptual processing of target stimuli (N1) is modulated by the instruction to enhance and decrease emotions. Furthermore, NSA, but not HSA participants showed emotion regulation effects on the late positive potential (LPP) in response to faces presented without a chemosensory context. An enhanced processing of the facial stimuli (N170, LPP) in HSA participants may account for this effect. Overall, the chemosensory context stimuli enhanced early perceptual processing (N1, N170), but diminished late evaluative (P3, LPP) processing of the faces. Correspondingly, no emotion regulation effects on the LPP were found when the faces were presented with contextual chemosensory stimuli. The current results highlight the unique role of olfaction in emotion perception, and shows that already early electrophysiological responses to fearful facial expressions can be altered using cognitive linguistic strategies.

Introduction

Emotion regulation has been defined as the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying the intensity and temporal features of emotional reactions (Thompson, 1994). One example for such processes is the voluntary reappraisal of emotion eliciting situations (Gross, 2002). The efficacy of reappraisal in regulating negative emotional states has been repeatedly demonstrated: Self-reported emotions, neuronal activity (Ochsner et al., 2002), as well as a number of physiological responses to threatening pictures, can be significantly increased or decreased using reappraisal(Gross, 2002; Jackson et al., 2000). Recently, several studies have demonstrated emotion regulation effects on brain electrical activity using event related potentials (ERPs) (Hajcak & Nieuwenhuis, 2006; Moser et al., 2006; Moser et al., 2009). The amplitude of the late positive potential (LPP), linked to the facilitated perceptual processing of arousing stimuli (Cuthbert et al., 2000; Schupp et al., 2000; Schupp et al., 2003; Schupp et al., 2004), was shown to decrease during the instruction to down regulate and to increase during the instruction to enhance emotions elicited by unpleasant pictures. However these studies did exclusively focus on the LPP, leaving open the question, whether also other processes of encoding or decoding are also affected by emotion regulation.

So far, emotion regulation research has focused almost exclusively on unpleasant non-social scenes in order to elicit emotions. To our knowledge, only one study, using threatening facial expressions (Goldin et al., 2009) has shown that on a verbal report level, emotion regulation is effective in response to social emotional stimuli. This is surprising, because mostly all emotion regulation efforts are made in social situations (Gross et al., 2006). Moreover, social fearful facial expressions provide an important channel for the communication of potential danger. Therefore, the rapid perception of these cues is discussed to serve to enhance awareness and behavioral responses toward emotionally relevant stimuli (Vuilleumier, 2002). Consequently facial displays of fear elicit rapid adaptations in the

perceiver. For example, in comparison to neutral faces fearful expressions elicit larger positive ERPs in latency ranges related to the P3/LPP (Eimer & Holmes, 2002; reviewed in Eimer & Holmes, 2007; Krolak-Salmon et al., 2001; Mühlberger et al., 2009). Furthermore, even early ERPs like the N170 component, which is thought to reflect the structural encoding of facial features and configurations (Bentin et al., 1996), has been found to be larger in response to fearful in comparison to neutral facial expressions (Batty & Taylor, 2003; Mühlberger, et al., 2009). However, whether these early face processing components are also sensitive to emotion regulation has yet to be determined. Aside from facial expressions, there is a growing body of evidence that anxiety can also be communicated chemosensorily. Chemosensory signals of anxiety alter neuronal activity within emotion processing brain areas (Mujica-Parodi et al., 2009; Prehn-Kristensen et al., 2009) and enhance withdrawal related motor activity (Pause et al., 2009; Prehn et al., 2006). Moreover, a recent ERP study reported an early processing advantage (N1), as well as enhanced elaborated processing of chemosensory anxiety signals (P3) in comparison to sport stimuli (Pause et al., 2010).

Taken together, the aim of the present study is to assess emotion regulation in response to emotional facial expressions in the context of chemosensory signals of anxiety in a time sensitive manner using ERPs. It has been demonstrated that chemosensory and visual signals when perceived together do perceptually integrate (Pause et al., 2004; Zhou & Chen, 2009), but it has yet to be determined whether this concurrent presentation results in an altered neuronal processing and has any effect on the ability to regulate the emotions elicited by the faces. Thus we presented the fearful expressions either with or without a social chemosignal (anxiety, sport). Finally, emotion regulation has strong clinical importance, since many psychological disorders include disturbances in regulatory processes (Cole et al., 1994). Thus, in assessing a group of high socially anxious individuals, it was aimed to assess whether these participants show an enhanced neuronal processing of the social fear signals (as

indicated by previous studies: Mühlberger, et al., 2009; Pause, et al., 2009), and whether socially anxious individuals show emotion regulation deficits in response to these cues.

Because it has been shown that emotion regulation effects most reliably occur for late positive ERPs, we assessed the P3 and the LPP components. Moreover, to determine whether also earlier processes are affected, we also measured the N1, and N170 component elicited in response to the faces.

Material and Methods

Participants

Thirty six non-smoking female students from the Heinrich-Heine-University of Düsseldorf were classified as either non-socially-anxious (NSA, scores < 18, n=18) or high-socially-anxious (HSA, scores > 20, n=18) based on their trait social anxiety scores (Social InteractionAnxiety Questionnaire, SIAS, Stangier et al., 1999). All reported a regular menstrual cycle (16, N=8 HSA, participants reported to use hormonal contraceptives), not to use any medication, not to suffer from mental and physical diseases or general hyposmia. All scored low on social desirability (<5 on the lie scale of the Eyesenck Personality Inverntory, EPI, Eggert & Ratschinski, 1983). HSA participants scored within normal range for trait anxiety (State Trait Anxiety Inventroy, STAI, Laux et al., 1981) and depressive feelings (Depression Scale, DS, von Zerssen & Koeller, 1976), while NSA participants scored low on both questionnaires. Both groups scored within the medium range for the frequency of everyday-life use of reappraisal (Emotion RegulationQuestionaire, ERQ, Abler & Kessler, 2009), and for empathy (German version of the Interpersonal Reactitivity Scale, IRI, Paulus, 2009 2009 #1731), and scores did not differ between groups (Table 1 shows detailed questionnaire data). The two groups did not differ for age, $p > 0.20$ (M=23.72, SD=4.86, range 19-42). All participants were paid for participation and gave written informed consent. The study was approved by the ethics committee of the German Psychological Society (DGPs).

Stimulus Material

To assess the chemosensory stimulus material used in the present study sweat from both axillae was sampled from 20 healthy non-smoking male students (mean age 24.90, SD=2.47)

of European descent in an anxiety condition (AC, waiting for an oral examination at the university in order to reach an academic degree) and a sport control condition (SC, ergometer training). During the AC, the donors felt more anxious, less happy (self rating using 10 cm Visual Analogue Scales), more unpleasant, more aroused, and less dominant (SAM ratings) than during the SC. The donors' physiological arousal did not differ between the two conditions (heart rate). (For a detailed description of the sampling procedure see supplementary material available on-line). Prior to use, the sweat samples were pooled with distinction to the respective donation conditions and stored at −20°C. As visual stimuli, 60 pictures from 30 male actors showing anxious facial expressions with an averted gaze to the left and right were taken from the Karolinska Directed Emotional Faces set (Lundqvist et al., 1997).

Stimulus Presentation

Stimulus presentation was controlled with the Presentation® software (Version 12, Neurobehavioral Systems, USA). The chemosensory stimuli were presented with a constant-flow (50ml/ s) 5-channel olfactometer (Prehn-Kristensen, et al., 2009) including glass bottles containing 1.2g of each stimulus (anxiety, sport, cotton pad). Stimuli were presented in three counterbalanced blocks (enhance, down-regulate, watch) of 60 trials each. During each trial the same facial expression was presented prior to and after a visual instruction to start emotion regulation. During the second presentation, the face was paired with a chemosensory context cue (Figure 1). During the Interstimulus Interval, participants rated their current emotional state for valence and arousal (SAM, Bradley & Lang, 1994). After the presentation of 30 trials (10 minutes) a five minute break was included. During each block, the 60 facial expressions were presented in random order, and paired with either a chemosensory anxiety (n=20 trials), or sport stimulus (n=20 trials), or cotton pad control (n=20 trials). Chemosensory stimuli were

equally distributed within blocks, and the same chemosensory stimulus did not occur during more than three consecutive trials.

Procedure

After having received detailed breathing instructions (figure 1) and only after they were able to breathe correctly, participants were given detailed instructions to use cognitive linguistic emotion regulation strategies (as derived from Jackson, et al., 2000). They were asked to start emotion regulation with the onset of the visual emotion regulation instruction and not to stop regulating until the offset of the following picture stimulus. Prior to the beginning of data recording, participants practiced at least 10 learning trials of each experimental condition. In total, the experimental procedure lasted about three hours.

Data recording

The EEG was recorded with Ag/AgCl electrodes (inner diameter 6 mm) from 25 scalp locations (AF7,FP1, FPz, FP2, AF8, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, PO7, O1, Oz, O2, PO8) and both earlobes using an electrode cap (EasyCap GmbH, Germany) in reference to the average across all electrodes. Two electrodes were placed near the right eye (3 cm above, inside the vertical pupil axis and 1.5 cm below, outside the vertical pupil axis) for the recording of vertical and horizontal eye movements. The impedance of the electrodes was kept below 10 kΩ.

The physiological data were recorded, amplified, and filtered with the BrainVision Recorder software (Brain Products GmbH, Munich, Germany) using a sampling rate of 250 Hz, a low-pass filter of 40 Hz (24 dB/ octave) and a 50 Hz notch filter. Offline, EEG signals were re-referenced to linked ear lobes and high pass filtered (0.04 Hz, 24 dB/ octave), afterwards corrected for eye movements (Gratton et al., 1983) and baseline-corrected (0-200

ms before picture onset). Subsequently, trials contaminated with artifacts (due to sweating, movements, or pronounced alpha-activity: 0.25%) and insufficient inhalation of the chemosensory stimuli (begin of inhalation > 300ms before picture onset or end of inhalation < 700 ms after picture onset: 3.5%) were eliminated. Prior to averaging, signals were again low pass filtered (20 Hz, 24 dB/ octave).

Data Analysis

The N1 amplitude was quantified as the maximum peak at frontopolar, frontal and central electrode sites (70-140 ms). The N170 amplitude was analyzed as maximum peak over parietal and occipital electrode sites (130-180 ms). The P3 and the LPP were extracted from all electrodes (P3 peak: 300 to 500 ms, LPP mean activity: 400 to 600 ms).

ERPs were subjected to repeated measure mixed model analysis of variance (ANOVA). For the N1 component the ANOVA included the between subject factor group (HSA, NSA participants) and the within subject factors context (chemosensory anxiety, chemosensory sport, cotton pad control), instruction (enhance, down regulate, watch), sagittal electrode sites (frontopolar, frontal, central), and transversal electrode sites (lateral left, left, midline, right, lateral right). For the N170 (detected at parietal and occipital sites) the factor sagittal had two levels (parietal, occipital), while for the P3 and the LPP (detected at all electrodes) it had five levels (frontopolar, frontal, central, parietal, occipital). For reasons of brevity, effects including only electrode factors are presented without follow-up tests.

Mean ratings of valence and arousal were calculated within participants according to the conditions and were subjected to a repeated measures mixed model analysis of variance including the between subject factor group, and the within subject factors instruction (enhance, down regulate, watch), and chemosensory context (anxiety, sport, cotton pad control).

Cohen's effect-size *f* was calculated. Huyn-Feldt corrections of degrees of freedom were applied, and corrected *p*-values are reported. Subsequent nested effects (Page et al., 2003) and t-tests were calculated. An alpha level of 5 % was used for all statistical tests.

Results

Chemosensory stimulus ratings

Prior to the experimental session, participants were asked to judge the chemosensory stimuli for intensity, pleasantness, unpleasantness and familiarity (10cm visual analogue scales). Anxiety stimuli were perceived as more intense, $t(35)=3.38$, $p=.002$, than sport stimuli, and cotton pad control, $t(35)=5.15$, $p<.001$ (main effect stimulus $F[2, 68]=13.96$, $p<.001$, $f=0.64$). They were also perceived as more unpleasant, $t(35)=2.21$, $p=.034$, than sport stimuli, and cotton pad control, $t(35)=3.64$, $p=.001$. (main effect stimulus, $F[2, 68]=7.57$, $p=.001$, $f=0.47$), and as more familiar than cotton pad control, $t(35)=2.72$, $p=.010$, but not than sport stimuli, $t(35)=1.85$, $p=.073$ (main effect stimulus, $F[2, 68]=4.57$, $p=.015$, $f=0.37$). Intensity ($p=.068$), unpleasantness ($p=.073$) and familiarity ratings ($p=.149$) between sport and cotton pad control did not differ. There were no differences in pleasantness ratings between any of the stimuli.

Afterwards, participants were asked to specify their feelings of happiness and arousal (SAM) in response to the chemosensory stimuli. The participants rated themselves to feel more unpleasant (SAM valence) when perceiving the chemosensory anxiety signals as compared to cotton pad control, $t(35)=2.50$, $p=.017$ (main effect stimulus $F[2, 68]=3.33$, $p=.042$, $f=0.31$). There were no more differences between the chemosensory signals or between HSA and NSA participants concerning the ratings.

Nineteen (53%) of the participants were able to differentiate both chemosensory stimuli from cotton pad control (two correct detections for each stimulus within three-alternative forced choice tests including cotton pads from either condition, and two non-used cotton pads, administered via the olfactometer for 2.5 s).

Self reported emotions during emotion regulation

SAM Valence

Overall, participants described themselves to feel less negative during the down-regulate (NSA: t[17]= 5.31, p<.001, HSA: t[17]= 2.42, p=.027) and during the watch condition (NSA: t[17]= 2.17, p=.045, HSA: t[17]= 3.04, p=.007) as compared to the enhance condition (main effect instruction, F[2, 68]= 24.53, p<.001, f=0.85) (for descriptive statistics see Table 2). However, when down regulating their emotion NSA (t[17]= 2.17, p=.045), but not HSA, participants (p>.10) described themselves to feel less negative as compared to the watch condition (interaction instruction by anxiety F[2, 68]= 3.68, p<.043, f=0.33).

SAM Arousal

Participants described themselves to feel less aroused during the down-regulate (NSA: t[17]= 6.28, p<.001, HSA: t[17]= 3.97, p<.001) and during the watch condition (NSA: t[17]= 3.71, p=.002, HSA: t[17]= 3.12, p=.006) as compared to the enhance condition (main effect instruction, F[2, 68]= 36.52, p<.001, f=1.04). Like for self reported valence, when down regulating their emotion NSA, t(17)= 5.16, p<.001, but not HSA participants, p>.10, described themselves to feel less aroused as compared to the watch condition (interaction instruction by anxiety, F[2, 68]= 3.87, p<.027, f=0.34).

Participants reported to feel more aroused when the faces were presented in the context of chemosensory anxiety signals (M=5.17, SD=1.14), t(35)=2.19, p=0.035, and sport stimuli (M=5.08, SD=1.01), t(35)=2.35, p=0.024, as compared to cotton pad control (M=4.98, SD=0.98). Arousal ratings between faces presented in the context of chemosensory anxiety signals and sport stimuli did not differ, p>.100 (main effect context, F[2, 68]= 3.83, p=.041, f=0.34).

ERP results

Effects of electrode positions

The N1 amplitude was largest at frontopolar and midline electrode sites (main effect transversal, F[2,68]=19.58, p<.001, f=0.76 and sagittal, F[2,68]=26.67, p<.001, f=0.89), and largest amplitudes were observed over central and frontal midline electrodes (Fz/ Cz, interaction sagittal by transversal, F[8,272]= 13.70, p<.001, f=0.63).

The N170 amplitude was largest at right lateral electrode sites (main effect transversal, F[4,136]=22.36, p<.001, f=0.81), and largest amplitudes were observed over P8 (interaction sagittal by transversal, F[4,136]=6.92, p=.001 f=0.45).

Results indicate that P3 amplitude was larger over left, midline and right electrode sites than over lateral electrode sites (main effect transversal, F[4, 136]=13.67, p<.001, f=0.76), and larger over occipital than parietal electrode sites (main effect sagittal, F[4, 136]=53.29, p<.001, f=0.89). However, the largest P3 amplitude were observed over Pz (interaction sagittal by transversal, F[16,544]= 7.67, p<.001, f=0.63).

Finally, the LPP was largest over parietal and occipital electrode sites (main effect sagittal, F[4,136]=32.60, p<.001, f=0.98), and central and right electrode sites (main effect transversal, F[4,136]=16.02, p<.001, f=0.69). However, the largest LPPs were observed over Pz, and Oz (interaction sagittal by transversal, F[16, 544]= 7.86, p<.001, f=0.48).

Effects of regulation instruction

N1. Participants showed larger N1 amplitudes when they were instructed to enhance (M=-3.36, SD=1.71), as compared to the instruction to down-regulate their emotions (M=-2.90, SD=1.51), t(35)=2.40, p=.022 (main effect instruction, F[2, 68]=3.00, p=.056, f=0.81).

Amplitudes did not differ between the enhance and watch (M=-3.29, 2.21), p>.100, and between the down regulate and watch conditions, p=0.073.

LPP. Because previous studies show regulation effects mainly for the LPP, the interaction group by regulation by chemosensory context by transversal electrode sites which was significant as a trend, F(16, 544)= 1.90, p= .066, f=0.24, was explored. Results indicate that the LPP in response to the faces varied with emotion regulation instruction in NSA participants only (Figure 2C). NSA participants showed larger LPPs when they were instructed to enhance their emotion as compared to the watch condition in lateral right electrode sites, t(17)=2.51, p=.023. There were no differences between the enhance and down regulate, p>.100, and between the watch and down regulate condition, p=.098 (nested effects for interaction group by regulation by chemosensory context by transversal: interaction group by instruction by transversal within cotton pad context, F[8, 272]=3.07, p=.016., f=0.30, group by regulation within transversal , F[2, 68]=5.03, p=.009, f=0.38, regulation within right electrode sites within NSA participants, F[2, 68]=4.43, p=.015, f=0.36, regulation within right electrode sites within HSA participants, p>.100).

N170/ P3. There were no effects of emotion regulation instruction.

Effects of social anxiety

N170. When they were instructed to watch and to down regulate (see Grand Average in Figure 2A and B), HSA participants showed larger N170 amplitudes than NSA participants at left, and central electrode sites (interaction group by transversal by regulation by context, F(16, 544)= 2.45, p=.007, f=0.27, nested effects: group by instruction by transversal within

cotton pad context, F[8, 272]=2.66, p=.024, f=0.28, group by transversal within watch, F[4, 136]=3.66, p=.031, f=0.33, group within left electrode sites within watch, F[1, 34]=5.91, p=.021, f=0.42, group within central electrode sites within watch, F[1, 34]=4.88, p=.034, f=0.38, group by transversal within down regulate, F[4, 136]=3.90, p=.026, f=0.34, group within central electrode sites within down regulate, F[1, 34]=5.18, p=.029, f=0.39). During the enhance condition, there were no differences between HSA and NSA participants, p>.100.

LPP. As suggested by previous studies an enhanced processing of chemosensory anxiety signals in NSA individuals was also found in the present study. When the facial expressions were presented in the context of the cotton pad control stimuli, HSA participants showed larger LPPs in the watch, and as a trend, in the down regulate condition than NSA participants (Figure 2 A and B, interaction group by regulation by chemosensory context by transversal, F[16, 544]= 1.90, p= .066, f=0.24,nested effects: group within right lateral electrode sites within watch, F[1, 34]=9.87, p=.003, f=0.54, group within right lateral electrode sites within down regulate, F[1,34]=3.60, p=.066, f=0.33). Moreover, HSA participants showed larger LPPs during the watch (HSA: M=2.89, SD=2.41; NSA: M=0.13, SD=2.15), and the enhance condition (HSA: M=2.90, SD=3.10; NSA: M=0.60, SD=2.97) towards anxious facial expressions in the context of chemosensory anxiety signals (significant nested effects: group by regulation instruction by context within right lateral electrode sites, F[4, 136]=3.98, p=.004, f=0.34, group by context within watch within right lateral electrode sites, F[2,68]=5.81, p=.005, f=0.41, group within watch within chemosensory anxiety signal within lateral right electrode sites, F[1, 34]=13.17, p=.001, f=0.62, group by context within enhance within lateral right electrode sites, F[2,68]=5.42, p=.007, f=0.40, group within enhance within chemosensory anxiety signal within right lateral electrode sites, F[1, 34]=5.19, p=.029, f=0.39).

N1/ P3. There were no differences between HAS and NSA participants.

Effects of chemosensory context

N1. The N1 amplitude appeared with larger amplitudes at central electrode sites for faces presented in the context of chemosensory anxiety signals, t(35)=2.71, p=.010, and sport stimuli, t(35)=1.99, p=.054 as compared to faces presented in the context of control stimuli (Figure 3). (interaction sagittal by context, F[4,136]=2.99, p=.041, f=0.30, nested effects, context within central electrode sites, F[2,68]= 5.54, p=.008, f=0.40). N1 amplitudes for faces presented in the context of anxiety or sport signals did not differ, p>.100.

N170. As for the N1 component, N170 amplitudes were larger for faces presented in the context of chemosensory anxiety, t(35)=2.38, p=.023, and sport signals, t(35)=2.04, p=.049 as compared to faces presented in the context of control stimuli (Figure 3, main effect context, F[2,68]=3.21, p=.046, f=0.31). Amplitudes for faces presented in the context of anxiety or sport signals did not differ, p>.100. Nested effects for the interaction group by transversal by regulation by context, F(16, 544)= 2.45, p=.007, f=0.27, revealed significant effects in the cotton pad control condition only. However, this effect is already described above.

P3. Amplitudes were larger for faces presented in the context of control stimuli, as compared to those presented alongside with sport stimuli, t(35)=2.80, p=.008 (Figure 3, Main effect for context, F[2,68]=3.56, p=.034, f=0.32). P3 amplitudes did not differ between faces presented in the context of anxiety signals as compared to sport, or control stimuli, both p>.100.

LPP. The LPP was larger for faces presented in the context of control stimuli, as compared to those presented alongside with anxiety signals, t(35)=2.33, p=.026, and sport stimuli, t(35)=2.96, p=.006. (Figure 3, main effect context, F[2,68]=5.04, p=.009, f=0.38). The LPP did not differ between faces presented in the context of anxiety signals and sport stimuli, p>.100.

Discussion

The present study investigates ERP correlates of emotion regulation in response to facial expressions presented in the context of a control stimulus, or in the context of human chemosensory signals (sport, anxiety) in a group of HSA and a group of NSA individuals.

Within the N1 latency range ERPs were larger during the instruction to enhance the as compared to down regulate the emotions. The N1 component is especially sensitive to selective attention (Hillyard et al., 1998). Interestingly, results from a recent emotion regulation study using eye tracking show that selective attention was controlled by the participants differently depending on whether the regulatory goal was to decrease or increase emotions (van Reekum et al., 2007), suggesting that in the present study attention may have been allocated automatically in dependence of the regulatory goal. In contrast to the N1 results, the face specific N170 component was not affected by emotion regulation. Early responses at central scalp locations (N1 in the present study) index general aspects of selective attention, while ERPs in the latency range of the N170 reflect modality-specific processing stages (van Voorhis & Hillyard, 1977). Thus the results observed for the N170 and the N1 in the present study may arise from distinct aspects of perceptual stimulus processing, and suggest that the structural encoding of facial expressions (N170) may not necessarily rely on the allocation of attentional resources. Taken together, the present study shows for the first time that also ERPs as early as the N1 are affected by emotion regulation. Furthermore, they support the assumption that attention selection is a frequently used emotion regulation strategy in everyday life (Gross, et al., 2006). Further research is needed to disentangle the differential effects of emotion regulation on early stimulus processing.

As in previous studies, results indicate that NSA participants rated themselves to feel less negative, and less aroused when down regulating their emotions, while they described themselves to feel more negative and more aroused when enhancing their emotions, indicating

successful regulation of subjective emotional experience. In terms of ERPs, emotion regulation was first analyzed in response to anxious expressions presented in the context of control stimuli (cotton pad). In line with previous reports (Moser, et al., 2009), the LPP was larger when NSA participants were instructed to enhance their emotions, as compared to the watch condition, indicating effective enhancement of emotional responses to fearful facial expressions. We did not find the expected reduction of the LPP in the down regulation condition, as reported previously (Hajcak & Nieuwenhuis, 2006; Moser, et al., 2006; Moser, et al., 2009). This could be due to the nature of the facial stimuli. Emotional reactions to faces are often described as only mildly arousing (Adolph & Alpers, 2010; Britton et al., 2006) as compared to those elicited by high arousing scenes as used in other emotion regulation studies. Moreover during the course of the experiment participants were confronted with a large number of trials and thus habituation of emotional responses cannot be ruled out. This may have caused a rather low emotional involvement of the NSA participants, leading to the present null results for the down regulation condition. However, in general the present results indicate that emotions elicited by threatening social stimuli can be manipulated using cognitive linguistic emotion regulation strategies. When the faces were presented in the context of chemosensory signals (anxiety, sport), no emotion regulation effects on late positive ERP components were found. This result corresponds with a preferential processing of contextual chemosensory information, as indexed by reduced elaborative processing (LPP) of faces presented in the context of the chemosensory stimuli as compared to faces presented with cotton pad control. It has already been shown that olfactory and visual information is integrated on a neuronal level (Gottfried & Dolan, 2003), and cross-modal integration has been demonstrated for chemosensory signals and facial expressions (Pause, et al., 2004; Zhou & Chen, 2009). Moreover, a recent study demonstrated that the perception of chemosensory information (sport/ anxiety), although perceived at the threshold level, elicits large P3 amplitudes (Pause, et al., 2010), suggesting that the processing of these information depends

on the allocation of neuronal resources. Thus the additional chemosensory context information in the present study might have distracted neuronal resources from the elaborative processing of the concurrently presented facial expressions, leading to reduced late ERPs towards the faces. Interestingly, in contrast to the results for late ERPs, larger early (N1/ N170) ERPs for facial expressions presented in a chemosensory context were found, suggesting an enhancement of early stimulus processing stages for the faces through human chemosensory signals. A recent study on cross-modal integration using ERPs has shown that emotional prosody enhances early stimulus processing of concurrently presented visual cues (Brosch et al., 2009). Thus, the current results extend previous findings on cross-modal stimulus integration and show that human chemosensory signals can enhance the perceptual processing of concurrently presented facial expressions at an early processing stage.

HSA participants as compared to NSA participants showed enhanced neuronal processing of the fearful expressions presented without a chemosensory context. This is reflected in enhanced early (N170) and late (LPP) ERPs in HSA participants. In general, social anxiety is characterized by abnormal processing of social threat information, involving processing biases in attention, interpretation and memory (Hirsch & Clark, 2004). In line with this, previous studies have shown enhanced automatic guidance of motivated attention (Schupp, et al., 2004) towards fearful faces in social anxiety (Mühlberger, et al., 2009). Our results extend on these findings and suggest that even components related to the early structural encoding (N170) of fearful facial expressions are enhanced in socially anxious individuals. In addition, the observed enhanced LPPs in HSA participants indicate an enhanced elaborative processing of fearful facial expressions as compared to NSA participants (see also Kolassa & Miltner, 2006; Moser et al., 2008). Enhanced LPPs in anxious individuals were also found for faces presented in the context of chemosensory anxiety signals. In line with this, it could be shown that HSA, in comparison to NSA participants exhibit larger withdrawal related motor behavior in response to chemosensory

anxiety signals (Pause, et al., 2009), and respond to angry, or fearful faces with increased amygdala activation (Phan et al., 2006; Straube et al., 2004). Thus converging evidence from previous and the current study suggest a general negativity bias in response to threatening (angry, fearful) faces and chemosensory signals of anxiety in high HSA participants, as indexed by deviant stimulus processing during late elaborative and early processing stages. In correspondence with this, no emotion regulation effects on late positive components (P3/LPP) were found for HSA participants in response to the fearful facial expressions. HSA participants showed large LPPs during the watch, and down regulate condition as compared to NSA participants. This indicates a ceiling effect of emotional engagement in HSA participants towards fearful faces which could not be altered using cognitive emotion regulation. These findings provide further evidence that emotion regulation might be deficient in social anxiety disorders, and underline the assumption that the alteration of antecedent focused reappraisal should be a key goal of cognitive behavior treatment of anxiety disorders (Barlow et al., 2004).

Results indicate that the chemosensory anxiety signals were perceived as more intense, unpleasant, and familiar as the sport signals and as cotton pad control. Therefore it cannot be completely ruled out that some of the observed effects on ERPs occurred because the context stimuli were perceived differently. However, overall, the chemosensory stimuli were described as low in intensity, and as only mildly unpleasant. The subjective emotional responses towards them were described as rather neutral. Furthermore, while differences in ERP effects were observed for anxiety and sport signals in comparison to cotton pad control, differences in subjective ratings were evident for anxiety in comparison to sport stimuli and cotton pad control. Finally, in line with previous reports, the effects of chemosensory stimuli occurred largely independent of conscious stimulus processing. Only 50% of the participants were able to consciously distinguish the chemosensory stimuli from cotton pad control.

Therefore it seems rather unlikely that the observed ERP effects are due to the differences in the cognitive evaluation of the chemosensory stimuli.

Conclusion

Taken together, the present study shows that electrophysiological responses to fearful facial expressions can be altered using cognitive linguistic strategies, while this effect was absent in high socially anxious individuals, and when participants perceived contextual human chemosensory signals. Importantly, the current study shows for the first time that also ERPs occurring as early as 100ms after stimulus onset were affected by emotion regulation attempts, indicating that very early perceptual processing is affected by emotion regulation.

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Table1

Personality profile of the NSA and HSA participants

	NSA		HSA		
	M	SD	M	SD	p
SIAS	11.61	3.36	31.22	8.32	≤0.001
STAI X2	35.50	5.23	47.22	8.63	≤0.001
DS	5.44	2.81	9.89	4.60	≤0.001
ERQ_{reap}	4.61	0.80	4.73	1.12	≥0.200
SPF	30.33	4.95	31.39	5.80	≥0.200

Note. SIAS= Social Interaction Anxiety Schedule, STAI= State Trait Anxiety Inventory Trait Form, DS= Depression Scale, SPF=Saarbrücker Personality Questionnaire, ERQ_{reap} = Reappraisal subscale of the Emotion Regulation Questionnaire, p-values are given for the direct comparison between NSA and HSA participants (t-Tests)

Table 2

Mean (+/- SD) self reported emotional valence and arousal ratings during emotion regulation

Emotion regulation condition	NSA				HSA			
	Valence		Arousal		Valence		Arousal	
	M	SD	M	SD	M	SD	M	SD
Enhance	-1.46	0.63	5.99	0.98	-1.13	0.85	5.65	1.14
Down regulate	-0.28	0.82	4.15	1.17	-0.62	0.46	4.70	1.22
Watch	-0.73	0.50	5.03	1.04	-0.74	0.62	4.94	1.47

Note. SAM Valence rang -4 - 4, SAM Arousal Range 1 - 9

Table 3

Mean intensity, pleasantness, unpleasantness, and familiarity ratings of the chemosensory stimuli

	Anxiety		Sport		Cotton pad control	
	M	SD	M	SD	M	SD
Intensity	4.64	1.68	3.39	1.66	2.72	1.75
Pleasantness	2.61	1.48	2.78	1.64	2.64	2.05
Unpleasantness	3.47	2.35	2.56	1.76	2.03	1.52
Familiarity	3.69	1.95	3.17	2.08	2.64	2.02

Note. Range 1-9

Table 4

Mean valence and arousal ratings of the chemosensory stimuli

	Anxiety		Sport		Cotton pad control	
	M	SD	M	SD	M	SD
Valence	-0.81	1.06	-0.36	1.42	-0.11	1.14
Arousal	4.72	1.52	4.81	1.51	4.25	1.50

Note. SAM Valence rang -4 - 4, SAM Arousal Range 1 - 9

Figure Legends

Figure 1

At the beginning of each trial an anxious facial expression was presented for 1s to prepare the participant for the upcoming emotion regulation task. After the written emotion regulation instruction was presented for 1.5s a ball on the monitor whose size decreased continuously across a period of 2.5s instructed the participants to exhale. After the exhalation instruction vanished the participants started with the inhalation. Randomly (1-2s) after the participants started with inhalation, the chemosensory stimulus was presented for 2.5s. One second after the beginning of this presentation the same facial expression was presented again for 1.5s. Participants were instructed keep inhaling until the end of the picture presentation. During the following Inter Trial Interval (duration random between 11-13s) participants rated their current emotional state using valence and arousal ratings. Mean trial duration was 20s.

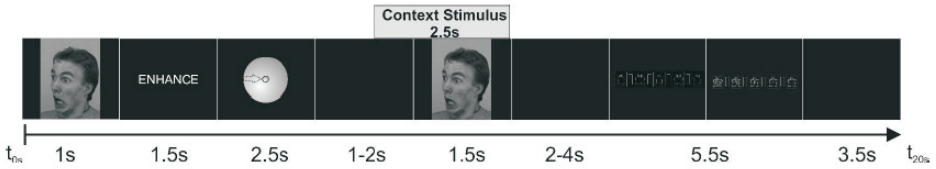
Figure 2

Grand averages waveforms in response to facial expressions presented in the context of cotton pad control stimuli during the watch condition (A) and during the down regulate condition (B) for NSA (black lines) and HSA (grey lines) participants. Mean LPP (+SEM) over right lateral electrode sites (including AF8, F8, T8, P8, PO8) for HSA and NSA participants in response to emotional facial expressions presented in the context of control stimuli during the watch, enhance, and down regulate condition.

Figure 3

Mean (+SEM) ERPs for facial expressions presented in the context of chemosensory anxiety stimuli (black bars), chemsensory sport stimuli (grey bars) and control stimuli (white bars) for the N1 amplitude (central electrode sites: AFz, Fz, Cz) (A), for the N170 amplitude (occipital,

and parietal electrode sites) (B), for the P3 amplitude (all electrodes) (C), as well as for the LPP (all electrodes) (D). Note: * p<.05, + p=.054.



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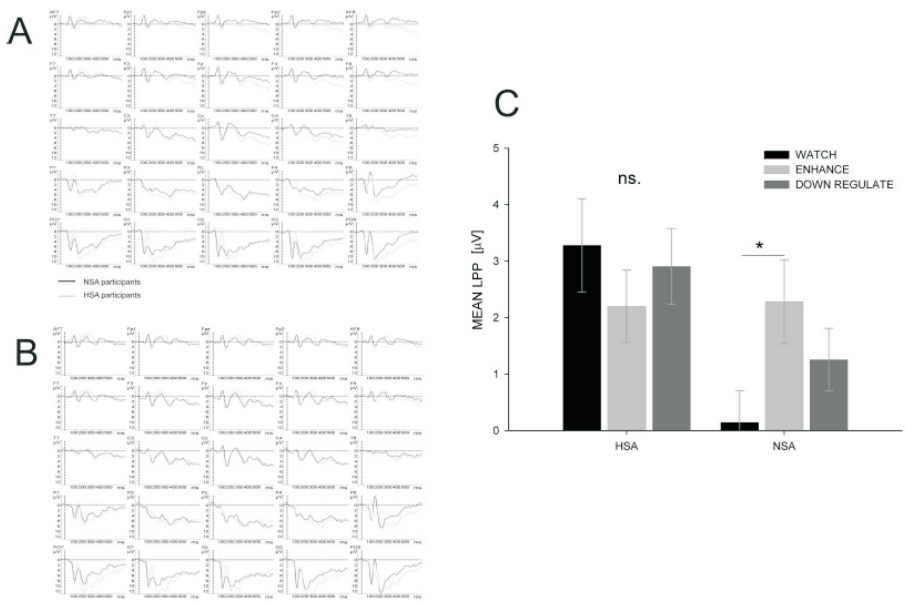

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106x68mm (600 x 600 DPI)

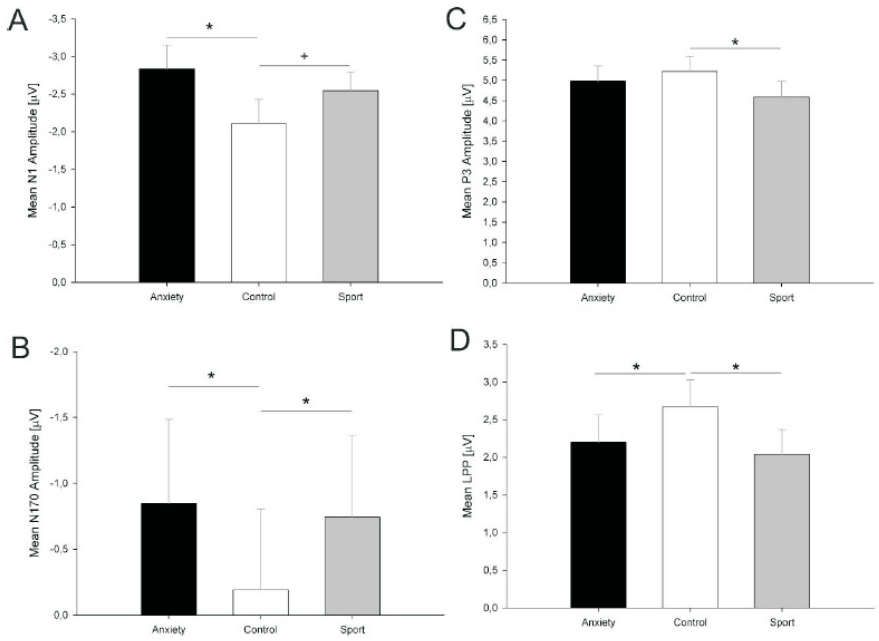

Figure 3. Mean (+SEM) ERPs for facial expressions presented in the context of chemosensory anxiety stimuli (black bars), chemsensory sport stimuli (grey bars) and control stimuli (white bars) for the N1 amplitude (central electrode sites: AFz, Fz, Cz) (A), for the N170 amplitude (occipital, and parietal electrode sites) (B), for the P3 amplitude (all electrodes) (C), as well as for the LPP (all electrodes) (D). Note: * p<.05, + p=.054.
258x184mm (600 x 600 DPI)

Collection of chemosensory stimuli

Chemosensory stimuli were sampled from 20 male students of European descent. Their age ranged from 22 to 30 (M=24.90, SD=2.47). Their body mass index was within the normal range (range: 19.60 - 27.30, M=23.16, SD=1.89), and all reported to have a regular sleep-wake-cycle. All described themselves as healthy, especially with respect to hormonal, neurological, immunological, cardiological, and diseases of the axillae. They were within the normal range for trait anxiety (as assessed with the State Trait Anxiety Inventory, STAI, Laux, Schaffner, Glanzmann, & Spielberger, 1981)(M=36.85, SD=7.04). All donated sweat from both axillae for 90 minutes within two donation situations using cotton pads (Ebelin Maxi Pads, dm-drugstore, Germany) following a well established sampling protocol (Pause, et al. 2009; Pause et al., 2004; Prehn-Kristensen et al., 2009; Prehn et al., 2006). During an interview session, the donors gave written informed consent to procedures and were instructed to refrain from eating garlic, onions, asparagus or spicy food, not to use deodorants and to wash their armpits exclusively with an unperfumed medical soap (Eubos®, Dr. Hobein GmbH, Germany) within 24 hours prior to donation. The anxiety condition consisted of waiting for an important oral examination at the university in order to assess an academic degree (subjective importance, M=8.29, SD=0.87, scale range 0-10), while the sport control condition consisted of ergometer training. During the donation conditions, the donors' emotional experience was assessed using the Self Assessment Manikin (SAM, Bradley & Lang, 1994) (valence: -4 – 4, arousal: 1-9, dominance: 1-9), and the intensities of the six basic emotions (Ekman & Friesen, 1971) (using 10 cm visual analogue scales). During the anxiety condition, the donors felt more anxious, and less happy, as compared to the sport control condition. There were no differences in ratings of disgust, sadness, surprise, or anger between the donation conditions. In accordance with the anxiety ratings, the donors reported to feel more unpleasant during the anxiety condition. They also felt more aroused, and less dominant during the anxiety condition (see Table S1). To control for physiological arousal, the donors'

heart rate was sampled during the interview session (baseline) and in the test conditions. During the sport control condition the heart rate did not differ from the anxiety condition, p=.792 (anxiety condition: M=91.25, SD=22.07 beats per minute, sport control condition, M=90.95, SD=19.61 beats per minute). However, both heart rates were higher than during baseline recording (M=68.80, SD=11.22), both p <.001. The sport control condition took place on average 6 (SD = 4.13) days after the anxiety condition, while the time of day was held constant (M = 83.75, SD = 85.65 minutes difference between the beginning of the two donation situations).

The sweat samples were pooled with distinction to the respective donation conditions and stored at −20°C. For the experiment, the homogenized samples were divided into small portions (1.2 g each).

Table S1.

Self reported feelings of the intensities of basic emotions and SAM ratings of the sweat donors.

	Anxiety Condition		Sport-Control Condition		Significance
	M	SD	M	SD	p
Anxiety	6.68	1.69	0.46	0.58	<0.001
Happiness	3.89	2.37	7.09	2.26	<0.001
Anger	1.74	1.42	1.18	1.54	>0.200
Disgust	0.90	1.28	0.66	1.23	>0.450
Sadness	1.78	1.91	1.05	1.06	>0.125
Surprise	3.04	2.18	2.65	2.45	>0.450
$SAM_{valence}$	-0.05	1.76	2.20	1.28	<0.001
$SAM_{arousal}$	7.35	0.88	3.85	1.60	<0.001
$SAM_{dominance}$	4.50	1.70	6.70	1.31	0.001

Note: Basic Emotions range: 0 to 10cm visual analogue scale, $SAM_{valence}$ range -4 to 4, $SAM_{arousal}$ and $SAM_{dominance}$ range: 1 to 9.

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Chemosensory signals of competition increase the skin conductance response in humans

Dirk Adolph [a], Sabine Schlösser [a], Maren Hawighorst [b], Bettina M. Pause [a,*]

[a] Department of Experimental Psychology, Heinrich-Heine-University Düsseldorf, FRG
[b] Building Science Group, Faculty of Architecture, Karlsruhe Institute of Technology (KIT), FRG

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ABSTRACT

In vertebrates, chemosensory signals of competition are communicated between conspecifics, eliciting behavioral and physiological adaptations in the perceiving animal. The current study investigates, whether chemosensory signals of competition are also communicated between humans, and whether they elicit physiological changes in the perceiver. It is further investigated whether personality traits alter this physiological responding. Axillary sweat was collected from six male donors during a competition (badminton match) and a sport control condition (running). The donors' testosterone rose stronger during the competition as compared to the sport control condition. The chemosensory stimuli were presented to 18 (9 male) participants through a constant-flow olfactometer, while the skin conductance response (SCR) was measured. Results reveal that the SCR was larger in response to chemosensory signals collected during the competition condition as compared to those collected during the sport control condition. Furthermore, regression analyses showed, that higher scores on trait social anxiety were related to larger SCRs towards the chemosensory signals of competition. The current result suggests that chemosensory signals of competition can be communicated between humans, and that they elicit orienting in the perceiving individual. These data are consistent with current research, suggesting that high socially anxious individuals process threatening social information preferentially. The current results add to the growing body of research into human chemosensory communication of social information, and extend previous research on the chemosensory communication of anxiety.

1. Introduction

Aggression is an evolutionary conserved behavior found throughout the animal kingdom with its neurophysiological mechanisms being similar in all vertebrates [1,2], which suggests that aggression might be critical to the survival of species. Rather than a single isolated phenomenon, aggression can be understood as a set of evolved adaptations or strategies with their occurrence being contingent on environmental circumstances [3]. As such, its function is thought to regulate reproduction, ultimately limiting population growth, to divide limited natural assets by actively competing for resources and to protect offspring [4]. Consequently, individuals might have a natural drive to strive for dominance in order to ensure access to vital and naturally limited resources.

Attention and orientation processes are relevant determinants affecting changes in animal behaviors that are biologically significant, that is allowing the organism to survive, grow and reproduce successfully. Chemosensory information has long been known to guide attention and orienting responses, and chemosensory communication of information about the sender's territory or social status in the animal kingdom has been a longstanding fact [5]. In rodent societies, territory owners scent mark their habitat at a higher rate than other mice to advertise their identity and competitive ability or dominance over their marked territory [6]. Although responses to scent marks can vary in relation to an animal's own competitive ability [7], male mice usually avoid male chemosignals of dominance/aggression [8] to elude costly conflicts. In terms of physiological responses, chemosensory cues exert a priming effect on perception and behavior, e.g. by allowing anticipation (attention and orientation) of an attack from another aggressor [6] and subsequent initialisation of withdrawal. So far, animal research has produced a substantial body of evidence that individual differences in inter-male aggressive behavior may be related to the recognition of chemosensory cues from the opponent before fighting [9,10], and that male mice produce a pheromone that elicits aggressive behavior in other males [11]. However, that substance is likely to be androgen-dependent [11] and not bladder borne [12]. Furthermore, oestrous female mice use scent marks as a reliable signal of high quality mates and show more

* Corresponding author. Department of Experimental Psychology, Heinrich-Heine-University Düsseldorf, Universitätsstraße 1, 40225 Düsseldorf, FRG. Tel.: +49 211 81 14384; fax: +49 211 81 12019.
E-mail address: bettina.pause@uni-duesseldorf.de (B.M. Pause).

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sexually related behavior when interacting with dominant territory owners [13].

Evidence from a recent study suggests that chemosensory cues associated with trait dominance may also be communicated between humans. It could be shown that women in the fertile phase of their menstrual cycle prefer body odor of men high in trait dominance [14]. In addition, previous work provided evidence that humans are also capable of chemosensorily communicating their emotional states. Chemosensory cues of anxiety alter visual social perception [15,16], activate withdrawal-related motor systems [17,18] and alter neuronal responses in the perceiver [19,20]. To our knowledge, there is yet no empirical evidence that humans perceive and react to olfactory signals of state dominance/aggression.

So far, human research into dominance/aggression has focused largely on the signalling characteristics of facial displays of anger, showing that angry facial expressions preferentially capture attention [21], are efficient cues for fear conditioning (for a review see [22]) and elicit autonomic changes while being perceived [23]. The aim of the present study was to test whether dominance/aggression is communicated by means of chemosensory perception between humans. Moreover, we aimed to test whether chemical signals of dominance/aggression are capable of altering physiological responses in the perceiver, and whether personality traits (social anxiety, aggression, and depression) modulate this responsivity. Therefore, chemosensory stimuli donated during a competitive encounter (a subjectively important badminton match—competition condition), and a sport control condition were sampled. In assessing sweat samples from winners in an ecologically valid competition situation (a sport contest), the collected sweat samples most likely relate to competitive behavior including both dominant and aggressive components. The pooled sweat samples were presented to participants through an olfactometer while the skin conductance response (SCR) was measured.

2. Materials and methods

2.1. Participants

Eighteen right-handed, non-smoking undergraduate students (9 males) volunteered to participate in this study. All participants reported to be non-smokers and of European origin. None of them suffered from any mental or physical diseases (self-report), especially not from diseases of the upper respiratory tract. All female participants reported to have a regular menstrual cycle (25–28 days), eight of them used contraceptive pills. The participants were on average 25.1 (SD = ± 4.5) years of age (range = 20–39 years), and males and females did not differ in age ($t(16) = 0.94$, $p = 0.361$).

Participants scored low on self-reported depressive feelings (M = 2.75, SD = ± 3.26, BDI, [24]). In addition, they scored within the medium range on trait aggression (M = 12.06, SD = ± 6.39, Freiburger Aggressions Fragebogen, FAF [25]), and social anxiety (M = 13.56, SD = ± 6.05, Social Interaction and Anxiety Schedule, SIAS [26]). Male and female participants did not differ in any of these questionnaires (BDI: $t(16) = 1.81$, $p = 0.097$; FAF: $t(16) = 1.21$, $p = 0.245$; SIAS: $t(16) = 0.53$, $p = 0.602$). The study was approved by the Ethical Committee of the Medical Faculty of the University of Kiel. All participants gave written, informed consent and were paid for their participation.

2.2. Chemosensory stimuli

2.2.1. Donors

A total of 6 male donors of a local badminton club (TSV Altenholz Kiel, Germany) donated axillary sweat while winning an important badminton match (competition condition) and during a sport control condition (running). The donors played on average 10.75 (SD = 3.82) years badminton. They were on average 23.33 (SD = ± 3.89, range 18–25) years of age, and their mean body-mass-index was 23.52 (SD = ± 2.49, range 21.77–28.41). Like the participants of the main experiment, all donors were of European descent, non-smokers and reported no use of any medication. In addition, for the sweat donors it was important to assure that they did not suffer from any medical disease, especially mental and metabolic diseases. To exclude the possibility that the sweat samples were contaminated, all donors were instructed to refrain from eating garlic, onions, asparagus or spicy food, not to use deodorants and to wash their armpits exclusively with an unperfumed medical soap (Eubos®, Dr. Hobein GmbH, Germany) within 24 h prior to donation. All donors gave written and informed consent, and were paid for their donation.

2.2.2. Sampling conditions

The donors' sweat was collected from both axillae (using cotton pads) for 1 h per sampling condition. The competition condition was a successfully finished badminton match (followed by a 30 min period of rest). All matches were important tournaments. The club's position table was based on the outcome of these tournaments. The badminton matches consisted of maximally three rounds, and lasted approximately 30 min. The sport control condition was designed to resemble this configuration. It consisted of jogging (three times for 7 min each, separated by 4 min breaks plus 30 min of rest).

Immediately before the match or the jogging began (baseline), at the end of the match or after the third jogging episode (t1) and after a 30 min period of rest (t2, 60 min after the beginning), saliva samples were collected to determine testosterone and cortisol levels (SaliCaps, IBL, Germany). Contrary to the participants of the main experiment, where it was aimed to assess several personality traits, it was important to assess the donors' current emotional state during the two sampling situations. Therefore, the emotional dimensions valence, arousal and dominance (Self Assessment Manikin, SAM [27]), and the intensity of six basic emotions (fear, anger, surprise, sadness, disgust, and happiness [28], on 10 cm visual analogue scales) were assessed at t1. To control for physiological arousal and physical activity, the donors' heart rates were sampled in the competition condition (t1). During the sport control condition these heart rates were held constant (t1). For this purpose, all donors wore a heart rate monitor watch (Polar Electric, USA) during both conditions. During the sport control condition, the donors were asked to adjust their heart rate to the mean heart rate of the competition condition, by adjusting their running speed. After 30 min of rest (t2), the cotton pads were removed. The sport control condition took place on average 3.5 (SD = ± 1.52) days after the competition condition, while the time of day was held constant (with M = 35.5, SD = ± 36.4 min difference between the beginning of the two donation situations).

2.2.3. Ratings, heart rate, and endocrine data of the donors

Prior to the analyses, change scores were calculated for the cortisol and testosterone measure (i.e., t1—baseline, t2—baseline) and the data were then averaged across t1 and t2. T-tests were run for the endocrine data and for the subjective ratings and heart rate.

As intended, the donors' heart rates did not differ between both sessions (competition condition, M = 153.67, SD = ± 22.85; sport control condition, M = 161.33, SD = ± 15.00). However, the testosterone increase was higher during the competition, as compared to the sport control condition ($t(5) = 2.06$, $p = 0.048$, Cohens' $d = 0.50$, one tailed). Pairwise comparisons of the donors' ratings did not reveal any significant differences between the competition and the sport control condition (all $p > 0.10$). However, as a trend, the donors described their mood (SAM valence) to be more positive during the competition, as compared to the sport control condition ($t(5) = 2.15$, $p = 0.084$, Cohens' $d = 0.88$). Descriptive statistics for the donors' ratings, and hormonal data are reported in Tables 1–3.

Table 1
Mean ratings of basic emotions of the donors in the competition and the sport control condition.

	Competition condition		Sport control condition		t-Test
	M	SD	M	SD	p
Happiness	7.78	2.24	5.61	2.52	0.165
Anger	0.41	0.51	0.09	0.10	0.169
Sadness	0.10	0.13	0.13	0.17	0.759
Anxiety	0.09	0.09	0.09	0.15	1.000
Disgust	0.12	0.16	0.54	0.80	0.196
Surprise	1.79	3.11	1.58	3.05	0.517

Note. Ratings of basic emotions range: 0–10; p-values are given for direct comparisons (t-Test) between the sampling conditions.

2.3. Stimulus presentation

The sweat samples were pooled with distinction to the respective donation conditions and stored at −20 °C. For the experiment, the homogenized samples were divided into small portions (0.4 g) and renewed after each experiment. The chemosensory stimuli were presented in accordance with the method described by Kobal [29]. A constant flow (100 ml/s), six channel olfactometer (OM6b, Burghart, Germany) was used to stimulate both nostrils simultaneously. Both air streams were controlled by separate mass flow controllers. In the olfactometer, the glass tubes containing the stimuli were stored in a warm-water chamber, and the chemosensory stimuli were delivered through a Teflon tube. The temperature of the gas flow at the exit of the olfactometer was 37 °C and the relative humidity above 80%.

2.4. Olfactory hyposmia screening

In order to assess general hyposmia, all participants had to identify a bottle containing phenylethyl alcohol (PEA, 99%, Fluka, Germany, 1:200 (v/v) diluted in 1,2-propanediol) from a series of three bottles (two consecutive trials). The remaining two bottles contained the same volume of solvent. No subject had to be excluded due to general hyposmia.

2.5. Stimulus detection and ratings

To determine participants' detection performance, the chemosensory stimuli were administered via the olfactometer (duration = 0.5 s). Participants were asked to select the most intense stimulus from a series of three stimuli, (three-alternative forced choice, including one worn cotton pad, either from the competition or from the sport condition, and two blank odors consisting of clean room air). This procedure was carried out twice. Participants who failed once to detect the test stimulus were defined as non-detectors. Ratings of the chemosensory stimuli for intensity, pleasantness, unpleasantness, and familiarity were carried out using visual analogue scales (presented on a computer screen, range 0–500: 0 = no smell, 500 = strongest smell). To determine participants' ratings of emotional responses to the chemosensory stimuli, the SAM scale was applied (valence: −4–+4, arousal: 1–9, dominance: 1–9).

Table 2
Mean ratings of emotional states of the donors in the competition and the sport control condition.

	Competition condition		Sport control condition		t-Test
	M	SD	M	SD	p
SAM valence	8.00	0.89	6.83	0.75	0.084
SAM arousal	4.67	1.86	4.67	1.63	1.000
SAM dominance	7.17	0.98	7.17	0.75	1.000

Note. SAM ratings range: 1–9; p-values are given for direct comparisons (t-Test) between the sampling conditions.

Table 3
Mean hormonal changes of the donors in the competition and the sport control condition.

	Competition condition		Sport control condition		t-Test
	M	SD	M	SD	p
Testosterone (pg/ml)	55.33	51.43	25.33	37.66	0.048
Cortisol (pg/dl)	0.24	0.56	0.01	0.08	0.164

Note. Values represent changes from baseline-level; p-values are given for direct comparisons (t-Test) between the sampling conditions.

2.6. Procedure

Prior to the SCR recording, participants practiced the velopharyngeal closure technique [30]. The chemosensory stimuli (competition and sport control) were presented non-synchronously to breathing (duration = 0.5 s, inter stimulus interval = 9 s) within an olfactory oddball paradigm, consisting of two blocks of 100 pseudo-randomized trials each (25 deviant stimuli in a train of 75 standard stimuli, during the two blocks, the competition and the sport control stimuli, served either as the standard or the deviant stimulus). A short break (10 min) was introduced after the first 100 trials were carried out. An EEG was also recorded. However these data will be reported elsewhere.

2.7. Data recording, data reduction, and data analysis

The EDA data were recorded from 0–40 Hz using two Ag/AgCl electrodes (4 mm inner diameter) placed on the thenar and hypothenar of the non-dominant hand [31]. The EDA data were recorded, amplified (factor: 250) and filtered with Acquire software (version 4.2, NeuroScan Inc., Virginia, USA), sampled at 200 Hz, and filtered on-line using a 50 Hz notch filter.

Offline, the raw EDA signal was low-pass filtered (0.64 Hz, 24 dB/octave [31]) and very few trials with necessary DC-corrections were excluded (0.01%, n = 39, trials in the competition condition, 0.01%, n = 32, trials in the sport control condition). The EDA data were then corrected for baseline (500 ms before—500 ms after stimulus onset) and the SCR was extracted as the maximum deflection in an interval from 1000 to 5000 ms after stimulus onset. Finally, mean SCRs were calculated for the competition and the sport control condition within each participant. The SCRs were then standardized within participants.

For the ratings and the skin conductance data, ANOVAs including the within subject factor chemosensory condition (competition and sport control) and the between subject factor sex of participant (male and female) were run using SPSS 15.0. For significant effects Cohens' effect-size f (ANOVA) or Cohens' d (t-Test) were calculated. Huyn–Feldt corrections of degrees of freedom were applied, and corrected p-values are reported. An alpha level of 5% was used for all statistical tests. Binomial and Fisher tests were used to analyze the detection rates.

A stepwise multiple linear regression model including trait social anxiety, depression, and trait aggression as predictors was run to explain the SCRs to chemosensory stimuli donated in the competition situation.

3. Results

3.1. Stimulus detection and ratings

Mean detection rates were 61.1% for chemosensory stimuli donated in the competition condition and 44.4% for chemosensory stimuli donated in the sport control condition. However, only six participants (30%) were able to detect both stimuli. There were no significant differences (all $p > 0.20$) between the detection rates for chemosensory stimuli donated in either condition (Binomial tests), and between male and female participants (Fisher tests).

The chemosensory stimuli were rated as mildly intense (M = 217.14, SD = ± 143.40) and mildly unpleasant (M = 195.25, SD = ± 152.71), as well as low in pleasantness (M = 37.28, SD = ± 45.96), and familiarity (M = 37.00, SD = ± 56.57; see Table 4). The participants described their

emotional reactions to the stimuli as neutral (SAM valence, M = 4.72, SD = ± 1.54, SAM arousal, M = 4.89, SD = ± 1.11, SAM dominance, M = 4.94, SD = ± 1.21). Female participants experienced more emotional arousal when perceiving the chemosensory stimuli than male participants, F (1, 16) = 5.84 p = 0.028, Cohens' f = 0.60 (main effect for sex of the participant, female participants, M = 5.44, SD = ± 1.21, male participants, M = 4.33, SD = ± 0.66). The ANOVAs revealed no further significant effects for the ratings of intensity, pleasantness, unpleasantness, familiarity, SAM valence, and SAM dominance.

3.2. Skin conductance response

All participants were included in the SCR analysis, whether or not they could detect an odor deriving from the sweat samples. Chemosensory stimuli donated in the competition condition elicited larger SCRs than chemosensory stimuli donated in the sport control condition (main effect for chemosensory condition, F (1, 16) = 5.10, p = 0.038, Cohens' f = 0.57, see Fig. 1). There was no significant main effect for sex of the perceiver and no significant interaction between chemosensory condition and sex of the perceiver.

3.3. Regression analysis

To test whether the SCRs to the chemosensory stimuli donated in the competition situation can be explained by means of personality traits, participants' scores on trait aggression, trait social anxiety and depressive feelings were entered into a regression analysis. Results revealed that only trait social anxiety was related to participants' electrodermal responding (β = 0.50, t (16) = 2.31, p = 0.035, see Table 5). This indicates that participants with higher scores on trait social anxiety exhibit larger SCRs to chemosensory stimuli collected in the competition condition, while depression and trait anxiety are not related to the SCR towards these stimuli (as the SCR data were standardized across conditions, the regression model for the sport control stimulus reveals the reciprocal results). Overall, the model explained 25% of variance ($R^2 = 0.25$, F (1, 16) = 5.33, p = 0.035).

4. Discussion

The present study investigated, whether competition is communicated chemosensorily between humans, and whether chemical signals of competition alter physiological responses in the perceiver. Therefore, chemosensory stimuli, donated during a competitive encounter and a sport control situation were sampled. During the competition condition the testosterone increase was higher than during the sport condition. However, as the endocrine data were collected during the match as well as after the match, the increase in testosterone may be due to the competitive behavior (aggression) during the match, and to the perceived dominance of the winners after the match. The pooled odor samples were presented while the skin conductance response was measured. Results clearly indicate that chemosensory stimuli, donated during the competition situation elicited larger SCRs than chemosensory control stimuli. To investigate whether the physiological responses were altered by personality traits, a regression analysis was carried out. Results indicate that higher scores on trait social anxiety are related to higher SCRs to the stimuli donated in the competition situation.

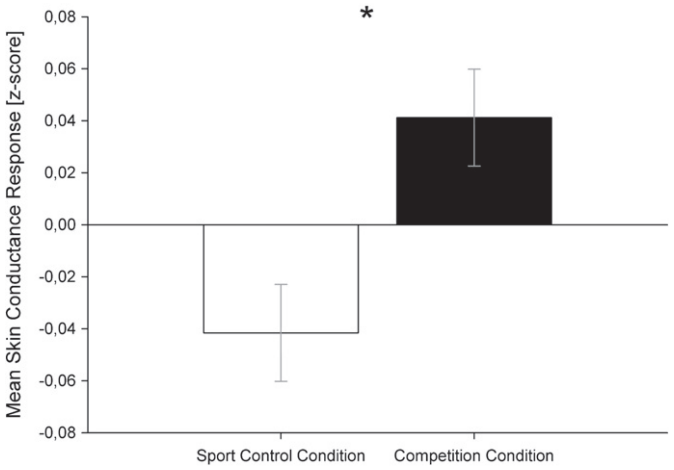

Fig. 1. Mean (±SEM) standardized SCR to chemosensory stimuli donated in the sport control and the competition condition. The SCR was larger in response to chemosensory stimuli donated in the competition than to those donated in the sport control condition (*p<0.05).

To achieve the chemosensory stimuli associated with competition, sweat samples were collected from winners of a badminton match. All donors stated that the upcoming match was important for them, that they occasionally became angry during, and felt dominant after winning an important match. Moreover, the donors' testosterone levels rose stronger during the competition as compared to the sport control condition, and as a trend, the donors described their mood to be more positive during the competition condition as compared to the sport control condition.

In general, athletic competitions are formalized contests for status that are convenient to study competitive behaviors [32]. Winning such contests is achieved through dominant behaviors like staring, threatening gestures, and most important, physical aggression [33]. In humans, testosterone is associated with competitive and dominant behaviors [34–36]. It can be assumed that the donors' rise in testosterone occurred due to the competitive nature of the match, and their willingness to win the contest to achieve social dominance. Also, the donors' mood was more positive in the competition, as compared to the sport control situation. Previous research has verified that positive mood change is associated with higher testosterone change in winners of human competitions [32]. Human research into competition (aggression/dominance), has previously shown that rises in testosterone levels are higher in winners than in losers of tennis matches [32]. Moreover, testosterone levels are positively correlated to the amount of attacks in judo fights [37] and to aggressive behaviors (amount of electro shocks administered) towards an opponent in a competitive reaction time task [38]. According to the "biosocial theory of status" [39] an individual's testosterone level is associated with the person's willingness to compete in contests for higher status, and reciprocally, the experience of winning such contests produce a rise in testosterone.

Table 4
Mean (M) intensity, pleasantness, unpleasantness, and familiarity ratings of the chemosensory stimuli donated in the competition, and the sport control condition.

	Competition condition		Sport control condition		ANOVA
	M	SD	M	SD	p
Intensity	255.06	172.33	179.22	162.08	0.088
Pleasantness	38.00	39.60	36.56	59.05	0.884
Unpleasantness	215.22	201.05	175.28	181.99	0.488
Familiarity	53.44	114.16	20.56	22.37	0.253

Note. Ratings range: 0–500; p-values are given for main effect donation condition (ANOVA).

Table 5
Regression analyses on SCRs to chemosensory stimuli donated in the competition condition using trait social anxiety (SIAS), depression (BDI), and aggression (FAF) scores.

	β	t	df	p
Social anxiety	0.50	2.31	16	0.035
Depression	−0.25	−1.11	16	0.284
Aggression	0.05	0.19	16	0.856

No difference was found in the donors' physiological (as measured with heart rate) and self-reported levels of arousal (as measured with the arousal scale of the SAM [27]), between the two donation situations. This is important, because changes in physiological responses in the perceiver of the chemosensory stimuli cannot be explained by differences in arousal of the donors during the donation situations.

In the main experiment, the skin conductance response was enhanced during the perception of chemosensory signals donated during the competition situation as compared to those donated in the sport control condition. Skin conductance is a marker of sympathetic autonomic activity, associated with arousal and orienting towards a meaningful stimulus [40]. Emotionally significant stimuli elicit larger skin conductance responses than neutral objects [41]. In line with the current results, it has been shown that angry facial expressions preferentially capture attention [21] and elicit higher skin conductance responses than neutral (and happy) expressions [23].

Mammalian evolution has required the successful development of systems to cope with potential dangers, including aggression from conspecifics. Facial expressions of threat (e.g. angry expressions) provide an important channel of communication in the maintenance of established dominance hierarchies among conspecifics [42]. This has also been shown for chemosensory signals of dominance/aggression in the animal kingdom [6,13]. Thus, the present results may indicate that chemosensory signals of competition, like facial expressions of anger, are potent signals of threat to conspecifics and thus preferentially elicit the automatic allocation of attention and orienting (as is the case for angry facial expressions [42]).

However, just recently, it has been reported that women in the fertile phase of their menstrual cycle prefer body odors of dominant males (as assessed by questionnaire) [14]. This suggests that body odors from dominant men may also have appetitive properties. Since highly arousing appetitive stimuli preferentially elicit attention and orienting [41], it cannot be ruled out that especially the female perceivers in the current experiment showed larger skin conductance responses as a result of the appetitive nature of the competition cue. This interpretation is also in line with findings of oestrus female rodents preferring the odors of dominant males which won a single encounter with a male conspecific [43].

Taken together, the current result suggests that chemosensory signals of competition can be communicated between humans, and that they preferentially elicit orienting in the perceiving individual. Further research is needed to clarify in detail which mechanisms come into play to enhance orienting towards chemosensory signals of dominance/aggression. It is hypothesized that chemosensory signals of competition evoke a higher SCR in male perceivers, because a potential threat could be indicated. However, for female perceivers the same signals may have appetitive properties in terms of mate selection.

Higher social anxiety is associated with higher SCRs to chemosensory stimuli donated in the competition situation. These data are consistent with current research suggesting that high socially anxious individuals process threatening facial expressions preferentially [44,45], and that social phobia is associated with an increased neuronal activity within the amygdala in reaction to angry faces [46]. In the context of chemosensory anxiety signals, the priming of withdrawal reflexes is intensified in non-clinical socially anxious participants [18]. The current results extend these findings to chemosensory signals of competition, suggesting a more generalized hyperreactivity of socially anxious individuals towards social threat. Furthermore, the arousal response observed in the present study may indicate withdrawal-related motivational priming in high socially anxious individuals.

As expected, in the present study, the detection rates of both chemosensory stimuli were considerably low. Only 30% of the participants were able to detect both stimuli. The current results are in accordance with previous research on human chemosensory communication, postulating that the effects of chemosensory stimuli are not necessarily dependent on attentional resources and conscious stimulus processing [16,18,19]. Consequently, the chemosensory stimuli were described as low in intensity and only mildly unpleasant. As a trend, the chemosensory stimuli donated in the competition condition were rated as slightly more intense as the stimuli donated during the control condition. Therefore, it cannot be completely ruled out that the SCR was affected by the perceived stimulus intensity. However, as most of the participants could not even detect an odor from the sweat samples, an effect of intensity on the SCR seems to be rather unlikely. As the ratings of the stimuli themselves do not differ between male and female participants, female participants experienced more emotional arousal in response to the chemosensory stimuli. This is concordant with previous research suggesting that women are more sensitive to chemosensory cues than men [15,47]. However, concerning the results for the psychophysiological data, the observed gender differences in subjective emotional arousal were not evident in the SCR data.

Taken together, the current results add to the growing body of research into human chemosensory communication of social information. It extends current research on the chemosensory communication of anxiety/stress. It could be shown that social chemosensory stress-signals are capable of priming defensive motivational systems in the perceiver [17], and to alter the neuronal responses in emotion-related brain areas [19,20]. The current results provide evidence that this communication channel is also evident for chemosensory signals of competition. Furthermore, chemosensory competition signals initiate physiological changes in the perceiver which are associated with attention and orienting.

The present study shows, that the perception of chemosensory signals of competition is altered in socially anxious participants. It remains to be an open question, whether the observed effect is reversed in anti-social personality disorder. Finally, the knowledge about an intensified processing of social chemosensory signals in socially anxious individuals might form the basis for developing chemosensory related therapeutic treatments.

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Erklärung

Die hier vorgelegte Dissertation habe ich eigenständig und ohne unerlaubte Hilfsmittel angefertigt. Die Dissertation wurde in vorliegender oder in ähnlicher Form bei keiner anderen Institution eingereicht. Ich habe bisher keine erfolglosen Promotionsversuche unternommen.

Dirk Adolph