The Role of Attentional Control and Fear Acquisition and Generalization in Social Anxiety Disorder

Die Rolle von Aufmerksamkeitskontrolle und Furchtlernen und Generalisierung bei Sozialer Angststörung

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Abstract

Although Social Anxiety Disorder (SAD) is one of the most prevalent mental disorders, still little is known about its development and maintenance. Cognitive models assume that deviations in attentional as well as associative learning processes play a role in the etiology of SAD. Amongst others, deficits in inhibitory attentional control as well as aberrations during fear generalization, which have already been observed in other anxiety disorders, are two candidate mechanisms that might contribute to the onset and retention of SAD. However, a review of the literature shows that there is a lack of research relating to these topics. Thus, the aim of the present thesis was to examine in which way individuals with SAD differ from healthy controls regarding attentional control and generalization of acquired fear during the processing of social stimuli.

Study 1 tested whether impairment in the inhibitory control of attention is a feature of SAD, and how it might be influenced by emotional expression and gaze direction of an interactional partner. For this purpose, individuals with SAD and healthy controls (HC) participated in an antisaccade task with faces displaying different emotional expressions (angry, neutral and happy) and gaze directions (direct and averted) serving as target stimuli. While the participants performed either pro- or antisaccades in response to the peripherally presented faces, their gaze behavior was recorded via eye-tracking, and ratings of valence and arousal were obtained. Results revealed that both groups showed prolonged latencies and increased error rates in trials with correct anti- compared to prosaccades. However, there were no differences between groups with regard to response latency or error rates, indicating that SAD patients did not exhibit impairment on inhibitory attentional control in comparison to HC during eye-tracking. Possible explanations for this finding could be that reduced inhibitory attentional control in SAD only occurs under certain circumstances, for example, when these individuals currently run the risk of being negatively evaluated by others and not in the mere presence of phobic stimuli, or when the cognitive load of a task is so high that it cannot be unwound by compensatory strategies, such as putting more effort into a task.

As not only deviations in attentional, but also associative learning processes might be pathogenic markers of SAD, these mechanisms were further addressed in the following experiments. Study 2 is the first that attempted to investigate the generalization of conditioned fear in patients with SAD. To this end, patients with SAD and HC were conditioned to two neutral female faces serving as conditioned stimuli (CS+: reinforced; CS-: non-reinforced) and a fearful face paired with a loud scream serving as unconditioned stimulus (US). Fear generalization was tested by presenting morphs of the two faces (GS: generalization stimuli), which varied in their similarity to the original faces. During the whole experiment, self-report ratings, heart rate (HR) and skin conductance responses (SCR) were recorded. Results demonstrated that SAD patients rated all stimuli as less

pleasant and more arousing, and overestimated the occurrence of the US compared to HC, indicating a general hyperarousal in individuals with SAD. In addition, ratings and SCR indicated that both groups generalized their acquired fear from the CS+ to intermediate GSs as a function of their similarity to the CS+. However, except for the HR data, which indicated that only SAD patients but not HC displayed a generalization response in this measure, most of the results did not support the hypothesis that SAD is characterized by overgeneralization. A plausible reason for this finding could be that overgeneralization is just a key characteristic of some anxiety disorders and SAD is not one of them. Still, other factors, such as comorbidities in the individuals with SAD, could also have had an influence on the results, which is why overgeneralization was further examined in study 3.

The aim of study 3 was to investigate fear generalization on a neuronal level. Hence, high (HSA) and low socially anxious participants (LSA) underwent a conditioning paradigm, which was an adaption of the experimental design used study 2 for EEG. During the experiment, steady-state visually evoked potentials (ssVEPs) and ratings of valence and arousal were recorded. Analyses revealed significant generalization gradients in all ratings with highest fear responses to the CS+ and a progressive decline of these reactions with increasing similarity to the CS-. In contrast, the generalization gradient on a neuronal level showed highest amplitudes for the CS+ and a reduction in amplitude to the most proximal, but not distal GSs in the ssVEP signal, which might be interpreted as lateral inhibition in the visual cortex. The observed dissociation among explicit and implicit measures points to different functions of behavioral and sensory cortical processes during fear generalization: While the ratings might reflect an individual's consciously increased readiness to react to threat, the lateral inhibition pattern in the occipital cortex might serve to maximize the contrast among stimuli with and without affective value and thereby improve adaptive behavior. As no group differences could be observed, the finding of study 2 that overgeneralization does not seem to be a marker of SAD is further consolidated.

In sum, the conducted experiments suggest that individuals with SAD are characterized by a general hyperarousal during the exposition to disorder-relevant stimuli as indicated by enhanced arousal and reduced valence ratings of the stimuli compared to HC. However, the hypotheses that reduced inhibitory attentional control and overgeneralization of conditioned fear are markers of SAD were mostly not confirmed. Further research is required to elucidate whether they only occur under certain circumstances, such as high cognitive load (e.g. handling two tasks simultaneously) or social stress (e.g. before giving a speech), or whether they are not characteristics of SAD at all. With the help of these findings, new interventions for the treatment of SAD can be developed, such as attentional bias modification or discrimination learning.

Zusammenfassung

Obwohl die Soziale Angststörung (SAS) eine der häufigsten psychischen Erkrankungen ist, ist über ihre Entstehung und Aufrechterhaltung noch wenig bekannt. Kognitive Modelle nehmen an, dass Abweichungen sowohl in Aufmerksamkeits- als auch assoziativen Lernprozessen eine Rolle bei ihrer Entwicklung spielen. Unter anderem werden Defizite in der Aufmerksamkeitskontrolle sowie Abweichungen während der Generalisierung von konditionierter Furcht als für die Ätiologie potentiell bedeutsame Faktoren gehandelt, da diese Auffälligkeiten bereits bei anderen Angststörungen beobachtet wurden. Eine Literaturübersicht zeigt jedoch, dass zu dieser Thematik ein Mangel an Forschung besteht. Das Ziel der vorliegenden Doktorarbeit war es daher zu untersuchen, auf welche Weise sich Individuen mit Sozialer Angststörung bei der Verarbeitung sozialer Stimuli von gesunden Kontrollprobanden in Hinblick auf ihre Aufmerksamkeitskontrolle und die Generalisierung gelernter Furchtreaktionen unterscheiden.

Studie 1 testete, ob das Vorliegen einer Beeinträchtigung der inhibitorischen Aufmerksamkeitskontrolle ein Merkmal der SAS ist, und auf welche Weise diese vom emotionalen Gesichtsausdruck sowie der Blickrichtung von Interaktionspartnern beeinflusst werden kann. Zu diesem Zweck nahmen Patienten mit SAS und eine gesunde Kontrollgruppe (KG) an einer Antisakkaden-Aufgabe teil, bei welcher Gesichter mit unterschiedlichem emotionalen Ausdruck (wütend, neutral und fröhlich) und unterschiedlicher Blickrichtung (direkter und abgewandter Blick) als Stimuli dienten. Während die Probanden in Abhängigkeit eines Hinweisreizes entweder Pro- oder Antisakkaden in Reaktion auf die peripher präsentierten Gesichter ausübten, wurde ihr Blickverhalten mittels Eye-Tracking aufgezeichnet. Außerdem wurden anschließend Valenz- und Arousal-Ratings der Stimuli erfasst. Die Ergebnisse zeigten, dass beide Gruppen erhöhte Latenzzeiten sowie Fehlerraten in Durchgängen mit korrekt ausgeführten Antisakkaden im Vergleich zu Prosakkaden aufwiesen. Jedoch gab es keinen Gruppenunterschied in Bezug auf die Antwortlatenz und Fehlerrate, was darauf hindeutet, dass Patienten mit SAS im Vergleich zur KG kein Defizit der inhibitorischen Aufmerksamkeitskontrolle während des Eye-Trackings erkennen ließen. Eine mögliche Ursache für diesen Befund könnte sein, dass eine reduzierte inhibitorische Aufmerksamkeitskontrolle bei SAS nur unter bestimmten Umständen auftritt, beispielsweise, wenn betroffene Individuen akut Gefahr laufen von anderen negativ bewertet zu werden, und nicht bloß phobischen Stimuli ausgesetzt sind, oder wenn die kognitive Belastung durch eine Aufgabe so groß ist, dass sie nicht durch kompensatorische Strategien, wie beispielsweise mehr Anstrengung, ausgeglichen werden kann.

Da nicht nur abweichende Aufmerksamkeitsprozesse, sondern auch abweichende assoziative Lernprozesse pathogene Marker von SAS sein könnten, wurden letztere in den folgenden

Experimenten genauer untersucht. Studie 2 stellt den ersten Versuch dar die Generalisierung konditionierter Furcht in Patienten mit SAS zu erforschen. Hierfür wurden sowohl SAS Patienten als auch eine KG auf zwei neutrale, weibliche Gesichter konditioniert, welche als Konditionierungsstimuli (conditioned stimuli [CS]: CS+: verstärkt; CS-: unverstärkt) dienten. Bei dem unkonditionierten Stimulus (unconditioned stimulus [US]) handelte es sich um die bereits bekannten Gesichter mit ängstlichem Ausdruck, die mit einem lauten Schrei gepaart wurden. Die Furchtgeneralisierung wurde mittels der Präsentation von Gesichtern, welche aus den beiden Ursprungsgesichtern gemorpht worden waren und als Generalisierungsstimuli (generalization stimuli [GS]) dienten, getestet. Während des Experiments wurden Selbstauskunftsratings sowie Herzrate (heart rate [HR]) und Hautleitfähigkeit (skin conductance response [SCR]) aufgezeichnet. Die Ergebnisse zeigten, dass Patienten mit SAS im Vergleich zur KG alle Stimuli als unangenehmer und aufregender bewerteten sowie die Auftretenswahrscheinlichkeit des US überschätzten, was auf eine generelle Übererregung in Individuen mit SAS hinweist. Darüber hinaus ergaben die Ergebnisse, dass beide Gruppen ihre erworbene Furcht vom CS+ in Abhängigkeit ihrer Ähnlichkeit mit dem CS+ auf intermediäre GSs übertrugen. Allerdings stützen abgesehen von den Daten der Herzrate, in denen nur SAS Patienten und nicht die KG eine Generalisierungsreaktion zeigten, die meisten Befunde nicht die Hypothese, dass Übergeneralisierung ein Merkmal von SAS ist. Eine mögliche Ursache dieses Ergebnisses könnte sein, dass Übergeneralisierung nur ein wichtiges Merkmal einiger bestimmter Angststörungen ist und SAS nicht zu ihnen gehört. Dennoch könnten auch andere Faktoren, wie beispielsweise die Komorbiditäten der untersuchten SAS Patienten, einen Einfluss auf die Ergebnisse gehabt haben. Aus diesem Grund wurde Übergeneralisierung in Studie 3 näher untersucht.

Das Ziel von Studie 3 war es Furchtgeneralisierung auf neuronaler Ebene zu untersuchen. Folglich wurde das Paradigma der zweiten Studie an einen Versuchsplan, der für die Messung von neuronaler Aktivität mittels EEG geeignet war, angepasst und auf eine hoch (high socially anxious [HSA])- sowie eine niedrig sozialängstliche Gruppe (low socially anxious [LSA]) angewandt. Während des Experiments wurden sowohl steady-state visually evoked potentials (ssVEPs) als auch Valenz- und Arousal-Ratings erfasst. Die Analyse ergab signifikante Generalisierungsgradienten in allen Ratings mit der höchsten Furchtreaktion auf den CS+ und einem fortschreitenden Abfall der Reaktion auf die GSs mit zunehmender Ähnlichkeit zum CS-. Im Gegensatz dazu zeigte sich in der ssVEP-Amplitude ein anderes Muster: hier erreichte der Generalisierungsgradient zwar auch die höchste Amplitude in Reaktion auf den CS+, jedoch eine anschließende Reduktion der Amplitude auf den nächst proximalen, nicht jedoch distale GS, was ein Hinweis auf laterale Hemmungsprozesse im visuellen Kortex sein könnte. Die beobachtete Dissoziation zwischen expliziten und impliziten Maßen könnte auf unterschiedliche Funktionen von behavioralen und sensorischen kortikalen Prozessen während der Generalisierung von Furcht hinweisen: Während die Ratings möglicherweise die

bewusste Bereitschaft eines Individuums auf Bedrohung zu reagieren widerspiegeln, könnte das Muster lateraler Hemmung im okzipitalen Kortex dazu dienen den Kontrast zwischen Stimuli mit und ohne affektivem Wert zu maximieren und somit adaptives Verhalten verbessern. Da zwischen beiden Gruppen keine signifikanten Unterschiede gefunden wurden, untermauerte Studie 3 das Ergebnis von Studie 2, welches bereits eher dagegen sprach, dass Übergeneralisierung von Furcht ein Merkmal von Individuen mit SAS sei.

Insgesamt suggerieren die Ergebnisse der durchgeführten Studien, dass Individuen mit SAS während der Exposition von störungsspezifischen Reizen im Vergleich zu Kontrollprobanden durch eine generelle Übererregung gekennzeichnet sind, was an erhöhten Arousal- und verringerten Valenz-Ratings erkennbar war. Jedoch konnten die Hypothesen, dass reduzierte Aufmerksamkeitskontrolle sowie Übergeneralisierung Merkmale von Individuen mit SAS sind, zum größten Teil nicht bestätigt werden. Weitere Forschung ist nötig um herauszufinden, ob diese Phänomene nur unter besonderen äußeren Umständen, wie beispielsweise hohen kognitiven Anforderungen (e.g. bei der Bearbeitung zweier Aufgaben gleichzeitig) oder sozialem Stress (e.g. vor dem Halten einer Rede), auftreten, oder ob sie gar kein Merkmal von SAS darstellen. Mit Hilfe der sich daraus ergebenden Befunde könnten neue Interventionen für die Behandlung von SAS entwickelt werden, wie beispielsweise Aufmerksamkeitsbias-Modifikations-Trainings oder Diskriminationslernen.

Abbreviations

ACC	Anterior cingulate cortex
ACT	Attentional control theory
ANOVA	Analysis of variance
BDI	Beck Depression Inventory
CNV	Contingent negative variation
CS	Conditioned stimulus
CSs	Conditioned stimuli
CS+	Conditioned fear cue
CS-	Conditioned safety cue
CTI	cue-target interval
DLPFC	Dorsolateral prefrontal cortex
DSM	Diagnostic and Statistical Manual of Mental Disorders
EEG	Electroencephalogram
ERP	Event-Related Potential
FEF	Frontal eye fields
fMRI	Functional magnetic resonance imaging
FPS	Fear-potentiated startle
GAD	Generalized anxiety disorder
GS	Generalization stimulus
GSs	Generalization stimuli
HC	Healthy controls
HR	Heart rate
HSA	High socially anxious
IADS	International affective digitized sounds database
ICD	International Statistical Classification of Diseases and Related Health Problems
LSA	Low socially anxious
LSAS	Liebowitz Social Anxiety Scale
NIMH	National Institute of Mental Health
PANAS	Positive and Negative Affect Schedule
PD	Panic disorder
PTSD	Posttraumatic stress disorder

RDoC	Research Domain Criteria
SAD	Social anxiety disorder
SAM	Self-Assessment Manikin (Scale)
SCR	Skin conductance response
SPAI	Social Phobia and Anxiety Inventory
STAI	State-Trait Anxiety Inventory
SSVEP	Steady-state Visually Evoked Potentials
US	Unconditioned stimulus
VLPFC	Ventrolateral prefrontal cortex

Introduction

‘A solitary, unused to speaking of what he sees and feels, has mental experiences which are at once more intense and less articulate than those of a gregarious man. They are sluggish, yet more wayward, and never without a melancholy tinge. Sights and impressions which others brush aside with a glance, a light comment, a smile, occupy him more than their due; they sink silently in, they take on meaning, they become experience, emotion, adventure. Solitude gives birth to the original in us, to beauty unfamiliar and perilous - to poetry. But also, it gives birth to the opposite: to the perverse, the illicit, the absurd’ (Mann, 1913).

Thomas Mann, *Death in Venice*

In his novel *Death in Venice* published in 1913, Thomas Mann describes the sensations and impression of the book’s main character Gustav von Aschenbach, an introverted and highly reflected writer, who – after many years of work in reclusiveness- decided to go on a journey. Von Aschenbach - being confronted with a large amount of new impressions on that trip - feels that he is different from most other people in several ways: He perceives his mental impressions to be ‘more intense and less articulate than those of a gregarious man […] and never without a melancholy tinge’, which indicates his experiences deviate in both quantity (articulation) and quality (intensity) in comparison to others. Also, he concedes that his perception might be biased by an affectively negative connotation (melancholy tinge). With regard to the duration that von Aschenbach spends to process encounters with other people, he realizes that more social people push aside negligible experiences ‘[…] with a glance, a light comment, a smile’, while he ruminates on them excessively and puts more meaning to them over time than necessary. Finally, he concludes that solitude can be a resource by evoking ‘beauty unfamiliar and perilous’, which might not be accessible for a social person, but likewise a risk factor, as it can also elicit ‘the perverse, the illicit, [and] the absurd.’

Albeit modern psychology as we know it today was in its infancy at the time the novel was written, Mann creates the picture of von Aschenbach’s inner experience so accurate and sound that individuals who suffer from a mental illness, which is nowadays referred to as social anxiety disorder (SAD), might identify with him. However, the aforementioned traits and affective states do not exclusively occur in SAD, but – to a certain degree - in healthy people, too. Therefore, the present dissertation aims at investigating and explaining in which way individuals with SAD differ from healthy individuals regarding particular cognitive processes in order to broaden the knowledge on the etiology and maintenance of this disorder.

1 Theoretical Background

1.1 Social Anxiety and Social Anxiety Disorder

Human beings are social animals by nature. Starting with birth, their feeding, hygiene and movement depend on an adult's care until they are grown-up and can look after themselves. And even when they are grown up, they need each other to make friends, enter into partnerships, start families and live in communities. This kind of behavior is not displayed without a reason: life in a group comes along with many benefits, which enhance the odds of survival for both the individual and the species. However, it also has its costs, as every member of the party does not only have to follow its own needs, but must consider the ones of others, too. While in ancient times pure physical strength paired with a certain shrewdness and audacity might have sufficed to secure an individual's position in the group, the present-day human being has to possess social skills to stand its ground in a community, for example verbal communication skills, persuasiveness, assertiveness, empathy, and adaptability to new situations. If an individual owns such competences, it is likely that it will interact with others without provoking undue disharmony or conflicts and hence be accepted as a member of the group, but if it does not, it runs the risk of being socially excluded.

Researchers found that the development and maintenance of stable interpersonal relationships is a fundamental human need (Baumeister & Leary, 1995; Vervliet, Vansteenwegen, Baeyens, Hermans, & Eelen, 2005). Social isolation does not only prevent reproduction and decrease the individual's chance to survive, but can also lead to anxiety, unhappiness, depression, low self-esteem and decrease prosocial behavior (Leary, 1990; Twenge, Baumeister, DeWall, Ciarocco, & Bartels, 2007). For that reason, human beings strive for attachment and try to avoid social exclusion (Eisenberger, 2012). This is not only true for human beings, but social species in general. For example, rats, which live in communities and belong to the most social rodents of all, show increased anxious behavior when they are socially isolated (Lee & Noh, 2015).

Within this context, it is plausible that human beings are concerned about what others might think of them, because it is "the others" who ultimately decide whether or not an individual is accepted as a member of the whole group. However, the degree to which an individual fears the judgement of other people might differ between participants. It can be assumed that the majority of the human population is familiar with the feeling of being nervous before social or performance situations, such as giving a speech in front of an audience or attending a party where most of the guests are unknown. Situations like this make people fear that others could notice they are not proficient speakers or do not know what to say during a light party small talk. In most of the cases, though, it does not take long until they realize that this fear was exaggerated and find themselves

giving a pointed speech or having an entertaining conversation with several new acquaintances. Yet, in some individuals, the fear in the presence of others is so intense that their regular performance is actually disturbed.

The fact that social fears and worries are so wide-spread among society makes it difficult to define at which point a person ranks among those with common shyness or those with a clinically diagnosable disorder. This is particularly true against the background that from an evolutionary perspective, social fears can be regarded as adaptive - especially for individuals who are lower in hierarchy - , because submissive behavior protects from being attacked by dominant conspecifics (Öhman, 1986). Thus, it is important to bear in mind that the fear of being evaluated in social situations is not a dichotomous trait, but exists along a continuum across the whole population, which ranges from fearlessness to average levels of anxiety and finally to extreme anxiety with psychopathological relevance (McNeil, 2010). Albeit there is no strict criterion for a psychopathological diagnosis, an important factor which is often consulted to separate regular timidity from social anxiety seems to be an impairment in social and occupational functioning and the personal suffering and distress that comes along with it (McNeil, 2010; Stangier & Fydrich, 2002).

From a historical perspective, the earliest description of extreme shyness within a medical context is accredited to Hippocrates (460-370 BC). He described an overly shy patient as someone who "through bashfulness, suspicion, and timorousness, will not be seen abroad" and "dare not come into company for fear he should be misused, disgraced, overshoot himself in gestures or speeches, or be sick; he thinks every man observes him, aims at him, derides him, owes him malice" (Hippocrates, lib. de insania et melancholia). The terms *social phobia* (phobie des situations sociales) and *social neurosis* just came up long after that at the beginning of the 20th century in France (Haustgen, 2004). However, it was not before the publication of the third edition of the Diagnostic and Statistical Manual of Mental Disorders in 1980 that social phobia was acknowledged as an own mental disorder (American Psychiatric Association, 1980). Since then, the definition has been revised several times, and as the original diagnosis only included fear of a specific situation and did not do justice to those individuals who feared several social situations, the name was changed to *social anxiety disorder (SAD).*

1.1.1 Definition

The most recent definition of social anxiety disorder in the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders) is considered to be the most definitive and clearest to date (American Psychiatric Association, 2013). It describes SAD as "a persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be

embarrassing and humiliating." This definition does not only include performance situations in which the actor is in the center of attention, but also situations such as going to the movies, to concerts or to dinner, because some individuals with SAD fear to eat, drink or make phone calls in public. A further criterion is that the exposure to social situations must usually lead to anxiety and can even take the form of panic attacks, which is why social situations are avoided. Typically, individuals who suffer from SAD also recognize that their fear is unreasonable or excessive, but this is not an obligatory criterion anymore. Beyond, the appearance of fear, anxiety and/or avoidance has to be persistent to give the diagnosis, which means it should last six or more months, and interferes with the individual's occupational functioning, ordinary routine or social activities and relationships (American PsychiatricAssociation, 2013).

1.1.2 Epidemiology

With an estimated life-time prevalence of approximately 7% in Europe and 13% in the United States, SAD belongs to one of the most prevalent mental disorders following major depression and alcohol abuse (Fehm, Pelissolo, Furmark, & Wittchen, 2005; Kessler, Chiu, Demler, & Walters, 2005; Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). However, it usually does not get as much attention as more expressive mental disorders, such as schizophrenia or bipolar disorders, although SAD also provokes severe emotional distress and suffering and causes a large amount of health care costs. Besides its comparably inconspicuous appearance, a reason could be that social anxiety among other anxiety disorders is typically treated in ambulant settings, as it comes along with a higher level of global functioning.

Researchers found the median age-of-onset in individuals with SAD at about 13 years with a narrow interquartile range (the number of years between the 25^{th} and 75^{th} percentiles of the age-of-onset distribution) of only 7 years, which means that the majority of the patients develop social anxiety during adolescence (Kessler, Berglund, et al., 2005). The most common fears at the age of 12-17 include test and performance situations (31.1%) followed by speaking in public (19.7%) (Essau, Conradt, & Petermann, 1999). More than half of the patients with SAD suffer from another anxiety disorder at some point in their lives, such as agoraphobia, specific phobia, panic disorder (PD) or generalized anxiety disorder (GAD), and/or major depression, but other comorbidities can also occur, such as obsessive-compulsive disorder, alcohol abuse or post-traumatic stress disorder (PTSD) (Kessler, Chiu, et al., 2005).

As the historical outline above has shown, pathological social anxiety has always existed in humans. Nevertheless, there is an ongoing public discussion on the question whether the prevalence of SAD has increased over the course of time. A cause which gave an impulse to this debate could have been the observation that modern societies favor individuals who are self-confident,

extraverted and bold; who are open for new experiences, love to socialize and quickly adapt to the environmental, political or societal changes in times of globalization. However, it is difficult to test this hypothesis for several reasons: first, the approval of SAD as a diagnose dates back only a few decades to the year 1980 when the DSM-III was published. Records from older investigations cannot be reliably compared to modern studies as they might have measured different constructs. Second, there is a lack of epidemiologic surveys which measured the occurrence of social anxiety and repeated the investigation in the same population after a certain time. There is only one large study conducted in the USA which meets this demands: the National Comorbidity Survey from 1994 (Kessler et al., 1994) and its replication approximately 10 years later (Kessler, Chiu, et al., 2005). This study did not support the hypothesis of an increased prevalence for SAD, though, as the observed twelve-month prevalence remained relatively stable with 7.9% in 1994 compared to 6.8% in 2005. A German meta-analysis including 27 studies from 16 European countries found twelve-month prevalence rates ranging from 0.6 to 7.9%, which were a little lower than those in the United States (Wittchen & Jacobi, 2005). However, it is very likely that this variation can be explained by methodological and diagnostically differences (Bandelow & Michaelis, 2015; Wittchen & Jacobi, 2005). Finally, researchers found that genetic factors play a noteworthy role in the development of social anxiety disorder as indexed by heritability estimates of about 30 to 60% (Scaini, Belotti, & Ogliari, 2014; Shimada-Sugimoto, Otowa, & Hettema, 2015). These findings are also in contrast to the hypothesis that the number of individuals suffering from SAD has increased, because disorders with a genetic influence do not change fundamentally during such a short period of time. In summary, it can be assumed that the occurrence of social anxiety disorder remained relatively constant over time. Nevertheless, the results on genetics denote in reverse that environmental factors explain 40 to 70% of the variance in SAD. This issue should be outlined in the following chapter.

1.2 The Development and Maintenance of Social Anxiety Disorder: Cognitive Models

Like for many other mental disorders, researchers assume that the onset and retention of SAD is caused by an interplay of genetic and environmental factors (e.g. Butcher, Mineka, & Hooley, 2009). The first include the individual's variation of genes inherited by his or her parents, while the second might comprise negative life events, parenting style and aversive learning experiences as well as cognitive and attentional biases that are accompanied with it. Also, there are parameters which are considered to be mixtures of both, such as personality traits and temperament, which are partially the result of genetic factors and therefore relatively stable over time, but can be influenced by personal experiences (Eysenck & Eysenck, 1985). Albeit all of these fields have to be considered to gain a holistic knowledge on the etiology and maintenance of SAD, they are too complex to be dealt

with in just one dissertation. Therefore, a selection had to be made with the result that the focus of the current work was laid on cognitive processes in individuals with SAD, particularly on attentional processes and learning experiences. The following section briefly summarizes the most influential cognitive views on the development and maintenance of SAD.

1.2.1 Schema-driven processing in anxiety disorders (Beck et al., 1985)

Contemporary models of SAD highlight the role of cognitive processes in the maintenance of the disease (Beck, Emery, & Greenberg, 1985; Clark & Wells, 1995; Mogg & Bradley, 1998; Rapee & Heimberg, 1997). One of the first who emphasized the meaning of the mind's cognitions in determining behavior were Aaron Beck and his colleagues, who hypothesized that so-called *dysfunctional thoughts* have an important influence on an individual's emotion and behavior (Beck et al., 1985). These thoughts can be related to the self ("I am boring!") or to others ("The others won't like me, because I have nothing to say!"). As a consequence, individuals with SAD tend to expect contemptuousness and rejection in the interaction with others, which in turn leads to a feeling of being vulnerable in the presence of other people. Once the individuals are in such an anxious state, information processing is biased with regard to attention, memory, and interpretation in equal measure, in a way that ambiguous or dismissive reactions by others are noticed more often, better remembered and interpreted more negatively compared to positive reactions. Eventually, this might influence an individual's behavior to that effect that he or she might avoid social situations if possible (Beck et al., 1985; Beck, Emery, & Greenberg, 2005).

1.2.2 The cognitive model of Clark and Wells (1995)

Based on the idea of Beck (Beck et al., 1985), the information processing model by Clark and Wells assumes that individuals with SAD developed several dysfunctional beliefs of themselves and others due to past negative experiences (Clark & Wells, 1995). These thoughts might include exaggerated standards for social performance ("I must not stutter!"), which are even hard to hold for non-anxious individuals, as well as conditional beliefs about the consequences that are accompanied with deficient performance ("If I stutter, people will think I am stupid!"). Consequently, Clark and Wells propose four different processes which lead to the maintenance of the individuals' maladaptive beliefs: first, the perception of social situations as potentially dangerous leads to close *observation and monitoring* of the self. The thereby gained internal information is used to derive the – in most cases negative - impression that others might have of oneself, for example: "I feel anxious, so I must look anxious!" Accordingly, the attentional self-focus prevents the socially anxious individual from disconfirming their negative beliefs, for example by avoidance of eye-contact and being inattentive for the verbal or non-verbal feedback of the counterpart. Second, social situations

evoke a *hypervigilance* for and continuous checking of anxiety symptoms, which use so much cognitive capacity that they might induce an actual performance deficit. Also, the information processing is biased in a way that individuals with SAD are faster at detecting threatening or ambiguous social cues, which might be interpreted negatively. Third, individuals with SAD typically engage in *safety behaviors* to minimize fear. Examples for safety behaviors are the wearing of neutral clothing to avoid attention, taking drugs before social situations to feel less anxious, asking the dialog partner questions to keep the focus off of oneself or wearing scarfs to cover blushing. However, these strategies are a major cause of persisting anxiety, because if a social interaction turns out well, individuals with SAD do not attribute the outcome to their personal skills, but to the safety behavior. Fourth, socially anxious tend to show so called *post-event rumination*, during which they mentally review the last social situation in detail. Usually, they hereby focus on ambiguously successful or unsuccessful social encounters or past failures, with the consequence that they judge a situation to be more negatively than it actually was. As a result, their fear of future social interactions is reinforced (Clark & Wells, 1995).

1.2.3 The cognitive-behavioral model of Rapee and Heimberg (1997)

Only two years later, Rapee and Heimberg (Rapee & Heimberg, 1997) postulated a similar model (see Figure 1: The model of the generation and maintenance of anxiety in social/evaluative situations of Rapee and Heimberg. Reprinted from Behaviour Research and Therapy, Vol. 35, No. 8, Ronald M. Rapee & Richard G. Heimberg, A cognitive-behavioral model of anxiety in social phobia, pp. 741-756, 1997, with permission from Elsevier.), which begins with a hypothesis first made by Leary and colleagues in 1988 (Leary, Kowalski, & Campbell, 1988). The hypothesis states that individuals with SAD act on two assumptions: First, they presume that other people are inherently critical. Second, they believe it to be of the utmost importance to be liked and positively seen by others. Hence, if individuals with social anxiety encounter a social event, they build a mental representation of their image as presumably seen by others and at the same time focus their attention onto both the described internal representation and any perceived threat in the social environment, particularly indicators of negative evaluation or ridicule, such as signs of boredom or mocking in the audience. Furthermore, the individuals formulate a prediction of the performance standard which they expect the audience to have and compare it with their mental self-image, which is created by input retrieved form internal cues (e.g. physiological anxiety symptoms, proprioception), external cues (e.g. feedback from the audience) and long-term memory (e.g. past experiences). Based on the presumption that other people are scrutinizing by nature, it is likely that not only threatening, but also ambiguous or neutral external cues are negatively evaluated by socially anxious individuals, and that therefore, they are also more prone to remember negative past

experiences. Consequently, a discrepancy among the socially anxious' perception of the audience's evaluation of their performance (*actual self*) and the individuals' assumption according to the audience's standard for the evaluation of their performance (*ought self*) evolves. This in turn causes the perceived likelihood of negative evaluation by others, which further exacerbates the anxiety of social situations on a behavioral, cognitive and physiological level. The anxiety symptoms again influence the individuals' negative idea of how they are seen by others and thereby lead to the retention of a self-energizing downward spiral.

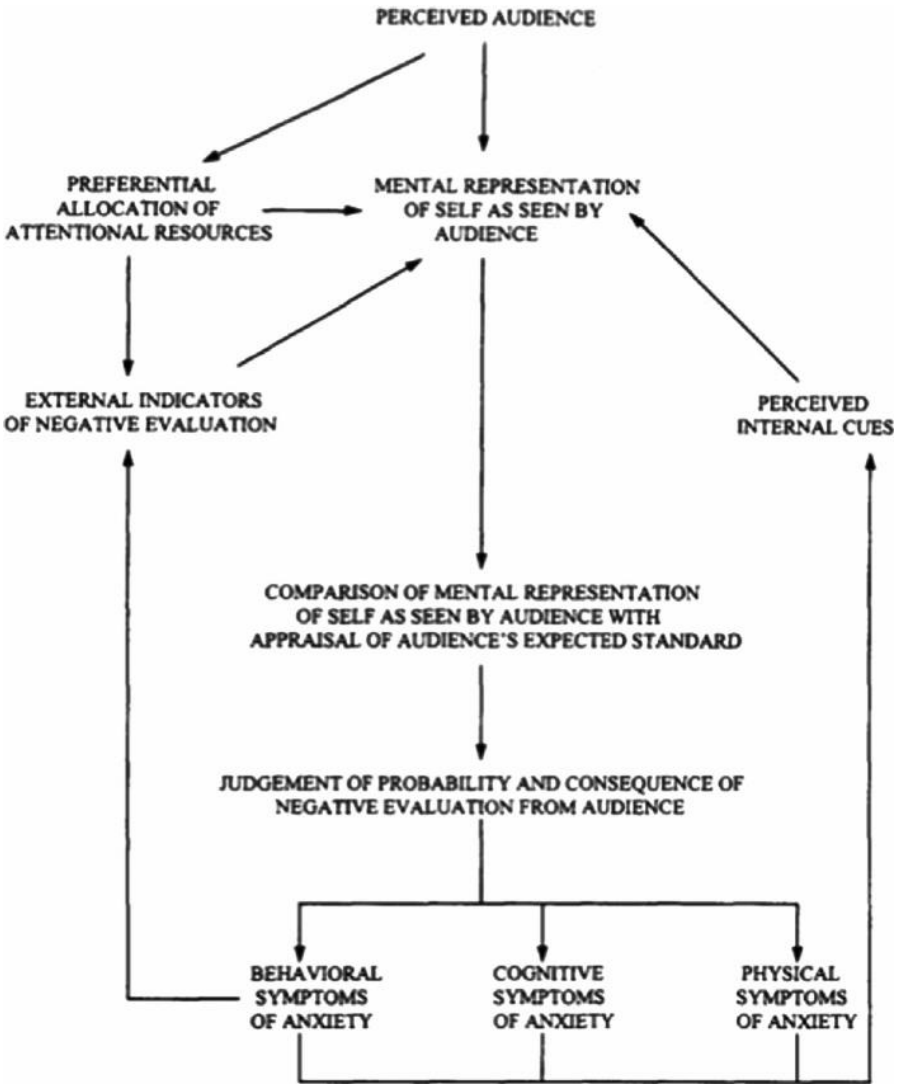

Figure 1: The model of the generation and maintenance of anxiety in social/evaluative situations of Rapee and Heimberg. Reprinted from Behaviour Research and Therapy, Vol. 35, No. 8, Ronald M. Rapee & Richard G. Heimberg, A cognitive-behavioral model of anxiety in social phobia, pp. 741-756, 1997, with permission from Elsevier.

1.2.4 The attentional control theory (ACT)

The attentional control theory (ACT) is an approach which deals with the effects of anxiety on cognitive performance (Eysenck, Derakshan, Santos, & Calvo, 2007). It hypothesizes that anxiety has a negative impact on cognitive performance, more specifically on the efficiency of the central executive, which is a part of Baddeley's working memory model with limited capacity (Baddeley, Baddeley, & Braddlely, 1986; Baddeley & Hitch, 1974). The authors explain this impairment as a misbalance between two attentional systems: a stimulus-driven or *bottom-up* system, which is influenced by salient information in the environment, and a goal-oriented or *top-down* system, which is driven by a person's current goals (Eysenck et al., 2007). If there is no threat to an individual's goals, the two systems mutually equilibrate each other, but if a goal gets threatened, the balance can be disrupted (Power & Dalgleish, 1997, 2015). According to the ACT, the hereby caused anxiety leads to the automatic allocation of attention to the source of threat with the aim to prepare an adequate defending response. As a consequence, this reflexive shift of attention might reduce volitional attentional control and make individuals lose track of their original goal, especially in situations where new stimuli pop up in the environment (Eysenck et al., 2007). In addition to reducing attentional control, anxiety thereby enhances attention to threat related stimuli.

Importantly, the model differentiates between processing *effectiveness* and processing *efficiency* even at primary stages of the ACT, as stated by Eysenck (Eysenck & Calvo, 1992; Eysenck & Derakshan, 2011; Eysenck et al., 2007). Performance effectiveness is defined as the quality of performance, measured by error rate, while processing efficiency relates to the relationship among performance effectiveness and the use of resources or effort. In other words, processing efficiency is high when performance effectiveness is high and the use of resources is low, and it is low when performance effectiveness is low but the use of resources is high (Eysenck & Derakshan, 2011). Therefore, the ACT assumes that anxiety impairs processing efficiency to a greater extent than performance effectiveness, which has been supported by several studies (as reviewed in Eysenck et al., 2007). Altogether, the ACT provides a comprehensive model of mechanisms determining the effects of anxiety on performance, which should be further investigated in study 1.

1.2.5 Interim Summary

The preceding section illustrates that the cognitive mechanisms involved in threat processing in SAD are explained by a diversity of views. The different approaches include the assumption that socially anxious individuals have dysfunctional thoughts or beliefs about themselves and others, recall threatening compared to neutral events from memory more easily (memory bias), pay more attention to threatening information (attentional bias) and are more likely to interpret neutral or

ambiguous stimuli as being threatening (interpretation bias) (Mathews & MacLeod, 1994; Van Bockstaele et al., 2014). The most common models of attentional (see 1.3), learning and memory biases (see 1.4) as well as empirical evidence for and against the different accounts will be introduced in more detail in the following chapters.

1.3 The Contribution of Deviant Attentional Processes to Social Anxiety and its Modulation by Emotions and Gaze Direction

1.3.1 Attentional biases in Social Anxiety

Several cognitive models assume that aberrations in attentional processes play a major role in SAD (Clark & Wells, 1995; Rapee & Heimberg, 1997). Especially biases in the processing of threat-related information seem to be a characteristic of these patients (e.g. Amir, Foa, & Coles, 1998; Beck et al., 1985; Mogg, Bradley, De Bono, & Painter, 1997; Öhman, 1986; Öhman & Soares, 1993; Williams, Watts, MacLeod, & Mathews, 1988), even when the threat is irrelevant for task performance (Lichtenstein-Vidne et al., 2017; Okon-Singer, 2018). Interestingly, albeit the scientific community agrees upon the idea that attentional biases exist in SAD, the assumptions about the nature of these biases strongly vary among research groups. Hence, evidence for and against the most important approaches is considered below.

1.3.1.1. Hypervigilance to threat

During their research to explore in which way individuals with anxiety disorders differ from healthy controls (HC) relating to their cognitive processes, scientists discovered that anxious individuals tend to reflexively direct their attention towards threatening information (Beck et al., 1985; Mathews & MacLeod, 1994; Williams et al., 1988). Actually, this finding was corroborated by studies detecting that the emotional evaluation of stimuli could even occur in the absence of awareness, which means it was carried out at a very early stage of processing (LeDoux, 1995; Öhman & Soares, 1994). Hence, researchers supposed that anxious individuals had an attentional system which was abnormally sensitive to threat-related stimuli (Eysenck & Calvo, 1992; Williams et al., 1988).

In this context, Eysenck posited an influential model on anxiety, in which he stated that an attentional bias for threat is a cognitive vulnerability factor for the development of anxiety disorders (Eysenck, 1997; Eysenck, 2014; Eysenck & Calvo, 1992). He defined the attentional bias as *hypervigilance*, which comprised not only a propensity to attend selectively to threat-related rather than neutral stimuli, as it is often used in the present literature. Eysenck also understood it as a

general distractibility to attend to any task-irrelevant stimuli, a high rate of environmental scanning, a broadening of attention prior to the detection of the target stimulus and a narrow attentional focus after the stimulus has been detected (Eysenck, 2013; Eysenck & Calvo, 1992). In the framework of a diathesis-stress-model, Eysenck assumed that highly anxious individuals only develop a disorder if they are exposed to stressful life events, but that their scanning behavior of the environment increases the chance to detect threatening stimuli and thereby makes the onset of a clinical disorder more likely.

To test the hypervigilance hypothesis, a lot of experimental studies using different paradigms were conducted. Indeed, there were many which found results in favor of the hypervigilance hypothesis, for example, that high socially anxious individuals reacted faster to probes following social threat words compared to neutral or physical threat words in a dot-probe paradigm (Asmundson & Stein, 1994), showed longer latencies for social rather than physical threat words in a revised Stroop color-naming task (Hope, Rapee, Heimberg, & Dombeck, 1990; Mattia, Heimberg, & Hope, 1993), recognized more critical than accepting faces in an unexpected recognition task (Lundh & Öst, 1996) and responded faster to probes occurring in the location of masked threat compared to neutral faces in a modified visual probe task (Mogg & Bradley, 2002). However, there is also evidence suggesting not only a greater orienting toward threat, but to emotional stimuli in general (Garner, Mogg, & Bradley, 2006; Wieser, Pauli, & Mühlberger, 2009).

1.3.1.2. Avoidance of threat and self-focused attention

In contrast, some research findings seem not to fit the picture, but rather suggest quite the opposite idea, namely that social anxiety is associated with an *avoidance* of threat information (Amir et al., 1996; Chen, Ehlers, Clark, & Mansell, 2002; Mansell, Clark, Ehlers, & Chen, 1999). These results fit approaches which stress the role of an internal focus of attention (or *self-focused attention*) in the development and maintenance of SAD (Hartman, 1983; Hope, Gansler, & Heimberg, 1989) and is also in line with recent cognitive models of social anxiety (Clark & Wells, 1995; Rapee & Heimberg, 1997). Self-focused attention, however, prohibits socially anxious individuals from being attentive to environmental information or feedback, and might cause a social performance deficit and manifest negative beliefs about the self.

Further evidence in compliance with the avoidance theory provided a study showing that the interference effect in the Stroop task (i.e. socially anxious are slower at color-naming of socially threatening compared to non-threatening words) reverses under high anxiety, such as before giving a speech. The authors interpret this finding as the ability of socially anxious to override attentional biases with regard to social threat words when they are highly anxious (Amir et al., 1996). Another study found that patients with SAD were faster at detecting the probe in a modified dot probe

paradigm when it appeared in the location of household objects compared to faces no matter what kind of expression (positive, neutral or negative) they had (Chen et al., 2002). The authors argue that these findings are a hint for reduced processing of external social cues in individuals with SAD. Also, they propose that high socially anxious individuals avoid detailed processing of social cues when they are in an anxious state, and disengage the attention from threat stimuli and attend non-social cues instead to decrease discomfort.

1.3.1.3. The vigilance-avoidance hypothesis

Due to the contradictory results in literature, researchers proposed that the pattern of attentional biases in SAD is more complex than assumed to begin with. They suggested that one should not only look at the initial response to threat stimuli in anxious individuals, but investigate the time course of their attentional processes (Mogg et al., 1997). Based on findings that anxious individuals initially direct their attention towards the threatening stimulus (*vigilance)*, but in a second step avoid the stimulus to prevent its detailed processing (*avoidance*), the *vigilance-avoidance hypothesis* was stated (Mogg, Bradley, Miles, & Dixon, 2004; Mogg, Mathews, & Weinman, 1987). Researchers explain the vigilance-avoidance pattern as an attempt of anxious individuals to reduce their anxiety, but suggest that the opposite is the case: as avoidance behavior prevents habituation to or the objective evaluation of an ambiguous stimulus (Rachman, 1980) - for example, the reappraisal of a dialog partner's yawning as a sign of fatigue rather than a lack of interest - that stimulus retains its fear-eliciting properties. In this way, the anxious state of the individual is maintained. To date, there is an established body of evidence speaking in favor of an enhanced initial attentional bias to threat stimuli in anxiety (for a review, see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007), while study results for threat avoidance are more inconsistent (as reviewed in Cisler & Koster, 2010). With regard to SAD in particular, studies investigating the vigilance-avoidance-hypothesis are limited. However, one study supported the view. It found that patients with generalized SAD showed an initial activation of threat-relevant information in response to sentences with socially relevant homographs, followed by an enhanced avoidance of such information (Amir et al., 1998).

1.3.1.4. Disengagement deficit

As already suggested by Rapee & Heimberg (Rapee & Heimberg, 1997), several researchers propose that anxiety has not only an influence on the initial allocation of attention in response to threat cues, but rather a strong effect on modulating the maintenance of attention on the source of threat, resulting in a reduced ability to disengage from social threat cues (Amir, Elias, Klumpp, & Przeworski, 2003; Fox et al., 2000). This effect is referred to as *disengagement deficit* and explains the maintenance of anxiety disorders by an excessive occupation with the threat stimulus combined

with a simultaneous reduction of available resources for actively coping with the threat (Fox, Russo, Bowles, & Dutton, 2001; Koster, Crombez, Verschuere, & De Houwer, 2004). Research testing the hypothesis found evidence for the difficulty in disengagement among anxious participants using the spatial cueing task (Fox et al., 2001; Fox, Russo, & Dutton, 2002), the visual search task (Gilboa-Schechtman, Foa, & Amir, 1999; Miltner, Krieschel, Hecht, Trippe, & Weiss, 2004) and the dot probe task (Koster, Crombez, Verschuere, & De Houwer, 2006).

1.3.1.5. Interim Summary

Regarding the different models of attention and cognitive correlates of anxiety, various aberrations in threat processing are suggested to be associated with anxiety, such as hypervigilance to threat, avoidance of threat, initially vigilance followed by avoidance and a disengagement deficit. Some researchers explain the discrepancy in the findings by the application of inapplicable research methods. They argue that some of the paradigms used to measure attentional processes at the beginning of anxiety research, such as the Stroop task, the dot-probe task and the visual search task, were not adequate for this purpose, because they were no direct measure of attention, but only measured reaction times (Schofield, Johnson, Inhoff, & Coles, 2012). To overcome these methodological problems, researchers focused on another paradigm in their recent work: the measurement of eye movements. The advantage of this method is that it allows a direct and overt measure of visual attention, as the allocation of attention and eye-movements are strongly associated with each other (Findlay & Gilchrist, 2003).

1.3.2 Measuring the temporal course of visual attention: Eye-tracking

1.3.2.1. The correlation of eye-movements and attention

As attention is a very complex construct including cognitive and behavioral processes, attempts to define it vary, but most researchers agree that it incorporates the allocation of limited resources to discrete aspects of information in the environment while other aspects are ignored (e.g. Anderson, 2005). A very popular metaphor of attention is the comparison with a spotlight with an adjustable beam (Norman, 1968). With regard to visual attention, it has been proposed that it strongly correlates with the movement of the eyes (Hofmann, Gerlach, Wender, & Roth, 1997; Rizzolatti, Riggio, Dascola, & Umiltá, 1987). Albeit it is well known today that attention does not necessarily require the movement of the eyes – a phenomenon referred to as “covert attention” (Posner, 1980; von Helmholtz, 1866) – the two go along in most cases (Klein, Kingstone, & Pontefract, 1992). Hence, the measurement of eye-movements, the so-called *eye-tracking*, allows the online recording of locations onto which the current visual attention lies and of attentional shifts via

saccadic eye-movements, which typically occur at a rate of 3-4 per second (Becker, 1989; Hoffman, 1998).

There are already several eye-tracking studies showing that eye-movement and the allocation of attention are interconnected (see Findlay & Gilchrist, 2003 for a review). In contrast to the earlier described classical paradigms, which only capture short excerpts of attention, it permits the investigation of early and late components of attention (Weierich, Treat, & Hollingworth, 2008), the examination of engagement and disengagement processes (Salemink, van den Hout, & Kindt, 2007), and testing of the vigilance-avoidance hypothesis (Henderson, 1992; Schofield et al., 2012). Therefore, eye-tracking is a valuable method to record visual attention processes.

1.3.2.2. Eye-tracking studies in Social Anxiety

Due to its methodological advantages, there are already a number of studies investigating attention in social anxiety with eye-tracking to date. One study recorded the subject's visual scan-paths to different facial expressions (angry, sad, neutral and happy) to investigate how participants with SAD process different facial expressions (Horley, Williams, Gonsalvez, & Gordon, 2003). Previous examinations in healthy participants found that the scan-paths usually follows a triangular pattern with fixations on the most salient facial features, namely the eyes and the mouth region (Walker-Smith, Gale, & Findlay, 1977). In contrast, Horley and colleagues detected that patients with SAD displayed *hyperscanning*, which is characterized by an enhanced raw scan-path length and a reduced number of abbreviated fixations, as well as avoidance of the eye-region compared to controls in response to emotional faces (Horley et al., 2003). Also, it was found that this effect was especially pronounced for angry faces (Horley, Williams, Gonsalvez, & Gordon, 2004). A second study examined eye movements in response to facial expressions (angry, neutral and happy) and objects under a no-stress and a social stress (giving a speech) situation in individuals with high (HSA) and low social anxiety (LSA) (Garner et al., 2006). The study revealed that HSA individuals compared to LSA demonstrated a stronger orientation towards social stimuli compared to objects in the no-stress condition. Under social-stress, right before giving a speech, HSA showed a faster orientation to emotional compared to neutral faces, followed by disengagement. The authors interpret these findings to be consistent with a two-stage pattern of attentional bias as described in the vigilance-avoidance hypothesis. A third study explored the time-course of attentional biases in patients with SAD and HC by showing them a) pairs of objects and faces or b) emotional (angry and happy) and neutral faces (Gamble & Rapee, 2010). Analyses yielded that SAD patients in comparison to controls were vigilant for angry compared to neutral faces, but only during the first 500 ms of stimulus presentation. Also, both SAD patients and controls were vigilant for happy compared to neutral

faces. The authors suggest that social phobics show hypervigilance to social threat stimuli in early, but not sustained stages of attentional processing.

Furthermore, there is research examining visual attention in non-clinical social anxiousness. For example, a study made participants view actors with happy or angry facial expressions in a virtual elevator situation and discovered that high socially anxious individuals initially avoided both emotional facial expressions compared to low anxious individuals, which is in contrast to an initial hypervigilance towards threat (Mühlberger, Wieser, & Pauli, 2008). Another experiment showed their low (LSA), medium (MSA) and high (HSA) socially anxious participants animated movie clips of actors with neutral facial expression and varied gaze direction (direct vs. averted). Results revealed that HSA displayed a stronger cardiac acceleration in response to faces with direct gaze, indicating that direct gaze may be fear-relevant for them, but surprisingly also fixated the eye region longer than MSA and LSA (Wieser, Pauli, Alpers, & Mühlberger, 2009). Finally, there is a new approach which argues that the significant findings with regard to social stimuli are not the result of social phobics being hypervigilant to angry faces, but of HC preferentially attending to happy faces and avoiding angry ones instead of (Schofield, Inhoff, & Coles, 2013). Overall, more research is needed on visual attention in SAD due to the contradictory results. Also, the role of gaze perception in SAD should be further clarified.

1.3.2.3. Testing attentional control: The antisaccade paradigm

An established research method to measure attentional control is the *antisaccade paradigm* (Hallett, 1978). In this tasks, participants first have to look at a fixation point, which is followed by one of two cues specifying the nature of the upcoming task: one serves as a signal to look directly at the consequently in the periphery presented target stimulus (prosaccade), while the other informs the subject to look at the opposite direction, mirroring the position of the target stimulus (antisaccade). Due to the sudden onset of the peripheral target stimuli, prosaccades are considered to be measures for reflexive, non-volitional attentional processes (*bottom-up* driven). Contrary, antisaccades serve as measures for volitional control (*top-down* driven), as they demand executive functions to inhibit the automatically triggered prosaccade and actively program the eye-movement to the mirror-image of the stimulus (e.g. Everling & Fischer, 1998). *Inhibition*, defined as the ability to deliberately inhibit a dominant, automatic, or pre-potent response when necessary (Miyake et al., 2000), is crucial in everyday life to follow internal goals and not being driven by stimuli appearing in the environment. In the antisaccade task, inhibition is measured via latency and error rates.

Interestingly, there is a growing body of evidence showing that several psychiatric and neurological disorders positively correlate with an impairment to inhibit prosaccades, such as schizophrenia (Fukushima et al., 1988), ADHD (Klein, Raschke, & Brandenbusch, 2003; Nigg, Butler,

Huang-Pollock, & Henderson, 2002), bipolar disorder (Gooding & Tallent, 2001) and frontal lobe damage (Guitton, Buchtel, & Douglas, 1985) (for a review, see Hutton & Ettinger, 2006). Healthy participants typically show error rates of about 20% (Ettinger et al., 2005; Everling & Fischer, 1998), while those of patients are significantly higher, for example, among 25% and 70% in schizophrenia, which is to date the best studied group with regard to the antisaccade paradigm (Broerse, Crawford, & den Boer, 2001; Hutton & Ettinger, 2006). In matters of social anxiety, the evidence is contradictory: one study also found significantly enhanced error rates in HSA (25%) compared to LSA (18%) individuals (Wieser, Pauli, & Mühlberger, 2009), while two investigations did not detect any group differences with regard to the error rate in the antisaccade task (Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009; Sluis, Boschen, Neumann, & Murphy, 2017). Overall, there are only a few studies investigating SAD with the antisaccade task, and further research is required to clarify if individuals with SAD show an inhibition deficit in attentional control compared to HC.

1.3.3 Avoidance of gaze in Social anxiety

Eye-contact is one of the most important sources of information during social interactions. It provides knowledge on several aspects, such as to whom a message is sent, to signal intimacy, to regulate turn-taking during conversations or to demonstrate submissive behavior as well as power and social control (see Kleinke, 1986, for a review). Dependent on the context of a situation, eye-contact can be a sign of kindness or interest in the other person, but also of anger and hostility (Abele, 1986; Driver IV et al., 1999; Emery, 2000).

Moreover, the gaze direction has an impact on the processing of emotional facial expressions. Studies demonstrated that emotions which typically go along with approach behavior, such as happiness or anger, can be more easily processed in combination with direct gaze (Hess, Adams, & Kleck, 2007), while emotional expressions which are often accompanied by avoidance, such as fear of sadness, are better processed in faces with averted gaze (Adams & Kleck, 2003, 2005), especially when the observer has high levels of trait anxiety (Fox, Mathews, Calder, & Yiend, 2007; Tipples, 2006). In addition, studies demonstrated that direct gaze is associated with enhanced levels of autonomic activation and higher arousal ratings in both healthy and socially anxious participants (Kleinke, 1986; Wieser, Pauli, Alpers, et al., 2009).

While healthy participants typically pay attention to the eye-region of their interactional partners, clinical observations as well as experimental research suggest that *avoidance of eye-contact* is a key characteristic of individuals with SAD (Horley et al., 2003; Howell, Zibulsky, Srivastav, & Weeks, 2016; Moukheiber et al., 2010; Schneier, Rodebaugh, Blanco, Lewin, & Liebowitz, 2011; Terburg et al., 2016; Van Dillen, Enter, Peters, van Dijk, & Rotteveel, 2017; Weeks, Howell, & Goldin, 2013). For example, studies showed that they had less eye-contact with their dialog partner

compared to low socially anxious individuals during interviews (Daly, 1978), looked less frequently at their audience while giving a speech (Eves & Marks, 1991), exhibited less gaze fixations on the eyes of faces during eye-tracking studies (Horley et al., 2003; Horley et al., 2004; Moukheiber et al., 2010) and showed less eye-contact during social conversations (Baker & Edelmann, 2002). Also, analysis of the Liebowitz Social Anxiety Scale (LSAS) (Liebowitz, 1987) revealed that there was a positive correlation between the item "fear of eye-contact" and the severity of SAD (Baker & Edelmann, 2002; Safren et al., 1999). Lastly, a recent study found that patients with SAD showed stronger gaze avoidance compared to controls in response to simulated positive and negative social encounters (Weeks et al., 2013).

As eye-contact is one of the most important social signals which provides information on an individual's identity, intentions, and emotional and mental states (Emery, 2000), not paying attention or even avoiding it can have negative consequences for the socially anxious individual. For example, social information might be missed or dialog partners could misinterpret the avoidance of eye-contact and a sign of disinterest and therefore show no longer motivation to keep up the conversation with the anxious individual, leading to a negative experience confirming the patient's believes. Due to the fact that avoidance of eye-contact may contribute to the onset and retention of SAD, it requires further investigation.

1.3.4 Neuronal correlates of anxiety and attentional control

Despite its major role in public health, the neurobiology of SAD is still poorly understood (Bell, Malizia, & Nutt, 1999). Imaging studies on anxiety in general indicated that it goes along with a dysfunction in a circuit of cortical and subcortical structures, including the amygdala, which plays a primary role in the processing of emotional reactions, and both the dorsolateral (DLPFC) and the ventrolateral prefrontal cortex (VLPFC), which are – amongst others – responsible for the top-down regulation of attention (Bishop, Duncan, Brett, & Lawrence, 2004; Shin & Liberzon, 2010; Taylor & Whalen, 2015). Highly anxious individuals are characterized by enhanced amygdala and reduced DLPFC and VLPFC activity (Bishop et al., 2004; Bishop, 2007). There are also several investigations on SAD in particular, which found a hyperactivity of the amygdala during the processing of negative emotional stimuli or the anticipation of stressful situations, such as giving a speech (Lorberbaum et al., 2004; Phan, Fitzgerald, Nathan, & Tancer, 2006; Stein, Goldin, Sareen, Zorrilla, & Brown, 2002; Straube, Kolassa, Glauer, Mentzel, & Miltner, 2004).

Also, it has been shown that high compared to low anxious individuals display reduced activity in the anterior cingulate cortex (ACC) and prefrontal cortex (PFC) in expectancy of threatening face stimuli, which is interpreted as a reduced recruitment of brain areas, which correlate with cognitive and attentional control (Carter et al., 1998; MacDonald, Cohen, Stenger, &

Carter, 2000). Overall, the described fear network is associated with the detection and evaluation of threat cues, emotional responses and their regulation, and fear learning and fear extinction (LeDoux, 2012). Neuroimaging studies measuring attentional control via antisaccade performance in healthy individuals detected that this task recruits a fronto-parieto-subcortical network including the ACC, lateral PFC, the frontal eye fields (FEF), the posterior parietal cortex and the thalamus (Müri et al., 1998; O'Driscoll et al., 1995; Sweeney et al., 1996). Hence, this network shows a great overlap with brain regions which are involved in attentional control (Ettinger et al., 2007). Event-related functional magnetic resonance imaging (fMRI) research further disentangled that, for example, activity is higher in the FEF during the preparation for anti- compared to prosaccades, which is interpreted as an additional requirement of preparation (Connolly, Goodale, Menon, & Munoz, 2002). Also, patients with acquired brain lesions were subject to research with the aim to identify the brain regions involved in antisaccades performance. These investigations revealed that DLPFC lesions led to increased error rates, while FEF lesions caused prolonged antisaccades latencies (Pierrot-Deseilligny, Ploner, Müri, Gaymard, & Rivaud-Pechoux, 2002). Moreover, performance deficits have been observed after ventral PFC and ACC lesions (Gaymard et al., 1998; Walker, Husain, Hodgson, Harrison, & Kennard, 1998). On the whole, the results of most neuroimaging studies support the finding of behavioral and reaction time studies that individuals with anxiety disorders compared to HC are characterized by an impairment of attentional control, indicated by activity enhancement and decrement, respectively, in brain areas known to be responsible for attentional control.

1.3.5 Summary and conclusion

The method of eye-tracking overcame the prior methodological problem of only being able to indirectly measure attention and was more and more established over the years (e.g. Findlay & Gilchrist, 2003; Garner et al., 2006; Schofield et al., 2012; Wieser, Pauli, Weyers, Alpers, & Mühlberger, 2009). A commonly applied task to measure attentional control, which can easily be combined with eye-tracking, is the antisaccade paradigm (Hallett, 1978). It is suitable to test for inhibitory deficits, which are supposed to be a characteristic of SAD, because it requires both the inhibition of the orienting reactions towards a new stimuli and the volitional programming of an antisaccade instead. However, eye-tracking studies investigating attentional control in social anxiety are still rare and the results inconclusive, which is why more research on this topic is needed, and previous experimental designs might profit from some changes. First, all eye-tracking studies applying the antisaccade task tested analogue samples instead of clinically diagnosed patients (Derakshan et al., 2009; Sluis et al., 2017; Wieser, Pauli, & Mühlberger, 2009). Most likely, this can be explained by the difficulty to recruit a sufficient sample of SAD patients as they fear performance situations. However, SAD patients should directly be investigated to make valid predications upon

this disorder. Second, the stimulus material of former studies was either not disorder-relevant (Derakshan et al., 2009) or consisted of computer animated instead of real photographs (Wieser, Pauli, & Mühlberger, 2009). These two issues should be addressed in study 1 of this thesis by investigating clinically diagnosed SAD patients and using photographs of real faces as stimulus material. Furthermore, another important aspect of social interactions should be examined, namely the influence of gaze direction on attentional processes in SAD. As illustrated in section 1.3.3, eye-contact plays a very important role during social interactions. Though, there is evidence that patients with SAD avoid direct gaze, which may lead to a significant loss of information that contributes to the maintenance of the disorder. Hence, it was the aim of study 1 to test whether attentional control in response to emotional faces was further modulated by their gaze direction. For the whole study, see chapter 2.

However, aberrations in attentional processes are not the only cognitive mechanisms which are discussed in conjunction with SAD. A second approach regards deviations in associative fear learning processes to be a key component in the onset and retention of SAD. Therefore, the next chapter is dedicated to this view and its current state of research.

1.4 On the Role of Associative Fear Learning in the Etiology of Social Anxiety

This chapter starts with a short overview on two important principles of associative learning, namely fear conditioning and fear generalization. After addressing this topic, the most common associative fear learning theories will be introduced and empirical evidence from fear generalization research, particularly in due consideration of SAD, is summarized. Subsequently, the neuronal processes underlying fear generalization and a recent model of fear generalization are presented. Finally, a conclusion with regard to future research on this topic will be drawn.

1.4.1 Fear conditioning and fear generalization

Many etiological approaches of anxiety disorders suggest *classical fear conditioning* to be a good translational model of the acquisition of clinically relevant fear (Mineka & Zinbarg, 2006). Classical fear conditioning describes the process through which a neutral *conditioned stimulus (CS)* acquires the ability to elicit fear (*CR: conditioned response*) following its co-occurrence with an aversive *unconditioned stimulus (US)* (Pavlov, 1927). The first popular experiment addressing fear conditioning was conducted in 1920 by John Watson and Rosalie Rayner. In their “Little Albert” experiment – a human case study on a nine-month old baby – the experimenters first exposed infant Albert to a white rat and made a very loud noise every time he touched the animal. In a second step, they observed Albert’s response to the rat alone and found him crying and distressed without any

noise being present (Watson & Rayner, 1920). They concluded that the pairing of the originally neutral stimulus (rat) with an aversive stimulus (loud noise) could evoke a fear reaction in response to a primary harmless object, and thereby serve as a model for the development of phobias. Due to its non-experimental design and its disputable ethical standards - Little Albert's conditioned fear reaction was never extinguished – Watson's and Rayner's work was harshly criticized (e.g. Harris, 1979). Nonetheless, it cleared the way for conditioning experiments in humans as well as it put emphasis on the interrelation among learning experiences and the development of anxiety disorders. However, subsequent conditioning researchers decided to focus on animal research for the time being, as seen first and foremost in the work of Ivan Pavlov and his dogs (Pavlov, 1927).

Aside from the fact that Little Albert feared rats after the conditioning procedure, Watson and Rayner observed that the infant also feared other white and furry objects, such as rabbits, some dogs and a Santa Claus mask (Watson & Rayner, 1920). This process of transmitting Little Albert's fear from the rat to similar objects is referred to as *generalization*, and was later confirmed in many other studies examining classical as well as operant conditioning (e.g. Hull, 1943; Pavlov, 1927). Researchers detected that fear learning was rarely limited to the specific US-CS combination which was conditioned in the first place, but could be broadened to both stimuli (*stimulus generalization*) and situations (*context generalization*) that were qualitatively similar to the original association cues (CSs) (as reviewed in Bouton, 2004; Dymond, Dunsmoor, Vervliet, Roche, & Hermans, 2015).

To a certain degree, fear generalization is reasonable, because potentially threatening stimuli do not necessarily look exactly the same in every situation. For example, after getting stung by a wasp, an individual might learn that not only that particular wasp, but other wasps or similar looking insects, such as bees, can cause painful bites, too (stimulus generalization). To this extent, generalization is adaptive. Moreover, in the case of fear compared to other emotions - when a stimulus predicts an aversive outcome - it makes even more sense to show generalization, because a miss is more costly than a false alarm (Dunsmoor & Paz, 2015). Likewise, it is essential to discriminate among different stimuli in order to conserve resources and diminish redundant fight-or-flight reactions or avoidance behavior when there is no threat. In our example, for instance, it would be exaggerated to broaden the fear of wasps to insects in general, as many of them are harmless. Avoiding all of them would cause unnecessary costs and no benefit.

Summing up, learning experiences seem to play a major role in the genesis and maintenance of anxiety and anxiety disorders, and thus may also play a role in SAD. Differences in the way information is absorbed, processed, stored and retrieved may later decide whether an individual develops an anxiety disorder or not.

1.4.2 Associative fear learning theories

Since decades, researchers have tried to identify at which point patients with anxiety disorders deviate from HC in fear learning processes. According to associative fear learning theories, enhanced conditionability, resistance to extinction, inhibition deficits and overgeneralization of conditioned fear are discussed as possible factors (Briscione, Jovanovic, & Norrholm, 2014; Duits et al., 2015; Lissek et al., 2005). In contrast, non-associative accounts postulate the existence of a limited number of evolutionary-important, innate fears and claim that changes in behavior take place without conditioning, but, for example, through habituation or sensitization processes (Poulton & Menzies, 2002). At present, associative fear learning relating to anxiety disorders is in the spotlight of research, which is why it is gets the most attention in the following chapters. Empirical evidence speaking in favor or against the different conditioning approaches is summarized, with a special emphasis on SAD and fear generalization. The interested reader who wants to learn more about non-associative accounts is at this point referred to the aforementioned detailed review article (Poulton & Menzies, 2002).

1.4.2.1. Enhanced conditionability

One account trying to explain the etiology of anxiety disorders is *enhanced conditionability*, which describes an increased ability to associate an US with a CS. According to this theory, individuals with anxiety disorders are predisposed to acquire conditioned fear responses, which makes it later more difficult to extinct these strong associations. A study comparing patients with post-traumatic stress disorder (PTSD) and trauma-exposed HC found that patients were easier conditioned to the CS, which was expressed in higher differential heart rate, EMG and skin conductance responses, compared to controls (Orr et al., 2000). A further study on PTDS supported these findings (Wessa & Flor, 2007). Also, a meta-analysis of fear conditioning studies detected a modest elevation in the acquisition of fear in anxiety patients (Lissek et al., 2005). On the contrary, there are several studies which did not find enhanced fear conditionability in anxious individuals, such as panic disorder (PD) (Michael, Blechert, Vriends, Margraf, & Wilhelm, 2007) or patients with specific phobias when conditioned to non-feared but fear-relevant animal stimuli (Soares & Öhman, 1993).

With regard to SAD in particular, the results of conditioning studies are mixed. One study investigating conditioning processes with disorder-relevant stimuli found facilitated acquisition of fear responses measured by fear- potentiated startle (FPS) in SAD patients compared to HC (Lissek, Levenson, et al., 2008). Furthermore, a second study which examined healthy participants during a social conditioning paradigm observed a positive correlation between social anxiety (measured via SPIN scores) on the neural (activation in the left amygdala and hippocampus) as well as on the subjective level (valence and fear ratings) (Pejic, Hermann, Vaitl, & Stark, 2011). In contrast, a study

examining healthy participants with high and low levels of social anxiety using neutral faces (CS) paired with auditory insults, compliments of neutral comments (US) as stimuli did not find differences in conditionability in participants with high compared to low levels of social anxiety (Ahrens, Mühlberger, Pauli, & Wieser, 2014). In an fMRI study that compared individuals with SAD with HC using neutral facial expressions as CS and a negative odor as US, researchers also detected no group differences on a behavioral level (valence ratings) during acquisition. In fact, groups differed in fMRI data: SAD patients show enhanced activity in the amygdala and the hippocampus in response to the reinforced danger (CS+) compared to the non-reinforced safety cue (CS-), whereas an opposite decrease was revealed in the control group (Schneider et al., 1999). However, the authors did not interpret this result as enhanced conditionability, but a delayed habituation, as a repetitive presentation of the same stimuli can cause a rapid habituation (a signal decrease) of the amygdala in HC (LeDoux, 1995). Furthermore, the results of a study using neutral faces (CS) and painful pressure (US) indicated that not social phobics, but HC showed enhanced conditioning during acquisition (Veit et al., 2002). Admittedly, one has to take into consideration that they only examined very small sample sizes (seven healthy participants and four patients with SAD), which is why results should be interpreted with caution. Moreover, a study using neutral faces and aversive odors as CS and US, respectively, did not find evidence for an enhanced conditionability in social phobics (Hermann, Ziegler, Birbaumer, & Flor, 2002). They rather showed an increased US expectancy and delayed extinction which will be discussed in the following paragraphs.

1.4.2.2. Resistance to extinction

Understanding the underlying processes of *extinction* riddles the scientific community since decades. Definitions have been repeatedly revised over the years, and still new knowledge is gained every year. First, it is important to note that against conventional expectations, extinction does not equal forgetting. It is not sufficient that time passes by to observe extinction, particularly not in the case of disproportionately solid fear memories, because it requires the presentation of the CS in the absence of the US (Myers & Davis, 2007). When Pavlov discovered the *extinction* phenomenon, he described it as a procedure in which "…the positive conditioned stimulus is temporarily transformed into a negative or inhibitory one by the simple method of repeating it several times in succession without reinforcement" (Pavlov, 1927, p. 68). Consequently, it was assumed that there is just one memory trace for the association of two stimuli, which can be either strengthened through multiple pairings of CS and US (conditioning) or weakened through single presentations of the CS (extinction training), meaning extinction training should result in unlearning of the previously acquired CS-US-association (e.g. Rescorla, 1972). However, subsequent studies found that extinguished fear responses were not permanent, but returned under certain circumstances, for example with the

passage of time (spontaneous recovery), when participants were re-exposed to the US alone (reinstatement), or when the conditioned stimulus was presented in a new context (renewal) (for a review, see Myers & Davis, 2007). This observation served as evidence that extinction training does not erase fear memories, but instead builds a new inhibitory memory which can become strong enough to suppress the competing expression of the previously acquired fear response (e.g. Bouton, 1993, 2004). With regard to anxiety disorders, it seems plausible that spontaneous recovery, reinstatement and renewal are more pronounced compared to healthy control participants.

Deficits in or resistance to extinction in the absence of threat can bring on the persistence of fear in situations when it is no longer adaptive, which is why it is discussed as a characteristic trait of individuals with anxiety disorders (e.g. Eysenck, 1981). Interestingly, Pavlov has already made the observation that nervous dogs show slower extinction than quiet, more even-tempered dogs, and noted: "First among these [conditions the extinction rate depends on] come any individual peculiarities of the nervous organization of the animal […]. In excitable dogs, the reflexes are mostly slow of extinction, but in quiet animals extinction is rapid" (Pavlov, 1927, p. 51). A considerable amount of fear conditioning studies in humans has been conducted ever since. Results of a meta-analysis including 20 fear conditioning studies in anxiety patients revealed in line with Pavlov's observation that also anxious humans are more resistant to extinction (Lissek et al., 2005). It has to be noted, though, that most of these effects were measured in *single-cue conditioning* paradigms, in which only danger and no safety cues are presented as in *differential conditioning*. Yet, a recent meta-analysis including 44 studies confirmed the prior finding that anxiety patients exhibit increased fear responses to the CS+ during extinction which might indicate resistance to or delayed extinction (Duits et al., 2015).

There are only a few studies testing resistance to extinction in SAD. One study investigating patients with anxiety disorders including five individuals with SAD found that patients showed slower extinction in their skin conductance response than controls in reaction to angry compared to neutral facial expression (Pitman & Orr, 1986). Another study detected that social phobics compared to controls showed delayed extinction to neutral faces that had been paired with an aversive odor, measured as well in skin conductance response (Hermann et al., 2002). Contrary, a conditioning study with fMRI did not discover any differences between SAD patients and HC with regard to fear extinction (Schneider et al., 1999). Further research is needed to clear the role of aberrant extinction processes in the etiology of SAD.

1.4.2.3. Inhibition deficit & impaired discrimination learning

As discussed in the previous chapter, an extinction deficit can result from *difficulties in inhibitory learning*. Conditioned fear inhibition describes the process of differentiating between

danger (CS+: paired with aversive US) and safety cue (CS-: single presentation) by suppressing the fear response in the presence of the latter stimulus. Accordingly, individuals with anxiety disorders might show fear responses in the absence of threat. Interestingly, the idea that individuals suffering from anxiety disorders have a failure to inhibit fear is not restricted to extinction, but may as well apply to the acquisition phase (Davis, Falls, & Gewirtz, 2000). Support for this account stems from studies which found enhanced fear responses to safety cues in individuals with anxiety disorders (Jovanovic et al., 2010; Peri, Ben-Shakhar, Orr, & Shalev, 2000) and individuals with high-levels of anxiety (Grillon & Ameli, 2001) compared to controls.

Another explanation for the observation that individuals with anxiety disorders exhibit smaller differences in fear responses to the danger and safety signals than healthy individuals was postulated by Grillon (Grillon, 2002). He suggests that anxious individuals show impaired acquisition of the conditioned fear response due to *associative learning deficits*. Under regular circumstances, the initial presentation of the US during fear conditioning is unpredictable, which is why fear generalizes to the surrounding contextual cues. With an increased number of CS-US pairings, individuals learn to identify the danger signal, and fear to the context is inhibited. However, if individuals with anxiety disorders are unable to learn the contingency among CS+ and US, it enhances uncertainty about what is happening next. As anxious individuals are especially apprehensive about unpredictability, Grillon posits that their anxiety is enhanced, which leads to a decreased memory performance (Grillon, 2002; Grillon & Morgan III, 1999). The idea that constant anxiety impairs learning is also in line with the *processing efficiency theory* (Eysenck & Calvo, 1992) and was further supported by a quantitative review of conditioning studies in anxiety disorders including over 450 anxiety patients as well as the same number of HC (Lissek et al., 2005). A more recent meta-analysis also found prove for enhanced fear responses to safety cues in individuals with anxiety disorders compared to controls (Duits et al., 2015). However, it is still unclear whether this effect is caused by impaired inhibition skills or excessive fear generalization.

In SAD, there are only a few studies addressing conditioned discrimination learning. One study using neutral faces (CS) and painful pressure (US) reported insufficient differentiation among the CS+ and the CS- in SAD patients compared to control participants (Veit et al., 2002). In line with this, another study with colored lights serving as CS and air puffs serving as US detected that while HC kept their eyes open in response to the non-reinforced light, SAD patients did not only blink as a reaction to the danger, but also to the safety signal (Sachs, Anderer, Doby, Saletu, & Dantendorfer, 2003). A third study using neutral faces (CS) and aversive odor (fermented yeast) (US) as stimuli reported that participants with SAD differentiated between CS+ and CS- in startle response, but not in corrugator activity, whereas HC discriminated the stimuli in both measures. Furthermore, SAD patients showed an impaired acquisition of the CS- as safety signal in the US expectancy ratings,

visible as enhanced US expectancy ratings although the CS- had never been paired with the US (Hermann et al., 2002).

Overall, there is growing evidence that some anxiety disorders including SAD are accompanied with difficulties in discriminative learning. Possible explanations could be an impairment of differentiating ability (Sachs et al., 2003) or difficulties in learning that social cues can serve as safety signals in particular (Hermann et al., 2002). Furthermore, an increased fear response to safety cues can be explained by *overgeneralization*.

1.4.2.4. Overgeneralization

A further approach trying to elucidate the mechanisms involved in the development and maintenance of anxiety disorders is *overgeneralization*. While fear generalization describes the transfer of an conditioned fear response to stimuli which are similar to the CS+ (Pavlov, 1927), the term overgeneralization is used when the regular, adaptive generalization process is exceeded by broadening the conditioned fear to a disproportionately high number of other, just slightly similar stimuli (e.g. Lissek, Biggs, et al., 2008; Lissek & Grillon, 2012; Lissek et al., 2009). According to this account, it is assumed that individuals with anxiety disorders are more ready to react to threat stimuli compared to HC, which is why a smaller resemblance of a stimulus with the CS+ is sufficient to elicit a fear response. Like the conditioned fear inhibition and the associative learning deficit theory, the overgeneralization account predicts increased fear responses to the safety cues, and meta-analyses show that there is solid evidence for this assumption (Duits et al., 2015; Lissek et al., 2005).

Fear generalization has been explored in animals (Hull, 1943; Pavlov, 1927) and humans (Bass & Hull, 1934; Hovland, 1937) for almost a century. However, as this field of research has then been neglected for several decades after the initial interest, surprisingly little is known about this phenomenon, especially in clinical populations. To further disentangle if and to which amount the overgeneralization of conditioned fear plays a role in the etiology of anxiety disorders, scientists brought generalization again into focus of their work. They started to develop paradigms which transcend the simple differentiation between two stimuli, as often seen in previous conditioning studies, by using a larger number of safety signals. The following chapter will provide a consolidated summary of the recent work in this field.

1.4.3 Empirical evidence from fear generalization research

During the last years, researchers gained new interest in stimulus generalization and designed novel paradigms to explore it. One of the most prominent was developed by Lissek and utilizes 10 rings of increasing diameter (Lissek, Biggs, et al., 2008). The largest and smallest rings

serve as CS+ and CS-, while intermediate stimuli are used as *generalization stimuli* (GSs), and an electric shock as US. Notably, this paradigm consists of a larger number of stimuli resembling the CS+ and thereby allows a more precise grading of stimulus generalization. Instead of just reporting that, for example, anxiety patients react with enhanced fear responses to the CS+ in comparison to controls, this paradigm enables the description in terms of a number of categories to which a population has generalized their conditioned fear response. Thereby, more precise information on learning differences among patient and control samples can be gained. Also, a larger amount of data points allows the calculation of curve progression. Studies utilizing the paradigm of gradually increasing rings detected that the generalization gradients of HC follow quadratic trends, whereas anxiety patients showed linear declines (e.g. Lissek et al., 2014; Lissek et al., 2009).

Researchers tested generalization paradigms in both healthy individuals (e.g. Norrholm et al., 2014; Vervliet, Vansteenwegen, & Eelen, 2004) and patients with anxiety disorders (for a review, see Dymond et al., 2015). So far, the data revealed overgeneralization of fear in PD (Lissek et al., 2009) and, as mentioned above, PTSD (Lissek & Grillon, 2012). In other words, patients did not only show fear responses to the CS+, but also to GSs, and this fear was pronounced to a greater extent than it was in control participants.

Interestingly, a recent study compared fear generalization between healthy adults and children and found that children – similar to anxiety patients – displayed heightened fear generalization in both explicit (arousal ratings) and implicit (skin conductance response) measures (Schiele et al., 2016). The authors suppose that enhanced fear generalization in children might be related to the insufficient maturation of brain structures responsible for the discrimination among danger and safety cues such as the prefrontal cortex. In a similar vein, the question arises whether the functioning of the same structures is impaired in anxiety patients. Further studies on psychiatrically HC with low and high spider-fearfulness (Dymond, Schlund, Roche, & Whelan, 2014) or with low and high characteristics of obsessive-compulsive disorder (OCD), such as washing, obsessing, hoarding, ordering, checking and neutralizing, indicated by elevated scores on the Obsessive-Compulsive Inventory-Revised (OCI-R) (Kaczkurkin & Lissek, 2013), also found that these individuals overgeneralized their fear compared to controls. These outcomes still have to be confirmed by studies testing clinical populations, though.

In contrast, results are ambiguous in some anxiety disorders: with regard to generalized anxiety disorder (GAD), one study confirmed the overgeneralization theory (Lissek et al., 2014), while others failed to detect overgeneralization in behavioral or psychophysiological responses (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Tinoco-González et al., 2015). Consistent with these mixed results, another investigation with a sample of high trait anxious students observed no overgeneralization compared to low trait anxious students (Torrents-Rodas et al., 2013).

In sum, results are contradictory, which is why the role of overgeneralization as a marker for anxiety disorders has not been fully clarified. With regard to SAD, empirical evidence is particularly scarce, as to our best knowledge, no study on this topic has been published yet.

1.4.4 The neuronal basis of fear generalization

On a neuronal level, there are only a few studies on fear generalization to date, but a preliminary understanding of involved brain circuits has begun to emerge. In humans, the first fMRI study on fear generalization (Dunsmoor, Prince, Murty, Kragel, & LaBar, 2011) using moderately fearful faces (CS+) paired with shocks (US) compared with neutral faces (CS-) found generalized enhancement of activity to stimuli which were similar to the CS+ within regions involved in the acquisition and expression of conditioned fear, such as the thalamus, insula and caudate. On the contrary, participants displayed generalized neural activity to stimuli approximating the CS- in the ventromedial prefrontal cortex (vmPFC). Further studies found similar results, including positive generalization gradients - indicated by a decrease in activity as the presented stimulus differs from the CS+ - in the dorsomedial prefrontal cortex (dmPFC), caudate, insula, anterior cingulate cortex (ACC), right supplementary motor area (SMA), as well as negative gradients in the hippocampus and vmPFC (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Lissek et al., 2013).With regard to anxiety disorders, there is only one fMRI study investigating generalization processes in GAD patients and the authors reported a flat, less discriminant vmPFC response slope in the GAD group, while healthy participants showed enhanced activity to GSs that resembled the CS- (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013). This impairment to recruit the vmPFC by safety signals is hypothesized to be associated with wider fear generalization (Dunsmoor & Paz, 2015). Altogether, these findings indicate that fear generalization engages similar neural areas involved in the acquisition and regulation of conditioned fear (Dymond et al., 2015).

A summary of the results by Lissek and colleagues led to a *neurobiological model of fear generalization* which comprises a network of brain areas including the hippocampus with connections to sensory cortices and brain areas associated with fear inhibition (vmPFC) and fear excitation (e.g. insula, ACC and amygdala) (Lissek, 2012; Lissek et al., 2013). According to this model, the exposure to GSs simultaneously spreads sensory information via two pathways proposed by LeDoux (LeDoux, 1998): a ‘quick and dirty’ route leading directly to the amygdala, which immediately initiates a conditioned fear response, and a ‘slow but elaborated’ route via the thalamus and visual cortices, which compares the new information of the GSs to the previously encoded CS+ through schematic matching. If there is a large overlap, the hippocampus reactivates the neural representation of the CS+ through *pattern completion* (Treves & Rolls, 1994) and thereby evokes a conditioned fear response. In contrast, insufficient overlap leads to the initiation of *pattern*

separation (McHugh et al., 2007), which activates structures associated with fear inhibition, which in turn decrease the activity in the amygdala.

However, a recent fMRI study using a circular fear-generalization paradigm with visual, circular cues, did not report a typical generalization gradient in all areas. Rather, the authors observed a high pattern-similarity between the CS+ and the US in the insula encoding the aversive quality of the CS+, and activity related to ambiguity-based outcome uncertainty indicated by differentiating intermediate stimuli from both the CS+ and CS- in the inferior temporal cortex (Onat & Büchel, 2015). The authors concluded that stimulus generalization is not only passively driven by perceptual similarity, but an active process which integrates activity from different areas related to threat identification and outcome uncertainty, and which can actively widen the scope of threat to perceptually similar stimuli. In line with this, a recent study which examined the involvement of the human visual cortex in the formation of learned perceptual biases with ssVEPs found two distinct tuning patterns in the cortex during an aversive conditioning paradigm: while the ssVEP amplitude displayed over parietal regions matched the typical generalization pattern of enhanced activation for the most proximate GS and also occurred in the measures of FPS and verbal reports, the ssVEP activity over the visual cortex reflected lateral inhibition, indicated by enhanced ssVEP amplitude in response to the CS+ and a suppression of activity for the most proximate, but not distal GSs relating to the CS+ (McTeague, Gruss, & Keil, 2015). These results suggest that different neural processes take place in the human cortex during fear generalization with lateral inhibition serving as a temporary process involving implicit modulation of visual cortex activity, and parietal generalization patterns, which are associated with psychophysiological measures and ratings, reflecting explicit processes and persistent emotional responses (Todd & Manaligod, 2017).

1.4.5 Summary and Conclusion

Given the present literature on associative fear learning, there is solid evidence that aberrations in fear conditioning and fear generalization processes contribute to the development and maintenance of anxiety disorders. However, it appears that there are several fields which would benefit from additional research. In particular, fear generalization has been tested only in a few anxiety disorders excluding SAD, albeit there is literature proposing that patients with SAD have difficulties to discriminate among danger and safety signals (Hermann et al., 2002; Sachs et al., 2003; Veit et al., 2002) and thereby are predisposed to display overgeneralization as well. Therefore, study 2 of the present thesis tested whether patients with SAD showed overgeneralization as well. Moreover, little is known about the neuronal basis of fear generalization, and previous findings are mostly based on investigations in healthy participants. For this reason, study 3 examined the neuronal basis of fear generalization in social anxiety.

1.5 Research Questions and Main Hypotheses of the Thesis

In the following, the three experimental studies of the present thesis will be shortly introduced, which had the purpose to advance the understanding of the development and maintenance of SAD. In particular, we aimed to investigate in which way differences in attentional (study 1) as well as learning and memory processes (study 2 and 3) contribute to the etiology of SAD.

As summarized in chapter 1.3, it is assumed that an attentional bias – the tendency to let prior experiences, expectations and recurring thoughts affect one's perception - towards threat-related information is a characteristic of individuals suffering from anxiety disorders. According to the ACT (see chapter 1.2.4), this effect emerges, because anxiety strains the central executive's capacity of the working memory and thereby reduces inhibitory control (Eysenck et al., 2007). Moreover, the impact of anxiety is said to be larger on performance efficiency (measured as latency time) compared to performance effectiveness (measured as error rate). In **study 1**, a deficit in inhibitory control was tested as a possible factor contributing to the development of SAD with the help of an antisaccade-paradigm (see chapter 1.3.2.3). As a bias towards threat should be especially pronounced in the presence of disorder-relevant stimuli, the experimental design included two phases: one using geometric figures as baseline measure and the other using faces with different emotional expressions (angry vs. neutral vs. happy) as target stimuli. Notably, the gaze direction of the applied faces was also varied (direct vs. averted), because it should be explored in which way the inhibitory control of attention was modulated by direct eye-contact or averted gaze, respectively (see chapter 1.3.3). Based on previous antisaccade-studies, it was hypothesized that both SAD patients and HC would show prolonged latencies and enhanced error rates in response to anti- compared to prosaccades during the first part of the experiment with geometric figures. Moreover, it was supposed that this effect would be more pronounced in SAD patients in the second part of the experiment using faces as target stimuli, and that it would concern response efficiency more than response effectiveness. Regarding the faces, it was expected that SAD patients would show weakest inhibitory control in response to the most-threatening faces (angry facial expression), followed by ambiguous faces (neutral facial expression) and harmless faces (happy facial expression). In addition, faces with negative (angry) or ambiguous (neutral) expression and a direct compared to averted gaze were hypothesized to have a larger, negative impact on inhibitory control in patients with SAD, displayed as enhanced error rates and prolonged latencies during antisaccades in response to those stimuli.

Besides an attentional bias towards threat, commonly discussed mechanisms contributing to the development of anxiety disorders are aberrations in associative learning processes (see chapter 1.4). Especially, overgeneralization of conditioned fear reactions became a focus of interest and was

demonstrated in patients with PD, PTSD and GAD. However, to this date, there are no studies investigating fear generalization in patients with SAD. As those patients have difficulties to discriminate between danger and safety signals in differential conditioning studies, it seemed plausible that they would also transmit a once acquired fear reaction to stimuli which were similar to the original CS+. Therefore, individuals with SAD and HC underwent a generalization paradigm in **study 2**, which used two neutral female faces serving as CS and a fearful face paired with a loud scream serving as US. Fear generalization was tested by presenting morphs of the two faces (GS: generalization stimuli) which varied in their similarity to the original faces. During the whole experiment, self-report ratings and skin conductance responses (SCR) were recorded. In line with former investigations in different clinical populations, it was hypothesized that both groups would generalize the fear reaction of the CS+ to the GS. However, it was assumed that SAD patients would transmit their fear to more categories of GSs in comparison with healthy participants indicating overgeneralization, which should also be reflected in linear instead of quadratic generalization gradients. Furthermore, it was expected that patients with SAD would show elevated levels of fear reactions (hyperarousal) compared to controls due to the application of disorder-relevant stimuli.

Up to now, fear generalization had just been recorded in terms of explicit ratings or peripheral physiological measures, such as heart rate, skin conductance and startle response. **Study 3** aimed at elucidating if there were already differences among high and low socially anxious participants during early stages of information processing, which could be measured as the activity of the brain's sensory neurons in the visual cortex. Therefore, the paradigm of study 2 was implemented in EEG, and steady-state Visually Evoked Potentials (ssVEPs) were recorded. So far, differential conditioning studies measuring ssVEPs revealed increased amplitudes in the visual cortex in response to the CS+ compared to the CS- (Moratti & Keil, 2005; Moratti, Keil, & Miller, 2006). Based on this finding and prior generalization studies[1], it was hypothesized that the pattern of electrical brain responses in the occipital cortex would be a reproduction of the pattern found in peripheral physiological measures. It was presumed that the neuronal activity would be highest in response to the CS+ and decrease in response to the GSs as a function of similarity with the CS- in both groups. Furthermore, it was expected that high socially anxious participants would generalize their conditioned fear reaction to more categories of the GSs and show linear generalization profiles compared to low socially anxious, which were assumed to display generalization to less categories combined with quadratic generalization profiles.

[1] There is one recent study which already investigated fear generalization with ssVEPs using a series of Gabor gratings as CS and GS, and a white noise as US (McTeague et al., 2015). Interestingly, analyses found highest ssVEP amplitudes in response to the sound-paired grating (CS+) and a suppression of the amplitude in response to the grating with the highest similarity to the CS+, which the authors interpreted as lateral inhibition among orientation-selective neuronal populations in the occipital cortex. However, this study had not been published yet when study 3 was conducted, which is why it did not have an influence on the hypotheses.

2 Study 1: The Influence of Emotions and Gaze on Attentional Control in Social Anxiety Disorder

2.1 Introduction

Attentional control can be described a person's ability to decide to what information he or she wants to pay attention to and what information he or she wants to ignore. As human beings are exposed to an infinite number of potentially relevant stimuli and distractors at the same time, attentional control is an indispensable skill required to pursue a person's goals and ensure a high task performance. Anxiety, however, seems to impair the functioning of attentional control (Eysenck & Calvo, 1992; Eysenck & Derakshan, 2011; Hembree, 1988). Experimental studies repeatedly provided profound evidence of attentional biases in patients with anxiety disorders, for example a hypervigilance for or an avoidance of threat (see Bar-Haim et al., 2007, for a review). These biases has also been well shown in SAD in particular (as reviewed in Morrison & Heimberg, 2013). Moreover, social anxiety patients seem to have difficulties to inhibit undesired, automatic attention allocation to stimuli (inhibition deficit) as well as to shift their attention from irrelevant to goal-relevant stimuli (disengagement-deficit) (Chen & Clarke, 2017).

One prominent model, which tries to illustrate attentional control processes in the context of anxiety and cognitive performance, is the attentional control theory (Eysenck et al., 2007) (see also chapter 1.2.4). According to this model, anxiety does not only lead to an attentional bias towards threat, but also impairs attentional control, because it disturbs the balance between two hypothesized attentional systems – a stimulus-driven and a goal-oriented system- at expense of the latter one. Consequently, individuals with high levels of anxiety are supposed to display a reduced performance in tasks which require attentional control compared to non-anxious individuals.

Study 1 aimed to examine whether an imbalance of reflexive and volitional control also appears in SAD and thereby potentially contributes to its development, maintenance and exacerbation. For this purpose, we recorded the eye-movements of SAD patients and HC during an antisaccade task (Hallett, 1978). Due to the stimulus-driven character during prosaccades and the inhibition of the orientation reaction as well as the volitional programming of a saccade in the opposite direction during antisaccades, the antisaccade task served as a suitable method to measure executive functions, such as reflexive and inhibitory attentional control (Broerse et al., 2001; Hallett, 1978). Faces displaying different emotional expressions (angry, neutral and happy) were used as target stimuli to investigate the influence of different emotions on task performance. In comparison to neutral stimuli, such as geometric figures, faces are disorder-relevant for individuals with SAD, which is why they should evoke more arousal and be rated as less pleasant by SAD patients

compared to HC. As patients with anxiety disorders typically react with an enhanced attention allocation towards threatening stimuli (Asmundson & Stein, 1994; Gilboa-Schechtman et al., 1999), it was expected that faces with angry expression interfered most with the patient's inhibitory control, as these expressions might embody scrutiny, degradation or criticism in general. Also, it was assumed that neutral faces interfered with the SAD patient's inhibitory control– albeit we expected the effects to be weaker in comparison with angry faces. This assumption was based on past studies which showed that the ambiguous nature of neutral facial expressions unsettled individuals with SAD (Birbaumer et al., 1998; Moser, Huppert, Duval, & Simons, 2008; Somerville, Kim, Johnstone, Alexander, & Whalen, 2004; Yoon & Zinbarg, 2007). Besides the presentation of different facial expressions, the depicted actor's line of vision had also been varied (direct vs. averted gaze). Past experiments suggested that individuals with SAD fear eye-contact and try to avoid it, which was indicated as less gaze fixations on the eyes of faces during eye-tracking studies (e.g. Horley et al., 2003; Horley et al., 2004; Moukheiber et al., 2010) and less eye-contact during social conversations (e.g. Baker & Edelmann, 2002; Howell et al., 2016). Therefore, it was assumed that direct eye-contact would make individuals with SAD feel more uncomfortable with regard to faces with angry and neutral expression, because they might interpret these expressions as a sign of scrutiny or rejection.

The experimental design of study 1 included two parts: during the first part, a geometric figure (ellipse) was presented as target stimulus to get a baseline measure, while during the second part, faces with different emotional expressions (angry vs. neutral vs. happy) and varied gaze direction (direct vs. averted) were shown to the participants. The hypotheses of study 1 at a glance were the following:

Part 1 (geometric figure):

1. Both SAD patients and HC show prolonged latencies in response to anti- compared to prosaccades.
2. Both SAD patients and HC exhibit enhanced error rates in response to anti- compared to prosaccades.
3. There are no differences among groups (SAD patients do not suffer from a general inhibition deficit).

Part 2 (emotional facial expressions):

1. Both groups show a) prolonged latencies and b) enhanced error rates in response to anti- compared to prosaccades.
2. SAD patients exhibit an inhibition deficit in response to disorder relevant stimuli (faces) indicated by a) longer latencies and b) enhanced error rates in the antisaccade task compared to HC. The effect is more pronounced with regard to the latency time, as the ACT states that anxiety has a stronger impact on performance efficiency compared to performance effectiveness.

3. The inhibition deficit is especially pronounced for angry (threatening), but also neutral (ambiguous) compared to happy faces (hypervigilance for threat).
4. Faces with direct compared to averted gaze have a stronger impact on the inhibitory control of SAD patients.
5. SAD patients rate the faces to be less pleasant and more arousing compared to HC (general hyperarousal in response to social stimuli).

2.2 Material and Methods

2.2.1 Participants

A total of thirty-three patients with a current ICD-10 diagnosis (International Statistical Classification of Diseases and Related Health Problems 10) (World Health Organization, 1992) of SAD and thirty-four HC took part in the study. Due to technical problems, three HC and two SAD patients had to be excluded. Furthermore, three SAD patients dropped out of the investigation, because they started to feel sick after the experiment had started, so that on the whole 30 HC (M_{age} = 26.40 SD_{age} = 6.41; 9 female) and 27 SAD patients (M_{age} = 27.96, SD_{age} = 10.40; 10 female) were included in the statistical analyses. Groups did not differ on neither age (p = .504) nor gender (p = .574).

All patients were recruited at a large mental health clinic in Germany (Schoen Klinik, Bad Bramstedt), and diagnoses were determined by experienced local staff psychologists. Only patients with SAD as primary diagnosis of discomfort were included in the study. Unfortunately, it was not allowed to bring non-patients to the clinic. Consequently, controls had to be recruited through advertisements on a local internet platform and tested at the University of Würzburg. After arriving at the laboratory, participants completed the informed consent form and some questionnaires. First, they filled in the German version of the Social Phobia and Anxiety Inventory (SPAI; Fydrich, 2002; Turner, Beidel, Dancu, & Stanley, 1989) as well as the Liebowitz Social Anxiety Scale (LSAS; Heimberg et al., 1999) to measure the severity of SAD symptoms. German scores of the SPAI were translated into the original scores (Turner et al., 1989). Moreover, participants filled in a socio-demographic questionnaire and the German versions of the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970), the Beck Depression Inventory (BDI: Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Hautzinger, Bailer, Worall, & Keller, 1994), and the Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988). To check if the SAD patients and HC differed with regard to their social anxiety, *t*-tests were calculated. Results revealed significant group differences in the total scores of the SPAI ($t(55) = 12.78$, $p < .001$; SAD: M = 134.4, SD = 26.56; HC: M = 58.88, SD = 17.28) and LSAS ($t(55) = 11.53$, $p < .001$; SAD: M = 85.31, SD = 24.18; HC: M = 21.23, SD = 16.65). Means and standard deviations for all questionnaires are presented in Table 1.

Exclusion criteria for all participants were 1) pregnancy, 2) current use of illicit drugs and 3) neurological disorders or other medical conditions that interfered with the objectives of the study. Additionally, HC reported no current or past AXIS I psychiatric diagnosis and psychopharmacologic medication (self-report). SAD patients were excluded if they had 1) a history of alcohol or substance abuse, 2) a current or past diagnosis of psychosis or delusional disorders and 3) current suicidal ideation. Psychiatric comorbidities among patients included major depression (n = 27), personality disorders (n = 13), eating disorders (n = 4), pathological gambling (n = 4), somatoform disorders (n = 4), other anxiety disorders (n = 5), dissociative and conversion disorder (n = 2) and sexual disorders (n = 1). Ethical permission for the study was granted by the ethical committee of the medical faculty of the University of Würzburg (reference number 86/13).

Table 1: Questionnaire characteristics of the participants of study 1.

	HC		SAD			
Variable	*M*	*SD*	*M*	*SD*	*t(59)*	*p*
SPAI	1.84 (58.88)	0.54	4.20 (134.4)	0.83	12.78	$p < .001$*
LSAS	21.23	16.65	85.31	24.18	11.53	$p < .001$*
BDI	6.40	4.89	25.81	11.60	7.97	$p < .001$*
STAI State	33.13	8.04	52.41	10.43	7.86	$p < .001$*
STAI Trait	33.72	7.88	61.78	7.91	13.29	$p < .001$*
PANAS_PA	28.67	6.53	23.41	7.16	2.90	$p = .006$*
PANAS_NA	11.40	3.69	22.37	8.68	6.09	$p < .001$*

SPAI, Social Phobia and Anxiety Inventory; LSAS, Liebowitz Social Anxiety Scale; BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; PANAS, Positive and Negative Affect Scale (PA, positive affect; NA, negative affect).

2.2.2 Stimuli

Pictures with different emotional expressions taken from the Radboud Faces Database (Langner et al., 2010) served as stimuli. In total, 72 photographs were presented, which differed with regard to gender (2: female vs. male), actor (3: character 1 vs. 2 vs. 3), emotion (3: angry vs. neutral vs. happy), gaze (2: direct vs. averted) and gaze direction (2: left vs. right) (see Figure 2). For each trial, a centrally presented cue indicated whether a prosaccade ("(Schau) hin!" ["Look!"]) or an antisaccade ("(Schau) weg!" ["Look away!"]) should be performed.

Design and procedure

To measure top-down attentional control, the current study applied the antisaccade paradigm (Hallett, 1978). In this task, participants had either to look towards an abruptly presented target stimulus as fast as possible (prosaccade), or to suppress the reflexive saccade in response to the suddenly appearing target and look in the opposite direction instead (antisaccade). Meanwhile, eye-movement data were recorded via eye-tracking.

When the participants arrived at the laboratory, they first completed the informed consent form and the questionnaires described above. Afterwards, they were seated in a chair and an eye-tracker was applied. Before the actual experiment began, participants underwent a 12-point calibration procedure to synchronize the participants' pupil with the eye-tracker. Subsequently, the experimental session started with eight practice trials, in which the task was explained. After the experimenter had ascertained by visual inspection of task performance that participants understood what they were asked for, the first of altogether four blocks with 2 (female vs. male) x 3 (character 1 vs. 2 vs. 3) x 3 (angry vs. neutral vs. happy) x 2 (direct vs. averted gaze) x 2 (left vs. right gaze direction) = 72 trials each (288 trials in total) started.

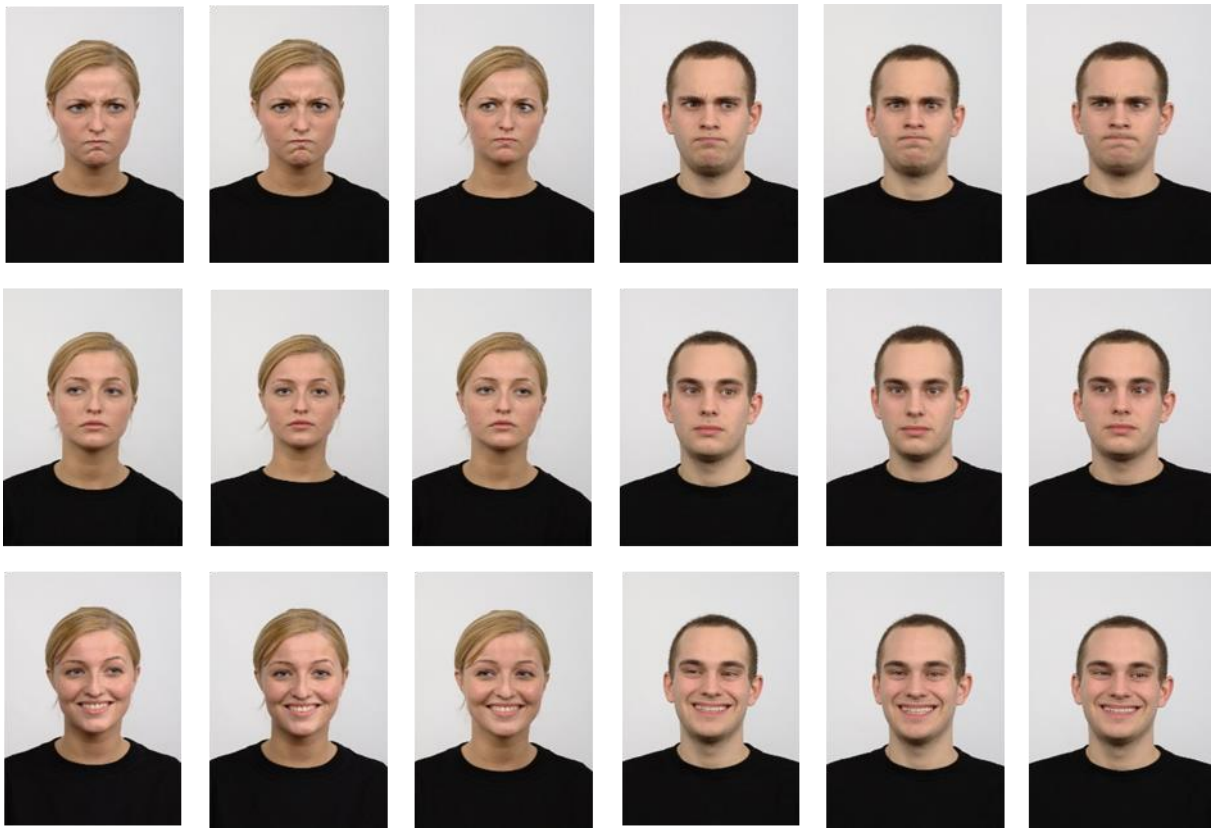

Figure 2: Example stimuli used in study 1. Faces varied with regard to gender (female vs. male), emotion (angry vs. neutral vs. happy), and gaze direction (direct vs. averted).

Each trial comprised three components: a fixation cross (500 ms), a cue (500 ms) and a target (1000 ms). At the beginning of each trial, a fixation cross was shown on a dark gray background to focus the participants' gaze at the center of the screen. In a second step, it was followed by one of two cues ("Hin!"/"Toward!" or "Weg!"/"Away!"), and provided information on the task the participants should perform (pro- or antisaccade, respectively). Finally, the actual target stimuli - pictures with angry, neutral and happy facial expression - were presented, and called on the participants to perform a pro- or antisaccade (see Figure 3). The inter-trial interval varied between 750 and 1500ms. The presentation order of the stimuli was random for each participant. After each block, participants were given the opportunity to make a break and relax their eyes as long as they wanted. To prevent possible movement artifacts, the calibration procedure was repeated subsequent to each break before a new block started. At the end of the experiment, participants were asked to rate the target stimuli with regard to valence and arousal on a 9-point SAM scale (valence: from 1 = unpleasant to 9 = pleasant; arousal: from 1 = low arousal to 9 = high arousal) (Self-Assessment Manikin; Bradley & Lang, 1994).

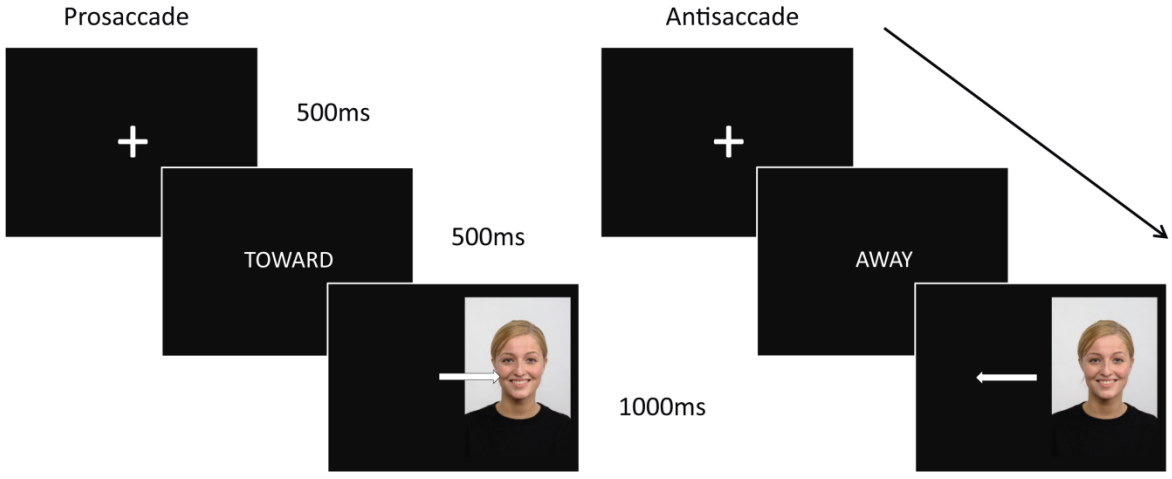

Figure 3: Schematic overview of the experimental procedure of study 1 (pro- and antisaccade trial). Stimuli are randomly presented for 1000ms; the fixation cross and cue were presented for 500ms each.

2.2.3 Data recording and analysis

During the whole experiment, the eye movement of the participants was recorded via an infrared head-mounted ViewPoint Eye-Tracker (Arrington Research, Scottsdale, AZ, USA) and a Z800 head mounted display (HMD) (eMagin Inc., Bellevue, Washington, DC) including the corresponding software. A pair of OLED (organic light-emitting diode) displays with magnifying lenses provided a 40-degree diagonal field of view and displayed images with a resolution of 800 x 600 pixels. The

sampling rate was 60 Hz. To program and display the antisaccade task, the software Presentation (Neurobehavioral Systems, Albany, CA) was used.

Eye-tracking data were processed offline using the software BrainVision Analyzer (Brain Products, Munich, Germany) and imported using an in-house written macro for BrainVision Analyzer. In a first step, data were preprocessed. For that purpose, they were segmented to extract the regions in which target stimuli were shown, and baseline corrected (-200 ms to stimulus onset) to compensate for shifting of the eye-tracker within blocks. Secondly, saccades were identified and artifacts were excluded. A saccade was defined as a horizontal eye movement faster than 30°/s and minimum amplitude of 1.5°. Saccades which had an onset shorter than 80 ms after stimulus onset were classified as anticipatory saccades (Reuter, Jäger, Bottlender, & Kathmann, 2007) and excluded from further analysis as well as trials containing movement artifacts, recording artifacts or eye-blinks. To assess task performance, two parameters were calculated: the onset latency and the number of errors the participants made. The latency was defined as the duration between stimulus onset and the starting point of the saccade (Reuter, Herzog, & Kathmann, 2006). With regard to the error rates, correctly performed pro- and antisaccades were counted as such. Prosaccadic errors were counted when participants made a primary saccade (amplitude >3°) in the opposite direction of the peripheral target stimulus on prosaccade trials; antisaccade errors were counted when participants performed a primary saccade towards the target picture on antisaccade trials. Percentages of reflexive prosaccades and of antisaccades were computed relative to the number of valid trials in each participant. If trials included recording artifacts or eye blinks, they were excluded from analysis. On average, 94.69% of trials were included. All remaining trials were exported for further analysis.

2.2.4 Statistical analysis

The preprocessed data were imported to SPSS 22 (IBM, Chicago, IL) and contained information on onset latencies and error rates. Percentages of correct pro- and antisaccades were computed relative to the number of valid trials for each participant. Participants with less than 66.67% valid trials were excluded from the experiment. Mean latencies and error rates were then calculated by repeated measures ANOVAs with group as between-subjects factor (2: SAD vs. HC), and emotion (3: angry vs. neutral vs. happy), gaze direction (2: direct vs. averted) and task (2: prosaccade vs. antisaccade) as within-subjects factors. Valence and arousal ratings were also analyzed by repeated measures ANOVAs with group as between-subjects factor (2: SAD vs. HC), and emotion (3: angry vs. neutral vs. happy) and gaze direction (2: direct vs. averted) as within-subjects factors.

A significance level of $p < 0.05$ (two tailed) was defined for all analyses. In case of violation of sphericity, Greenhouse–Geisser epsilon (GG-ε) and uncorrected degrees of freedom are reported (Picton et al., 2000). Significant interactions were followed up with ANOVAs and post hoc *t*-tests

using the Bonferroni adjustment of alpha level. As a measure of effect size, the partial eta-squared (ηp^2) is reported.

2.3 Results

2.3.1 Eye-Tracking

Part I: Geometric figures

Latency: For the eye-movement data, the repeated measures ANOVA revealed a significant main effect of task [$F(1,55) = 127.61$, $p < .001$, $\eta p^2 = .70$]. As expected, participants responded faster to pro- (M = 223.61 ms SD = 36.95) compared to antisaccades (M = 304.32 ms, SD = 61.88) (see Figure 4). The main effects of group [$F(1,55) = 0.03$, $p = .872$, $\eta p^2 < .001$] as well as the task x group interaction [$F(1,55) = 1.40$, $p = .242$, $\eta p^2 = .03$] did not reach significance.

Error rate: The repeated measures ANOVA for the error rate also yielded a significant main effect of task [$F(1,55) = 70.68$, $p < .001$, $\eta p^2 = .56$] as seen in the latency data (see also Figure 4). Participants made more errors in response to anti- (M = 32.41 %, SD = 22.76) compared to prosaccades (M = 10.58 %, SD = 12.74) [$t(56) = 8.17$, $p < .001$]. However, neither the main effect of group [$F(1,55) = 0.74$, $p = .392$, $\eta p^2 < .01$] nor the task x group interaction [$F(1,55) = 3.16$, $p = .081$, $\eta p^2 = .05$] were significant, indicating that SAD patients do not show a general inhibition deficit compared to HC.

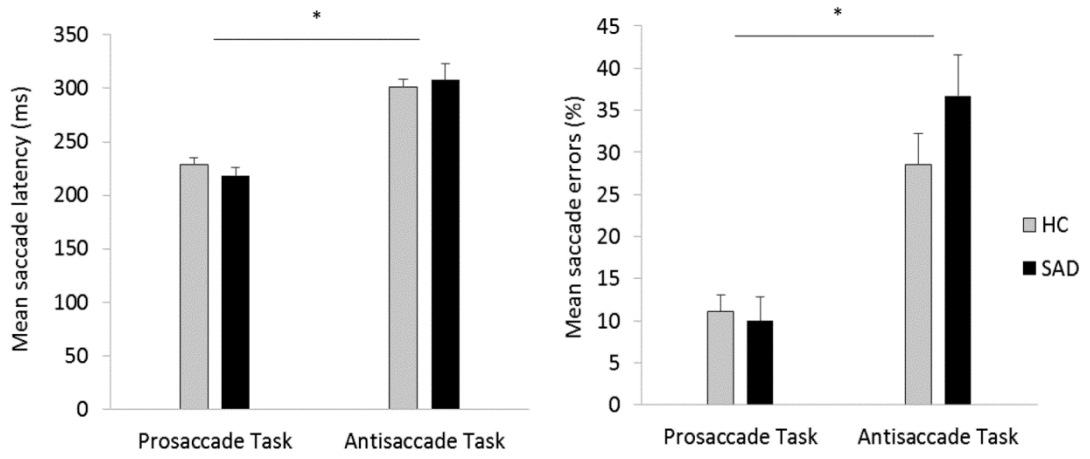

Figure 4: Mean correct saccade latencies (left) and mean percentage of errors (right) with standard errors by group in the non-social pro- and antisaccade task are displayed. The asterisks represent a significance level of p < .05.

Part II: Facial expressions

Latency: Eye-movement data were analyzed by a 2 (group: SAD vs. HC) x 3 (emotion: angry vs. neutral vs. happy) x 2 (gaze direction: direct vs. averted) x 2 (task: prosaccade vs. antisaccade) repeated measures ANOVA. Results showed only a significant main effect of task [$F(1,55) = 283.11$, $p < .001$, $\eta p^2 = .84$], which indicated that participants responded faster to pro- (M = 222.28 ms SD = 36.37) compared to antisaccades (M = 303.25 ms, SD = 46.66) (see *Figure 5*).

The main effects of group [$F(1,55) = 0.74$, $p = .394$, $\eta p^2 = .01$], gaze [$F(1,55) = 1.73$, $p = .194$, $\eta p^2 = .03$] and emotion [$F(2,110) = 0.07$, $p = .093$, $\eta p^2 < .01$], as well as the interactions task x group [$F(1,55) = 0.15$, $p = .705$, $\eta p^2 < .01$], gaze x group [$F(,55) < 0.01$, $p = .998$, $\eta p^2 < .01$], emotion x group [$F(2,110) = 0.10$, $p = .909$, $\eta p^2 = .04$], task x gaze [$F(1,55) = 0.59$, $p = .445$, $\eta p^2 = .01$], task x gaze x group [$F(1,55) = 0.06$, $p = .814$, $\eta p^2 < .01$], task x emotion [$F(2,110) = 0.60$, $p = .549$, $\eta p^2 = .01$], task x emotion x group [$F(2,110) = 0.23$, $p = .795$, $\eta p^2 < .01$], gaze x emotion [$F(2,110) = 0.01$, $p = .986$, $\eta p^2 < .01$], gaze x emotion x group [$F(2,110) = 1.15$, $p = .322$, $\eta p^2 = .02$], task x gaze x emotion [$F(2,110) = 2.24$, $p = .112$, $\eta p^2 = .04$] and task x gaze x emotion x group [$F(2,110) = 1.01$, $p = .368$, $\eta p^2 = .02$] did not reach significance.

Error rate: For the analysis for the error rate, a 2 (group: SAD vs. HC) x 3 (emotion: angry vs. neutral vs. happy) x 2 (gaze direction: direct vs. averted) x 2 (task: prosaccade vs. antisaccade) repeated measures ANOVA was also calculated. As for the latency, a significant main effect of task [$F(1,55) = 85.25$, $p < .001$, $\eta p^2 = .61$] was found. Furthermore, the gaze x group interaction was significant [$F(1,55) = 8.00$, $p = .007$, $\eta p^2 = .13$].

As expected, participants responded with more errors to anti- (M = 30.93%, SD = 20.66) in comparison to prosaccades (M = 8.94%, SD = 9.79). Furthermore, post-hoc t-tests of the gaze x group interaction yielded that HC made less mistakes in response to faces with direct (M = 18.13%, SD =12.31) compared to averted gaze (M = 19.21%, SD = 12.24) [$t(29) = 2.09$, $p = .046$]. In SAD patients, there was no significant difference between faces with direct (M = 22.04%, SD =15.09) compared to averted gaze (M = 20.65%, SD = 14.89) [$t(26) = 1.93$, $p = .065$], but the data suggest by trend that the response pattern was reversed in comparison to HC.

The main effects of group [$F(1,55) = 0.56$, $p = .459$, $\eta p^2 = .01$], gaze [$F(1,55) = 0.12$, $p = .732$, $\eta p^2 < .13$] and emotion [$F(2,110) = 0.39$, $p = .678$, $\eta p^2 < .01$], as well as the interactions task x group [$F(1,55) = 0.21$, $p = .647$, $\eta p^2 < .01$], emotion x group [$F(2,110) = 1.64$, $p = .198$, $\eta p^2 = .03$], task x gaze [$F(1,55) = 0.30$, $p = .586$, $\eta p^2 < .01$], task x gaze x group [$F(1,55) = 0.46$, $p = .502$, $\eta p^2 < .01$], task x emotion [$F(2,110) = 0.99$, $p = .376$, $\eta p^2 = .02$], task x emotion x group [$F(2,110) = 0.23$, $p = .796$, $\eta p^2 < .01$], gaze x emotion [$F(2,110) = 0.08$, $p = .928$, $\eta p^2 < .01$], gaze x emotion x group [$F(2,110) = 0.51$, $p = .605$, $\eta p^2 = .01$], task x gaze x emotion [$F(2,110) = 0.86$, $p = .427$, $\eta p^2 = .02$] and task x gaze x emotion x group [$F(2,110) = 0.28$, $p = .754$, $\eta p^2 < .01$] were not significant (see *Figure 5*).

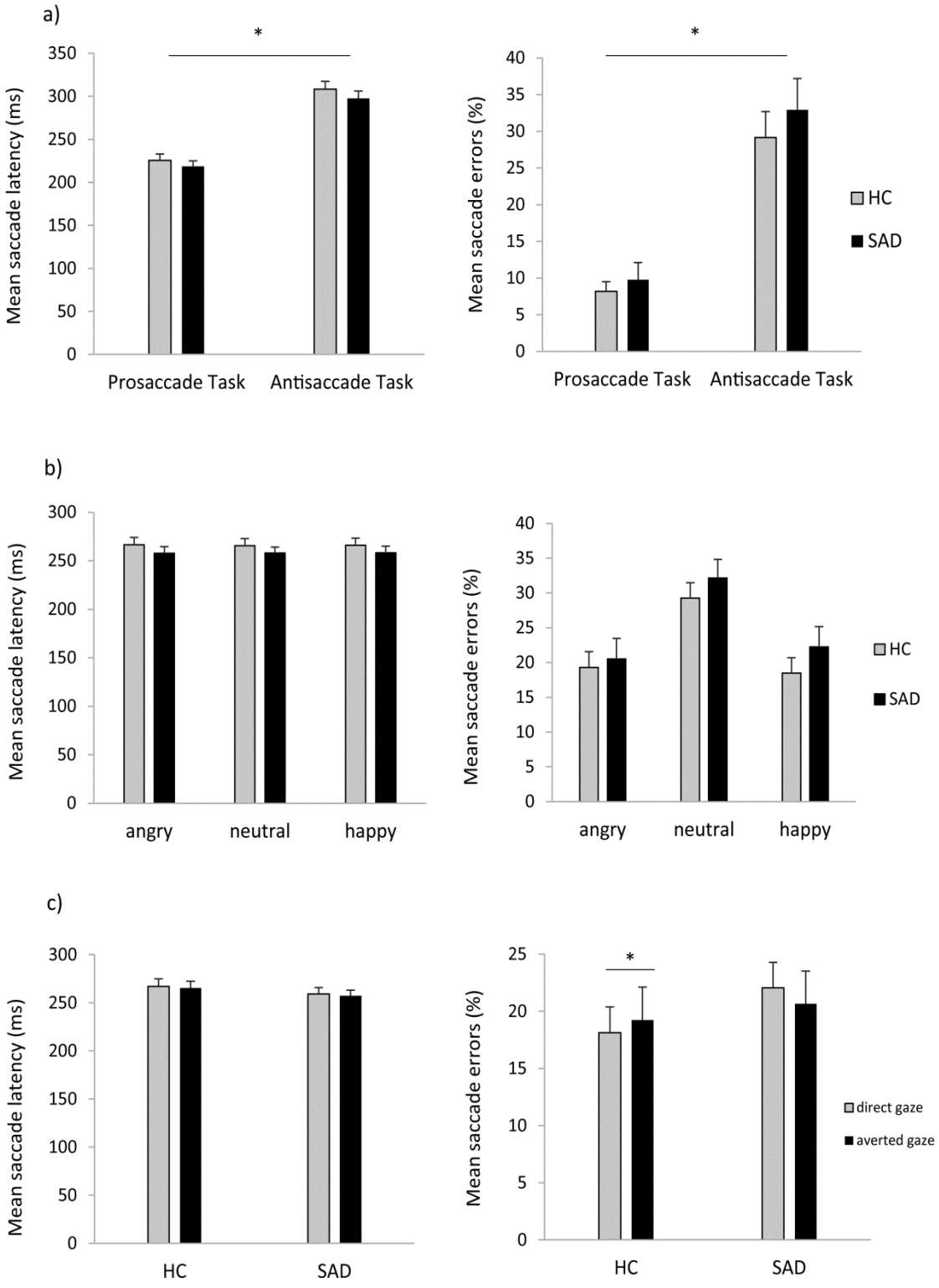

Figure 5: Mean correct saccade latencies (left) and mean percentage of errors (right) with standard errors in the social antisaccade task are displayed. Data were collected for pro- and antisaccades in the social task by group (a); for angry, neutral and happy facial expression by group (b); and for direct vs. averted gaze by group (c) (= p < .05).*

2.3.2 Ratings

Valence: The 2 (group: SAD vs. HC) x 3 (emotion: angry vs. neutral vs. happy) x 2 (gaze direction: direct vs. averted) repeated measures ANOVA revealed significant main effects of group [$F(1,55) = 6.79$, $p = .012$, $\eta p^2 = .11$] and emotion [$F(2,110) = 61.34$, GG- $\varepsilon = .76$, $p < .001$, $\eta p^2 = .53$]. Also, there was a significant gaze x group [$F(1,55) = 5.16$, $p = .027$, $\eta p^2 = .09$] and a marginally significant emotion x group interaction [$F(2,110) = 2.85$, GG- $\varepsilon = .76$, $p = .077$, $\eta p^2 = .05$] (see Figure 6). The main effect of gaze [$F(1,55) = 0.28$, $p = .599$, $\eta p^2 = .01$], the emotion x gaze interaction [$F(2,110) = 2.41$, GG- $\varepsilon = .84$, $p = .105$, $\eta p^2 = .04$] and the emotion x gaze x group interaction [$F(2,110) = 0.66$, GG- $\varepsilon = .84$, $p = .520$, $\eta p^2 = .01$] were not significant.

Regarding the significant main effect of group, patients with SAD ($M = 4.81$, $SD = 1.09$) rated the stimuli in general as less pleasant compared to HC ($M = 5.52$, $SD = 0.93$). Furthermore, three paired samples *t*-tests were calculated to follow up the significant main effect of emotion. Analyses showed that participants rated angry faces ($M = 4.03$, $SD = 1.43$) as less pleasant compared to neutral ($M = 5.43$, $SD = 1.19$) [$t(56) = 10.32$, $p < .001$] and happy ones ($M = 6.10$, $SD = 1.41$) [$t(56) = 8.52$, $p < .001$]. The difference among neutral and happy faces was significant, too [$t(56) = 3.76$, $p < .001$]. Follow-up independent samples *t*-tests for the gaze x group interaction revealed that SAD patients rated faces with direct gaze ($M = 4.73$, $SD = 1.07$) to be less pleasant compared to the control group ($M = 5.55$, $SD = 0.91$) [$t(55) = 2.95$, $p = .005$]. After alpha-adjustment, there was no difference among groups with regard to faces with averted gaze [$t(55) = 2.28$, $p = .027$], although the same tendency – namely that SAD patients rated the faces as less pleasant ($M = 4.89$, $SD = 1.07$) than controls ($M = 5.50$, $SD = 0.96$) – could be observed. Post-hoc calculated *t*-tests for the emotion x group interaction yielded significant differences for angry [$t(55) = 3.33$, $p = .002$] and neutral [$t(55) = 2.46$, $p = .017$], but not happy faces [$t(55) = 0.65$, $p = .517$] between the two groups. SAD patients rated angry ($M = 3.42$, $SD = 1.39$) and neutral faces ($M = 5.04$, $SD = 1.11$) as less pleasant compared to HC ($M = 4.58$, $SD = 1.25$; and $M = 5.79$, $SD = 1.17$, respectively), while happy faces were similarly rated (SAD: $M = 5.97$, $SD = 1.45$; and HC: $M = 6.21$, $SD = 1.39$, respectively).

Arousal: Analysis with the 2 (group: SAD vs. HC) x 3 (emotion: angry vs. neutral vs. happy) x 2 (gaze direction: direct vs. averted) repeated measures ANOVA showed significant main effects of group [$F(1,55) = 8.06$, $p = .006$, $\eta p^2 = .13$] and emotion [$F(2,110) = 244.59$, GG- $\varepsilon = .58$, $p < .001$, $\eta p^2 = .82$]. Moreover, the emotion x group [$F(2,110) = 4.79$, $p = .027$, $\eta p^2 = .08$] and the emotion x gaze interaction [$F(2,110) = 11.12$, GG- $\varepsilon = .89$, $p < .001$, $\eta p^2 = .17$] were significant. The main effect of gaze [$F(1,55) = 0.03$, $p = .995$, $\eta p^2 < .01$], the gaze x group interaction [$F(1,55) = 2.36$, $p = .131$, $\eta p^2 = .04$] and the emotion x gaze x group interaction [$F(2,110) = 1.60$, GG- $\varepsilon = .89$, $p = .210$, $\eta p^2 = .03$] did not reach significance.

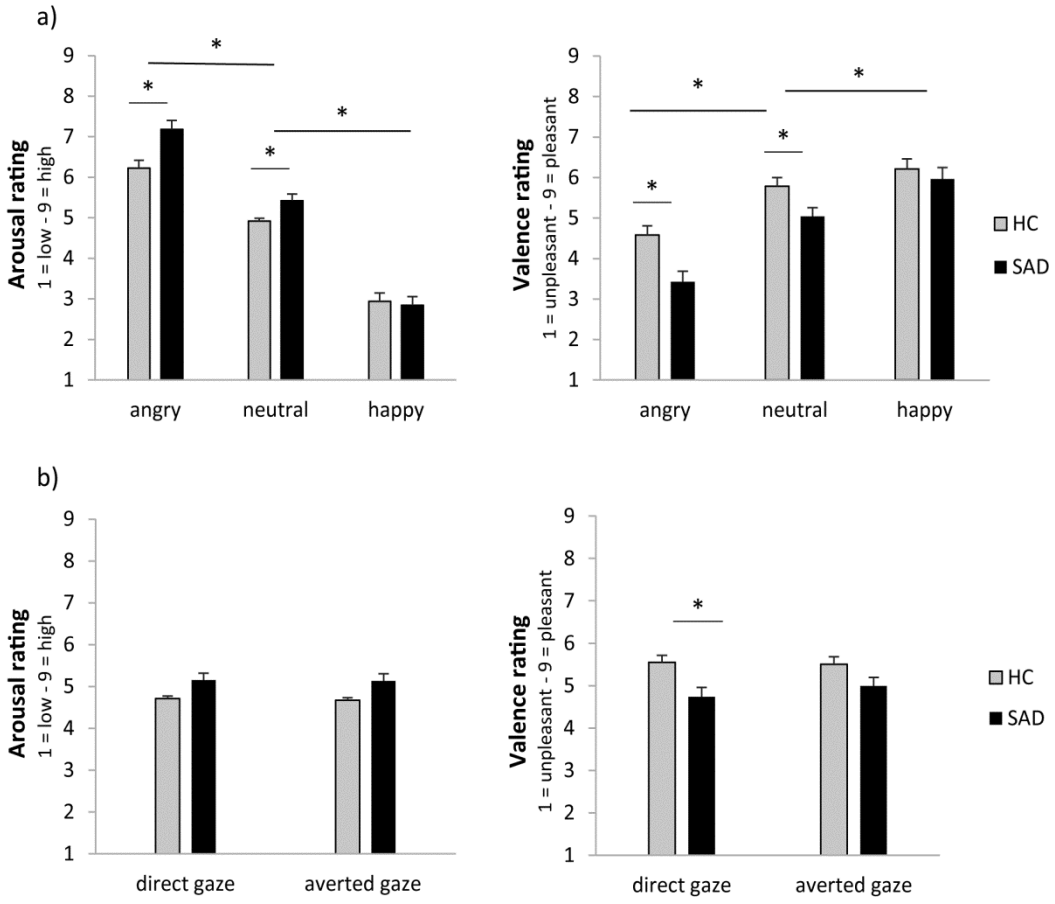

Figure 6: Mean arousal (left) and valence ratings (right) obtained at the end of the experiment in response to happy, neutral and angry faces (a) and in response to faces with direct compared to averted gaze (b) by group. Error bars represent standard errors of the mean, asterisks indicate significant differences (p < .05).

SAD patients rated the faces as more arousing (*M* = 5.15, *SD* = 0.87) compared to controls (*M* = 4.69, *SD* =0.31). Post-hoc analysis of the significant main effect of emotion revealed that participants rated angry faces (*M* = 6.68, *SD* = 1.20) as more arousing compared to neutral (*M* = 5.16, *SD* = 0.71) [*t*(56) = 12.31, *p* < .001] and happy ones (*M* = 2.89, *SD* = 1.10) [*t*(56) = 15.54, *p* < .001]. Beyond, the ratings of neutral and happy faces also varied significantly [*t*(56) = 15.98, *p* < .001]. Just as found in the valence ratings, the post-hoc analysis of the significant emotion x group interaction discovered significant differences for angry [*t*(55) = 3.26, *p* = .002] and neutral [*t*(55) = 2.72, *p* = .010], but not happy faces [*t*(55) = 0.33, *p* = .745] between the two groups. In comparison to HC (M_{ang} = 6.22, *SD* = 1.06; and M_{neu} = 4.92, *SD* = 0.40, respectively), SAD patients rated angry (*M* = 7.18, *SD* = 1.15) and neutral faces (*M* = 5.42, *SD* = 0.88) to be more arousing, while happy faces were rated equally arousing (SAD: *M* = 2.84, *SD* = 1.09; and HC: *M* = 2.94, *SD* = 1.129, respectively) (see Figure 6).

Figure 7: Mean arousal (left) and valence ratings (right) in response to happy, neutral and angry faces by gaze direction. Error bars represent standard errors of the mean, asterisks indicate significant differences ($p < .05$).

Follow-up *t*-tests for the gaze x emotion interaction revealed that angry faces with direct gaze (M =6.78, SD = 1.25) were rated as more arousing compared to angry faces with averted gaze (M = 6.57, SD = 1.16) [$t(56) = 5.11$, $p = .005$]. In contrast, participants rated happy faces with direct gaze (M = 2.84, SD = 1.11) to be less arousing compared to happy faces with averted gaze (M = 2.95, SD = 1.11) [$t(56) = 2.48$, $p = .016$]. There was no significant difference between faces with neutral gaze (M_{direct} = 5.15, SD = 0.71; and $M_{averted}$ = 5.24, SD = 0.95, respectively) [$t(56) = 1.24$, $p = .220$] (see Figure 7).

2.4 Discussion

Study 1 investigated the differences in gaze behavior between patients with SAD and HC during the performance of a saccade task with non-social and social stimuli (faces) varying in terms of emotion as well as gaze direction. In this way, it was examined whether social anxiety comes along with an imbalance of reflexive and volitional control in response to social stimuli as predicted by the ACT (Eysenck & Derakshan, 2011; Eysenck et al., 2007) resulting in an inhibition deficit in SAD patients. In order to extend previous research on this topic, this study investigated clinically diagnosed patients instead of an analogue sample of high and low socially anxious individuals (e.g. Ansari, Derakshan, & Richards, 2008), used photographs of human faces instead of computer-generated faces (e.g. Wieser, Pauli, & Mühlberger, 2009), and manipulated the gaze direction of the target stimuli to examine the role of eye-contact on attentional control. Furthermore, a non-social antisaccade task was conducted before the social antisaccade task to rule out that SAD patients are characterized by a general inhibition deficit. During the experiment, eye-movements as well as ratings of valence and arousal were recorded.

As predicted, results replicated the findings of prior studies using the saccade task that participants exhibited prolonged latencies and enhanced error rates in trials with anti- compared to prosaccades (see Hutton & Ettinger, 2006, for a review). This effect was observable in both parts of the experiment (geometric figures and faces as target stimuli), indicating that the experimental procedure per se was successful and that the results were in line with previous antisaccade studies on social anxiety using emotional faces as target stimuli (Ansari et al., 2008; Wieser, Pauli, & Mühlberger, 2009). Moreover, there were no further differences among groups in the non-social saccade task, which shows that SAD patients did not suffer from a general inhibition deficit.

However, the hypothesized effects for the eye-tracking data in the social task were not found as expected: both groups did not differ in terms of the error rates. This finding is opposed to a prior study conducting an antisaccade task paradigm in HSA and LSA individuals, which detected an enhanced error rate in response to facial expressions in HSA compared to LSA participants during antisaccades (Wieser, Pauli, & Mühlberger, 2009) and concluded that this result might indicate a lowered executive functioning and attentional control in reaction to facial expressions. In contrast, there is also evidence from other experiments supporting the findings of the present study as they did not find group differences regarding the error rates as well among high and low anxious participants (Derakshan et al., 2009) and high and low socially anxious participants (Sluis et al., 2017). In line with this, one study also found that low and high socially anxious individuals did not differ in attention to facial expressions; differences were only found when participants were exposed to social-evaluative threat (Mansell et al., 1999). A possible explanation for these mixed results could be that anxiety leads to an enhanced use of resources, and thereby affects performance efficiency (the relationship between the effectiveness of performance and the effort or resources spend in task performance) more that effectiveness (the quality of task performance or response accuracy), because only the latter can be counterbalanced by compensatory strategies, for example increased effort (Eysenck et al., 2007). In some cases – like the present study - the effect of compensatory strategies might be so strong, that performance effectiveness is not affected *less* than performance efficiency, but rather not *at all*.

However, there was a significant gaze x group interaction for response accuracy in study 1: SAD patients made slightly more errors in response to faces with direct compared to averted gaze, while HC reacted the other way around. A possible explanation could be that SAD patients normally tend to avoid eye-contact and felt uncomfortable when being confronted with direct gaze, while HC normally use direct eye-contact as source of information on the affective state of their conversational partners and felt awkward when the counterpart did not look them in the eyes. There are several studies which have observed reduced maintenance of attention towards eye regions of presented faces in patients with SAD and high socially anxious individuals (Horley et al., 2003; Horley

et al., 2004; Howell et al., 2016; Moukheiber, Rautureau, Perez-Diaz, Jouvent, & Pelissolo, 2012; Moukheiber et al., 2010; Weeks et al., 2013). It has to be mentioned, though, that there are also a few studies which detected the opposite pattern (Boll, Bartholomaeus, Peter, Lupke, & Gamer, 2016; Brunet, Heisz, Mondloch, Shore, & Schmidt, 2009). Furthermore, other studies showed that the severity of SAD positively correlated with the magnitude of eye-contact avoidance in clinical patients (Horley et al., 2004; Moukheiber et al., 2012; Moukheiber et al., 2010). Yet, this finding should be interpreted with caution, because the follow-up calculated *t*-tests were not significant in both groups after alpha adjustment. This could be explicated by either a lack of statistical power or by the prediction of the ACT that anxious individuals respond to processing ineffectiveness by using compensatory strategies, such as the use of processing resources or putting more effort into the task (Eysenck et al., 2007). Another possibility is that the influence of direct gaze on the attentional control of SAD patients was not as strong as expected, because the operationalization of direct gaze was not ideal. In the present experiment, faces with direct gaze were presented in the periphery of the participants' visual field, which makes it possible that participants did not have the impression that the presented faces were looking at them but something else. A better way to operationalize it in future studies might be the presentation of faces with averted gaze that are looking towards the fixation cross, because that is exactly the spot the participants are looking at during the beginning of each trial, too. In this way, participants might rather feel observed.

Moreover, the predicted impact on performance efficiency indicated by response latency, which could be interpreted as a sign of reduced inhibitory control, failed to appear in SAD patients. This is surprising, given the results of several studies finding a hypervigilance for threat in socially anxious children and adults, which is interpreted as a lack of voluntary control over attention in the presence of threatening stimuli (e.g. Mathews & MacLeod, 1994; Seefeldt, Krämer, Tuschen-Caffier, & Heinrichs, 2014; Shechner et al., 2013; Stevens, Rist, & Gerlach, 2011; Williams et al., 1988). However, two other studies investigating attentional control with the antisaccade task in analogue samples of low and high socially anxious individuals also detected no difference with regard to performance efficiency in terms of latency in response to pro- and antisaccades (Sluis et al., 2017; Wieser, Pauli, & Mühlberger, 2009). It could be argued that the parametric value of social anxiety in the high socially anxious students of those two investigations was not comparable to clinically diagnosed social phobics, but this explanation does not apply to the current study, as high socially anxious inpatients served as participants.

One possibility to explain this finding is that the stimuli used in study 1 were not suitable to depict social threat. The target stimuli consisted of faces with angry, neutral and happy expression, whereas the angry condition was considered to be the most threatening one. However, there was no cover story explaining that the faces looked angry, happy or neutral at the participants themselves or

in response to anything the participants had done before. Consequently, it is possible that participants did not attribute the emotional reactions to themselves, but the situation in general, and were less frightened. This might indicate that looking at angry faces alone does not necessarily lead to social anxiety, but that either (the threat of) a negative evaluation of others or self-evaluation is required to induce social anxiousness. However, a recent experiment combined the antisaccades with a threat of a speech task (e.g. Garner et al., 2006; Hinrichsen & Clark, 2003; Mühlberger et al., 2008; Vassilopoulos, 2005; Wong & Moulds, 2011) to elicit social evaluative threat and also found a null result with regard to antisaccades latency differences among low and high socially anxious participants all the same (Sluis et al., 2017).

Another reason for the finding that SAD patients did not show impaired attentional control could have been the participants' degree of motivation. There is evidence from previous experiments which underlines the influence of motivation on cognitive control (Botvinick & Braver, 2015; Kouneiher, Charron, & Koechlin, 2009). As individuals with SAD are afraid to perform poorly in a testing situation, it can be assumed that they put extra effort into the antisaccade task and thereby compensated for possible inhibitory deficits. Future studies should test these influences, for example by enhancing the social threat during the experiment (e.g. giving a speech in front of an audience/ a video camera on an unknown topic) (for examples, see Garner et al., 2006; Wong & Moulds, 2011) or manipulating the amount of cognitive load of the experimental task to a level that cannot be compensated by motivational factors alone (e.g. giving participants a second task to deal with simultaneously to the antisaccade task).

With regard to the ratings of the stimulus material applied in the social antisaccade task, analyses demonstrated that there were distinctions among SAD patients and HC with regard to *emotions*: the SAD patients rated the faces on average to be more arousing and less pleasant compared to HC, which suggests that the disorder-relevant stimuli caused a feeling of discomfort in the group of patients. This observation might be interpreted as a sign of general hyperarousal for situations in which individuals with SAD are confronted with social stimuli and is in line with one of the diagnostic criteria of SAD in the DSM-5 (American Psychiatric Association, 2013) and previous experiments, which detected similar effects (Erwin, Heimberg, Marx, & Franklin, 2006; Etkin & Wager, 2007). A more detailed analysis of the response to the three different categories of faces revealed that SAD patients rated just angry and neutral faces to be more arousing and less pleasant compared to healthy participants, while the analysis of both groups with regard to happy faces did not reach significance. This is in accordance with our hypothesis supposing that not only angry, but also neutral faces appear threatening and unsettling to SAD patients as observed in previous studies (Birbaumer et al., 1998; Somerville et al., 2004; Yoon & Zinbarg, 2007). Neutral faces are more difficult to interpret in comparison to other emotions displaying more salient features, such as a

smile indicates happiness or puckered brows are a signal of anger, and thereby might have led to insecurity in the SAD patients. For that reason, it seems plausible that angry and neutral faces elicited a stronger fear reaction in patients with SAD than harmless happy faces.

Regarding the *gaze direction*, the group differences were even more pronounced for faces with direct compared to averted gaze as indicated by a significant interaction of gaze x group in the valence ratings. While there was no group difference in response to faces with averted gaze after alpha-adjustment, SAD patients rated faces with direct gaze to be less pleasant than HC. This finding punctuates earlier research mentioned above which also detected that SAD patients feel uncomfortable when they are exposed to eye-contact or even try to avoid it (Heuer, Rinck, & Becker, 2007; Horley et al., 2003; Horley et al., 2004; Howell et al., 2016; Lange et al., 2011; Moukheiber et al., 2010; Roelofs et al., 2010; Weeks et al., 2013). The analysis of the arousal rating data yielded a significant emotion x gaze interaction, which resulted from higher arousal ratings to angry faces with direct compared to averted gaze, while it was the other way around for happy faces. An explanation for this finding could be that angry faces have a stronger signaling character when they are directed towards their conversational partner, because in this case the respondent will relate the messenger's facial expression to themselves instead of the environment. Consequently, the behavioral response resulting from the anger would be directed towards the conversational counterpart instead of something in the environment. While healthy participants typically react with approach behavior towards threat, the findings of the present study support that SAD patients show avoidance behavior instead. Relating to happy faces, the motivational effect is typically also to approach it, which is why it is more rewarding and simultaneously less arousing when somebody is directly looking at someone else compared to the situation when the messenger is just happy about something in the environment. Lastly, there was no difference between neutral faces with direct versus averted gaze. As neutral faces are not typically linked to avoidance or approach, it seems plausible that there was no difference in gaze direction relating to this category of facial expression. Yet, it would have also been plausible if participants reacted with more arousal in response to direct neutral compared to averted gaze, because neutral expressions are barely experienced in real-life conversations, which is why they might lead to uncertainty or ambiguity regarding the conversational partner's intentions (e.g. Birbaumer et al., 1998; Moser et al., 2008). However, this is in line with another study investigating the effect of gaze direction on social avoidance elicited by emotional faces in high socially anxious (HSA) individuals (Roelofs et al., 2010). Overall, the results of the ratings corresponded with our expectations.

In line with the growing body of literature on attentional control in SAD, the results of the present study suggest that the underlying mechanisms of SAD are more complex than current theoretical models are able to represent. Contrary to the premises of the ACT (Eysenck et al., 2007),

the present study provided no evidence for reduced inhibitory control in SAD patients compared to controls during an antisaccade task with emotional faces serving as target stimuli, albeit SAD patients rated emotionally faces - particularly angry and neutral ones and those with direct compared to averted gaze – as more arousing and less pleasant than controls. However, it has to be stated that the reason why there were no group differences in the latencies of the eye-tracking data could be that deficits in attentional inhibitory control only occur under social threat and not just in the mere presence of phobic stimuli, that motivation has a strong impact on task performance and can compensate inhibitory deficits when the cognitive load is low, or even that several attentional biases occur at different stages of attention and cancel each other out. Therefore, future research is needed to explore the multiple underlying mechanisms associated with attentional inhibitory control in SAD to gain a better understanding of this disorder and provide new developments for interventions in SAD.

3 Study 2: Fear Conditioning and Stimulus Generalization in Patients with Social Anxiety Disorder

This study has been partly published in the *Journal of Anxiety Disorders* (Ahrens et al., 2016).

3.1 Introduction

Etiology models of anxiety postulate that aberrant learning and memory processes in patients compared to HC play a key role in the development and maintenance of these disorders (Mineka & Zinbarg, 2006). In addition to enhanced conditionability, resistance to extinction and an inhibition deficit, overgeneralization gained special interest in the scientific community (Duits et al., 2015; Lissek et al., 2005) (see also chapter 1.4.2.4). Overgeneralization is referred to as the process of transferring a conditioned fear response to similar stimuli in an exaggerated way and has been found in several anxiety disorders, such as PTSD, PD and GAD (Lissek & Grillon, 2012; Lissek et al., 2014; Lissek et al., 2009). However, as research on this topic has just begun, it is unclear whether overgeneralization is a marker of anxiety disorders in general or just occurs in specific clinical pictures. As SAD is one of the most prevalent anxiety disorders besides specific phobias, we aimed to examine whether or not it was linked to overgeneralization, too.

According to the DSM-5, SAD is characterized by a persistent fear of social or performance situations in which the individual feels self-conscious when exposed to strangers or potential scrutiny by others (American Psychiatric Association, 2013). As mentioned for anxiety disorders in general, previous conditioning studies have detected that the ability of patients with SAD to discriminate between danger and safety cues is diminished (for a recent meta-analysis, see Duits et al., 2015). A lack of this skill might lead to deficits in discrimination learning – a cognitive process opposite of generalization – and implicate an enhanced tendency to generalize conditioned fear. As a consequence, a negative experience with one particular person could, for example, be generalized to others without having previously met.

However, to test this assumption, a suitable paradigm was needed. Most previous studies on fear generalization applied the generalization paradigm developed by Lissek, which employs 10 rings of increasing diameter. The largest and smallest rings serve as CS+ and CS-, intermediate stimuli as GSs, and an electric shock as US (Lissek, Biggs, et al., 2008). Although this paradigm is well-suited to assess the generalization phenomenon on a basic level, we suspected it not be specific enough to disentangle the diverse mechanisms underlying different anxiety disorders.

Fear learning in vivo scarcely occurs to simple sensory cues, such as geometric figures or shocks, but involves more complex stimuli that may differ among disorders. Therefore, we

investigated fear generalization in SAD with an adaption of the "screaming-lady" paradigm (Lau et al., 2008). In this design, two neutral, female faces served as CS, and a fearful face paired with a loud scream as US. Intermediate stimuli - created by morphing the two original faces into each other - served as GSs. The screaming lady paradigm provides several advantages compared to the rings-of-increasing-diameter-design: first, it utilizes social instead of non-social stimuli, which likely are disorder-relevant for SAD patients and enhance the ecological validity of the design. Several studies have shown that successful conditioning in high socially anxious individuals or patients with SAD can not only be evoked by efficacious non-social unconditioned stimuli, such as electric shocks, aversive odors and geometric figures (e.g. Hermann et al., 2002; Schneider et al., 1999), but also by social stimuli, such as emotional facial expressions paired with compatible verbal feedback (Lissek, Levenson, et al., 2008) or isolated verbal comments (Ahrens et al., 2014). Comparisons between conditioning studies with disorder-relevant and disorder-non-relevant stimuli detected that the former design leads to faster fear learning, stronger fear responses, and greater resistance to extinction (as reviewed in Lissek et al., 2005; Öhman & Mineka, 2001). Second, the screaming-lady paradigm has been particularly developed for vulnerable populations, such as children or clinical samples (Haddad, Pritchett, Lissek, & Lau, 2012), which makes it potentially advantageous for the recruitment of anxiety patients. Finally, we expected better learning effects in both groups due to the high belongingness between the CS (faces) and the US (scream). During the whole experiment, skin conductance response (SCR), heart rate (HR) and ratings of valence, arousal and US expectancy were recorded. Based on the aforementioned findings, the hypotheses for study 2 were the following:

1. Both groups generalize their conditioned fear of the CS+ to morphs of the original stimuli (GS) as a function of their similarity to the CS+.
2. Patients with SAD compared to HC show overgeneralization of conditioned fear responses measurable as a) significantly enhanced fear responses in reaction to more categories of GSs and b) linear instead of quadric declines (as seen in HC) of the generalization gradient.
3. Patients with SAD display elevated levels of fear in both physiological measures and ratings compared to HC due to a general hyperarousal in response to social stimuli.

3.2 Material and Methods

3.2.1 Participants

Thirty-one patients with a current ICD-10 diagnosis of SAD and thirty-one HC took part in the study. Two HC had to be excluded due to technical problems and five patients with SAD dropped out of the study, so that 29 HC (*M* = 27.66 *SD* = 7.05; 12 female) and 26 SAD patients (*M* = 26.46, *SD* =

8.37; 8 female) were included in the statistical analyses. Groups did not differ on age (p = .568) or gender (p = .414).

Patients were recruited at the same mental health clinic in Germany as in study 1 (Schoen Klinik, Bad Bramstedt), where again experienced local staff psychologists diagnosed the SAD patients according to the criteria of the ICD-10 (World Health Organization, 1992). For all patients, SAD was the primary source of current discomfort. Controls were recruited through advertisements on a local internet platform and tested at the University of Würzburg, as non-patients were not allowed to enter the clinic of the inpatients. To measure symptom severity, all participants completed the German version of the SPAI (Fydrich, 2002; Turner et al., 1989) and the LSAS (Heimberg et al., 1999). German scores of the SPAI were transformed into the original scores (Turner et al., 1989). As expected, significant group differences were found in the total scores of the SPAI ($t(53) = 11.20$, $p < .001$; SAD: M = 136.96, SD = 30.72; HC: M = 61.12, SD = 18.56) and LSAS ($t(53) = 11.66$, $p < .001$; SAD: M = 87.54, SD = 23.49; HC: M = 24.38, SD = 15.36). Participants also completed a socio-demographic questionnaire and the German versions of the STAI (Spielberger et al., 1970), the BDI (Beck et al., 1961; Hautzinger et al., 1994) and the PANAS (Watson et al., 1988). Means and standard deviations for all questionnaires are presented in Table 2.

Table 2: Descriptive variables of both groups of study 2.

	HC		SAD			
Variable	*M*	*SD*	*M*	*SD*	*t(53)*	*p*
SPAI	61.12	18.56	136.96	30.72	11.20	$p < .001$*
LSAS	24.38	15.36	87.54	23.49	11.66	$p < .001$*
BDI	7.07	6.19	23.92	12.52	6.18	$p < .001$*
STAI State	34.97	8.58	55.73	9.70	8.43	$p < .001$*
STAI Trait	34.97	9.19	60.81	8.45	10.81	$p < .001$*
PANAS_PA	30.10	5.98	21.85	4.42	5.77	$p < .001$*
PANAS_NA	12.38	4.21	21.85	8.36	5.21	$p < .001$*

SPAI, Social Phobia and Anxiety Inventory; LSAS, Liebowitz Social Anxiety Scale; BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; PANAS, Positive and Negative Affect Scale (PA, positive affect; NA, negative affect).

All participants gave written, informed consent prior to participation. Exclusion criteria for SAD patients included: 1) a history of alcohol or substance abuse, 2) a current or past diagnosis of psychosis or delusional disorders and 3) current suicidal ideation. Psychiatric comorbidities among patients included major depression (n = 31), personality disorders (n = 19), eating disorders (n = 5), pathological gambling (n = 7), somatoform disorders (n = 3), other anxiety disorders (n = 4),

dissociative and conversion disorder (n = 1) and sexual disorders (n = 2). HC were free of any current or past AXIS I mental disorder and psychopharmacologic medication (self-report). Further exclusion criteria were 1) pregnancy, 2) current use of illicit drugs and 3) neurological disorders or other medical conditions that interfered with the objectives of the study. Ethical approval for the study was granted by the ethical committee of the medical faculty of the University of Würzburg (reference number 87/13).

3.2.2 Stimuli

Two photographs of a blonde and a brunette actress with neutral facial expression (NimStim Set of Facial Expressions; Tottenham et al., 2009) served as threat (CS+) and safety cues (CS-). For half of the participants, the blonde actress served as threat cue and the brunette face as safety cue (counterbalancing order 1) and for the other half, the assignment was reversed (counterbalancing order 2). The US consisted of the respective CS+ face displaying a fearful expression and a simultaneously presented 95 dB shrill female scream of the International affective digitized sounds database (IADS; Bradley & Lang, 1999; Bradley & Lang, 2007). Four GS were created by morphing the two faces in 20% steps using the face-morphing software Squirlz Morph Version 2.1 (Xiberpix, Solihull, UK) with the GS most similar to the CS+ referred to as GS1 and the GS most similar to the CS- as GS4 (see Figure 8).

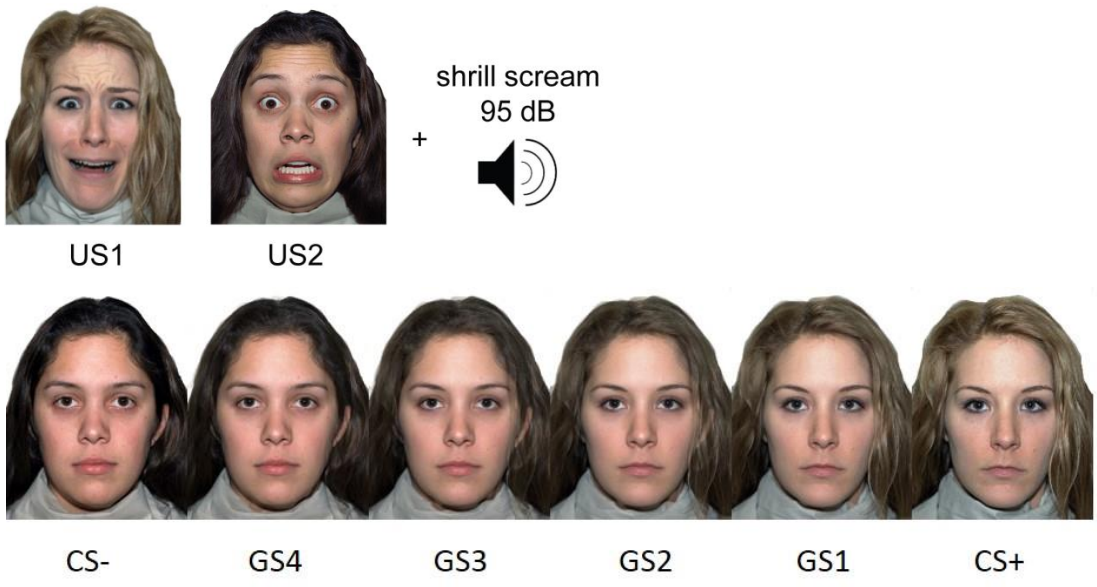

Figure 8: Unconditioned (US) (upper panel), conditioned (CS) and generalized stimuli (GSs) (lower panel) used in study 2. For half of the participants, the blonde face served as CS+ and the brunette face as safety signal (as depicted), while the order was reversed for the other half of participants (not depicted). GSs were created by morphing the two CS faces into each other in 20% steps with the GS1 being most similar and the GS4 being least similar to the CS+.

3.2.3 Design and procedure

The paradigm (adapted from Lau et al., 2008; Lissek, Biggs, et al., 2008) consisted of a habituation, acquisition and generalization phase. In each trial, either the CS+, CS- or one of the GS was presented for 6 s in a randomized order with no CS or GS occurring more than twice in a row. Reinforced trials were followed immediately by the US which lasted for 1.5 s. To prevent expectancy effects, the inter-trial interval varied among 9 and 12s.

Habituation consisted of 4 CS+ and 4 CS- presentations during which no US was presented (8 trials). Afterwards, valence and arousal ratings were obtained on a 9-point Likert scale. During acquisition, 12 CS+ and 12 CS- were presented (24 trials). 9 of 12 CS+ were instantly followed by the US using a 75% reinforcement schedule. This rate was used, because several studies have shown that partial reinforcement schedules are more resistant to extinction than continuous reinforcement schedules with highest resistance rates in the region between 50 and 80% (Lewis, 1960). Generalization consisted of the CS+, CS-, and the GSs 1-4, each presented 12 times (72 trials). While CS- and GSs were never reinforced, 6 of the 12 CS+ were still followed by the US to prevent early extinction (50% reinforcement) (see Figure 9). In addition to valence and arousal ratings, which were obtained after all of the three phases, participants were also asked to rate US expectancy after acquisition and generalization. Moreover, they were asked to evaluate the valence and arousal of the US at the end of the experiment. This was done to investigate whether the US was sufficiently aversive to elicit conditioning and if there were differences relating to the US among groups.

During the whole experiment, skin conductance response (SCR) and heart rate (HR) were recorded by a BrainVision Data acquisition system (V-Amp 16, Brain Products Inc., Munich, Germany). Participants were offered an extinction block in which the US never occurred to prohibit permanent fear conditioning, but only two participants accepted the offer.

3.2.4 Data recording and analysis

Physiological variables were processed offline with the Vision Analyzer (Version 2.0, Brain Products Inc., Munich, Germany). Skin conductance was recorded from the hypothenar eminence of the palmar surface of the non-dominant hand using two 8 mm Ag/AgCl electrodes filled with a 0.05 M NaCl electrolyte medium. The V-Amp system constantly delivered 0.5 V across the electrodes and sampled skin conductance at a rate of 1000 Hz. Skin conductance recording was filtered with a 50 Hz notch and a 1 Hz high cutoff filter. Skin conductance response (SCR) to the stimuli was defined as the base to peak difference (in µS) for an increase within 1-6 s after CS onset. The SCR was baseline-corrected with 1 s before CS onset. Responses lower than 0.02 µS were scored as zero. To normalize

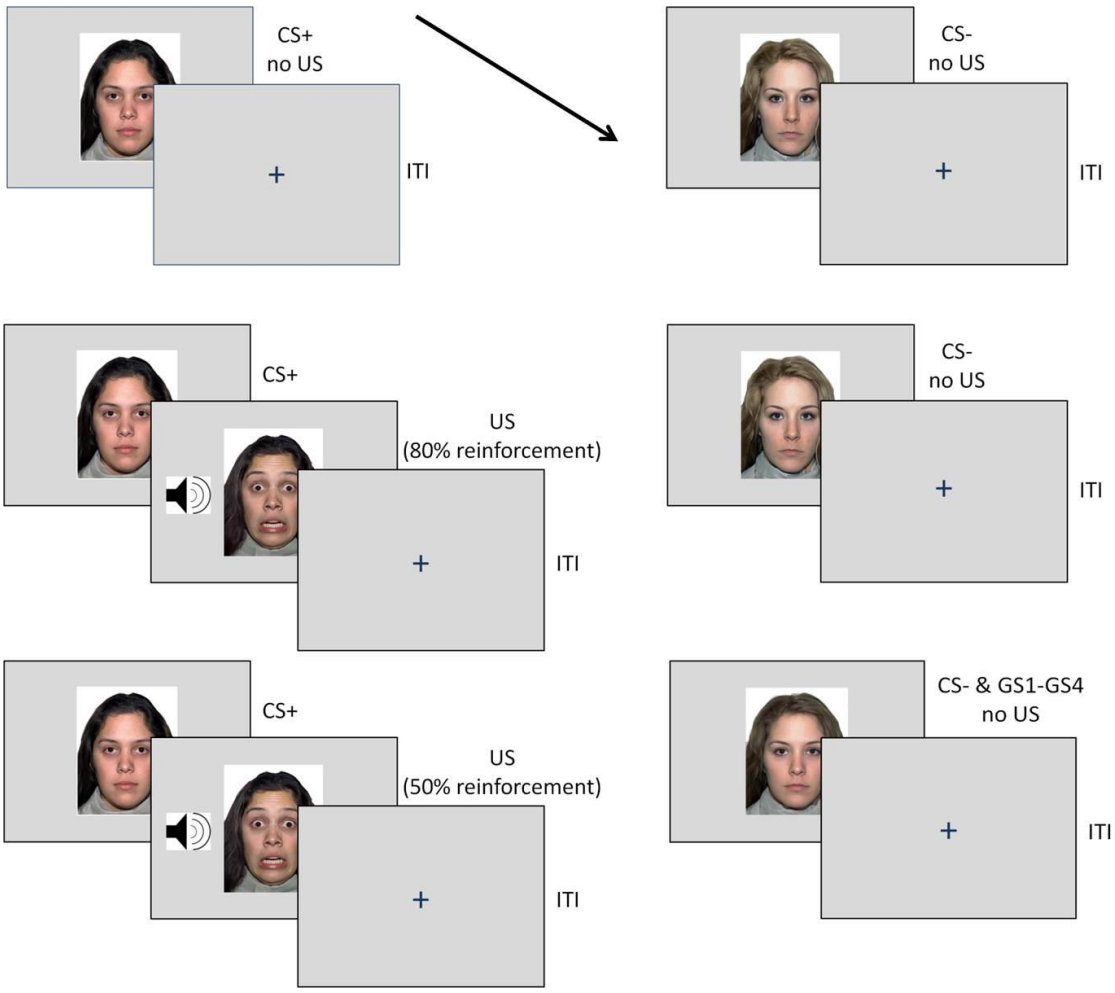

Figure 9: Schematic overview of the experimental design of study 2. Depicted are the habituation (upper panel), acquisition (middle panel) and generalization phase (lower panel). Stimuli were randomly presented for 6sec during each of the three parts of the experiment.

distribution, the logarithms of SCR values were calculated (SCR+1) (Venables & Christie, 1980). Scores for each CS were generated by computing the mean of all trials.

Heart rate was measured by recording an electrocardiogram with two adhesive Ag/AgCl electrodes, one placed on the sternum, the other placed on the left lateral margin of the chest in order to minimize movement artefacts (Jennings et al., 1981). A 5 mm electrode fixed to the "processus mastoideus" behind the left ear and a second one attached to the middle of the forehead right under the hairline served as reference and ground electrode, respectively. Impedances were kept below 10 kΩ. Offline, difference values between the heart rate electrodes were computed and the electrocardiogram (ECG) was filtered with a 50 Hz notch, a 30 Hz high cutoff filter and a time constant of 0.1. In a next step, R-spikes were automatically counted, the inter-beat-interval was calculated, and continuous heart rate (HR) estimates were determined per sampling point (sampling

rate: 1000Hz). Then, a baseline-correction of 1s was applied. Average changes in heart rate from baseline were calculated for each CS (0-6 s) in beats per minute (bpm).

3.2.5 Statistical analysis

Statistical analyses were conducted using SPSS (Version 22, SPSS Inc, Chicago, IL, USA). Acquisition of conditioning was analyzed with a 2 (Group: SAD vs. HC) x 2 (Stimulus: CS+ vs. CS-) analysis of variance (ANOVA) with repeated measures. Generalization effects were analyzed with a 2 (Group: SAD vs. HC) x 6 (Stimulus: CS+ vs. GS1 vs. GS2 vs. GS3 vs. GS4 vs. CS-) ANOVA with repeated measures. Significant effects were followed by either paired-samples t tests or trend analyses. With regard to the shape of the generalization curves, linear and quadratic trends were tested. For all analyses, a significance level of $p < .05$ (two-tailed) was defined. The partial eta-squared (ηp^2) is reported as a measure of effect size. In case of violation of sphericity, Greenhouse-Geisser epsilon (GG-ε) and uncorrected degrees of freedom are reported (Picton et al., 2000).

3.3 Results

3.3.1 Habituation

Psychophysiology: As expected, the 2 (group) x 2 (stimulus) ANOVA for the skin conductance response (SCR) revealed no significant main effect of stimulus type and no stimulus type x group interaction, indicating that none of the groups preferred one of the two presented faces. However, SAD (M = 0.15 µS, SD = 0.11) already showed a greater SCR in response to faces compared to HC (M = 0.08 µS, SD = 0.09) [$F(1,53) = 7.67$, $p = .008$, $\eta p^2 = .13$], which might point to a generally enhanced fear reaction in SAD patients in response to face stimuli. The analysis of the heart rate (HR) yielded neither a significant main effect for group nor interaction, but unexpectedly showed a significant main effect of stimulus type [$F(1,53) = 4.65$, $p = .036$, $\eta p^2 = .08$] with a decrease in heart rate in response to the CS+ (M = - 0.55 bpm, SD = 2.85) and an increase to the CS- (M = 0.45 bpm, SD = 2.17).

Ratings: While there was no significant main effect of stimulus type and no stimulus type x group in the valence and arousal ratings, significant main effects of group were detected [$F(1,53)$ = 7.21, $p = .010$, $\eta p^2 = .12$, and $F(1,53) = 8.82$, $p = .004$, $\eta p^2 = .14$, respectively], as SAD rated all faces to be less pleasant (M = 4.58, SD = 1.40) and more arousing (M = 4.37, SD = 1.51) than HC (M = 5.50, SD = 1.14 and M = 3.12, SD = 1.59, respectively) (see Figure 10). This is in line with the enhanced responses in SCR in SAD patients compared to HC. With regard to the US expectancy rating, neither the main effect of group nor the interaction was significant. However, an unexpected effect of stimulus type was found [$F(1,53) = 5.30$, $p = .025$, $\eta p^2 = .09$]: all participants expected the CS+ (M = 46.00%, SD = 28.97%) to be followed more often by a US relative to the CS- (M = 36.91%, SD = 24.64%) although no consequences were applied yet. One possibility is that this effect was an

incidental finding. Another explanation could be that the two faces were not of equal value regarding valence and/or arousal, and therefore elicited different assumptions regarding their pairing with the aversive scream.

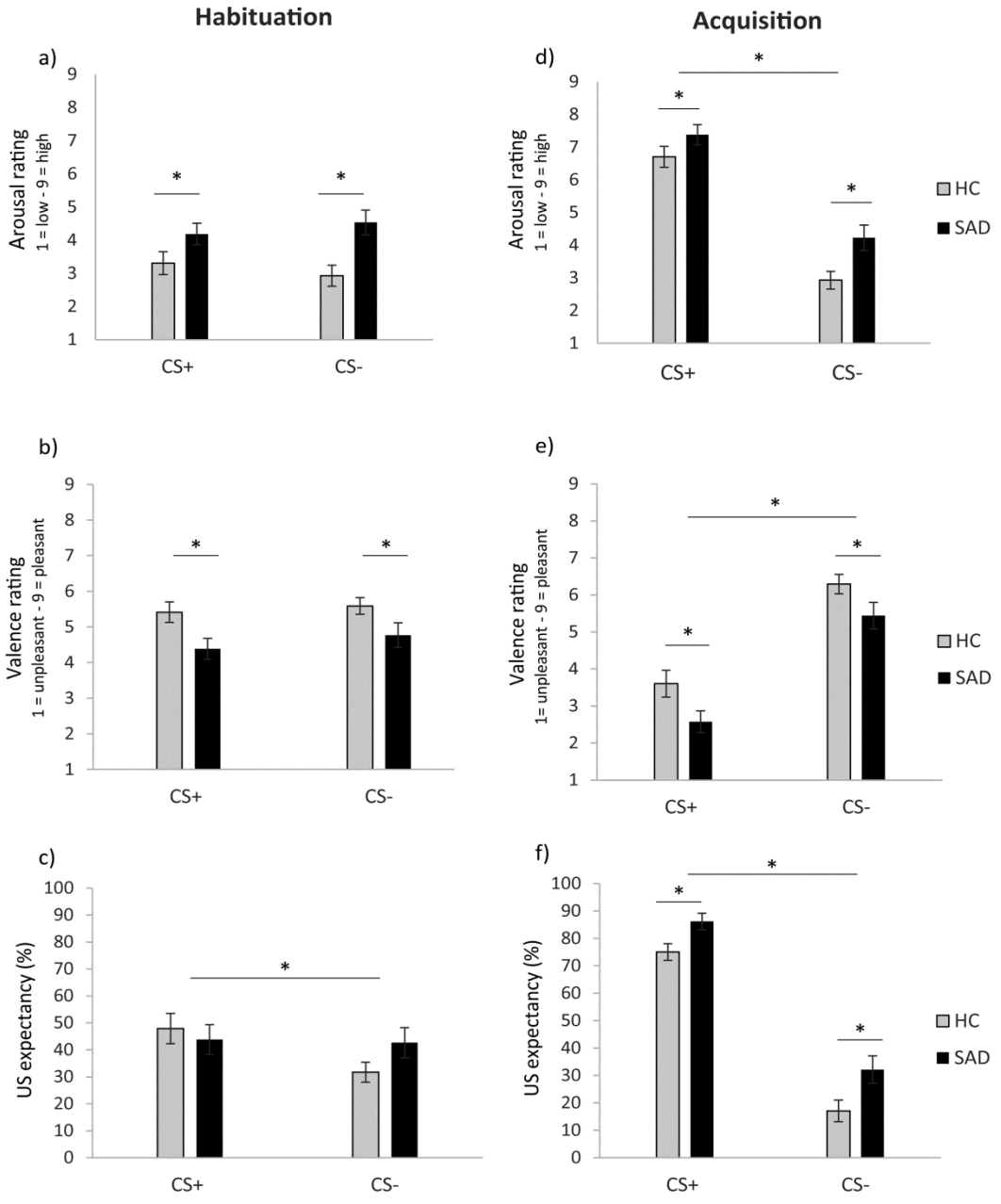

Figure 10: Mean arousal (a), valence (b) and US expectancy ratings (c) to the threat (CS+) and safety cue (CS-) by group during habituation (left panel) and acquisition (right panel). Error bars represent standard errors of the mean, asterisks indicate significant differences (p< .05).

Although effects like this usually do not occur due to the counterbalancing of experimental conditions, an unequal drop out might have caused the finding. In the experiment, two participants who were assigned to condition 1 (blonde face served as CS+) and five participants assigned to

condition 2 (brunette face served as CS+) had to be excluded. Comparison with a paired samples *t*-test yielded that in general, the blonde face (*M* = 47.82%, *SD* = 29.04) was expected to be followed by the US more often compared to the brunette face (*M* = 35.09%, *SD* = 23.72), (*t*(54) = 3.46, *p* = .001). As the blonde face served as the CS+ more often in the experiment due to dropout, a bias in the expectancy ratings of the whole sample cannot be ruled out.

3.3.2 Acquisition

Psychophysiology: Successful conditioning reflected in a significant stimulus type main effect was found for the SCR [$F(1,53) = 4.07$, $p = .049$, $\eta p^2 = .07$], indicating that all participants responded with significant higher SCR to the CS+ (*M* = 0.20 µS, *SD* = 0.18) compared to the CS- (*M* = 0.16 µS, *SD* = 0.13) (see Figure 11). Both the main effect of group [$F(1,53) = 1.24$, $p = .270$, $\eta p^2 = .02$] and the stimulus type x group interaction [$F(1,53) = 0.98$, $p = .326$, $\eta p^2 = .02$] were not significant.

In the HR, the main effect of stimulus type was also significant [$F(1,53) = 5.00$, $p = .030$, $\eta p^2 = .09$], but surprisingly revealed a greater HR deceleration to the CS- (*M* = -1.02 bpm, *SD* = 1.46) relative to the CS+ (*M* = -0.38 bpm, *SD* = 1.78). Furthermore, the main effect of group [$F(1,53) = 11.22$, $p = .001$, $\eta p^2 = .18$] showed that SAD (*M* = -1.24 bpm, *SD* = 1.28) exhibited a stronger HR deceleration than HC (*M* = -0.21 bpm, *SD* = 0.99) which again points in the direction of a generally stronger fear reaction of SAD in response to the presented faces compared to HC (see Figure 11). The stimulus type x group interaction did not reach significance [$F(1,53) = 0.21$, $p = .649$, $\eta p^2 < .01$].

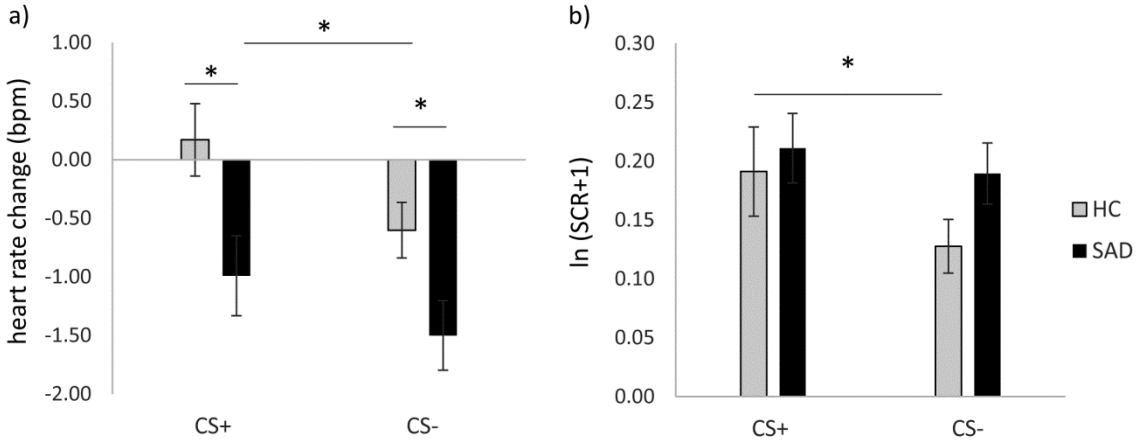

Figure 11: Averaged changes in heart rate (relative to baseline in beats per minute; bpm) (a) and skin conductance responses (b) in response to the threat (CS+) and safety cue (CS-) during acquisition differentiated for social anxiety disorder (SAD) and healthy control (HC) participants. Error bars represent the standard error of the mean. Asterisks indicate significant differences (p < .05).

Ratings: Confirming successful conditioning, main effects of stimulus type were found in the valence [$F(1,53) = 66.93$, $p < .001$, $\eta p^2 = .56$], arousal [$F(1,53) = 141.16$, $p < .001$, $\eta p^2 = .73$] and US

expectancy ratings [$F(1,53) = 178.52$, $p < .001$, $\eta p^2 = .77$], resulting from more negative valence ratings to the CS+ (M= 3.12, SD= 1.81) versus CS- (M = 5.89, SD = 1.67), more arousing ratings regarding the CS+ (M = 6.71, SD = 1.71) compared to the CS- (M = 2.93, SD = 1.45), and higher US expectancy ratings for the CS+ (M = 80.27%, SD = 16.87%) than for the CS- (M= 24.18%, SD = 24.30%). Also, significant main effects of group were revealed for all three measures (valence: [$F(1,53) = 9.52$, $p = .003$, $\eta p^2 = .15$]; arousal [$F(1,53) = 8.08$, $p < .006$, $\eta p^2 = .13$]; US expectancy: [$F(1,53) = 14.73$, $p < .001$, $\eta p^2 = .15$]), indicating that SAD rated all faces as less pleasant, more arousing, and overestimated the occurrence of the US compared to HC (see Figure 10). The stimulus type x group interaction never reached significance (valence: [$F(1,53) = 0.07$, $p = .797$, $\eta p^2 < .01$], arousal: [$F(1,53) = 1.14$, $p = .291$, $\eta p^2 = .02$] and US expectancy: [$F(1,53) = 0.22$, $p = .644$, $\eta p^2 < .01$], respectively).

3.3.3 Generalization

Psychophysiology: In line with our hypotheses, the 2 x 6 group by stimulus type repeated measures ANOVA yielded a significant effect of stimulus type [$F(5,265) = 18.30$, GG- $\varepsilon = .34$, $p < .001$, $\eta p^2 = .26$] for the SCR, which reflects that the participants differentiated among the six presented faces. The main effect of group [$F(1,53) = 0.23$, $p = .631$, $\eta p^2 < .01$] and the stimulus-type x group interaction [$F(5,265) = 0.77$, $p = .571$, $\eta p^2 = .01$] did not reach significance, though, depicting that there were neither quantitative nor qualitative differences among groups in the SCR. To follow up the significant main effect of stimulus-type, five paired t-tests were performed using the CS- as reference condition to identify precisely which GSs elicited generalized fear reactions. Results revealed significant differences between CS- and CS+ [$t(54) = 4.60$, $p < .001$], CS- and GS1 [$t(54) = 3.80$, $p = .001$], and a marginally significant difference between CS- and GS2 [$t(54) = 1.89$, $p = .064$]. No differences were found between the CS- and GS3 or GS4. This result points to generalization of conditioned fear reactions from the CS+ to the most similar morph.

To test the shape of the generalization gradients, trend analyses were performed for the SCR. As noted above, healthy participants typically exhibit quadratic shapes, while anxiety patients were found to display more linear gradients. Results showed a significant linear [$F(1,53) = 23.13$, $p < .001$, $\eta p^2 = .30$] and quadratic trend [$F(1,53) = 24.07$, $p < .001$, $\eta p^2 = .31$] for the CS type and a significant quadratic stimulus type x group interaction [$F(1,53) = 4.68$, $p = .035$, $\eta p^2 = .08$]. In order to explore group differences, a follow-up ANOVA of the significant quadratic trend interaction was performed. Significant quadratic trends of the stimulus type were found in both SAD patients [$F(1,25) = 5.78$, $p = .024$, $\eta p^2 = .19$] and controls [$F(1,28) = 19.69$, $p < .001$, $\eta p^2 = .41$], whereas it was more pronounced in the latter group (see Figure 12). The linear stimulus type x group interaction did not reach significance ($p = .692$).

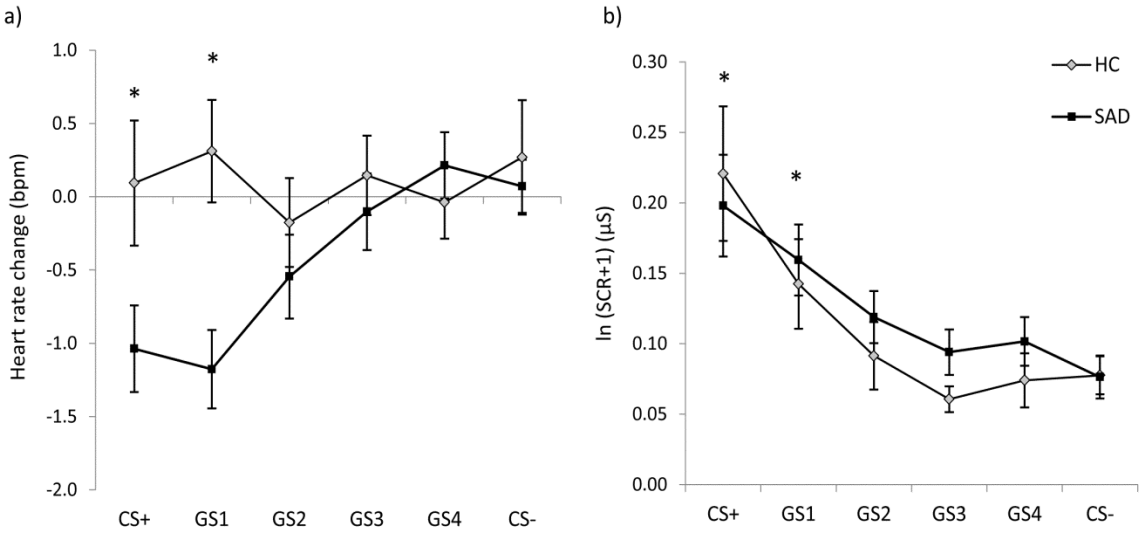

Figure 12: Results for heart rate change (a) and skin conductance response (b) during the generalization phase of study 2 to each stimulus category for patients with SAD and healthy controls. Error bars indicate the standard error of the mean, asterisks represent significant differences from the reference condition (CS-) (p < .05). Reprinted and adapted from the Journal of anxiety disorders, Vol. 44, Ahrens, L. M., Pauli, P., Reif, A., Mühlberger, A., Langs, G., Aalderink, T., & Wieser, M. J., Fear conditioning and stimulus generalization in patients with social anxiety disorder, pp. 36-46, 2016.

For the HR, analyses yielded a marginal effect of stimulus type [$F(5,265) = 2.08$, $p = .068$, $\eta p^2 = .04$], a significant main effect of group [$F(1,53) = 5.30$, $p = .025$, $\eta p^2 = .09$], and a significant stimulus type x group interaction [$F(5,265) = 2.64$, $p = .024$, $\eta p^2 = .05$], indicating differentiation among the six stimuli as well as quantitative and qualitative group differences. Follow-up ANOVAs for each group found no main effect of CS for HC ($p = .88$), but for SAD [$F(5,125) = 5.93$, $p < .001$, $\eta p^2 = .19$], reflecting that only the SAD patients differentiated between stimuli. Follow-up paired *t*-tests were performed for SAD using the CS- as reference condition and revealed a heart rate deceleration in response to the CS+ which spread to the GSs, indicated by significant differences between CS- and CS+ [$t(25) = 3.59$, $p = .001$] and CS- and GS1 [$t(25) = 3.77$, $p = .001$]. This shows that SAD patients transferred their conditioned fear from the CS+ to at least one GS. There were no differences between the CS- and GS2, GS3 or GS4, though.

Trend analyses for the HR revealed that there was a significant linear trend of stimulus type [$F(1,53) = 5.86$, $p = .019$, $\eta p^2 = .10$] as well as a linear stimulus type x group interaction [$F(1,53) = 5.52$, $p = .023$, $\eta p^2 = .09$]. A follow-up ANOVA for the significant linear trend interaction disclosed that this was due to a linear trend in SAD patients [$F(1,25) = 19.70$, $p < .001$, $\eta p^2 = .44$], whereas that trend could not be detected in HC ($p = .97$) (see Figure 12). The quadratic trends were not significant (stimulus type: $p = .912$; stimulus type x group interaction: $p = .390$).

Ratings: The 2 x 6 repeated-measures ANOVA demonstrated main effects of stimulus-type and group in all three measures: valence [$F(5,265) = 58.25$, GG- $\varepsilon = .45$, $p < .001$, $\eta p^2 = .52$ and $F(1,53) = 7.49$, $p = .008$, $\eta p^2 = .12$, respectively], arousal [$F(5,265) = 70.48$, GG- $\varepsilon = .39$, $p < .001$, $\eta p^2 = .57$ and

$F(1,53) = 6.34$, $p = .015$, $\eta p^2 = .11$] and US expectancy [$F(5,265) = 140.91$, GG- $\varepsilon = .62$, $p < .001$, $\eta p^2 = .73$ and $F(1,53) = 11.90$, $p = .001$, $\eta p^2 = .18$]. In order to test if the detected stimulus differences were in line with our hypothesis, five follow-up paired *t*-tests were calculated for each rating. In all three measures, participants generalized their conditioned fear reaction from the CS+ to at least to two GSs: In the valence ratings, differences were found between CS- and CS+ [$t(54) = 9.01$, $p < .001$], CS- and GS1 [$t(54) = 6.93$, $p < .001$] and CS- and GS2 [$t(54) = 2.95$, $p = .005$], but not between the CS- and the GS3 or GS4. In the other ratings, participants even distinguished for a further category in both arousal (CS- vs. CS+: $t(54) = 10.32$, $p < .001$; CS- vs. GS1: $t(54) = 7.93$, $p < .001$; CS- vs. GS2: $t(54) = 4.69$, $p = .005$; CS- vs. GS3: $t(54) = 2.80$, $p = .007$) and US expectancy rating (CS- vs. CS+: $t(54) = 18.52$, $p < .001$; CS- vs. GS1: $t(54) = 9.83$, $p < .001$; CS- vs. GS2: $t(54) = 6.33$, $p = .005$; CS- vs. GS3: $t(54) = 3.39$, $p = .001$), respectively. Also, as observed during acquisition, follow-up *t*-tests for the main effects of group showed that SAD rated the faces on average to be less pleasant and more arousing ($M = 5.31$, $SD = 1.52$ vs. $M = 4.36$, $SD = 1.27$), and overrated the occurrence of the US (see Figure 13) in comparison to HC. The stimulus type x group interactions were not significant for all three variables [(arousal: $F(5,265) = 0.86$, $p = .510$, $\eta p^2 = .02$), (valence: $F(5,265) = 0.78$, $p = .569$, $\eta p^2 = .01$), and (US expectancy: $F(5,265) = 1.76$, $p = .121$, $\eta p^2 = .03$) respectively].

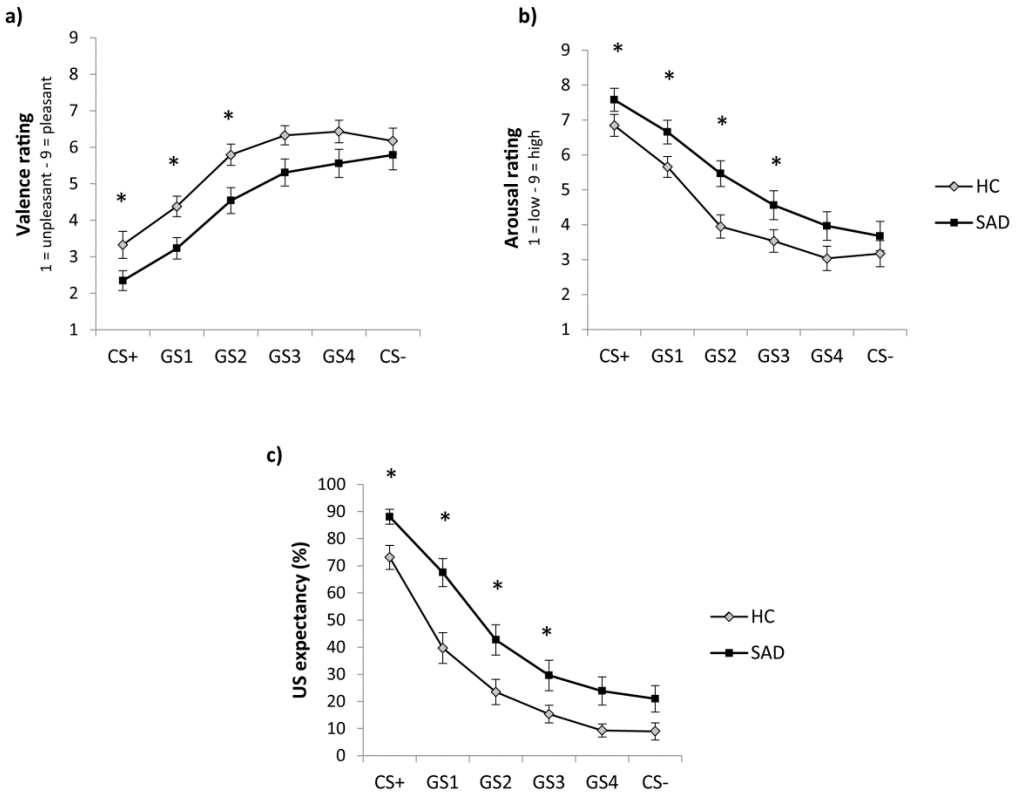

Figure 13: Results of the generalization phase for valence (a), arousal (b) and US expectancy ratings (c) to each stimulus category by group. Asterisks indicate significant differences from the reference condition (CS-) (p < .05). Reprinted and adapted from the Journal of anxiety disorders, Vol. 44, Ahrens, L. M., Pauli, P., Reif, A., Mühlberger, A., Langs, G., Aalderink, T., & Wieser, M. J., Fear conditioning and stimulus generalization in patients with social anxiety disorder, pp. 36-46, 2016.

Trend analyses revealed that both groups showed significant linear and quadratic trends in stimulus type in valence ([$F(1,53) = 82.62$, $p < .001$, $\eta p^2 = .61$] and [$F(1,53) = 35.20$, $p < .001$, $\eta p^2 = .40$]), arousal ([$F(1,53) = 97.47$, $p < .001$, $\eta p^2 = .65$] and [$F(1,53) = 30.78$, $p < .001$, $\eta p^2 = .37$]) and US expectancy ratings ([$F(1,53) = 304.07$, $p < .001$, $\eta p^2 = .85$] and [$F(1,53) = 77.92$, $p < .001$, $\eta p^2 = .60$]). In addition, there was an almost significant quadratic stimulus type x group interaction [$F(1,53) = 3.71$, $p = .060$, $\eta p^2 = .07$] in the arousal ratings. No other effects were significant.

Valence and Arousal of the US: The ratings for the US on a scale from 1 to 9 revealed that all participants rated the US to be very unpleasant ($M = 2.02$, $SD = 0.23$) and very arousing ($M = 7.65$, $SD = 0.23$), which indicates the US to be effective in eliciting fear. Independent samples *t*-tests found no group differences for the US ratings.

3.4 Discussion

The present study examined differences between SAD patients and HC regarding the acquisition of conditioned fear to a threat cue and its generalization to perceptually similar generalization cues. In this way, it should be investigated whether, for example, a negative experience with one particular person could be generalized to others without having previously met. During the experiment, SCR, HR and ratings of valence, arousal and contingency were recorded. In line with previous experiments (Haddad et al., 2012; Lau et al., 2008), the applied paradigm proved to be effective: after several pairings of a specific person's neutral face (CS+) with a loud scream and a fearful expression (US), both SAD and HC exhibited enhanced fear responses to that face compared to another person's neutral face (CS-) which never became associated with the US. Such successful fear conditioning was apparent in both SAD and HC reflected in verbal reports, i.e., valence, arousal and contingency ratings, and physiological responses, i.e., heart rate and skin conductance response. The subsequently conducted generalization test revealed that all participants generalized their conditioned fear from the CS+ to the new, similar stimuli (GSs) as a function of their similarity to the threat cue. Again, such generalization was detected for verbal reports and physiological responses. Importantly, quantitative differences of fear generalization between SAD patients and HC were discovered, while qualitative discrepancies were rare. The main evidence for elevated fear generalization in patients was found in HR, where only SAD showed fear generalization with fear bradycardia linearly increasing from CS- over the GSs to CS+, whereas HC did not differentiate among conditions at all.

With the generalization test, maladaptive fear generalization patterns were expected to be found in SAD patients as some previous studies observed overgeneralization to be a pathogenic marker of some anxiety disorders (Kaczkurkin & Lissek, 2013; Lissek & Grillon, 2012; Lissek et al.,

2014; Lissek et al., 2009). The HR finding was consistent with this hypothesis. During generalization, a significant stimulus x group interaction was detected, caused by a generalization gradient in SAD with most pronounced HR deceleration to the CS+ and least pronounced HR deceleration to the CS-. In animals, the appearance of a predator leads to an orientation reaction and freezing behavior, which is accompanied by a profound deceleration in heart rate labelled in the literature as "fear bradycardia" (Campbell, Wood, & McBride, 1997). Likewise, humans show a HR deceleration when seeing arousing pictures, and this is especially true for unpleasant compared to pleasant pictures (for a review, see Lang & Davis, 2006). In contrast, the HC in this study phase displayed equal levels of HR changes for all faces. This difference in HR decelerations in SAD patients compared to HC might be explained by the defense cascade model (for more details, see Lang, 1995; Lang, Bradley, & Cuthbert, 1997). It seems possible that while for SAD patients the stimuli were threatening enough to cause a shift from the pre- to the post-encounter stage and initiate fear bradycardia, HC might have perceived these stimuli as aversive, but not threatening enough to actually prepare a flight or fight reaction. Thus, HC stayed in the pre-encounter stage, whereas SAD patients may have been exhibiting an orienting reaction to the stimuli. Interestingly, this effect was absent during acquisition, where SAD in general showed stronger heart rate deceleration to both CS+ and CS-. This could point towards the difficulty of SAD patients of learning to discriminate between friends and foes (Ahrens et al., 2014; Hermann et al., 2002). However, it is puzzling that in the acquisition phase an overall enhanced HR acceleration in response to the CS+ was observed in both groups, which is in contrast to the later observed enhanced deceleration in SAD. Most likely, this overall pattern emerges due to individual differences with regard to either more pronounced deceleration or acceleration of HR in response to the CS+ (Sevenster, Hamm, Beckers, & Kindt, 2015). It has been argued that bradycardia as well as tachycardia may be observed, as the balance between the sympathetic and parasympathetic system is dynamic, in order to quickly respond to changing circumstances (Hagenaars, Oitzl, & Roelofs, 2014). Thus, it can be assumed that whereas during learning, variable HR reactions may lead to the observed indistinct pattern, whereas later on after learning, only SAD uniformly react with fear bradycardia to the CS+ and GS1.

With regard to SCR, the possibility of stronger fear generalization in SAD patients compared to controls was observed, indicated by a significant quadratic stimulus type x group interaction in the trend analysis, which resulted from a more pronounced quadratic trend in controls compared to patients. Moreover, overall elevated SCR levels in SAD patients compared to HC were detected as a further sign of their physiological hyperarousal.

For the other dependent variables, there were in contrast to the hypotheses no differences in generalization gradients, but again general group differences. The ratings revealed main effects in valence, arousal and US expectancy: phobic individuals reported to perceive all faces as less pleasant

and more arousing, and they overestimated the pairing of GSs and the CS- with the US, although those stimuli were never reinforced. These findings are congruent with previous studies on face perception in SAD, which detected that individuals with clinical or subclinical social anxiety rated angry faces to be more negative (Dimberg & Christmanson, 1991) and more arousing (Dimberg, 1997), and also rated happy faces as less pleasant (Straube et al., 2004). Furthermore, socially anxious individuals showed enhanced US expectancy ratings compared to controls, which might be interpreted as an illusory correlation related to enhanced anxiety (Wiemer & Pauli, 2016). Again, this is consistent with prior conditioning studies indicating that patients with SAD have bad stimulus discrimination skills and therefore show enhanced US expectancy ratings and (neuro-) physiological fear responses to safety cues (Ahrens et al., 2014; Hermann et al., 2002; Sachs et al., 2003).

Overall, the expected overgeneralization in patients with SAD compared to controls was not confirmed. Just two potential indices of aberrant fear generalization were observed in study 2: the first index emerged in the shape of the HR gradient, as SAD patients showed a linear decrease in HR from conditioned danger to conditioned safety cues. Linear curves in conditioned fear generalization seem to be characteristic for several anxiety disorders, whereas HC and animals usually display quadratic gradients (for a review, see Dymond et al., 2015). The second lead appeared in the SCR trend analyses, where a significant quadratic stimulus type x group interaction was found. Although a follow-up test indicated that the significant quadratic trend of the stimulus type occurred in both SAD patients and controls, it has to be noted that the quadratic shape was more distinct in HC. Hence, it can be interpreted as a slight cue that SAD patients generalize their conditioned fear reaction stronger that controls. Beyond that, no evidence for an overgeneralization of fear was found in the patients.

However, study 2 is not the first that did not clearly detect overgeneralization in anxiety disorders. In line with the results, a study with non-clinical individuals scoring high on trait anxiety (Torrents-Rodas et al., 2013) as well as two studies investigating generalization in GAD did not find signs of overgeneralization compared to controls (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Tinoco-González et al., 2015). This is unexpected, especially as one of these studies (Tinoco-González et al., 2015) even used the same paradigm as another study which found overgeneralization effects in GAD patients (Lissek et al., 2014). Accordingly, the question arises how the contradictory findings on overgeneralization can be explained.

One reason could be that most of the SAD patients in study 2 suffered from comorbidities, which could have distorted the results. The most prevalent comorbidity was depression, which was found to have an impact on the defensive reaction of patients with SAD in a previous study (McTeague et al., 2009). Depressed and non-depressed SAD patients as well as HC were asked to imagine neutral and fearful events, while eye-blink responses to startle probes, HR and SCR were

recorded. Results revealed that non-depressed SAD patients showed fear potentiation during social threat imagery compared to controls, while patients with generalized social phobia plus depression showed decreased affective modulation. This is in line with another study which reported that high levels of anxiety led to augmented startle responding, whereas high levels of depression were associated with a lack of startle modulation in response to affective film clips (Kaviani et al., 2004). Therefore, it can be argued that the defensive response in the patients of study 2 might have also been attenuated. To test this hypothesis, future studies could exclude patients with comorbid depression from the study.

In addition, the stimulus material might not have been suitable to investigate overgeneralization in SAD, because it was not disorder-specific enough. The fearful faces serving as CS and the scream serving as US were certainly more social in comparison to prior studies with rings and electric shocks, but still might not have been good representations of the fear of being negatively evaluated or laughed at which SAD patients experience. For this reason, the paradigm should be tested with more disorder-specific stimulus material, such as angry faces serving as CS, which can be interpreted as a sign of criticism, and verbal insults serving as US (Ahrens et al., 2014; Iidaka et al., 2010; Lissek, Levenson, et al., 2008).

Moreover, it is possible that the non-significant results were due to a lack of statistical power. To check this hypothesis, a post-hoc power analyses using the program GPower (Faul, Erdfelder, Lang, & Buchner, 2007) was conducted. The analyses were executed for repeated measures ANOVAs with α set at .05, power $(1 - \beta) = 0.80$ and the varying observed effect sizes f (calculated from the reported partial eta squared) for all five dependent variables of the present study, ($f_{scr} = 0.119$, $f_{HR} = 0.229$, $f_{arousal} = 0.128$, $f_{valence} = 119$, and $f_{USexpectancy} = 182$, respectively). Results revealed that sample sizes would have to rise up to n = 78 (SCR), n = 68 (arousal), n = 78 (valence) and n = 34 (US expectancy), respectively, to reach significance. These sample size however were not feasible to reach in the current study.

Furthermore, another possibility is that overgeneralization is not a distinguishing marker of all anxiety disorders, but only occurs in some of them excluding SAD. Until now, the most solid results have been detected in PD and PTSD (Lissek & Grillon, 2012; Lissek et al., 2009). It is also discussed as a characteristic of GAD, albeit the results are mixed (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Lissek et al., 2014; Tinoco-González et al., 2015). Beyond that, there exist no studies on fear generalization in other anxiety disorders including SAD. As to the findings of the present study, which discovered mostly quantitative, but not qualitative differences in conditioned fear generalization among patients with SAD and HC, overgeneralization is not a general pathogenic marker of SAD. A plausible reason could be that the fear of social scrutiny in SAD patients is relatively circumscribed, whereas PD and PTSD patients experience fear in multiple situations.

Further research is required to clarify the role of overgeneralization in the etiology of social anxiety, specifically whether the scarce evidence speaking in favor of overgeneralization was an incidental finding or not. Therefore, this topic was further addressed in study 3.

4 Study 3: Electrocortical Correlates of Fear Learning and Generalization in Social Anxiety

4.1 Introduction

Over the past decade, a growing amount of literature on fear generalization has developed which tried to uncover the contribution of aberrant associative learning mechanisms to the etiology of anxiety disorders (see Dymond et al., 2015, for a review). However, the results of previous studies are ambiguous. While some experiments revealed overgeneralization in patients with anxiety disorders (e.g. Lissek & Grillon, 2012; Lissek et al., 2014), others did not (Ahrens et al., 2016; Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Tinoco-González et al., 2015). In line with this, we detected some evidence speaking in favor of fear generalization in SAD in study 2 of the present thesis, but most of the results counted against it. Albeit chances are that overgeneralization is just a marker of some anxiety disorders and/or that differences in study design are responsible for the inconsistent findings, the contradictory results make clear how little is known about fear generalization in general and in anxiety patients in particular.

When an individual is in a state of fear, its defensive system is activated to prepare a fight or flight response. This physical activation can be captured by peripheral physiological measures, such as fear-potentiated startle (FPS), skin conductance (SCR) and cardiovascular parameters (e.g. HR), which is why these measures have commonly been used in previous fear generalization experiments (Lissek et al., 2009; Tinoco-González et al., 2015; Torrents-Rodas et al., 2013). Study 2 also concentrated on peripheral physiological aspects during fear generalization and revealed mostly quantitative, but not qualitative differences between patients with SAD and HC. These findings indicated that the SAD patient's fear reaction was in fact more intense than those of HC, but that the way it was generalized did not differ substantially with regard to evaluation and physiological reactions in the periphery (except for the HR response). However, fear does not only go along with changes in the peripheral physiological system of an organism, but also with variations in the central nervous system, which can be measured as changes in neuronal activity in different areas of the brain. Although findings in the central nervous system and the periphery often correlate with each other, this is not necessarily the case. For this reason, study 3 had the aim to examine fear generalization on a neuronal level.

One cognitive process, which plays an important role during learning, is visual attention. For example, studies proved that working memory for attended compared to unattended items is better (Bays & Husain, 2008; Griffin & Nobre, 2003; Murray, Nobre, & Stokes, 2011; Ravizza, Uitvlugt, & Hazeltine, 2016; Santangelo & Macaluso, 2013), which leads to the conclusion that attention

influences on how an individual perceives its environment. Prior studies investigating attention with indirect measures, such as reaction time experiments, showed that individuals hold an attentional bias towards cues or situations that might predict danger, and that this bias is especially pronounced in patients with anxiety disorders (Bar-Haim et al., 2007). As discussed earlier, paying more attention to threatening stimuli might be one perpetuating factor of SAD, and it can be measured as enhanced neuronal activity in occipital regions of the human brain – the center of visual information processing (Müller & Hübner, 2002; Müller, Teder-Sälejärvi, & Hillyard, 1998).

One way to capture visual attention in the brain is the recording of steady-state Visually Evoked Potentials (ssVEPs) (e.g. Müller et al., 1998). SsVEPs are oscillatory neuronal responses to flickering stimuli and reflect multiple excitations of the visual system over a limited period of time. Studies suggest that their origin is mostly located in the visual cortex, in particular V1, but also in higher order cortices (Di Russo et al., 2007) and extracortical structures (Pastor, Artieda, Arbizu, Valencia, & Masdeu, 2003; Srinivasan, Fornari, Knyazeva, Meuli, & Maeder, 2007). The enhancement of ssVEP amplitude marks increased visuocortical activation, whereas the decrease indicates diminished activation. Changes in electrocortical activity can be generated by both bottom-up driven sensory processing or top-down regulated higher order processing (Keil et al., 2003; Nunez & Srinivasan, 2006).

Compared to regular Event-Related Potentials (ERPs), ssVEPs provide a list of advantages for conditioning studies: as the frequency of the electrocortical reaction recorded via EEG equals the one of the driving stimulus, the ssVEP signal can be reliably separated from noise and quantified in the frequency domain (Müller et al., 1998; Regan, 1989). That is why - in comparison to single ERPs - ssVEPs are more robust to movement and eye blink artifacts and yield a better signal-to-noise-ratio (Perlstein et al., 2003). This is particularly beneficial for experiments with a restricted number of trials, such as generalization experiments. Also, ssVEPs are sensitive to emotional and attentional processes and show increased amplitudes for emotional and attended compared to neutral and unattended stimuli (Kemp, Gray, Eide, Silberstein, & Nathan, 2002; McTeague, Shumen, Wieser, Lang, & Keil, 2011; Müller, Teder, & Hillyard, 1997). Therefore, they provide a suitable account to measure attentional processes in response to emotional stimuli in a fear generalization paradigm.

SsVEPs and ssVEFs (steady-state Visually Evoked Fields) have already been applied in fear conditioning studies using two stimuli (CS+ and CS-) and proved to be effective in differentiating danger from safety signals (Moratti & Keil, 2005; Moratti et al., 2006). However, there were no studies investigating the more complex generalization paradigm with ssVEPs at the time study 3 was conducted. To close this gap, we decided to examine fear generalization with a similar design as used in study 2 and fit it to EEG (adapted from Lau et al., 2008) (see also chapter 3.2 for a detailed description).

The aim of study 3 was to investigate whether high (HSA) compared to low socially anxious (LSA) showed overgeneralization on a neuronal level. Instead of using peripheral physiological measures, brain activity during fear was recorded via ssVEPs. Based on the literature, it was hypothesized that the adaption of the conditioning paradigm with social stimuli (faces and screams) would be sensitive enough to differentiate among conditioned and generalization stimuli on a neuronal level. Moreover, we expected to reproduce the generalization pattern, which was found in peripheral physiological measures of former studies (e.g. Lissek et al., 2009), in both groups. Specifically, we expected the following:

1. Neuronal activity is highest in response to the CS+ and decreases in response to the GSs as a function of similarity with the CS- in both groups.
2. HSA display overgeneralization compared to LSA individuals, indicated by a) enhanced fear responses to a higher number of categories of the GSs and b) linear compared quadric generalization profiles.
3. HSA show enhanced levels of ssVEPs compared to LSA (hyperarousal).

4.2 Material and Methods

4.2.1 Participants

Participants were 67 undergraduate students (*M* = 24.10, *SD* = 6.33; 48 female) at the University of Würzburg without any past or present psychiatric diagnosis (self-report), who were paid or received course credit for participation. All participants reported normal or corrected to normal vision, and none of them had a family history of epilepsy. Prior to participation, written informed consent was obtained from each participant. The study was approved by the ethics committee of the medical faculty of the University of Würzburg.

Participants completed the German Version of the SPAI (Fydrich, 2002; Turner et al., 1989), the LSAS (Liebowitz, 1987; Stangier & Heidenreich, 1997), the STAI (Spielberger et al., 1970), the BDI (Beck et al., 1961; Hautzinger et al., 1994) and the PANAS (Watson et al., 1988). Participants were divided into two groups as a function of their SPAI-score (median split), with the lower half referred to as “low socially anxious” (LSA), and the upper half referred to as “high socially anxious” (HSA). *T*-tests were calculated to check if the HSA and LSA group differed with regard to their social anxiousness. Analyses showed significant group differences in the total scores of the SPAI ($t(65) = 9.16$, $p < .001$; HSA: $M = 2.57$, $SD = 0.52$; LSA: $M = 1.65$, $SD = 0.26$) and LSAS ($t(55) = 4.18$, $p < .001$; HSA: $M = 31.94$, $SD = 17.16$; LSA: $M = 17.61$, $SD = 10.17$). Three of the participants scored above the cut-off of the BDI indicating depression. Since the elimination of these participants from analyses did

not have a significant impact on the results, we decided to include them in the sample in order to enhance statistical power. Mean questionnaire scores are shown in Table 3.

Table 3: Questionnaire characteristics of both groups of study 3.

	LSA		HSA			
Variable	*M*	*SD*	*M*	*SD*	*t*(65)	*p*
SPAI	1.65 (52.8)	0.26	2.57a (82.24)	0.52	9.16	$p < .001$*
LSAS	17.61	10.17	31.94	17.16	4.18	$p < .001$*
BDI	5.27	6.29	5.09	5.20	0.13	$p = .896$
STAI State	32.12	5.47	35.76	7.85	2.20	$p = .031$*
STAI Trait	34.30	8.00	39.56	9.61	2.43	$p = .018$*
PANAS_PA	29.03	6.09	26.38	6.26	1.76	$p = .084$*
PANAS_NA	10.82	1.29	12.24	2.97	2.55	$p = .014$**

SPAI, Social Phobia and Anxiety Inventory; LSAS, Liebowitz Social Anxiety Scale; BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; PANAS, Positive and Negative Affect Scale (PA, positive affect; NA, negative affect).

4.2.2 Stimuli

The conditioned stimuli (CS) consisted of two pictures of female actresses with a neutral facial expression taken from the NimStim Set of Facial Expressions (Tottenham et al., 2009). Pictures were adjusted for luminance and brightness, converted to gray-scale and presented using Presentation (Neurobehavioral Systems, Inc., Albany, CA, USA). One of the actresses was randomly selected as threat cue for each participant (CS+) while the other served as safety signal (CS-). Pictures were shown on a gray background on a 17-inch monitor (resolution = 1280 x 1024 pixel) in a flickering mode at a frequency of 12 Hz in order to elicit ssVEPs. The US consisted of the respective CS+ face displaying a fearful expression and a simultaneously presented 95 Db shrill female scream of the IADS database (Bradley & Lang, 1999). Four GS were created by morphing the two faces together in 20% steps using a face-morphing software (Squirlz Morph; Xiberpix, Solihull, UK. http://www.xiberpix.net/SqirlzMorph.html). The GS most similar to the CS+ is referred to as GS1 and the GS most similar to the CS- as GS4 (see Figure 14).

4.2.1 Design and procedure

The experiment (adapted from Lau et al., 2008; Lissek, Biggs, et al., 2008) consisted of three

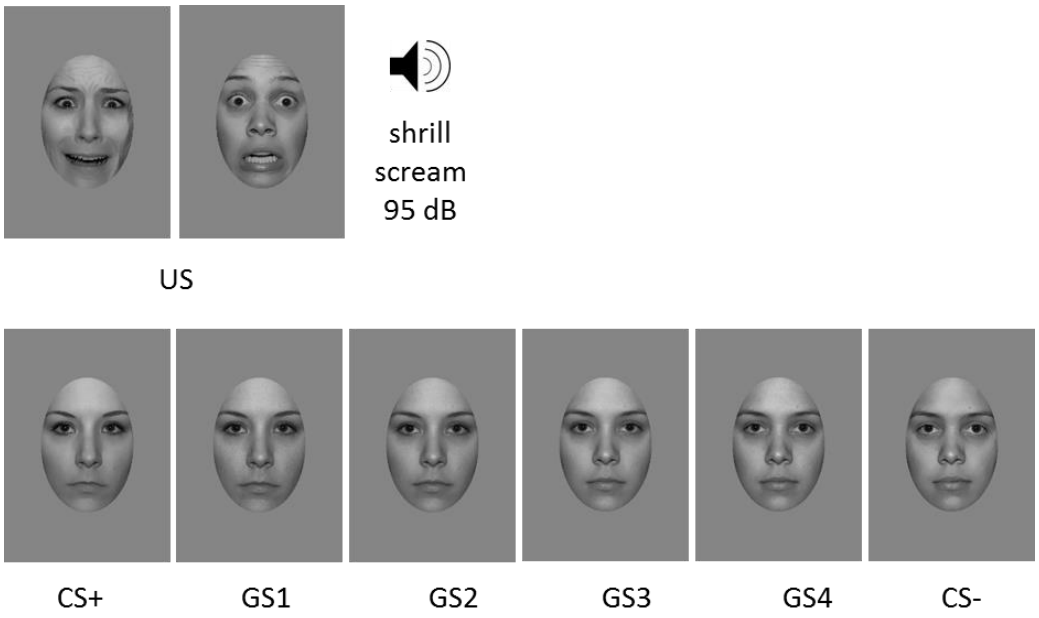

Figure 14: Unconditioned (US) (upper panel), conditioned (CS) and generalized stimuli (GSs) (lower panel) of study 3. For half of the participants, the left face served as CS+ and the right face served as safety signal (as depicted), while the order was reversed for the other half of participants (not depicted). GSs were created by morphing the two CS faces into each other in 20% steps with the GS1 being most similar and the GS4 being least similar to the CS+.

blocks (habituation, acquisition, generalization). Habituation and acquisition consisted of 30 trials (two faces, each presented 15 times), while there were 90 trials in the generalization phase (six faces, each presented 15 times), resulting in 150 trials in total.

After completing the questionnaires, EEG electrodes were applied to the participants and they were seated in a noise-reduced, darkened room one meter distant to the screen. Before the start of the experiment, participants were not informed of any specific relation among the CSs and the US. Then, the study began with the habituation phase, in which faces were presented for 3000 ms without reinforcement. During acquisition, one of the faces (CS+) was paired in 12 of 15 trials (80% reinforcement) with the US, which lasted 1500 ms and was replayed with a sound volume of 95 dB by Labtech speakers (Labtech International Ltd., Ringmer, East Sussex, GB) and a Kenwood KA-3010-Amplifier (Kenwood Electronics, Heusenstamm, GER). It was counterbalanced across participants which face served as the CS+ and which as the CS-. Generalization consisted of the CS+, CS-, and four GS, each presented 15 times (90 trials). While CS- and GSs were never reinforced, 6 of the 15 CS+ were still followed by the US to prevent early extinction (40% reinforcement) (see Figure 15). The presentation order of the faces within each block was pseudo-randomized such that no more than two of the same faces could occur in a row. After each trial, a gray screen with a fixation cross was presented. Inter-trial intervals differed between 2000 and 2500 ms to prevent expectancy effects.

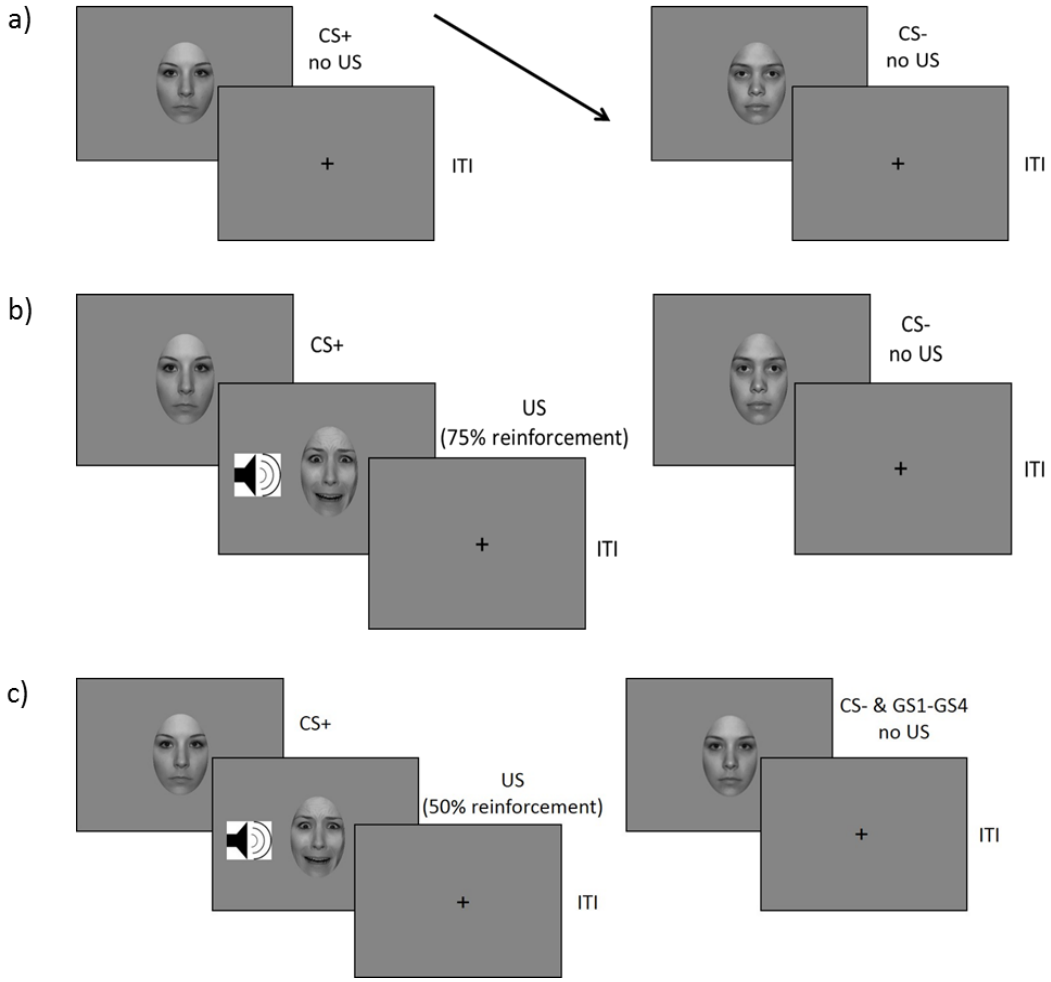

Figure 15: Schematic overview of the experimental design of study 3. Habituation (upper panel), acquisition (middle panel) and generalization phase (lower panel) are illustrated. Stimuli were randomly presented for 3 sec during each of the three parts of the experiment.

At the end of each phase, participants rated the valence and arousal of the faces using a computer-based version of the Self-Assessment Manikin Scale (SAM; Bradley & Lang, 1994). Moreover, participants were asked to rate US expectancy after acquisition and generalization in % as a response to the question "What is the likelihood that the currently presented face is followed by a scream?" to measure successful learning of the CS-US association.

4.2.2 EEG recording and analysis

Electrocortical activity was measured via 129 electrodes using an Electrical Geodesics (EGI, Eugene, OR, USA) high-densitiy EEG System referenced to Cz, recorded with a sampling rate of 250 Hz and online bandpass filtered with 0.1 and 100 Hz and a 50 Hz notch filter. The threshold of impedances was kept below 50 kΩ as recommended for the Electrical Geodesics high-impedance amplifiers.

Offline, EEG analyses were implemented using the software EMEGS (Electro Magnetic EncephaloGraphy) version 2.4 (Peyk, De Cesarei, & Junghöfer, 2011) and Matlab Version 7.11.1 (Matrix Laboratory; MathWorks, Natick, MA, USA). First, epochs of 600 ms pre-stimulus and 3600 ms post-stimulus onset were extracted, and data were filtered with a low-pass filter of 40 Hz. In a second step, artifact rejection was conducted (as proposed by Junghöfer, Elbert, Tucker, & Rockstroh, 2000) to create statistical indices of data quality. In this way, bad channels could be identified and interpolated from the full channel set and bad trials could be excluded from the analyses. Trials were rejected when more than 20 channels out of 129 were outliers as per the statistical parameters used for artifact identification (mean absolute amplitude, variability over time points, maximum first order derivate (gradient)). In a next step, the artifact-free trials were averaged for each subject according to the 10 different experimental conditions (habituation: CS+, CS-; acquisition: CS+, CS-; generalization: CS+, CS-, GS1-4). The preprocessed data were further analyzed by means of Hilbert transformation to determine the strength of the driving frequency (12 Hz) during the time course of each trial. First, data were bandpass-filtered with a 12th order Butterworth filter having a width of 0.5 Hz (48 dB/octave) around the target frequency. Second, amplitudes of the band-pass filtered signal were computed using the Hilbert function implemented in MATLAB. The Hilbert transformation possesses high temporal resolution for indexing rapid changes in ssVEP amplitude. The absolute value of Hilbert transform corresponds to the envelope of the averaged waveform. Thereupon, the mean ssVEP amplitude of each condition was assessed for the time interval between 200 and 3000 ms.

As found in previous studies with visually presented flickering stimuli (e.g. McTeague et al., 2011; Müller, Andersen, & Keil, 2007; Wieser, McTeague, & Keil, 2012) the ssVEP signal was most pronounced over medial occipital sensors. Therefore, ssVEP activity was spatially averaged across the Oz and 6 surrounding electrodes (EGI sensors 70, 71, 74, 75, 76, 82, 83) (see Figure 16).

4.2.3 Statistical analysis

Stimulus differences in ssVEP amplitudes as well as valence and arousal ratings during the habituation and acquisition phase were analyzed with paired samples *t*-tests. For the generalization phase, a repeated measures ANOVA with the within-subject factor CS-type (6: CS+, GS1-4, CS-) was conducted. In case of significant effects discovered by the ANOVA, analyses were followed by paired samples *t*-tests with the CS- as reference condition or trend analysis.

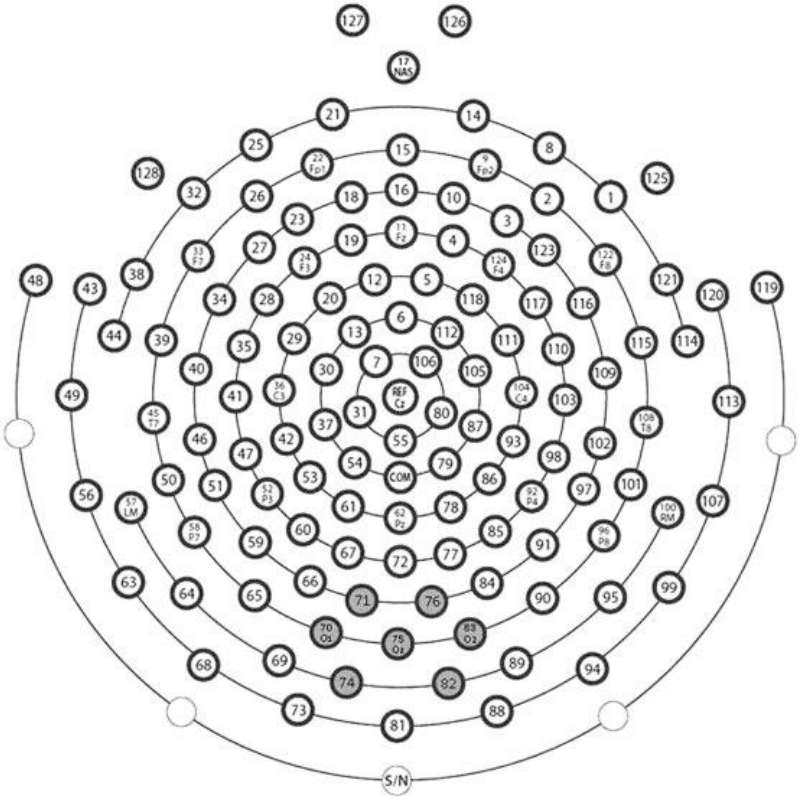

Figure 16: Sensor layout of the HydroCel Geodesic Sensor Net. Locations of the sensors included in the analysis are marked in gray. Sensor No. 75 corresponds to the Oz of the international 10-20 system.

US expectancy ratings underwent the same analyses with the exception of the habituation phase, because US expectancy ratings just started after the acquisition phase.

Alpha was set at $p < .05$ (two-tailed) and was corrected using the Bonferroni-Holm adjustment for multiple tests where appropriate. In case of violation of sphericity, Greenhouse-Geisser epsilon (GG-ε) and uncorrected degrees of freedom are reported (Picton et al., 2000). The partial eta-squared (ηp^2) is reported as a measure of effect size.

4.3 Results

4.3.1 Habituation

Steady-state Visually Evoked Potentials: As expected, the 2 (group: LSA vs. HSA) x 2 (stimulus: CS+ vs. CS-) ANOVA for the ssVEPs revealed no significant effects for stimulus type [$F(1,65) = 2.45$, $p = .123$, $\eta p^2 = .04$], group [$F(1,65) = 0.41$, $p = .525$, $\eta p^2 = .01$] or the stimulus type x group interaction [$F(1,65) = 1.67$, $p = .201$, $\eta p^2 = .03$] during habituation (see Figure 17). This demonstrates that both groups reacted with similar ssVEP amplitudes to both face stimuli at the beginning of the experiment.

Valence and arousal ratings: The 2 (group: LSA vs. HSA) x 2 (stimulus: CS+ vs. CS-) ANOVA for the valence ratings revealed neither a significant main effect of group [$F(1,65) = 2.11$, $p = .151$, $\eta p^2 = .03$] nor a significant stimulus type x group interaction [$F(1,65) = 0.35$, $p = .559$, $\eta p^2 = .01$]. However,

participants rated the CS+ (M = 5.40, SD = 1.22) as marginally more pleasant than the CS- (M = 5.01, SD = 1.25) [F(1,65) = 3.99, p = .050, ηp² = .06], indicating that they preferred by trend the face that was later on in the experiment paired with the US. Crucially, this pattern reversed during acquisition and can probably be interpreted as an incidental finding. With regard to the arousal rating, the 2 (group: LSA vs. HSA) x 2 (stimulus: CS+ vs. CS-) ANOVA did not reach significance in both main effects (stimulus type: [F(1,65) = 0.33, p = .570, ηp² = .01]; group: [F(1,65) = 1.06, p = .308, ηp² = .02]) and stimulus type x group interaction [F(1,65) = 0.06, p = .813, ηp² < .01] (see Figure 18). This result points out that none of the two faces elicited more arousal in any of the two groups at the beginning of the experiment.

4.3.2 Acquisition

Steady-state Visually Evoked Potentials: After the CS+ had been paired with the US, analyses yielded a significant main effect of stimulus type in the ssVEP amplitude [*F*(1,65) = 4.42, *p* = .039, ηp² = .06], demonstrating that participants reacted with higher amplitudes to the CS+ (*M* = 0.51, *SD* = 0.44) compared to the CS- (*M* = 0.47, *SD* = 0.50) (see Figure 17). The main effect of group [*F*(1,65) = 1.34, *p* = .252, ηp² = .02] and the stimulus type x group interaction [*F*(1,65) = 0.11, *p* = .744, ηp² < .01] were not significant, though. This shows that the conditioning procedure itself was successful, but there were no group differences among low and high socially anxious participants.

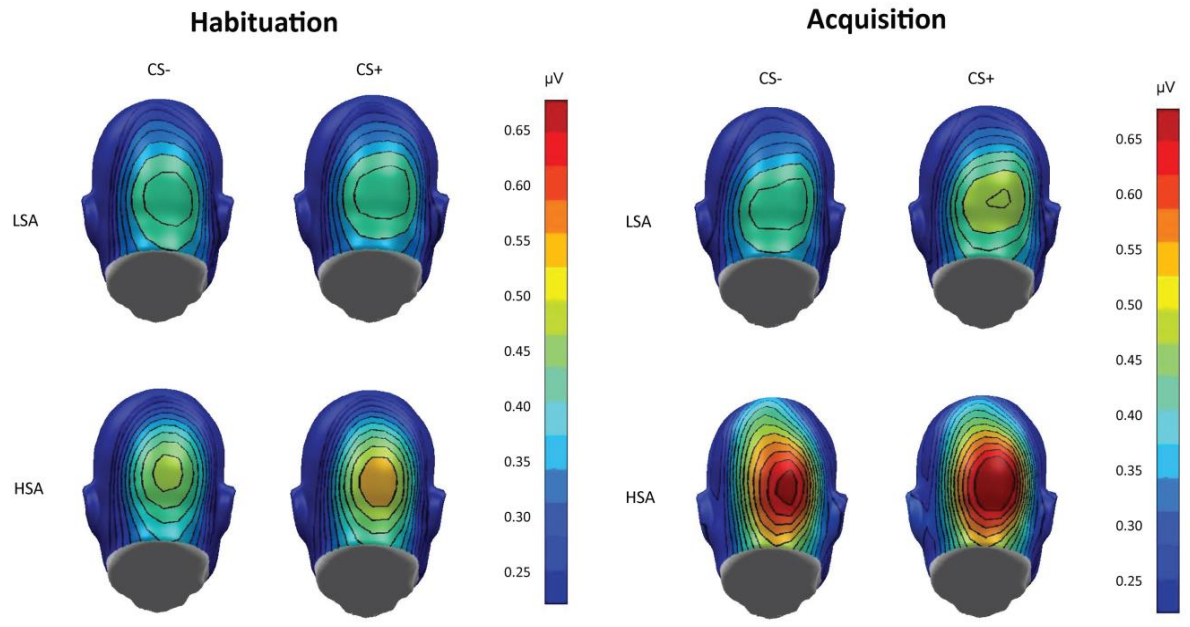

Figure 17: Grand mean topographic distribution of the ssVEP amplitudes across groups (LSA: low socially anxious group; HSA: high socially anxious group) in response to the CS+ and CS- during habituation (left panel) and acquisition phase (right panel).

Valence and arousal ratings: In the second phase of the experiment, there was a significant main effect of stimulus type in both valence [$F(1,65) = 49.80$, $p < .001$, $\eta p^2 = .43$] and arousal ratings [$F(1,65) = 89.45$, $p < .001$, $\eta p^2 = .58$], which notified that participants rated the CS+ as less pleasant (valence: CS+: M = 3.58, SD = 1.42; CS-: M= 5.27, SD = 1.34) and more arousing (CS+: M = 6.51, SD = 1.63; CS-: M = 3.69, SD = 1.94) compared to the CS- after the former had been paired with an aversive scream and fearful facial expression (see Figure 18).

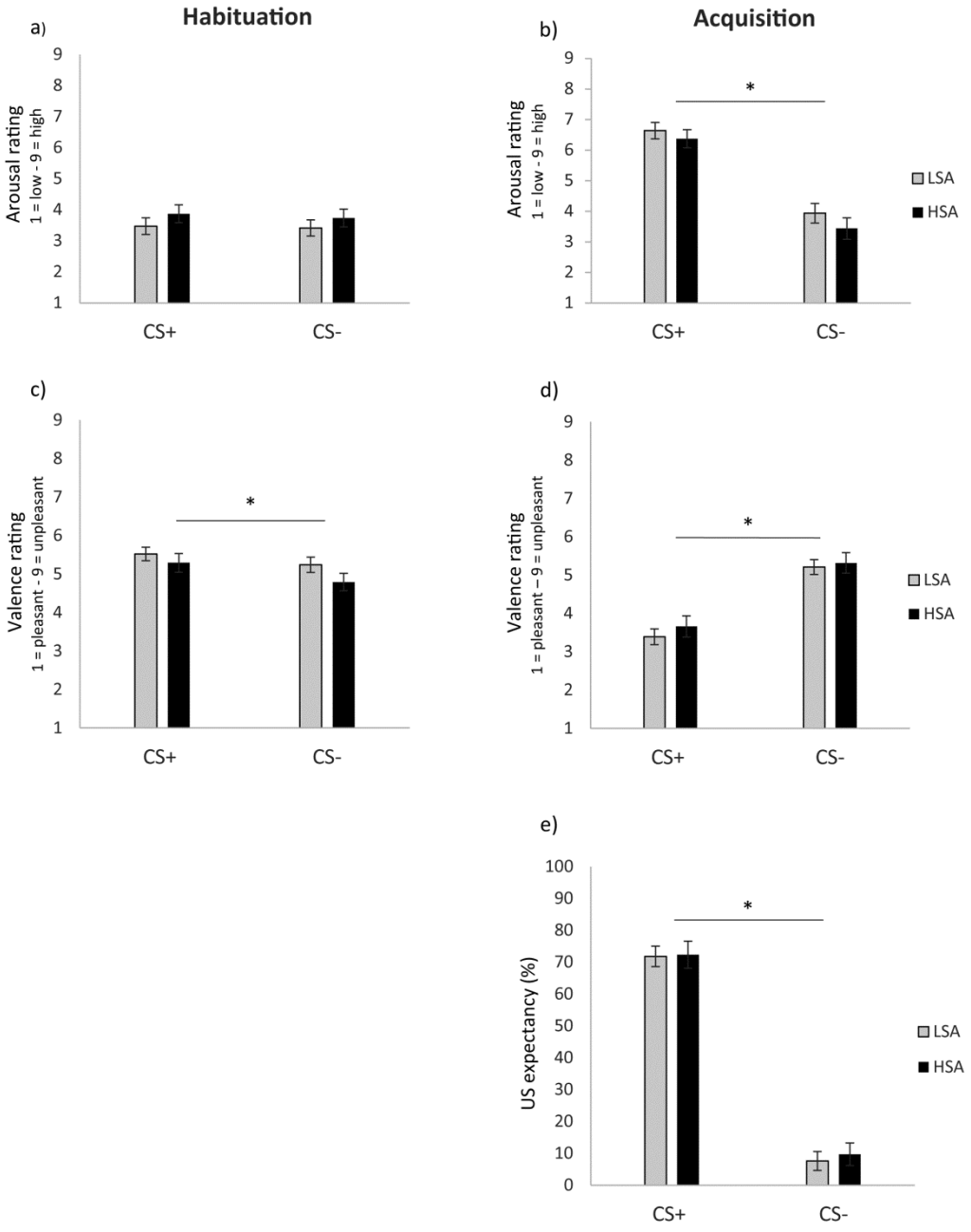

Figure 18: Mean arousal (a+b), valende (c+d) and US expectancy ratings (e) to the threat (CS+) and safety cue (CS-) by group during habituation (left panel) and acquisition (right panel) of study 3. Error bars represent the standard error of the mean, asterisks indicate significant differences (p < .05).

These results underpin the finding in the ssVEPs that the conditioning procedure was successful. However, neither the stimulus type x group interaction (valence: [$F(1,65) = 0.29$, $p = .590$, $\eta p^2 < .01$]; arousal: [$F(1,65) = 0.17$, $p = .683$, $\eta p^2 < .01$]) nor the main effect of group (valence: [$F(1,65) = 1.02$, $p = .317$, $\eta p^2 = .02$]; arousal: [$F(1,65) = 1.37$, $p = .246$, $\eta p^2 = .02$]) were significant in both ratings.

US expectancy rating: During acquisition, the analysis of the US expectancy ratings with a 2 x 2 ANOVA also detected a main effect of stimulus-type as in the other two ratings [$F(1,65) = 286.05$, $p < .001$, $\eta p^2 = .82$] (see Figure 18). The finding that participants gave higher US expectancy ratings for the CS+ ($M = 72.09\%$, $SD = 21.71\%$) compared to the CS- ($M = 8.66\%$, $SD = 18.74\%$) underlined that the experimental manipulation was effective. However, the stimulus type x group interaction [$F(1,65) = 0.05$, $p = .832$, $\eta p^2 < .01$] and the main effect of group [$F(1,65) = 0.16$, $p = .687$, $\eta p^2 < .01$] were not significant, indicating that there were no differences between the low and high socially anxious group.

4.3.3 Generalization

Steady-state Visually Evoked Potentials: Analyses with a 2 (group: LSA vs. HSA) x 6 (stimulus: CS+ vs. GS1-4 vs. CS-) repeated-measures ANOVA provided a significant main effect of stimulus-type [$F(5,325) = 5.39$, GG- $\varepsilon = .42$, $p < .001$, $\eta p^2 = .08$]. In order to test if this effect was in line with our hypothesis, five follow-up paired *t*-tests were calculated with the CS- as reference condition.

Surprisingly, results only revealed a marginally significant difference between CS- and CS+ [$t(66) = 1.91$, $p = .060$] and a significant difference between CS- and GS1 [$t(66) = 2.55$, $p = .013$], but not between CS- and GS2 [$t(66) = 0.47$, $p = .638$], CS- and GS3 [$t(66) = 1.00$, $p = .323$] or CS- and GS4 [$t(66) = 1.69$, $p = .096$] (see Figure 19). The main effect of group [$F(1,65) = 1.13$, $p = .292$, $\eta p^2 = .02$] and the stimulus type x group interaction [$F(5,325) = 0.67$, GG- $\varepsilon = .42$, $p = .522$, $\eta p^2 = .01$]) were not significant.

Trend analysis for the main effect of stimulus type in the ssVEPs revealed not the expected significant linear and quadratic trends ([$F(1,65) = 1.64$, $p = .205$, $\eta p^2 = .03$] and [$F(1,65) = 1.62$, $p = .208$, $\eta p^2 = .02$], respectively), but instead a significant cubic trend [$F(1,65) = 7.54$, $p = .008$, $\eta p^2 = .10$] as well as significant trends of 4th [$F(1,65) = 7.45$, $p = .008$, $\eta p^2 = .10$] and 5th order [$F(1,65) = 5.19$, $p = .026$, $\eta p^2 = .07$]. This indicated that the pattern of the generalization gradient diverged substantially in its shape from the linear and quadratic gradients found in previous studies which investigated stimulus generalization (e.g. Lissek, 2012; Lissek et al., 2010). Visual analysis revealed that the ssVEP amplitude was highest for the CS+ and lowest for the GS1, the most proximate GS. Afterwards, the ssVEP amplitude increases from GS2 to GS4 and decreased at the CS-. There were no significant trends for the stimulus type x group interaction.

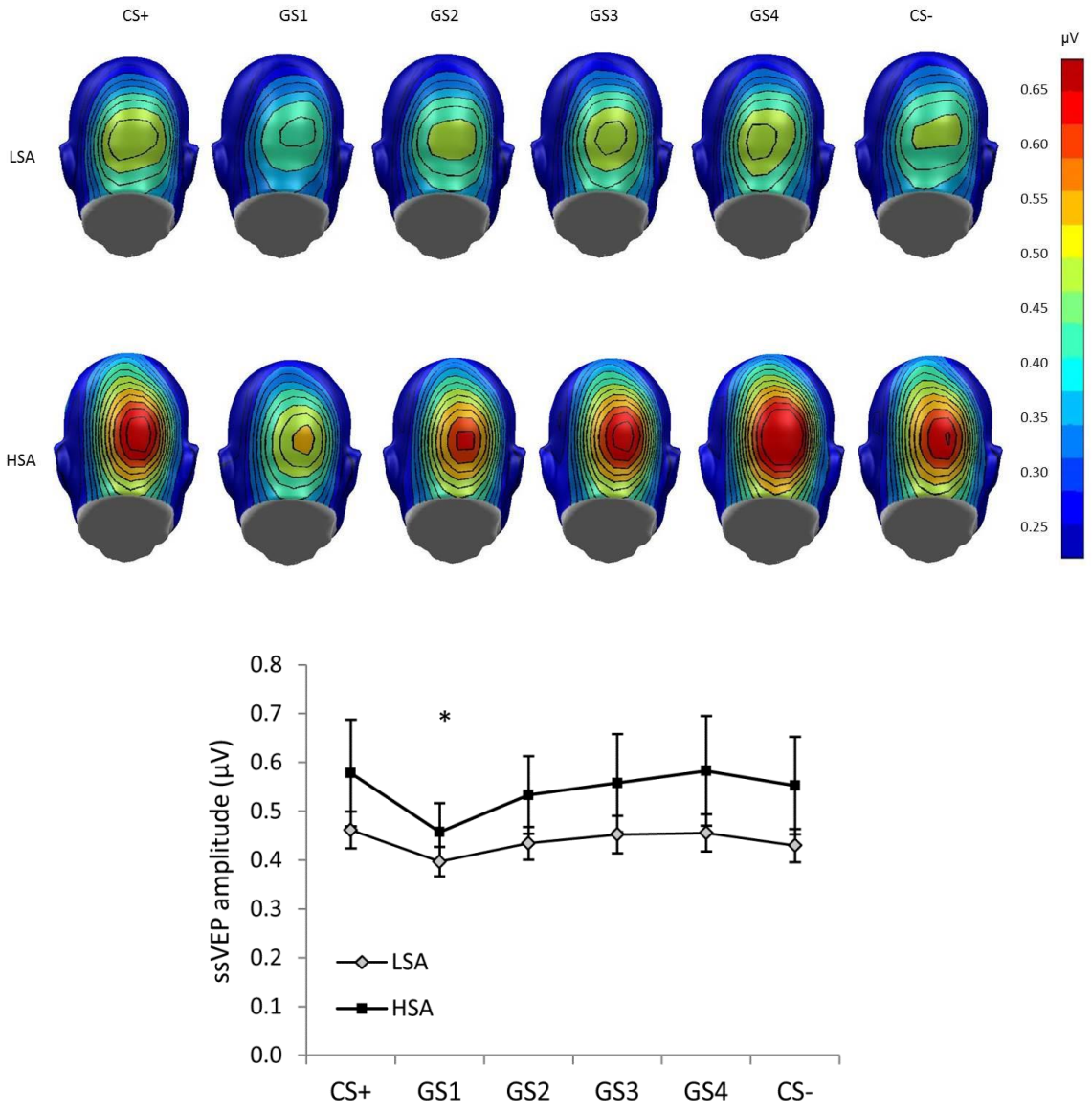

Figure 19: Grand mean topographic distribution (upper panel) and mean ssVEP amplitudes (lower panel) across groups (LSA and HSA) in response to the CS+, GS 1-4 and CS- during the fear generalization phase of study 3. Error bars indicate standard errors of the mean, asterisks indicate significant differences (p< .05).

Valence and arousal ratings: The 2 (group: LSA vs. HSA) x 6 (stimulus: CS+ vs. GS1-4 vs. CS-) repeated-measures ANOVA yielded a significant main effect of stimulus-type in both valence [$F(5,325) = 35.52$, GG- $\varepsilon = .62$, $p < .001$, $\eta p^2 = .35$] and arousal ratings [$F(5,325) = 66.44$, GG- $\varepsilon = .60$, $p < .001$, $\eta p^2 = .51$]. Following the procedure of the ssVEP analysis, five follow-up paired *t*-tests were performed. In the valence ratings, results showed differences between CS- and CS+ [$t(66) = 9.00$, $p < .001$], CS- and GS1 [$t(66) = 5.64$, $p < .001$], and CS- and GS2 [$t(66) = 3.34$, $p = .001$], but not between CS- and GS3 [$t(66) = 2.30$, $p = .025$] or CS- and GS4 after alpha adjustment [$t(66) = 0.88$, $p = .381$]. With regard to arousal, participants even differentiated among the CS- and the CS+ plus three GS: CS- and CS+ [$t(66) = 12.12$, $p < .001$], CS- and GS1 [$t(66) = 8.22$, $p < .001$], CS- and GS2 [$t(66) = 4.88$, $p = .005$], and CS- and GS3 [$t(66) = 4.33$, $p = .007$]. Only the test among CS- and GS4 [$t(66) = 1.84$, $p =$

.070] was not significant (see Figure 20). These results suggest that all participants transferred their fear response from the CS+ to at least two categories of GSs in both valence and arousal ratings. However, neither the main effect of groups (valence: [$F(1,65) = 0.78$, $p = .381$, $\eta p^2 = .01$]; arousal: [$F(1,65) = 0.83$, $p = .365$, $\eta p^2 = .01$]) nor the stimulus type x group interaction (valence: [$F(5,325) = 1.14$, GG- $\varepsilon = .62$, $p = .336$, $\eta p^2 = .02$]; arousal: [$F(5,325) = 0.41$, GG- $\varepsilon = .60$, $p = .841$, $\eta p^2 = .01$]) reached significance in both ratings, indicating that there were no differences among LSA and HSA participants.

Trend analysis for the main effect of stimulus type revealed significant linear and quadratic trends in valence (linear [$F(1,65) = 67.80$, $p < .001$, $\eta p^2 = .51$] and quadratic [$F(1,65) = 16.75$, $p < .001$, $\eta p^2 = .21$]) and arousal ratings (linear [$F(1,65) = 129.08$, $p < .001$, $\eta p^2 = .67$] and quadratic [$F(1,65) = 26.88$, $p < .001$, $\eta p^2 = .29$], respectively). There were no significant trends for the stimulus type x group interaction, which suggests that there were no group differences with regard to the shape of the generalization gradients.

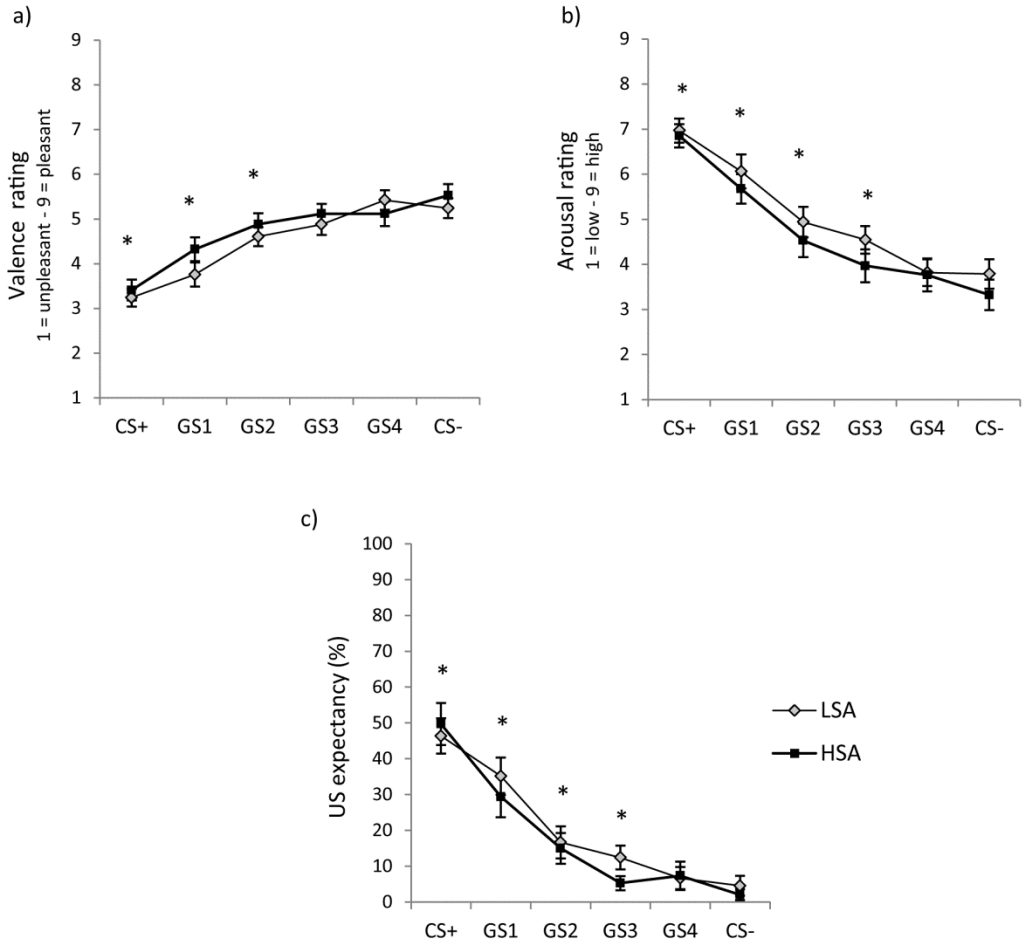

Figure 20: Mean valence (a), arousal (b) and US expectancy ratings (c) to each stimulus category for the high and low socially anxious group after the generalization phase of study 3. Asterisks indicate significant differences from the reference condition (CS-) (p < .05).

US expectancy ratings: Analysis with the 2 x 6 repeated-measures ANOVA revealed a main effect of stimulus-type [$F(5,325) = 56.99$, GG- $\varepsilon = .61$, $p < .001$, $\eta p^2 = .47$]. Post-hoc *t*-tests yielded significant effects for the comparison of CS- and CS+ [$t(66) = 11.26$, $p < .001$], GS1 [$t(66) = 7.63$, $p < .001$], GS2 [$t(66) = 4.33$, $p < .001$] and GS3 [$t(66) = 4.57$, $p < .001$]. The difference among CS- and GS4 was not significant [$t(66) = 1.76$, $p = .084$] (see Figure 20). As found in the valence and arousal ratings, participants showed an enhanced tendency to generalize their conditioned fear reaction, indicated by the fact that they expected the GS1-3 to be followed by the US, although they had never been paired with a fearful face and scream before. US expectancy ratings decreased when GSs became less similar to the CS+. The main effect of group [$F(1,65) = 0.28$, $p = .600$, $\eta p^2 < .01$] as well as the stimulus type x group interaction [$F(5,325) = 0.71$, GG- $\varepsilon = .61$, $p = .547$, $\eta p^2 = .01$] were not significant.

Trend analyses of the main effect of CS type detected that the generalization gradients followed a significant linear [$F(1,65) = 115.48$, $p < .001$, $\eta p^2 = .64$] and quadratic trend [$F(1,65) = 54.52$, $p < .001$, $\eta p^2 = .46$]. Participants gave highest US expectancy ratings for the CS+ ($M = 48.06\%$, $SD = 31.30\%$), intermediate ratings for the GSs and lowest for the CS- ($M = 3.28\%$, $SD = 12.72\%$). The stimulus type x group interaction was not significant.

4.4 Discussion

The present study aimed at investigating the discrepancies among individuals with high (HSA) and low socially anxious individuals (LSA) during fear generalization on a neuronal level. For this purpose, the generalization experiment applied in study 2 was fitted to EEG, so that brain activity in terms of steady-state Visually Evoked Potentials (ssVEPs) as well as valence, arousal and US expectancy ratings could be recorded. The results revealed a successful fear induction in both ssVEP amplitude and ratings during the acquisition phase, which was observable as higher neuronal activity in the visual cortex as well as enhanced arousal, decreased valence and increased US expectancy ratings in response to the CS+ compared to the CS- in high and low socially anxious individuals. With regard to the ensuing generalization phase, both groups generalized their conditioned fear reaction from the CS+ to similar GSs in valence, arousal and US expectancy ratings.

Surprisingly, however, the shape of the generalization gradients differed substantially on the neuronal level with highest amplitude in response to the CS+ as ever, but lowest amplitude in response to the GS1, the generalization stimulus which was most similar to the CS+, followed by a subsequent enhancement of amplitude for the GS2 to GS4 and CS-. Notably, analyses detected no differences among the low and high socially anxious group during all three phases of the experiment at all, neither in the ssVEP amplitude nor in the ratings, providing no hints that overgeneralization is a

marker of SAD. A reason for this finding could be that participants were healthy participants with low and high levels of SAD, and not clinically diagnosed patients.

The premise to interpret the findings of study 3 was a successful implementation of the generalization paradigm for the recording of ssVEPs. The biggest challenge of the adaption was to keep the six target stimuli distinguishable despite a necessary reduction of characteristic properties to make the paradigm work for ssVEPs. As ssVEPs are sensitive to luminance and color, the faces of study 2 had to be adjusted in brightness and converted to gray-scales, and the hair of the actresses had to be cut-off. As a consequence, it was substantially more difficult for the participants to discriminate between CS+, GSs and CS-. However, the analyses of the verbal measures yielded the expected generalization patterns with (a) highest arousal and US expectancy ratings and lowest valence ratings in response to the CS+, (b) intermediate levels of ratings in response to the GSs, which diminished as a function of similarity with the CS- in case of arousal and expectancy ratings and raised in case of the valence ratings, and (c) lowest arousal and US expectancy ratings and highest valence ratings in response to the CS-. This indicates – in combination with enhanced arousal and US expectancy ratings and decreased valence ratings for the CS+ in comparison to the CS- during the acquisition phase- that the conditioning and the generalization procedures were successful.

As there are studies which detected overgeneralization to be a characteristic of several anxiety disorders (Lissek & Grillon, 2012; Lissek et al., 2014; Lissek et al., 2009), the primary hypothesis of study 2 was that overgeneralization could be a marker of SAD, too. After receiving mixed results, which rather argued against overgeneralization, it should be tested if there were differences in fear generalization among high and low socially anxious individuals on a neuronal level. However, analyses revealed no signs of overgeneralization in the HSA group in the ssVEP amplitude, which indicated that the generalization pattern in neuronal measures resembled those of the LSA group. Furthermore, the non-significant differences in arousal, valence and US expectancy levels of study 2 were replicated, building up more evidence speaking against overgeneralization in SAD. Consequently, overgeneralization seems to be a pathogenic marker of just a subset of anxiety disorders which excludes SAD (for a detailed discussion, see chapter 5).

One of the most remarkable findings of study 3 was the shape of the generalization gradients on the neuronal level: the amplitude of the ssVEPs did not gradually diminish with increasing distance from the CS+ as observed in previous generalization studies (e.g. Kaczkurkin & Lissek, 2013; Lissek et al., 2009). Instead, analyses revealed the greatest ssVEP amplitude for the CS+, followed by an immediate reduction of ssVEP amplitude for the GS closest to the CS+ (GS1), and a slow increase in response to the remaining GSs and the CS-. A possible explanation for this observation might be gained from evidence in the field of visual neuroscience. The visual cortex of the brain is located in the occipital lobe at the back of the head and plays an important role in visual information

processing. After entering the retina, visual information is passed through the lateral geniculate nucleus of the thalamus to the primary visual cortex (V1) and then distributed to several areas in the extrastriate areas (e.g. V2, V3 and V4), which are sensitive to specific information, such as color, orientation or movement (e.g. Gazzaniga, 2004). Experiments have shown that the response amplitude to specific stimulus features is not static, but can be heightened if these features get associated with an affective or motivational value (Bradley, Keil, & Lang, 2012). From an evolutionary perspective, this makes sense, as the constant change of the environment the individual lives in demands a highly plastic physiological mechanism which is able to capture this dynamic (Miskovic & Keil, 2012). In line with this, the sensory cortex is more and more considered to be a kind of adaptive processor, which reacts with actual structural and functional changes within its substrate to new learning experiences, instead of just passively transmitting information (Gilbert & Sigman, 2007).

A popular subject of visual neuroscience are the neurons in the primary visual cortex, because while neurons in extrastriate areas may provide information about more complex attributes of an object, the great majority of the cells in the primary visual cortex is only sensitive to the orientation of a stimulus (Ferster & Miller, 2000). Previous research detected that the orientation-tuning functions of the visual neurons are static properties, but could be shaped over time by suppressive mechanisms, such as *lateral inhibition* (Dragoi, Sharma, & Sur, 2000).

To gain a more detailed insight in this phenomenon, a recent study aimed at examining the involvement of the human visual cortex in the formation of learned perceptual biases (McTeague et al., 2015). High-contrast grating stimuli (Gabor patches) in eight different orientations (CS) and a white noise (US) served as stimuli to study orientation tuning of neurons in the primary visual cortex during fear generalization. Analyses revealed a selective amplification in the visual cortex in response to the sound-paired grating (CS+), which was located in the middle of the stimulus continuum, and a suppression of the grating orientations with highest similarity to the CS+. This so-called *Mexican hat* tuning pattern suggests lateral inhibitory interactions among orientation-selective neuronal populations in the visual cortex (McTeague et al., 2015) and is consistent with the result of the ssVEP activity in study 3 – albeit the latter just provided 50% of the *Mexican hat* shape due to its different stimulus arrangement. The authors of the study also recorded startle reflex and arousal and valence ratings during their experiment, and found the regular generalization gradients that have already been reported in earlier studies. Accordingly, the findings suggest that there is dissociation in response patterns between efferent reflex systems and sensory systems. As it seems, it is most adaptive for the organism to enhance sensory specificity in the visual cortex to distinguish the motivational information-providing stimulus from the others, while the readiness to respond to a potential threat is generalized, because a false alarm is less costly than a miss.

In contrast to study 2, there were no differences among the LSA and HSA group at all. While there were at least quantitative distinctions in the fear ratings and HR deceleration in study 2 arguing for a general hyperarousal of SAD patients in comparison to HC, neither group x stimuli interactions nor main effects of group were significant in the third experiment. The most obvious explanation is that the two experimental groups of study 3 did not vary enough regarding their level of social anxiety to elicit group differences. In study 2, the two groups exhibited a large difference in view of their degree of social anxiousness: HC had a SPAI score of *M* = 1.93, *SD* = 0.57, whereas patients had an average score of *M* = 4.24, *SD* = 0.93. For comparison: Fydrich's norm of psychosomatic SAD patients was with *M* = 3.96 lower than the patient's average of the second experiment. In contrast, the participants of study 3 were all healthy and artificially divided into two groups by a median-split with the SPAI score serving as criterion. Although the resulting low *(M* = 1.65, *SD* = 0.26) and high (*M* = 2.57, *SD* = 0.52) socially anxious groups differed significantly in their level of social anxiety, this difference might not have been strong enough to discover discrepancies in behavioral ratings and neuronal activity during fear generalization.

Another explanation could be that the conditioned stimuli itself - fearful faces paired with a shrill scream - were threatening indeed, but not *socially* threatening and thereby did not elicit a high degree of fear in high socially anxious participants. Faces per se are certainly social stimuli, but they would probably have been more effective if the displayed emotion were anger or disgust instead of fear, as these emotions have a particularly strong impact on individuals with SAD (Amir et al., 2005; Rossignol, Anselme, Vermeulen, Philippot, & Campanella, 2007; Stark et al., 2007; Turner, Johnson, Beidel, Heiser, & Lydiard, 2003). Also, the impression of social threat might have been enhanced by using negative verbal comments or critique in place of the scream as audible cue, which was proven to be effective in several previous investigations (Ahrens et al., 2014; Iidaka et al., 2010; Lissek, Levenson, et al., 2008). Thereby, the experimental design would have been closer to a real-life social threat situation, whereby the experiment's ecological validity would have been improved. However, the reason for the fact that study 3 did not utilize more specific social threat stimuli was its affiliation to a larger project, which investigated fear generalization in several populations with different anxiety traits. As an attempt to maintain comparability among populations, the fear generalization paradigm and its stimuli were kept constant over groups. Nevertheless, it has to be argued that study 2 used the same stimuli and found at least quantitative differences among groups, which is why the lack of group differences cannot be completely attributed to the choice of stimuli.

A limitation of the present study is its sub-clinical sample. While the first and second study compared clinically diagnosed patients suffering from SAD with HC, study 3 examined low and high socially anxious participants. As the generalization paradigm with faces was newly adapted for ssVEPs, it should first be tested in a sample of healthy participants before bringing it to a more

vulnerable as well as more difficult and costly-to-recruit population of patients with SAD. Nevertheless, it has to be stated that if there were any qualitative aberrations during fear generalization in patients with social phobia, it would be more likely to detect them in a clinical sample which should be considered for further investigations, now that the paradigm itself has proven to be effective.

In conclusion, the results of study 3 argue against overgeneralization as a marker of individuals with social anxiety. To secure this finding, the experiment should be replicated, but with clinically diagnosed SAD patients and HC as participants instead of LSA and HSA individuals. Notably, the observation that the generalization pattern in the visual cortex dissociates with his half *Mexican-hat* shape from the commonly reported generalization gradients is highly remarkable and should be further examined in the future.

5 General Discussion

In the final chapter, the results of the conducted experiments of the thesis will be integrated, discussed and brought into a broader context. First, a short summary of the primary findings is provided, and methodological as well as theoretical questions will be answered. Second, clinical implications of the current findings will be discussed. Third, there will be a critical look at the limitations of the present studies. Finally, conclusions for future projects will be presented in a concise outlook.

5.1 Summary and Discussion of the Present Experiments

The aim of the present dissertation was to investigate how patients with SAD differ from healthy participants regarding certain cognitive processes to gain a better understanding of the etiology and maintenance of SAD. In particular, the thesis focused on attentional and learning processes, as there is a growing body of literature highlighting that these mechanisms play a key role in the onset and retention of SAD. Altogether, three studies add to the existing knowledge on visual attention and conditioning and generalization processes in socially anxious individuals.

5.1.1 The influence of emotions and gaze direction on inhibitory attentional control in SAD

The first aim of this dissertation was to investigate how aberrations in attentional processes in patients with SAD contribute to the development and maintenance of this disorder. For this purpose, study 1 presented pictures of different actors displaying various emotional expressions with direct or averted gaze during an antisaccade task in order to compare the differential processing of these stimuli among SAD patients and healthy participants. Hence, we sought to determine whether the presentation of disorder-relevant stimuli would lead to a reduction of inhibitory control in patients with SAD as predicted by the ACT (Eysenck et al., 2007) and thereby perpetuate social anxiousness. A particular focus was set on the modulating effect of different emotional expressions as well as gaze directions on attentional control. Task performance was assessed via eye-tracking as response latency and error rate, whereas the evaluation of the target stimuli was carried out via valence and arousal ratings at the end of the experiment.

In order to enhance the reliability and validity of the study, some adaptions on previous experimental designs were made: instead of using former indirect measures of attention, such as reaction time in the dot-probe or stroop task, we applied eye-tracking as a testing method in study 1. Eye-tracking gets more and more established in practice to gain a continuous, direct measure of visual attention (Garner et al., 2006; Rinck & Becker, 2006; Sluis et al., 2017). The advantage of this

method is that it allows the analysis of the time-course of attention. This reveals the difference between instantly, correctly executed saccades and antisaccades, and those which were erroneous at first, but later voluntarily corrected by the participants. Moreover, several experiments of the past used computer-generated actors and facial expressions as target stimuli in order to accomplish a high level of controllability (Derakshan & Koster, 2010; Wieser, Pauli, & Mühlberger, 2009). However, researchers found out that artificially created faces often either do not look human enough to make participants identify with them, or look so human that participants find their non-human imperfections unsettling (MacDorman, Green, Ho, & Koch, 2009; MacDorman & Ishiguro, 2006; Mori, 1970). The phenomenon that the relationship between the degree of an object's resemblance to a human being and empathetic responses in humans to such an object does not follow a simple linear curve, but displays a dip when the humanoid object appears to be almost, but not 100% human, is known as the *uncanny valley* (Mori, 1970). Consequently, when the computer-created target stimuli in psychological studies do not look human enough, participants might not show enough empathy or emotional arousal in response to them, making the experimental manipulation less effective. To bypass the risk of the uncanny valley, study 1 of this dissertation presented photographs of real human faces taken from a standardized picture data base as target stimuli (Langner et al., 2010). Further, in contrast to previous studies (Sluis et al., 2017; Wieser, Pauli, & Mühlberger, 2009), study 1 included not only the actual antisaccade task with social stimuli, but it also included a control task with non-social stimuli. This assured, a general inhibition deficit could be ruled out. In addition, prior studies often tested analogue samples with healthy participants characterized by high levels of social anxiety instead of diagnosed patients. As these experiments often lead to comparable results as in patients, it is logical to test new designs in easier-to-recruit individuals (non-patients) first. Yet, a generalization of such results might be rash and error-prone, for which reason study 1 and study 2 were conducted with clinically diagnosed patients.

However, the results of study 1 did not support our hypothesis. First, the results did not support the assumption of cognitive models that social anxiety is characterized by an attentional bias to external social threat cues (Clark & Wells, 1995; Rapee & Heimberg, 1997). Second, the results failed to support the ACT hypothesis, in which an anxiety-induced misbalance between the stimulus-driven bottom-up and the goal-oriented top-down attentional system leads to a reduction in volitional attentional control (Eysenck & Derakshan, 2011; Eysenck et al., 2007), as SAD patients showed neither enhanced error rates nor increased response latencies in comparison to non-patients in the eye-tracking data. The only difference between groups was found with regard to the error rates and gaze direction, as SAD patients made slightly more errors at the presence of faces with direct compared to averted gaze, whereas HC made less errors in response to faces with direct gaze. A plausable reason for this finding could be that SAD patients tend to avoid eye-contact (Horley et al.,

2003; Moukheiber et al., 2010; Weeks et al., 2013) and were more distressed by those stimuli. Overall, it is quite astonishing that there were almost no group differences in the eye-tracking data regarding the high number of studies which already detected a hypervigilance for threat in SAD (Mathews & MacLeod, 1994; Seefeldt et al., 2014; Shechner et al., 2013; Williams et al., 1988), which is why a further explanation is demanded.

As the findings of previous experiments that participants display enhanced error rates and prolonged latencies in antisaccade compared to prosaccade trials could be replicated in study 1 (for a review, see Hutton & Ettinger, 2006), it is not very likely that the experimental design itself was not suitable to measure attentional control. However, it is possible that SAD patients do not always suffer from an attentional bias towards threat, but only show this bias under certain circumstances. This hypothesis is underlined by the finding that study 1 is not the first experiment that did not observe differences among (socially) anxious groups regarding the error rate (Derakshan et al., 2009; Sluis et al., 2017) and response latency (Sluis et al., 2017; Wieser, Pauli, & Mühlberger, 2009). For example, one possibility could be that SAD patients only show an attentional bias towards threat when they are currently in a situation of potentially being negatively evaluated by others. The mere presentation of phobic stimuli as applied in study 1 might not be sufficient to elicit anxiety in SAD patients, because without an audience, participants never ran the risk of being judged or laughed at, and maybe did not even attribute the emotional reactions of the faces to themselves. Empirical evidence supporting this assumption provides a study using a modified dot-probe task, which presented pairs of faces with negative, neutral and positive emotional expression. It detected that HSA individuals only show an attentional bias compared to LSA in response to emotional faces under a social-evaluative threat condition (threat of giving a speech after the experimental task), but not under the control condition (Mansell et al., 1999). Moreover, another facial dot-probe study without a social threat induction also detected no attentional biases in HSA compared to LSA participants (Bradley et al., 1997). However, there is a recent antisaccade study which aimed at investigating the role of anticipatory processing as a maintaining factor of SAD and included a threat of a speech task before the antisaccade paradigm (Sluis et al., 2017). Surprisingly, they did not find impairment in attentional inhibition functions in HSA individuals who anticipated giving a speech compared to HSA individuals who did not anticipate giving a speech or LSA individuals in both conditions. They rather detected that LSA individuals in the experimental condition showed reduced response latencies compared to LSA individuals in the control condition, suggesting that the threat of giving a speech facilitated the inhibition functioning of the anticipating LSA participants. Altogether, the inconclusive results indicate that there must be further factors having an influence on attentional control in participants with SAD.

Another possible explanation could be that social anxiety might not be maintained by a hypervigilance to threat, but rather a deficit in the attentional processing of positive information. Support for this account stems from an investigation which found that attention to emotionally relative to neutral expressions did not vary by emotion for SAD patients but control patients in a probe detection task. HC preferred happy and avoided negative facial expressions over time while SAD patients did not show any difference (Schofield et al., 2013). Likewise, another study did not observe differences in attentional engagement with socially relevant emotional stimuli in SAD patients, but found faster attentional disengagement from positive stimuli relative to HC instead (Chen, Clarke, MacLeod, & Guastella, 2012). However, the current project did not find differences in the control group to support this hypothesis.

Furthermore, a reason for the findings could be that attentional control in SAD is not only characterized by a hypervigilance of threat, resulting in reduced inhibitory attentional control observable as shortened prosaccades and prolonged antisaccades in the presence of threatening faces, but by several biases in selective attention occurring at different stages of attention (see Chen & Clarke, 2017, for a review). Lang and Gray already posited in 1990 that an organism's motivational state conditions its readiness to approach or avoid a stimulus (Gray, 1990; Lang, Bradley, & Cuthbert, 1990). As earlier described (see chapter 1.4.1.3) socially anxious individuals might be in a conflict of response tendencies: the permanent vigilance and monitoring of threat to detect potential danger versus avoidance and escape strategies to reduce discomfort (Mogg & Bradley, 1998). Consequently, the focus of attention of SAD patients in this study might have been unstable and permanently shifting towards and away from threat after the initial orienting reaction, so therefore the biases canceled each other out, leading to a null result.

Another plausible reason for the finding that there were no differences regarding performance efficiency and effectiveness between SAD patients and the control group could be that motivation had an impact on the SAD patient's task performance. Although research on the relationship among attentional control and motivation is still in its early stages, several studies suggest that motivation can have a strong influence on cognitive and therefore also on attentional control (e.g. Botvinick & Braver, 2015; Kouneiher et al., 2009). It is possible that in study 1, the threat of doing poorly in the experimental task induced individuals with SAD to put more effort into task performance, which could have caused a compensatory effect on the results and led to a comparable level of performance effectiveness. Support for the idea that high versus low anxious participants exhibit greater cognitive effort in antisaccade tasks, at least during medium and long cue-target intervals (CTI), is provided by Ansari and colleagues, who measured cognitive effort by frontal contingent negative variation (CNV) activity (Ansari & Derakshan, 2011). This is in line with Eysenck's current update of the ACT, in which he hypothesized that anxiety can have two effects on attentional

control: it can either cause a deficit in recruiting attentional control resources in conditions involving low levels of motivation, such as in easy, undemanding task, or tasks without clear goals, or it can have the opposite effect of increased recruitment of attentional resources, when the level of motivation in the participants is high (Eysenck & Derakshan, 2011). More support for this idea provided a study which showed that high trait anxiety had a negative effect on task performance in a low-, but not high-motivation condition in a category learning task (Hayes, MacLeod, & Hammond, 2009).

Further research is required to disentangle the role of motivation on attentional control in SAD. To assess this question, researchers would have to manipulate the amount of cognitive load that participants handle during a task. According to ACT, anxious individuals try to avoid poor task performance by using the aforementioned compensatory strategies (Eysenck & Derakshan, 2011; Eysenck et al., 2007). However, this comes at a cost to processing efficiency and is also called the "hidden cost of anxiety" (Eysenck & Calvo, 1992). As a consequence, patients with SAD should be more easily overloaded by high task demands compared to healthy control participants. There are already a few studies which found that highly anxious individuals exhibited increased latencies to low anxious individuals in tasks with high cognitive load (Eysenck, Payne, & Derakshan, 2005; MacLeod & Donnellan, 1993). As we did not find enhanced latencies in the SAD patients compared to HC, it is possible that the cognitive load in study 1 was so low that SAD patients were able to compensate their lack of attentional control by putting more effort into their performance. To clarify whether this was the case, future studies should modulate the cognitive load of a task. For example, individuals should simultaneously perform a second task in addition to the antisaccade paradigm.

Albeit there were almost no discrepancies among groups with regard to visual attention measured by eye-tracking, the hypotheses regarding the evaluation of the stimuli via valence and arousal ratings applied to a great extent: as suggested by more and more studies (Birbaumer et al., 1998; Yoon & Zinbarg, 2007), study 1 revealed that SAD patients did not only judge angry faces to be more arousing and less pleasant in comparison to a healthy control group, but that this group difference also applies to neutral faces. An account to explain this effect could be that neutral facial expressions are difficult to interpret and cause a feeling of uncertainty in SAD patients (Birbaumer et al., 1998; Moser et al., 2008). In any case, this finding puts the utilization of neutral faces as control stimuli for individuals with SAD into question. Moreover, SAD patients rated faces with direct gaze to be less pleasant than faces with averted gaze, which is in line with former results showing that these patients try to avoid eye-contact during social interactions or feel very uncomfortable when they are exposed to it (e.g. Howell et al., 2016; Weeks et al., 2013). Overall, the results of the ratings

underline that both the facial expression and the gaze direction influence individuals with SAD compared to HC in a different way and therefore play an important role in their social interactions.

The fact that the results of the ratings altogether corresponded with our expectations, while the results of the eye-tracking data did not, requires an explanation. First, the finding of differences between implicit and explicit measures has been repeatedly reported (Bar-Haim et al., 2007; Moser et al., 2008; Wieser, McTeague, & Keil, 2011). A possible reason for this discrepancy could be that implicit compared to explicit measures underlie an enhanced error-proneness, because the former do not only require the press of a button or a the checking of a box on a questionnaire, but the correct installation of the measuring equipment as well as data recording and processing. Another explanation could be that rationally, SAD patients evaluated the angry and neutral faces with direct gaze to be less pleasant and more arousing, but as no social interaction with the actors was required afterwards, the mere presentation of socially threatening stimuli might not have activated social anxiousness in the SAD patients. This is why there was no interference from anxiety with the patient's task performance on the antisaccade paradigm. As mentioned above, this could be examined in the future by enhancing the level of social threat, for instance, by making participants give a speech in addition to the regular task.

Also, it is conceivable that the experimental design just led to a medium degree of social anxiety in the patients, which might have increased their task performance. According to the Yerkes-Dodson law (Yerkes & Dodson, 1908), which describes the relationship among arousal and task performance, the latter only positively correlates with arousal up to a certain point. When the level of arousal transcends this point, performance decreases. In other words: the relationship of arousal and performance is best described as a reversed u-shaped curve. Also, the Yerkes-Dodson law has shown that the level of arousal required for the best task performance varies as a function of task difficulty: easy tasks demanding persistence, such as the antisaccade task, are better performed with higher levels of arousal, because thereby motivation is enhanced, whereas difficult tasks require lower levels of arousal. Whether the degree of arousal and motivation played an important role in confounding the results should also be tested in future studies by manipulating the degree of arousal or cognitive load, respectively. For instance, a future experimental design would have participants work on two tasks simultaneously.

Altogether, the present findings have several implications for understanding the role of attentional control in SAD. Previous cognitive models of social anxiety disorder emphasize attentional biases to threat (Clark & Wells, 1995; Rapee & Heimberg, 1997) and thereby evoked interferences in inhibitory attentional control (Eysenck et al., 2007) as important features of this disorder, which contribute to its maintenance. However, there were no group differences in response latency and

error rate in a social antisaccade task among SAD patients and HC, indicating that some of the premises of prior models were not met by the current findings. Consequently, there seem to be more factors contributing to attentional control processes than actual models assume, such as motivation, the threat of negative evaluation or the amount of cognitive load, which suggests a specification or expansion of the models to gain a better knowledge on the etiology and maintenance of SAD. More research is required to determine the underlying mechanisms of attentional control processes in SAD and how they are modulated by other situational factors, such as cognitive load and motivation.

5.1.2 Fear conditioning and fear generalization in SAD

The second aim of the present dissertation was to explore whether individuals with SAD showed differences in associative fear learning processes compared to HC, which is purported to be a contributing factor to the etiology of SAD (Mineka & Zinbarg, 2006). Particularly, investigations are needed to determine whether SAD patients also show an overgeneralization pattern of conditioned fear, as it has been demonstrated for several other anxiety disorders (for a review, seeDymond et al., 2015). To this aim, two studies were conducted. In study 2, we first conditioned patients with SAD and HC to two neutral faces (CS), of which one (CS+) was paired with a fearful scream (US), while the other (CS-) remained unpaired. In the following generalization procedure, morphs of the two faces, which varied with regard to the degree of similarity with the original CS+, were presented while HR, SCR and valence and arousal ratings were recorded. Further work is needed to determine whether SAD patients would show overgeneralization indicated by an enhanced fear response to more GSs compared to the control group. In study 2, we focused on peripheral physiological measures (HR, SCR), while in study 3, we recorded neuronal activity of the brain (ssVEPs) during the generalization phase. In the third study, elements of the first two studies were combined: while the experimental paradigm was an adaption of the fear generalization paradigm of study 2, the dependent variable was again a measure of visual attention as in study 1. However, this time attention was not measured via eye-tracking, but neuronal activity in the visual cortex of the brain (ssVEPs). It should be tested whether there were already differences in information processing pointing to overgeneralization in HSA compared to LSA individuals on a neuronal level. As before, valence, arousal and US expectancy ratings of the stimulus material were obtained to add an explicit measure to the psychophysiological and neuronal assessment of anxiety.

To enhance the probability to detect group differences which could improve the knowledge on the etiology of SAD, we made some modifications to the design of previous studies examining similar problems in different anxiety disorders: previous studies on fear generalization mostly used non-social stimuli, such as electric shocks (Lissek, Biggs, et al., 2008), loud noise (Morris & Dolan, 2004) or aversive odors (Hermann et al., 2002; Schneider et al., 1999) as US. While those stimuli are

highly aversive and therefore effective, one of their disadvantages is the lack of ecological validity. To overcome this flaw, study 2 and 3 used an adaption of the "screaming-lady" paradigm developed by Lau and colleagues (Lau et al., 2008) with disorder-relevant stimuli serving as CS (human faces) and US (a shrill scream). Besides the ecological validity, the high belongingness of the target stimuli (face/scream) is an advantage of the design, because it ensures facilitated associative learning compared to experiments with stimuli without high belongingness (e.g. landscape/scream) (Hamm, Vaitl, & Lang, 1989). A further benefit of avoiding the until now frequently used electric shocks as US in conditioning experiments was that the paradigm was less questionable from an ethical perspective and even suitable for vulnerable populations, such as individuals with anxiety or other mental disorders.

With regard to the results, both study 2 and 3 indicated that the experimental procedure itself was successful, as the threat cue (CS+) elicited stronger fear responses compared to the safety cue (CS-) in both ratings and physiological measures after the conditioning procedure. Furthermore, both groups in both experiments generalized their conditioned fear of the CS+ to several GSs as a function of their similarity to the CS+ (with exception of the neuronal activity in study 3), speaking in favor of a successful generalization procedure. However, the main hypothesis that patients with SAD and high socially anxious participants would show overgeneralization compared to healthy or low socially anxious controls was not confirmed, as most of the results of study 2 and 3 – with the exception of the HR data - speak against this hypothesis.

This finding could be explained by several different reasons: first, it is possible that overgeneralization is only a feature of a subset of specific anxiety disorders, and SAD is not one of them. To date, overgeneralization is best documented for PD and PTSD (Lissek & Grillon, 2012; Lissek et al., 2009), and it might also be a marker of GAD (Lissek et al., 2014). However, there are also studies in anxiety patients and high and low anxious participants which did not observe overgeneralization in their samples. One generalization study in low and high trait anxious participants did not find greater fear generalization in the high anxious group. The authors conclude that overgeneralization of conditioned fear seems to be only characteristic for individuals with PD (Torrents-Rodas et al., 2013). They suggest that aberrant fear generalization is not a predisposing vulnerability mechanism, but rather acquired as a result of pathological processes. Two other studies investigated fear generalization in GAD, and in most indexes, their results speak against overgeneralization (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Tinoco-González et al., 2015), which is in contrast to the previously mentioned study of Lissek and colleagues (Lissek et al., 2014). With regard to SAD, there is no study which has tested fear generalization in SAD before. There is only a side note in one of Lissek's papers that he tested his generalization paradigm with non-social intermediary-sized rings in SAD and found no overgeneralization in this sample (Lissek,

2012). It has to be mentioned, though, that he did not expect SAD patients to show overgeneralization in this paradigm in the first place, because he used non-social stimuli (rings) as CSs and GSs. Moreover, the physical threat of electric shocks used in his investigation lies outside the content of the SAD patient's fear of social humiliation and scrutiny. To overcome this issue, we chose to apply socially relevant stimuli in study 2 and 3 of this dissertation, and yet we mostly did not find evidence speaking in favor of overgeneralization in SAD. One could argue that patients with PD, who are characterized by overgeneralization, fear a multiplicity of situations, whereas patients with SAD suffer from a comparatively circumscribed anxiety of social humiliation and scrutiny. Hence, patients with SAD do not show overgeneralization. However, there might be more factors which have to be taken in consideration as possible explanations for the current findings.

Another reason could be that the stimulus material of study 2 – the faces (CS) and the loud scream (US)- were an improvement compared to the geometric rings and startle probes regarding their disorder-specificity, but were still not threatening enough to elicit overgeneralization in SAD. Particularly, the human scream that was used as US might not have been disorder-specific enough to serve as a good model for the development of SAD. Future research should therefore address this question by investigating generalization in SAD with disorder-specific US, such as verbal insults (Ahrens et al., 2014; Davis, Johnstone, Mazzulla, Oler, & Whalen, 2009; Iidaka et al., 2010; Lissek, Levenson, et al., 2008). Also, it might make more sense to use angry instead of fearful faces, because anger can be more easily interpreted as a sign of disapproval or scrutiny. Yet, it might remain difficult to design an experimental setting which sufficiently represents the complexity of social interactions.

Beyond that, a plausible reason could be that study 2 and 3 examined stimulus but not context generalization. According to the DSM-5, SAD is characterized by an irrational fear of social and performance situations, in which one is exposed to possible scrutiny by others (American Psychiatric Association, 2013). As the definition already states, the fear does not refer to a certain stimulus, which is observed in specific phobia; but rather, the fear refers to the whole context in which one runs the risk of embarrassing oneself. Thus, future studies should examine SAD patients regarding generalization of contextual anxiety, perhaps following the design of Andreatta and colleagues, but with a social context (e.g. an audience) and US (negative verbal comments) (Andreatta, Leombruni, Glotzbach-Schoon, Pauli, & Mühlberger, 2015).

Furthermore, another reason for the fact that overgeneralization was not found in the SAD patients could be the high amount of comorbid disorders. Under the assumption that there is a positive correlation between SAD and overgeneralization, higher scores in SAD should be accompanied with more pronounced generalization effects. As the likelihood to detect a potential overgeneralization effect should be increased, patients with severe SAD were investigated. These patients could only be found in an inpatient setting and consequently, many of them suffered from

other psychopathologies, too. While we controlled for disorders which are often accompanied by a strong impairment in perception, learning and memory, such as alcohol or substance abuse as well as psychosis and delusional disorders, it cannot be ruled out that the findings were distorted by other mental disorders, especially depression. In this regard, a study investigating the influence of comorbid depression on SAD found that patients without depression showed defensive hyper-reactivity indicated by fear-potentiated startle responses during social threat imagery, while patients with comorbid depression demonstrated attenuated startle modulation, which might reflect a depression-associated psychomotor retardation and behavioral inhibition (McTeague et al., 2009). As depression was the most frequent comorbidity in the sample in the present study, these findings might have had an influence on the results as well. However, most of the other studies on overgeneralization also had included up to 50% individuals with comorbidities, albeit one could argue that many of them suffered 'only' from other anxiety disorders or major depression (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Lissek et al., 2014; Lissek et al., 2009). For future studies, it would be reasonable to tighten the exclusion criteria in order to minimize the influence of comorbidities. Nevertheless, it should be considered that testing SAD patients without further diagnosis – given the high number of comorbidities (Kessler, Chiu, et al., 2005) - is somewhat artificial, too.

Lastly, the fear-generalization process in study 2 and 3 was based on physical similarity. However, generalization might also occur on other dimensions, for example category or intensity (as reviewed in Dymond et al., 2015). In two generalization studies, it was examined in which way fear generalization is determined by the level of fear intensity in the CS- relative to a perceptually similar CS+ (Dunsmoor, Mitroff, & LaBar, 2009). Faces morphed between the endpoints of a neutral and a fearful expression were used as CS, and an electric shock served as US. The CS+ was always a face of 55% fear intensity, whereas the CS- was a neutral stimulus in experiment 1 and the most fearful stimulus in experiment 2. Interestingly, a peak shift to the most fearful face occurred in experiment 1, while generalization to the most fear-intense stimulus was reduced in experiment 2. These findings indicate that fear generalization is sensitive to the level of fear intensity in non-conditioned stimuli, but it can be attenuated by discrimination learning. Hence, further research is necessary to examine if SAD is characterized by aberrations in fear-generalization determined by the intensity of non-conditioned stimuli.

The hypothesis that SAD compared to HC would yield elevated fear reactions was confirmed in study 2. This was indicated by group differences in several measures: in general, the presented faces elicited greater HR decelerations, more negative valence ratings as well as enhanced arousal and US expectancy ratings in SAD patients in accordance with previous studies (Dimberg, 1997;

Dimberg & Christmanson, 1991; Straube et al., 2004). These findings do not speak for facilitated fear conditionability in SAD patients, though. As a matter of fact, such group differences have already been detected before fear conditioning, i.e. during habituation - albeit not always in the same measures. In the habituation phase, the SAD patients compared to HC showed a stronger SCR, likely indicating enhanced anxiety (Bradley, Codispoti, Cuthbert, & Lang, 2001), and increased arousal and more negative valence ratings. It can be assumed that the observed group differences are caused by a general hyperarousal of SAD patients triggered by the exposure to disorder-relevant face stimuli. Such responses actually constitute a diagnostic criterion of this anxiety disorder in the DSM-5 (American Psychiatric Association, 2013). In line with this, several studies have already observed enhanced activity in physiological measures during fear conditioning (Hermann et al., 2002; Lissek, Levenson, et al., 2008), face perception (Stein et al., 2002) and imagery of fearful events (McTeague et al., 2009) in SAD patients. This general effect is also in line with previous findings revealing a general biased processing of faces in social anxiety (Wieser, Pauli, & Mühlberger, 2009).

The reason why there was no group difference in study 3 could be that the difference regarding the level of social anxiety among the LSA (M_{SPAI} = 1.65, *SD* = 0.26) and HSA (M_{SPAI} = 2.57, *SD* = 0.52) was not large enough. After all, the samples consisted of healthy controls and not patients as in study 2 (HC: M_{SPAI} = 1.84, *SD* = 0.54; SAD: M_{SPAI}: 4.20, *SD* = 0.83). Moreover, it could be interesting to let participants not only rate indicators of fear and anxiety, such as valence and arousal ratings, but also their actual fear level in future investigations.

With regard to the overgeneralization hypothesis on a neuronal level, it was interesting to observe that study 3 did not only contradict overgeneralization in high compared to low socially anxious participants, but that the shape of the generalization gradients measured as ssVEP amplitude strongly diverged from what we had expected. Unfortunately, to date, there is only one other study that also explored fear generalization while recording ssVEPs (McTeague et al., 2015). In conformance with study 3, McTeague and colleagues also found highest neuronal activity in response to the CS+ coming along with a reduction of activity in response to the most proximal, but not distal GSs. For the authors, this finding was not too surprising, because there is evidence from animal research suggesting inhibitory interactions between orientation sensitive cells in the mammalian visual cortex (Freeman, Durand, Kiper, & Carandini, 2002; Li, Thompson, Duong, Peterson, & Freeman, 2006). As McTeague and colleagues used very basal stimuli (gabor patches) as CS, which differed in just one dimension (orientation), their results are in line with animal research. In contrast, the stimuli of study 3 (faces) were complex and multi-featured in comparison, which is why it could be assumed that the pattern of lateral inhibition should also be more complex and lead to distorted results. In this regard, McTeague and colleagues predicted that just those features of a CS+ would be

amplified which had a discriminative value, while irrelevant features or those which are shared with the CS- would be suppressed (McTeague et al., 2015). As a consequence, it could be hard to disentangle which features of complex stimuli are suppressed and which are amplified. Given this assumption, it is even more surprising that a similar activation pattern during fear generalization was found in study 3. Additional basic research with less-featured stimuli is needed to better understand the mechanisms in the human visual cortex during fear generalization. Furthermore, as it is so difficult to find SAD patients volunteering in clinical research, it would be reasonable to test the paradigm repeatedly in analogue samples first before bringing it to a clinical sample.

Due to the dissociation among peripheral psychophysiological and cortical sensory responses (u-shaped vs. half Mexican hat shaped generalization gradient), the question arises what function this discrepancy might have. It is possible that on the one hand, inhibitory interactions on the visual cortical level are adaptive, enabling enhancement of the sensory specificity of the CS+. On the other hand, the same process would be too costly for behavioral and peripheral psychophysiological systems, as it reduces the individual's preparedness to respond to a threat in the environment. Lastly, to exclude the possibility that the discrepancies in social threat processing in efferent defensive reflexes (study 2) and sensory aspects in the brain (study 3) are the result of different experimental paradigms, a future study on fear generalization should incorporate simultaneous measures of both cortical processes and defensive somatic reflexes.

Overall, the present results suggest that overgeneralization is not a key characteristic of SAD. This finding stands in contrast to Lissek's hypothesis that overgeneralization could be a pathogenic mechanism which occurs across traditional anxiety disorder categories (Lissek et al., 2014). A possible explanation could be that overgeneralization is only a marker of those anxiety disorders which come along with a broader anxiety concept (i.e. multiple situations are feared, such as in PD and PTSD), whereas anxiety disorders with a more circumscribed anxiety concept (i.e. less situations are feared, such as in specific phobia or social phobia) are not characterized by it. However, as study 2 and 3 of the present thesis are the first to assess fear generalization in SAD, it should not be ruled out that methodological aspects or other modulating factors of fear generalization discussed above are accountable for the present findings. Future research should address these questions, for example by exclusion of comorbid disorders in the sample, the application of even more disorder-relevant stimuli (such as angry faces and negative verbal comments) or the development of intensity- instead of similarity-based generalization paradigms. Lastly, generalization processes on a neuronal level should be further explored, preferably at first with less complex stimuli.

5.2 Clinical Implications

Given the fact that the purpose of clinical research is the development of new accounts to prevent, diagnose, or treat diseases more effectively than in the past, it is surprising how little these questions are directly addressed in a good deal of literature. It reveals that there is still a lot of potential to improve the communication among researchers and practicing clinicians. The following section aims at providing information on the treatment of SAD as well as conclusions for further improvement that can be drawn from the studies of the present thesis.

5.2.1 Treatment of anxiety induced attentional control deficits

As aberrations in attentional processes play a role in SAD, one promising account to treat them might be to retrain attentional biases. Over the last years, researchers have implemented the so-called *attention bias modification (ABM)*, which is a computer-delivered treatment with the aim to lower anxiety by reducing an attentional bias towards threat (MacLeod & Mathews, 2012; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). Albeit some studies have shown that ABM leads to reductions in anxiety symptoms (Amir, Beard, Burns, & Bomyea, 2009; MacLeod & Clarke, 2015; Price, Tone, & Anderson, 2011), recent findings suggest that its effectiveness is limited (Carleton et al., 2015; Cristea, Kok, & Cuijpers, 2015; Koster & Bernstein, 2015; Van Bockstaele et al., 2014). One reason could be that ABM training is repetitious, which might be boring for the participants and reduce treatment compliance (Mogg & Bradley, 2018). Another explanation could be that the most widely-used version, the *ABM-threat-avoidance training*, is not suitable for all anxiety patients, because some of them do not display an attentional bias towards threat, but are already avoidant (Eldar et al., 2012; Van Bockstaele et al., 2014). However, there is also an account which is potentially suitable for all individuals, the *ABM-positive-search training.* In this version of the visual-search task, an array including one positive stimulus (e.g. happy face) and many negative stimuli (e.g. angry faces) is presented to the participants, and they are instructed to look for the happy face while ignoring the angry ones (Dandeneau, Baldwin, Baccus, Sakellaropoulo, & Pruessner, 2007; De Voogd, Wiers, Prins, & Salemink, 2014; Waters, Bradley, & Mogg, 2014; Waters, Pittaway, Mogg, Bradley, & Pine, 2013; Waters et al., 2015). A meta-analysis revealed that studies using the ABM-positive-search training had larger effect sizes regarding symptom-improvement compared to those using the ABM-threat-avoidance training (Mogoaşe, David, & Koster, 2014) (for a review on ABM, see Mogg & Bradley, 2016).

Beyond that, the method of eye-tracking as used in study 1 could be a helpful tool for the treatment of anxiety-related performance deficits on attentional control, for example by pairing it with conditioning paradigms as used in study 2 and 3. Research in this area is just starting to emerge.

There are two studies which developed innovative paradigms to modify attentional biases. One study applied an operant-condition-based and eye-gaze-dependent approach to retrain maladaptive attentional patterns by reinforcing healthy participants every time they attended the correct emotional expression (happy vs. neutral condition) within an array of six different emotions (Price, Greven, Siegle, Koster, & De Raedt, 2016). Results showed that individuals who were trained to pay attention to happy faces were more resilient to stress in a later stress-inducing task compared to those who were trained to attend neutral faces, suggesting that attending to happy faces helps to stabilize the mood. This finding is in line with cognitive SAD models hypothesizing that maladaptive information processing patterns have downstream effects on emotional vulnerability (Clark, 1999; Clark & Wells, 1995). Another study tested patients with SAD in a newly developed gaze-contingent music reward therapy (Lazarov, Pine, & Bar-Haim, 2017). In this task, SAD patients were conditioned to direct their gaze toward neutral instead of threatening faces and were reinforced with their favorite music as long as they attended to the neutral faces. When they fixated on disgusted faces, though, the music stopped. Results indicated that the experimental compared to the control condition significantly reduced both self-reported and clinician-rated SAD symptoms after treatment, and that this effect was stable at a 3-month follow-up.

One aspect we investigated in study 1 was in which way gaze direction modulates attentional control. Although we found no group differences in the eye-tracking data, ratings suggested that SAD patients evaluated faces with direct compared to averted gaze as less pleasant compared to HC. Also, there is evidence that SAD patients try to avoid eye-contact more frequently or feel uncomfortable when they are exposed to it (e.g. Horley et al., 2003; Howell et al., 2016; Weeks et al., 2013). Consequently, a further account could be to train SAD patients to maintain eye-contact with their interactional partners. In this way, SAD patients would not lose important information, as suggested in theoretical models (Clark & Wells, 1995; Rapee & Heimberg, 1997), but instead they would benefit from important feedback on their actual-self as seen by others, which could decrease social anxiousness.

5.2.2 Treatment of generalized anxiety

With regard to fear generalization, there is even less literature on how the findings of clinical laboratory studies could improve the treatment of anxiety disorders in general and SAD in particular. This is not astonishing given the fact that this field of research just recently got into the focus of scientists – at least with regard to human and not animal studies – and cannot look back on a long history of etiological models and treatment accounts. Nevertheless, there are already some conclusions that can be drawn from previous investigations. First, the discovery of the generalization process itself (Pavlov, 1927; Watson & Rayner, 1920) is of great importance for *exposure therapy and*

response prevention. This technique is a key-component of cognitive behavioral therapy (CBT), which is applied mainly in anxiety disorders and involves the confrontation with the feared stimulus or context while the regular escape response is interrupted (e.g. Abramowitz, Deacon, & Whiteside, 2012). In this way, the patient makes a new learning experience, namely that the fear decreases over time without his or her help, which aids to overcome their distress and anxiety.

The lesson from fear generalization research is that fear can be triggered by stimuli that actually were never present at the original conditioning experience. Consequently, it is not sufficient to expose the patient to the primary CS, but rather to a number of similar stimuli and situations (perceptual generalization). Moreover, there is growing evidence that fear does not only generalize to perceptually similar stimuli, but also to more abstract and complex representations of object categories or verbal relations (non-perceptually based or conceptual generalization) (Dunsmoor & Murphy, 2015; Dunsmoor, White, & LaBar, 2011; Dymond et al., 2015; Hermans, Baeyens, & Vervliet, 2013). Based on animal research, it was believed that fear conditioning was an evolutionary conserved system which only mediated simple forms of learned behaviors (Dunsmoor & Murphy, 2015). However, this translational model has some limitations, because it does not take into account the human ability for abstract representations. This network of associations in the human brain can lead to the generalization of fear along arbitrary dimensions (Dymond et al., 2014), with the result that, for example, an individual who gets laughed at while giving a speech during class might not only fear giving speeches in front of this particular class, but an audience in general. He or she might also get afraid of classrooms, being in a performance situation or in the center of attention and avoid these situations in the future, which may lead to a loss of quality of life. Accordingly, the treatment of SAD requires a thorough assessment of relevant fear stimuli and their conditioning history. However, it is also possible that the original trigger cannot be traced, because the way from the actual fear to the eliciting stimulus might be too complex. Not identifying the original threat stimulus, or identifying it but finding it inaccessible (which is very common), can actually lead to further difficulties during therapy. While there is evidence that extinction of the primary CS spreads to GSs, the reverse does not necessarily apply (Roche, Kanter, Brown, Dymond, & Fogarty, 2008) and might even lead to a more extensive return of fear (Vervliet et al., 2005).

Further, overgeneralization in anxiety disorders may play a crucial role during the early diagnosis or even prevention of anxiety disorders. For example, adolescents with a higher risk to develop anxiety disorders (e.g. family history of anxiety disorders, growing up in a family with an overprotective parenting style) could be tested with regard to their generalization pattern, and, if they display overgeneralization, be offered therapeutic support and special interventions. Furthermore, individuals who had to make critical life experiences (e.g. failing during an important

performance situation, being bullied) could also profit from early interventions, so that the fear does not get the chance to spread.

Albeit the results of study 2 and 3 of the present thesis speak rather against the overgeneralization hypothesis in SAD, patients could also benefit from certain therapeutic methods as they show generalization at all. One potential candidate is *discrimination learning*, which is basically the opposite of generalization. During this training, individuals with SAD could learn of which stimuli or in which situations it makes sense to be afraid, and how these stimuli and situations could be separated from harmless perceptually or conceptually related stimuli or events (Vervliet, Kindt, Vansteenwegen, & Hermans, 2010). Overall, more knowledge on perceptual and non-perceptual fear generalization is necessary before further conclusions on how this information should influence the use of traditional therapeutic methods should be drawn.

5.3 General Limitations

Several limitations have already been discussed at the end of each of the single studies. Still, there are a number of critical theoretical and methodological aspects which have not been addressed yet and therefore should be disputed in the following section.

One important constraint when interpreting the results of study 1 and 2 is that the clinical and the control group were conducted at different locations which could have an impact on the results. While the patients with SAD were recruited at a psychosomatic clinic, the control group was tested at the University of Würzburg. This was eventually inevitable for two reasons: on the one hand, there were not enough volunteers with SAD in Würzburg to participate in the experiments. For this reason, the set-up had to be brought to a psychosomatic clinic which was specialized on the treatment of SAD, thereby providing a large pool of participants. On the other hand, non-patients were not allowed to enter the clinic, which is why the control group had to be tested at the University. To minimize artifacts, we conducted the experiments in similar rooms, and used the same experimental set-up and apparatus for both groups. Yet, future studies should avoid spatial separation of the experimental settings, whenever it is possible.

The second limitation is the fact that only two studies (1 and 2) tested clinically diagnosed SAD patients, while the participants of study 3 were undergraduate students. Although experiments with samples of healthy participants, which display high levels of the investigated target characteristic, often lead to similar results as experiments with real patients, the generalization of the results from an analogue sample to patients is risky. It must always be considered that any deductions or conclusions from these studies may be factually flawed. With two samples consisting of SAD patients and one consisting of healthy participants who share particular traits (social anxiousness) with the patient group, it is more difficult to bring the results of all three studies into a

broader context and derive clinical implications from the results. The reason for examining a sub-clinical sample in study 3 and taking this disadvantage into account was that in contrast to study 1 and 2, the ssVEP-adapted generalization paradigm had never been tested before. Individuals with diagnosed SAD are rare to find and – due to their nature – even more difficult to convince to take part in scientific experiments, because the situation of "being tested" itself makes them feel very uncomfortable. Therefore, it should first be tested whether the paradigm worked at all, before bringing it to such a difficult-to-acquire group as patients with SAD. Now that the paradigm proved to be effective, the next step would be to test diagnosed SAD patients with it.

A further limitation that comes along when working with inpatients is the high number of comorbidities in study 1 and 2. To minimize the influence of other disorders, we excluded those patients from participation which suffered from disorders known to go along with a strong impairment of attention, learning and memory, such as alcohol or substance abuse as well as psychosis and delusional disorders. However, comorbid depression occurred so frequently in the SAD patients of the present study that the elimination of all affected patients would have led to undersized samples. For the same reason, it was impossible to calculate the confounding effect of this covariate. Previous work shows that many studies with anxiety patients have to deal with the same difficulty (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Lissek et al., 2014; Lissek et al., 2009). One account for future studies could be to investigate a third group in addition to the SAD and the control group, such as clinically depressed patients. In this way, it could be compared if and to what extent patients with depression and SAD differ from each other with regard to attentional control, fear conditioning and generalization. There is already evidence from a recent study which investigated attentional biases in patients with anxiety disorders (SAD, GAD, PD and unspecified anxiety disorder) and depression in response to task-relevant and task-irrelevant emotional and special cues. The study detected that anxiety was associated with an attentional bias towards emotional information, even if they were task-irrelevant, while depression was not (Lichtenstein-Vidne et al., 2017). Another possibility, which has already been discussed in section 4.4., could be to sharpen the exclusion criteria to reduce the impact of comorbidities on the results. However, given the high number of comorbidities of SAD (Kessler, Chiu, et al., 2005), this proceeding neglects the fact that a "pure" SAD is very uncommon and might therefore also lead to distorted results and interpretations.

A new approach to deal with this challenge provides the National institute of Mental (NIMH) with its research Domain Criteria (RDoC) initiative to create a biologically-focused framework of mental disorders. This project emerged out of the need to define a new taxonomy for mental disorders by integrating research accounts from different fields, such as neuroscience, imaging, psychophysiology, genetics and behavioral science, and looks at different mechanisms and

phenotypes transdiagnostically (Cuthbert & Insel, 2013; Insel et al., 2010). The problem with the currently used taxonomy of the DSM is that it is based on traditional diagnostic categories, and that these categories are not adapted from objective laboratory measures, but rather from a consensus of experienced clinicians about clusters of clinical symptoms. For this reason, the DSM methodology has been criticized by describing it as "[…] at best, a dictionary, creating a set of labels and defining each" (Insel, 2013). And indeed, while the measurement of physiological variables is a basic procedure during the clinical assessment of mainly physical disorders, such as a heart attack or a cerebral haemorrhage, this is not the case for mental disorders, as diagnosis is mainly based on clinic interviews, observations and self-report data of the patients. For this reason, the RDoC account aims at investigating basic mechanisms underlying mental illness, unconstrained by diagnostic boundaries to explicate certain endophenotypes or response measures, such as startle reflex, heart rate and reaction times (McTeague & Lang, 2012). For future studies, this would mean that researchers should not investigate attentional control or learning aberrations in one diagnosis only, such as SAD, but concentrate on one mechanism and investigate across the anxiety disorder spectrum and potentially mood-disorders, as prior epidemiological phenotypic and genotypic factor analytic studies of anxiety disorders and mood disorders observed common internalizing dimensions (e.g. Kendler, Prescott, Myers, & Neale, 2003; Vollebergh et al., 2001).

Finally, as all three studies had the aim to investigate certain characteristics of an anxiety disorder, it would have been reasonable not only to gain arousal and valence ratings of the stimuli, but to additionally record an explicit measure of anxiety.

5.4 Conclusion and Outlook

The present thesis investigated aberrations in attentional and associative learning processes in SAD patients and high socially anxious individuals compared to HC with the aim to gain new knowledge on factors contributing to the development and maintenance of SAD. Overall, the results suggest that SAD is characterized by a general hyperarousal in response to disorder-relevant stimulus material, as indicated by the ratings: SAD patients perceived the presented faces to be less pleasant, more arousing, and expected them to be followed by an aversive US more often compared to HC. With regard to attentional processes, the hypothesis that SAD patients would show reduced inhibitory control as the result of an attentional bias towards threat was not confirmed. Further research is required to clarify whether reduced inhibitory control only occurs under certain conditions, such as very high social stress conditions (e.g. before giving a speech, being negatively evaluated by others) or high cognitive load (e.g. handling two tasks simultaneously), or whether it is not a characteristic of SAD at all. For this purpose, the current experimental design could be modulated, for example by telling participants that they will have to give a speech after performing

the antisaccade task (anxiety induction) or by giving participants a second task to solve on top of the antisaccade paradigm (enhance the amount of cognitive load).

Relating to associative learning processes, the results mainly suggest that overgeneralization is not a pathogenic marker of SAD. However, SAD patients displayed a fully embodied fear reaction in HR response to the face stimuli while HC did not, which might be interpreted as the only sign pointing towards overgeneralization or rather the fact that fear reactions can be triggered more easily in SAD patients than HC. To rule out the potential influence of comorbidities, investigations in the future should address this purpose by excluding patients with comorbidities from testing or by adding a third clinical sample, for example patients with major depression, to the experimental design. Also, it could be interesting to examine fear generalization with emotional facial expressions of varying intensity as GSs or generalization of contextual fear in SAD patients. Beyond that, the outcome that the shape of the generalization gradient on a neuronal level differed substantially from the findings in peripheral physiological measures deserves more scientific attention. Additional basic research on this topic, for instance, with less complex objects than faces as target stimuli, is required before bringing it to the next level (i.e. testing it on SAD patients).

Overall, this thesis shows that the development and maintenance of SAD is more complex than present models can represent and predict. Some of the examined factors contributing to SAD do not seem to be merely endogenous (i.e. a general inhibitory deficit), but these factors might only occur when an external stressor is added to the equation that cannot be compensated by motivation and effort (i.e. the inhibitory deficit might only occur under high cognitive load or high social stress). Future research on both attentional and learning mechanisms is needed to expand current theories on SAD, which should also take into account different subtypes of SAD patients, for example to discriminate among those individuals who are hypervigilant and those who are mainly avoidant to threat. The hereby gained insights can help to improve the treatment of SAD, for example by attentional bias modification training or discrimination learning for certain contexts and subtypes of SAD.

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7 Annex

A Screening questionnaire for study 1 - 3

B Demographic data questionnaire

C Informed consent study 1

D Informed consent study 2

E Informed consent study 3

F List of figures

G List of tables

A Screening questionnaire

Teilnehmer-Code: Vp……. Datum:_____

Screening KG

1. Alter (18-65):_____

2. Geschlecht: □ männlich □ weiblich

3. Sind Sie **schwanger**? □ ja □ **nein**

4. Nehmen Sie regelmäßig verschreibungspflichtige **Medikamente** ein?: □ ja □ **nein**

Falls ja: Welche?_____

Kontraindikation: Zentralnervös wirksame Medikamente, z.B. Neuroleptika, Antidepressiva, Antiepileptika, Opiate, Benzodiazepine

5. Leiden Sie an einer **psychischen Erkrankung** (Angststörungen, Depression, Schizophrenie, Alkohol-, Drogen-, Medikamentenabhängigkeit? □ ja □ **nein**

Falls ja: Welche?_____

Leichte isolierte Phobien (z.B. Spinnen, Spritzen) sind o.k.

6. Leiden Sie an einer **neurologischen Erkrankung**? □ ja □ **nein**

Falls ja: Welche?_____

Kontraindikation: Erkrankungen mit Beteiligung des ZNS, z.B. Schlaganfall, Gehirnblutungen, **Epilepsie**, Parkinson, MS

7. Leiden Sie an einer **sonstigen Erkrankung** (Tinnitus, Herz-Kreislauf, Blut, Lunge, Leber, Nieren, Schilddrüse, Augen, Magen-Darmtrakt, Stoffwechsel): □ ja □ **nein**

Falls ja: Welche?_____

Kontraindikation: schwere Erkrankungen

8. Wie viele Gläser Alkohol trinken Sie pro Woche? Menge:_____

Weniger als 15 Gläser Alkohol pro Woche: □ **ja** □ nein

9. Wie viele Zigaretten rauchen Sie täglich? Menge:_____

Nicht mehr als 20 Zigaretten pro Tag: □ **ja** □ nein

10. Wie viele Tassen Kaffee trinken Sie täglich? Menge:_____

Nicht mehr als 4 Tassen Kaffee pro Tag: □ **ja** □ nein

11. Konsumieren Sie illegale Drogen: □ ja □ nein

Name: _____ **Telefonnummer:_____**

Emailadresse:_____

Testdatum: _____ **Vp-Nr.: _____**

B Demographic data questionnaire

V O R B E F R A G U N G

Wir möchten Sie bitten, einige Angaben zu ihrer Person zu machen. Diese sind notwendig, da individuelle Faktoren (wie z.B. Ihr Alter) einen Einfluss auf die Testergebnisse haben könnten.

Sie können sich darauf verlassen, dass diese streng vertraulich bleiben.

1. Alter: : ……..

2. Geschlecht: männlich …… ☐
weiblich …… ☐

3. Familienstand: ledig ..... ☐
verheiratet ..... ☐
in Lebensgemeinschaft lebend ..... ☐
geschieden ..... ☐
getrennt lebend ..... ☐
verwitwet ..... ☐

4. Welchen Schulabschluss haben Sie ?_____
(z.B. Hauptschule, Realschule, Gymnasium, Studium mit/ohne Abschluss)

5. Was machen Sie beruflich?_____
(z.B. Angestellter, Freiberufliche Tätigkeit, Unternehmer, Beamter, Schüler, Student, Bund/FSJ, Hausfrau/-mann, Ausbildung, Rentner, Ruhestand…)

5. Händigkeit : ☐ rechts ☐ links ☐ beidhändig

6. Haben Sie eine Sehschwäche? ☐ ja ☐ nein

Wird Ihre Sehfähigkeit ausreichend korrigiert? ☐ ja ☐ nein

7. Leiden Sie an einer psychiatrischen oder neurologischen Erkrankung (wenn ja, welche)?

_____

8. Hatten Sie schon einmal einen epileptischen Anfall oder ist bei Ihnen in der Familie eine Epilepsieerkrankung bekannt?
☐ ja ☐ nein

9. Nehmen Sie regelmäßig oder zurzeit Medikamente (welche, wie oft)?

C Informed consent study 1

Julius-Maximilians-
UNIVERSITÄT
WÜRZBURG

Probandencode: _____

Datum: _____

Probandeninformation zur Studie

„Aufmerksamkeit auf emotionale Gesichter bei Sozialer Phobie“

Sehr geehrte(r) Proband(in),

wir möchten Sie bitten, an einer wissenschaftlichen Studie zur Verarbeitung von Gesichtern teilzunehmen. In dieser Studie werden Ihnen Bilder geometrischer Figuren oder verschiedener Personen gezeigt. Ihre Aufgabe wird es sein, auf ein Signal hin entweder direkt zu den gezeigten Bildern zu blicken oder in die entgegengesetzte Richtung zu schauen. Außerdem sollen Sie die Bilder während des Versuchs mehrfach bewerten. Durchgänge mit Blickbewegungen und Bewertungsdurchgänge werden sich während des Versuchs mehrfach abwechseln.

Ablauf:

Zunächst werden Sie gebeten, einige Fragebögen zu persönlichen Angaben, Ängstlichkeit und Stimmung auszufüllen. Bitte antworten Sie hierbei so spontan und ehrlich wie möglich! Anschließend wird Ihnen ein sogenannter Eye-Tracker aufgesetzt, welcher wie eine Art Brille aussieht und die Aufzeichnung Ihrer Augenbewegungen mit einer kleinen Kamera während der Untersuchung ermöglicht. Dies ist für Sie völlig unbedenklich.

Während der Untersuchung wird Ihnen auf dem Bildschirm des Eye-Trackers zunächst ein Punkt dargeboten, dem Sie mit dem Blick folgen sollen. Dies dient der Anpassung Ihrer Augenbewegungen an unser Messgerät. Danach wird Ihnen in mehreren Durchgängen ein Kreuz dargeboten, welches Sie aufmerksam betrachten sollen. Nach kurzer Zeit erscheint an der Stelle des Kreuzes entweder das Wort „HIN“ oder „WEG“ und daraufhin das Bild einer geometrischen Figur oder eines Gesichts. Erscheint das Wort „HIN“, sollen Sie so schnell wie möglich eine Blickbewegung zu dem daraufhin präsentierten Gesicht oder der daraufhin präsentierten geometrischen Figur machen. Erscheint das Wort „WEG“, sollen Sie bitte bei Erscheinen des daraufhin präsentierten Gesichts eine Blickbewegung in die entgegengesetzte Richtung durchführen. Sie erhalten die Möglichkeit, diese Aufgabe vor Beginn

der eigentlichen Untersuchung zu üben. Zudem sollen Sie die Gesichter mehrfach bewerten. Anschließend wird Ihnen der Eye-Tracker abgenommen und Sie sollen nochmals Fragebögen ausfüllen. Insgesamt wird der Versuch max. 1 Stunde in Anspruch nehmen.

Datenschutz:

Ihre Daten werden unter einer Codenummer abgespeichert. Dies erlaubt eine anonyme wissenschaftliche Auswertung der Daten. Eine Zuordnung der Daten zu bestimmten Personen ist nicht möglich. Die Zuordnung der Codenummer zu Ihrer Person wird getrennt von den Daten aufbewahrt und nach einem Jahr vernichtet. Bis dahin können Sie, auch ohne Angabe von Gründen, die Löschung Ihrer Daten verlangen. Es ist möglich, dass die anonymisierten Daten, die keiner Person mehr zugeordnet werden können, im Rahmen einer wissenschaftlichen Publikation veröffentlicht werden. Die anonymisierten Daten werden auf unbestimmte Zeit virtuell gespeichert. Eine Weitergabe der Daten an Dritte erfolgt nicht.

Nutzen der Untersuchung:

Wir weisen Sie ausdrücklich darauf hin, dass diese Untersuchung ausschließlich der Grundlagenforschung dient. Ein unmittelbarer Nutzen ist für Sie durch die Teilnahme nicht zu erwarten.

Freiwilligkeit der Teilnahme:

Bitte beachten Sie:

Die Teilnahme an der Untersuchung ist völlig freiwillig. Wenn Sie bereit sind, an dieser wissenschaftlichen Untersuchung teilzunehmen, bitten wir Sie, uns Ihr Einverständnis schriftlich zu erklären. Auch wenn Sie unterschrieben haben, können Sie natürlich jederzeit ohne Angabe von Gründen und ohne dass Ihnen daraus Nachteile entstehen, Ihr Einverständnis mündlich zurückziehen und die Untersuchung abbrechen.

Haben Sie noch Fragen? Dann stellen Sie diese bitte jetzt der Versuchsleitung.

-

Versuchsleiter:
Lea M. Ahrens, Dipl.-Psych.
Marcusstraße 9-11
97070 Würzburg
Tel: 0931/31-81929

Einverständniserklärung zur Datenerhebung im Rahmen der Studie „Aufmerksamkeit auf emotionale Gesichter bei Sozialer Phobie“

Name der Probandin / des Probanden (bitte Druckschrift)

_____

Ich habe das Informationsblatt zur Studie „Aufmerksamkeit auf emotionale Gesichter bei Sozialer Phobie“ gelesen und bin ausführlich über die geplante Untersuchung unterrichtet worden. Die Informationen habe ich inhaltlich verstanden und hatte die Gelegenheit, Fragen zu stellen. Mit den erhaltenen Antworten bin ich zufrieden.

Ich erkläre mich freiwillig mit der Datenerhebung einverstanden. Über mögliche Risiken wurde ich aufgeklärt. Ich weiß, dass die Untersuchung wissenschaftlichen Zwecken dient und es nicht möglich ist, Informationen über individuelle Untersuchungsergebnisse zu erhalten.

Ich hatte ausreichend Zeit, mir zu überlegen, ob ich an der Datenerhebung teilnehmen will, fühle mich ausreichend informiert und habe keine weiteren Fragen. Ich wurde darauf hingewiesen, dass ich jederzeit von dieser Untersuchung zurücktreten kann, ohne dass mir dadurch ein Nachteil entsteht. Die Daten werden in diesem Falle vernichtet.

Ich erkläre mich darüber hinaus damit einverstanden, dass die aus der Datenerhebung gewonnenen Informationen verschlüsselt, d.h. in unpersönlicher Form (ohne Namens- oder Initialen-Nennung) aufgezeichnet, für unbestimmte Zeit in Computern gespeichert und ausgewertet werden. Dabei gibt es keine Möglichkeit des Rückschlusses auf Einzelpersonen. Der Codierungsschlüssel wird 1 Jahr nach Abschluss der Studie vernichtet. Bis dahin kann ich, auch noch nach der Untersuchung, die Löschung meiner Daten verlangen.

Ich bin auch damit einverstanden, dass die Ergebnisse der Studie in Gruppen zusammengefasst wissenschaftlich veröffentlicht werden.

_____ _____

Ort, Datum Unterschrift der Probandin/des Probanden

_____ _____

Ort, Datum Unterschrift des aufklärenden Mitarbeiters

D Informed consent study 2

Julius-Maximilians-
UNIVERSITÄT
WÜRZBURG

Probandencode: _____

Datum: _____

Probandeninformation zur Studie

„Assoziatives Lernen und Stimulusgeneralisierung bei Sozialer Phobie“

Sehr geehrte(r) Proband(in),

wir möchten Sie bitten, an einer wissenschaftlichen Studie zur Verarbeitung von Gesichtern und Geräuschen teilzunehmen. In dieser Studie werden Ihnen Fotos von Personen gezeigt, die teilweise gleichzeitig mit einem unangenehmen, relativ lauten Geräusch dargeboten werden. Ihre Aufgabe wird es sein, die Bilder auf sich wirken zu lassen und während des Versuchs mehrfach zu bewerten. Betrachtungs- und Bewertungsdurchgänge werden sich während des Versuchs mehrfach abwechseln.

Ablauf:

Zunächst werden Sie gebeten, einige Fragebögen zu persönlichen Angaben, Ängstlichkeit und Stimmung auszufüllen. Bitte antworten Sie hierbei so spontan und ehrlich wie möglich! Anschließend werden Ihnen an der nicht-dominanten Hand (die Hand, die gewöhnlich im Alltag seltener verwendet wird) sowie am Oberkörper Elektroden zur Erhebung physiologischer Maße angebracht. Diese Messungen werden von fast allen Probanden nicht als störend empfunden.

Während der Untersuchung werden Sie Bilder von Gesichtern betrachten, die über einen Computerbildschirm präsentiert werden. Sie werden in regelmäßigen Abständen zu den Bildern befragt. Diese zeigen 2 weibliche Darsteller mit neutralem Gesichtsausdruck. Ab und an werden Sie zusätzlich einen ängstlichen Gesichtsausdruck sehen. Außerdem werden Sie in bestimmten Abständen über einen Kopfhörer ein unangenehmes, relativ lautes Geräusch hören. Dieses kann einen Augenblick lang unangenehme Gefühle sowie Erregungsgefühle auslösen, ist jedoch nicht gefährlich. Zudem sollen Sie die Gesichter mehrfach bewerten. Anschließend werden die physiologischen Messgeräte abgenommen und Sie sollen nochmals Fragebögen ausfüllen. Insgesamt wird der Versuch max. 1 Stunde in Anspruch nehmen.

Datenschutz:

Ihre Daten werden unter einer Codenummer abgespeichert. Dies erlaubt eine anonyme wissenschaftliche Auswertung der Daten. Eine Zuordnung der Daten zu bestimmten Personen ist nicht möglich. Die Zuordnung der Codenummer zu Ihrer Person wird getrennt von den Daten aufbewahrt und nach einem Jahr vernichtet. Bis dahin können Sie, auch ohne Angabe von Gründen, die Löschung Ihrer Daten verlangen. Es ist möglich, dass die anonymisierten Daten, die keiner Person mehr zugeordnet werden können, im Rahmen einer wissenschaftlichen Publikation veröffentlicht werden. Die anonymisierten Daten werden auf unbestimmte Zeit virtuell gespeichert. Eine Weitergabe der Daten an Dritte erfolgt nicht.

Nutzen der Untersuchung:

Wir weisen Sie ausdrücklich darauf hin, dass diese Untersuchung ausschließlich der Grundlagenforschung dient. Ein unmittelbarer Nutzen ist für Sie durch die Teilnahme nicht zu erwarten.

Freiwilligkeit der Teilnahme:

Bitte beachten Sie:

Die Teilnahme an der Untersuchung ist völlig freiwillig. Wenn Sie bereit sind, an dieser wissenschaftlichen Untersuchung teilzunehmen, bitten wir Sie, uns Ihr Einverständnis schriftlich zu erklären. Auch wenn Sie unterschrieben haben, können Sie natürlich jederzeit ohne Angabe von Gründen und ohne dass Ihnen daraus Nachteile entstehen, Ihr Einverständnis mündlich zurückziehen und die Untersuchung abbrechen.

Haben Sie noch Fragen? Dann stellen Sie diese bitte jetzt der Versuchsleitung.

-

Versuchsleiter:
Lea M. Ahrens, Dipl.-Psych.
Marcusstraße 9-11
97070 Würzburg
Tel: 0931/31-81929

Einverständniserklärung zur Datenerhebung im Rahmen der Studie „Assoziatives Lernen und Stimulusgeneralisierung bei Sozialer Phobie“

Name der Probandin / des Probanden (bitte Druckschrift)

_____

Ich habe das Informationsblatt zur Studie „Assoziatives Lernen und Stimulusgeneralisierung bei Sozialer Phobie“ gelesen und bin ausführlich über die geplante Untersuchung unterrichtet worden. Die Informationen habe ich inhaltlich verstanden und hatte die Gelegenheit, Fragen zu stellen. Mit den erhaltenen Antworten bin ich zufrieden.

Ich erkläre mich freiwillig mit der Datenerhebung einverstanden. Über mögliche Risiken wurde ich aufgeklärt. Ich weiß, dass die Untersuchung wissenschaftlichen Zwecken dient und es nicht möglich ist, Informationen über individuelle Untersuchungsergebnisse zu erhalten.

Ich hatte ausreichend Zeit, mir zu überlegen, ob ich an der Datenerhebung teilnehmen will, fühle mich ausreichend informiert und habe keine weiteren Fragen. Ich wurde darauf hingewiesen, dass ich jederzeit von dieser Untersuchung zurücktreten kann, ohne dass mir dadurch ein Nachteil entsteht. Die Daten werden in diesem Falle vernichtet.

Ich erkläre mich darüber hinaus damit einverstanden, dass die aus der Datenerhebung gewonnenen Informationen verschlüsselt, d.h. in unpersönlicher Form (ohne Namens- oder Initialen-Nennung) aufgezeichnet, für unbestimmte Zeit in Computern gespeichert und ausgewertet werden. Dabei gibt es keine Möglichkeit des Rückschlusses auf Einzelpersonen. Der Codierungsschlüssel wird 1 Jahr nach Abschluss der Studie vernichtet. Bis dahin kann ich, auch noch nach der Untersuchung, die Löschung meiner Daten verlangen.

Ich bin auch damit einverstanden, dass die Ergebnisse der Studie in Gruppen zusammengefasst wissenschaftlich veröffentlicht werden.

_____ _____

Ort, Datum Unterschrift der Probandin/des Probanden

_____ _____

Ort, Datum Unterschrift des aufklärenden Mitarbeiters

E Informed consent study 3

Julius-Maximilians-
UNIVERSITÄT
WÜRZBURG

Probandencode: _____

Datum: _____

Probandeninformation zur Studie

„Stimulusgeneralisierung bei Sozialer Ängstlichkeit“

Sehr geehrte(r) Proband(in),

wir möchten Sie bitten, an einer wissenschaftlichen Studie zur Verarbeitung von Gesichtern und Geräuschen teilzunehmen. In dieser Studie werden Ihnen Fotos von Personen gezeigt, die teilweise gleichzeitig mit einem unangenehmen, relativ lauten Geräusch dargeboten werden. Ihre Aufgabe wird es sein, die Bilder auf sich wirken zu lassen und während des Versuchs mehrfach zu bewerten. Betrachtungs- und Bewertungsdurchgänge werden sich während des Versuchs mehrfach abwechseln.

Ablauf:

Zunächst werden Sie gebeten, einige Fragebögen zu persönlichen Angaben, Ängstlichkeit und Stimmung auszufüllen. Bitte antworten Sie hierbei so spontan und ehrlich wie möglich! Während der Untersuchung werden Sie Bilder von Gesichtern betrachten, die über einen Computerbildschirm präsentiert werden. Die Bilder werden im so genannten Flicker-Modus gezeigt, d.h. sie werden sehr schnell hintereinander auf dem Bildschirm an- und ausgeschaltet. Falls in Ihrer Familie oder bei Ihnen bereits einmal ein epileptischer Anfall aufgetreten ist oder eine Epilepsie diagnostiziert wurde, sollten Sie nicht an diesem Versuch teilnehmen. Ansonsten ist die Teilnahme völlig unbedenklich.

Sie werden in regelmäßigen Abständen zu den Bildern befragt. Diese zeigen 2 weibliche Darsteller mit neutralem Gesichtsausdruck. Ab und an werden Sie zusätzlich einen ängstlichen Gesichtsausdruck sehen. Außerdem werden Sie in bestimmten Abständen über einen Kopfhörer ein unangenehmes, relativ lautes Geräusch hören. Dieses kann einen Augenblick lang unangenehme Gefühle sowie Erregungsgefühle auslösen, ist jedoch nicht gefährlich. Während des Versuchs wird ihre Gehirnaktivität mittels EEG aufgezeichnet. Dazu werden Sie ein Netz von Elektroden auf dem Kopf tragen, welches vorher in ein Salz-Wasser-Gemisch mit Shampoo eingelegt wurde und daher ein wenig feucht sein wird. In seltenen Fällen können dabei Hautirritationen auftreten.

Am Ende der Untersuchung sollen Sie nochmals Fragebögen ausfüllen. Insgesamt wird der Versuch max. 1 Stunde in Anspruch nehmen.

Datenschutz:

Ihre Daten werden unter einer Codenummer abgespeichert. Dies erlaubt eine anonyme wissenschaftliche Auswertung der Daten. Eine Zuordnung der Daten zu bestimmten Personen ist nicht möglich. Die Zuordnung der Codenummer zu Ihrer Person wird getrennt von den Daten aufbewahrt und nach einem Jahr vernichtet. Bis dahin können Sie, auch ohne Angabe von Gründen, die Löschung Ihrer Daten verlangen. Es ist möglich, dass die anonymisierten Daten, die keiner Person mehr zugeordnet werden können, im Rahmen einer wissenschaftlichen Publikation veröffentlicht werden. Die anonymisierten Daten werden auf unbestimmte Zeit virtuell gespeichert. Eine Weitergabe der Daten an Dritte erfolgt nicht.

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Freiwilligkeit der Teilnahme:

Bitte beachten Sie:

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Haben Sie noch Fragen? Dann stellen Sie diese bitte jetzt der Versuchsleitung.

Versuchsleiter:
Lea M. Ahrens, Dipl.-Psych.
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97070 Würzburg
Tel: 0931/31-81929

Einverständniserklärung zur Datenerhebung im Rahmen der Studie „Stimulusgeneralisierung bei Sozialer Ängstlichkeit“

Name der Probandin / des Probanden (bitte Druckschrift)

_____

Ich habe das Informationsblatt zur Studie „Stimulusgeneralisierung bei Sozialer Ängstlichkeit“ gelesen und bin ausführlich über die geplante Untersuchung unterrichtet worden. Die Informationen habe ich inhaltlich verstanden und hatte die Gelegenheit, Fragen zu stellen. Mit den erhaltenen Antworten bin ich zufrieden.

Ich erkläre mich freiwillig mit der Datenerhebung einverstanden. Über mögliche Risiken wurde ich aufgeklärt. Ich weiß, dass die Untersuchung wissenschaftlichen Zwecken dient und es nicht möglich ist, Informationen über individuelle Untersuchungsergebnisse zu erhalten.

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Ich erkläre mich darüber hinaus damit einverstanden, dass die aus der Datenerhebung gewonnenen Informationen verschlüsselt, d.h. in unpersönlicher Form (ohne Namens- oder Initialen-Nennung) aufgezeichnet, für unbestimmte Zeit in Computern gespeichert und ausgewertet werden. Dabei gibt es keine Möglichkeit des Rückschlusses auf Einzelpersonen. Der Codierungsschlüssel wird 1 Jahr nach Abschluss der Studie vernichtet. Bis dahin kann ich, auch noch nach der Untersuchung, die Löschung meiner Daten verlangen.

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_____	_____
Ort, Datum	Unterschrift der Probandin/des Probanden
_____	_____
Ort, Datum	Unterschrift des aufklärenden Mitarbeiters

F List of figures

G List of tables

8 Publication List

Research articles in peer-reviewed journals

Ahrens, L. M., Pauli, P., Reif, A., Mühlberger, A., Langs, G., Aalderink, T., & Wieser, M. J. (2016). Fear conditioning and stimulus generalization in patients with social anxiety disorder. *Journal of Anxiety Disorders*, 44, 36-46.

Ahrens, L. M., Mühlberger, A., Pauli, P., & Wieser, M. J. (2014). Impaired visuocortical discrimination learning of socially conditioned stimuli in social anxiety. *Social cognitive and affective neuroscience,* 10(7), 929-937.

Published abstracts

Ahrens, L.M., Reif, A., Pauli, P. & Wieser, M.J. (2016). Examining Fear Generalization with steady-state Visually Evoked Potentials. *Cognitive Neuroscience (CNS)*, New York City, NY, USA.

Ahrens, L.M., Pauli, P., Reif, A., Mühlberger, A., Langs, G., Pauli, P. & Wieser, M.J. (2015). Fear Conditioning and Stimulus Generalization in Social Anxiety Disorder. *Psychologie und Gehirn*, Frankfurt, Germany.

Ahrens, L.M., Mühlberger, A., Reif, A., Langs, G., Pauli, P. & Wieser, M.J. (2015). Social Anxiety Disorder is Associated with Impaired Psychophysiological Discrimination Learning during Fear Generalization. *Cognitive Neuroscience (CNS)*, San Francisco, CA, USA.

Ahrens, L.M., Mühlberger, A., & Wieser, M.J. (2014). Diminished Visuocortical Discrimination Learning of Socially Conditioned Stimuli in Social Anxiety. *Society for Psychophysiological Research (SPR)*, Atlanta, USA

Ahrens, L.M., Mühlberger, A., & Wieser, M.J. (2014). Impaired Cortical Discrimination of Socially Conditioned Faces in Social Anxiety. *Cognitive Neuroscience (CNS)*, Boston, MA, USA.

Ahrens, L.M., Mühlberger, A., & Wieser, M.J. (2013). Social conditioning in social anxiety-evidence from steady-state visual evoked potentials. *Psychologie und Gehirn*, Würzburg, Germany.

9 Curriculum Vitae

10 Affidavit

I hereby confirm that my thesis entitled “The Role of Attentional Control and Fear Acquisition and Generalization in Social Anxiety Disorder” is the result of my own work. I did not receive any help or support from commercial consultants. All sources and /or materials applied are listed and specified in the thesis.

Furthermore, I confirm that this thesis has not yet been submitted as part of another examination process neither in identical nor in similar form.

_____ _____

Place, Date Signature

Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt, die Dissertation „Die Rolle von Aufmerksamkeitskontrolle und Furchtlernen und Generalisierung bei Sozialer Angststörung“ eigenständig, d.h. insbesondere selbstständig und ohne Hilfe eines kommerziellen Promotionsberaters, angefertigt und keine anderen als die von mir angegebenen Quellen und Hilfsmittel verwendet zu haben.

Ich erkläre außerdem, dass die Dissertation weder in gleicher noch in ähnlicher Form bereits in einem anderen Prüfungserfahren vorgelegen hat.

_____ _____

Ort, Datum Unterschrift