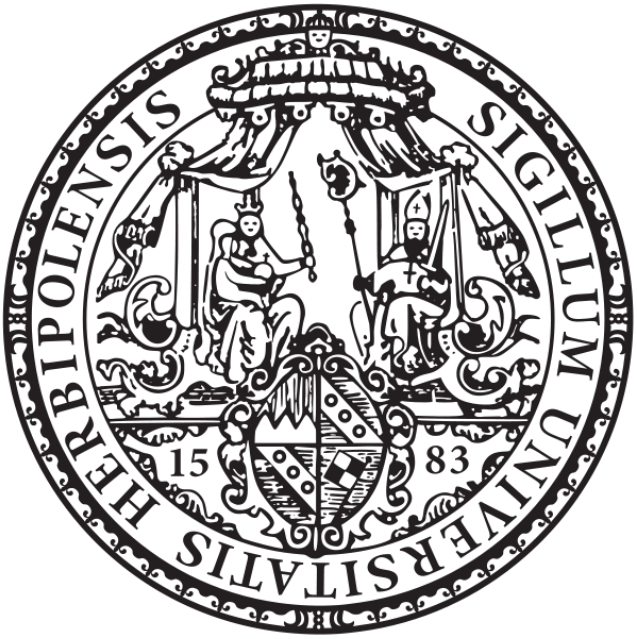
Fear conditioning, its generalization and extinction in children and adolescents under consideration of trait anxiety and anxiety sensitivity

Furchtkonditionierung, ihre Generalisierung und Extinktion bei Kindern und Jugendlichen unter Berücksichtigung von Ängstlichkeit und Angstsensitivität



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submitted by
Anna Slyschak
from
Pawlodar, Kazakhstan

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Submitted on: ……..

Members of the Thesis Committee:

Chairperson:	**Prof. Dr. Keram Pfeiffer**
Primary Supervisor:	**Prof. Dr. Marcel Romanos**
Supervisor (Second):	**Prof. Dr. Paul Pauli**
Supervisor (Third):	**Prof. Dr. Matthias Gamer**

Date of Public Defence:

Date of Receipt of Certificates:

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Abbreviations

ACC	anterior cingulate cortex
AD	anxiety disorder
ANOVA	analysis of variance
ANCOVA	analysis of covariance
CASI	childhood anxiety sensitivity index
CBT	cognitive behavioral therapy
CR	conditioned reaction, i.e. reaction triggered by a conditioned stimulus after fear conditioning
CS	conditioned stimulus
CS-	conditioned stimulus presented during fear conditioning, which never is associated with the unconditioned stimulus (→ safety cue/signal/stimulus)
CS+	conditioned stimulus presented during fear conditioning, which is associated with the unconditioned stimulus (→ danger/threat cue/signal/stimulus)
FIR	first interval responses
fMRI	functional magnetic resonance imaging
FPS	fear-potentiated startle
GS	generalization stimulus
GAD	generalized anxiety disorder
ITI	inter-trial interval (time span between the offset of a stimulus and the onset of the following stimulus)
mPFC	medial prefrontal cortex
PFC	prefrontal cortex
PTSD	post-traumatic stress disorder
RDoC	research domain criteria
SAD	social anxiety disorder
SCR	skin conductance response
SIR	second interval responses
STAIC	state-trait-anxiety inventory for children
TIR	third interval responses
US	unconditioned stimulus, i.e. stimulus, which causes unconditioned reactions without any learning (e.g. an electrical shock, a loud scream/an unpleasant noise)
vmPFC	ventromedial prefrontal cortex

Abstract

The propounded thesis investigated fear learning including fear conditioning, its generalization as well as its extinction in 133 healthy children and adolescents aged 8 to 17 years. The main goal was to analyze these processes also in the course of childhood and adolescence due to far less research in this age span compared to adults. Of note, childhood is the typical period for the onset of anxiety disorders. To achieve this, an aversive discriminative fear conditioning, generalization and extinction paradigm, which based on the "screaming lady paradigm" from Lau et al. (2008) and was adapted by Schiele & Reinhard et al. (2016), was applied. All probands traversed the pre-acquisition (4 x CS-, 4 x CS+, no US), the acquisition (12 x CS-, 12 x CS+, reinforcement rate: 83%), the generalization (12 x CS-, 12 x GS4, 12 x GS3, 12 x GS2, 12 x GS1, 12 x CS+, reinforcement rate: 50%) and the extinction (18 x CS-, 18 x CS+, no US). The generalization stimuli, i.e. GS1-GS4, were built out of CS- and CS+ in different mixtures on a percentage basis in steps of 20% from CS- to CS+. Pictures of faces of two actresses with a neutral expression were used for the discriminative conditioning, whereby the CS+ was paired with a 95-dB loud female scream at the same time together with a fearful facial expression (US). CS- and GS1-GS4 were never followed by the US. Subjective ratings (arousal, valence and US expectancy) were collected and further the psychophysiological measure of the skin conductance response (SCR). The hypotheses were 1) that underage probands show a negative correlation between age and overgeneralization and 2) that anxiety is positively correlated with overgeneralization in the same sample. ANOVAs with repeated measures were conducted for all four dependent variables with phase (pre-acquisition phase, 1. + 2. acquisition phase, 1. + 2. generalization phase, 1. - 3. extinction phase) and stimulus type (CS-, CS+, GS1-GS4) as within-subject factors. For the analyses of the modulatory effects of age and anxiety in additional separate ANCOVAs were conducted including a) age, b) the STAIC score for trait anxiety and c) the CASI score for anxiety sensitivity as covariates. Sex was always included as covariate of no interest. On the one hand, findings indicated that the general extent of the reactions (arousal, valence and US expectancy ratings and the SCR) decreased with growing age, i.e. the older the probands the lower their reactions towards the stimuli regardless of the type of dependent variable. On the other hand, ratings of US expectancy, i.e. the likelihood that a stimulus is followed by a US (here: female scream coupled with a fearful facial expression), showed better discrimination skills the older the probands were, resulting in a smaller overgeneralization within older probands. It must be emphasized very clearly that no causality can be derived. Thus, it was only an association revealed between

age and generalization of conditioned fear, which is negative. Furthermore, no obvious impact of trait anxiety could be detected on the different processes of fear learning. Especially, no overgeneralization was expressed by the probands linked to higher trait anxiety. In contrast to trait anxiety, for anxiety sensitivity there was an association between its extent and the level of fear reactions. This could be described best with a kind of parallel shifts: the higher the anxiety sensitivity, the stronger the fear reactions. Likewise, for anxiety sensitivity no overgeneralization due to a stronger extent of anxiety sensitivity could be observed.

Longitudinal follow-up examinations and, furthermore, neurobiological investigations are needed for replication purposes and purposes of gaining more supporting or opposing insights, but also for the profound exploration of the impact of hormonal changes during puberty and of the maturation processes of different brain structures. Finally, the question whether enhanced generalization of conditioned fear facilitates the development of anxiety disorders or vice versa remains unsolved yet.

Zusammenfassung

Die vorgelegte Doktorarbeit untersuchte Furchtlernen, wobei Furchtkonditionierung, ihre Generalisierung als auch ihre Extinktion bei 133 gesunden Kindern und Jugendlichen zwischen 8 und 17 Jahren betrachtet wurden. Das Hauptziel war es diese Prozesse auch im Laufe der Kindheit und Jugend zu analysieren, weil es sehr viel weniger Forschung für diese Altersspanne gibt im Vergleich zu Erwachsenen. Zu beachten ist, dass die Kindheit den typischen Zeitpunkt für den Beginn von Angsterkrankungen darstellt. Um dieses Ziel zu erreichen, wurde ein aversives Furchtkonditionierungs, -generalisierungs- und -extinktions-Paradigma verwendet, das auf dem „screaming lady paradigm“ von Lau et al. (2008) basiert und von Schiele und Reinhard et al. (2016) angepasst worden ist. Alle Probanden durchliefen die Prä-Akquisition (4 x CS-, 4 x CS+, kein US), die Akquisition (12 x CS-, 12 x CS+, Verstärkungsrate: 83%), die Generalisierung (12 x CS-, 12 x GS4, 12 x GS3, 12 x GS2, 12 x GS1, 12 x CS+, Verstärkungsrate: 50%) und die Extinktion (18 x CS-, 18 x CS+, kein US). Die Generalisierungsstimuli, d.h. GS1-GS4, wurden in unterschiedlichem Verhältnis aus CS- und CS+ auf einer Prozentbasis von 20%-Schritten zusammengesetzt (von CS- in Richtung CS+). Bilder von Gesichtern von zwei Schauspielerinnen mit einem neutralen Ausdruck wurden für die diskriminative Konditionierung verwendet, wobei CS+ mit einem 95-dB lauten weiblichen Schrei und gleichzeitig einem furchterfüllten Gesichtsausdruck verbunden worden ist (US). Auf CS- und GS1-GS4 folgte niemals US. Die subjektiven Ratings (Arousal, Valenz und die US expectancy) wurden erfasst und weiterhin auch die psychophysiologische Messung der Hautleitfähigkeit (SCR). Die Hypothesen lauteten, 1) dass minderjährige Probanden eine negative Korrelation zwischen Alter und Übergeneralisierung zeigen, und, 2) dass Ängstlichkeit positiv mit Übergeneralisierung in der selben Stichprobe korreliert ist. ANOVAs mit Messwiederholung wurden für alle vier abhängigen Variablen durchgeführt mit Phase (Prä-Akquisitionsphase, 1. + 2. Akquisitionsphase, 1. + 2. Generalisierungsphase, 1. – 3. Extinktionsphase) und Stimulustyp (CS-, CS+, GS1-GS4) als Inner-Subjektfaktoren. Für die Analysen zur modulierenden Wirkung von Alter und Ängstlichkeit wurden zusätzlich separate ANCOVAs durchgeführt mit a) dem Alter, b) dem STAIC-Score für die Trait Anxiety und c) dem CASI-Score für die Angstsensitivität als Kovariaten. Das Geschlecht wurde immer als Kovariate ohne Bedeutung, d.h. nur zur statistischen Kontrolle, eingeschlossen. Auf der einen Seite deuten die Ergebnisse darauf hin, dass das allgemeine Ausmaß der Reaktionen (Arousal, Valenz und US expectancy Ratings und die Hautleitfähigkeit (SCR)) mit steigendem Alter abnehmen, d.h. umso älter die Probanden sind, um so geringer sind ihre Reaktionen auf die

Stimuli ganz unabhängig von der Art der abhängigen Variable. Auf der anderen Seite zeigen die Ratings der US expectancy, d.h. der Wahrscheinlichkeit, das auf einen Stimulus ein US (hier: weiblicher Schrei verbunden mit einem furchterfüllten Gesichtsausdruck) folgt, bessere Diskriminations-/Unterscheidungsfähigkeiten umso älter die Probanden waren, was wiederum eine geringere Übergeneralisierung bei den älteren Probanden zur Folge hatte. Es muss sehr klar und deutlich betont werden, dass kein kausaler Zusammenhang abgeleitet werden kann bzw. darf. Somit wurde nur ein Zusammenhang zwischen dem Alter und der Generalisierung konditionierter Furcht entdeckt, der negativ ist.

Weiterhin konnte kein offensichtlicher Einfluss von Trait Anxiety auf die unterschiedlichen Prozesse des Furchtlernens gefunden werden. Insbesondere wurde keine Übergeneralisierung bei den Probanden mit höherer Trait Anxiety ausgedrückt.

Im Gegensatz zur Trait Anxiety gab es für die Angstsensitivität eine Verbindung zwischen ihrem Ausmaß und dem Level der Furchtreaktionen. Dies könnte am besten mit Hilfe von einer Art von Parallelverschiebungen beschrieben warden: je höher die Angstsensitivität, desto stärker die Furchtreaktionen. Gleichermaßen konnte auch für die Angstsensitivität keine Übergeneralisierung aufgrund eines stärkeren Ausmaßes an Angstsensitivität beobachtet werden.

Längsschnittliche Folgeuntersuchungen und weiterhin auch neurobiologische Untersuchungen werden für Replikationszwecke und weitere Zwecke gebraucht, um unterstützende oder gegensätzliche Erkenntnisse zu gewinnen, aber auch für die gründliche Exploration des Einflusses hormoneller Veränderungen während der Pubertät und von Reifungsprozessen verschiedener Gehirnstrukturen. Abschließend bleibt die Frage, ob die erhöhte Generalisierung konditionierter Furcht die Entwicklung von Angststörungen begünstigt oder vice versa, immer noch ungelöst.

1. Introduction

"*Angst ist für das Überleben unverzichtbar.*" was said by Hannah Arendt (1906-1975), the famous German-American political theoretician and publicist, which means freely translated "fear is indispensable for survival". It is crucial that threatening situations provoke fear, and furthermore, trigger an appropriate reaction in order to ensure the survival for all living beings. Thus, fear helped and helps mankind and the animal world to survive. A fear response is usually an adaptive reaction because it initiates a defensive reaction when confronted with real danger (Gazendam, Kamphius & Kindt, 2013; Beckers, Krypotos, Boddez, Effting & Kindt, 2012; Frijda, 1986). In this regard the better-safe-than-sorry strategy is noteworthy, which means that it is wiser from an evolutionary point of view to respond to a false alarm, i.e. mistakenly consider a harmless stimulus for a hazardous one, than failing in reacting to a hazardous stimulus erroneously considering it a harmless one (Dunsmore & Paz, 2015; Öhman, 2008). Fear learning is an essential process. For example, if a child was stung by a wasp and even had an allergic reaction to it, then it is reasonable and completely understandable if the child intends to avoid all wasps and even other similar flying insects after that incident. This effect is called generalization, i.e. it was learned to show a resembling response to stimuli, which are only similar to threatening objects, animals, situations or environments, but not dangerous in real life. The ability to generalize is crucial, especially for young children, who are lacking life experience and need a defensive mechanism protecting them from harm in everyday life. With accumulating life experience in the course of childhood via adolescence into adulthood less and less protection is necessary. There is research, which confirms this perspective with results showing less generalization with increasing age (Schiele & Reinhard et al., 2016). In this context, discrimination, i.e. the capability to differentiate correctly between danger and safety cues, is of importance. The skill of learning to discriminate between secure and threatening environments is crucial in order to survive for both, animals and humans (Christianson et al., 2012). Its lack, however, can lead to an exaggerated ongoing bodily and mental tension because of the inability to detect safe surroundings where it is possible to have a rest and feel safe (Reinhard, 2017). Studies show that the discrimination between safety and threat cues improves with growing age (e.g. Michalska et al., 2016; Glenn et al., 2012a; Lau et al., 2011; Gao, Raine, Venables, Dawson & Mednick, 2010).

Importantly, the terms fear and anxiety share similarities like the similar activated highly unpleasant state focused on menace, hazard, and danger with massive adverse feelings and heavy physical reactions (Öhman, 2008). However, they also must be distinguished regarding

some substantial differing splits: Whereas fear elicits reacting to particular and perceptible threats with the wish to flee from the specific situation, anxiety involves vague and intangible apprehensions (Öhman, 2008; Barlow, 2002).

Although a fear reaction is usually considered as situationally adaptive, it can also become maladaptive in some cases, for example, when the fear response is far too excessive and no longer appropriate regarding the faced danger (Dunsmoor & Paz, 2015; van Meurs, Wiggert, Wicker & Lissek, 2014; Öhman, 2009; Barlow, 2002). Fear conditioning and fear generalization are two important fear learning processes, whose abnormalities are thought to be related to various anxiety disorders (Lissek et al., 2010; Lissek et al., 2005; Lenaert, van de Ven, Kaas & Vlaeyen, 2016; Lissek et al., 2014b; Lissek & Grillon, 2012; Davis, Castagna, Shaheen & Reuther, 2017; Lissek et al., 2008; Wong & Lovibond, 2018). Imagining a person suffering from a specific phobia it is reasonable to retrace it to an awful past experience with the subject of the phobic fear. Further, thinking of generalization, the step towards a generalized anxiety disorder (GAD) is justifiable and this disorder is associated with diffuse and vague apprehensions where no trigger is necessary to cause intense anxiety or even panic. However, usually this is not the case. The described phenomena represent pathological features and are usually an exception. Of course, the question arises why the learned fear or anxiety gets that excessive and pathological for some persons, when it does not happen for the vast majority (Reinhard, 2017).

Anxiety disorders are common mental diseases with a lifetime prevalence of about 28.8% (Mineka & Zinbarg, 2006; Kessler et al., 2005; Kim & Richardson, 2010) and typically have an early onset. For elementary-school-age children aged 6 to 12 years, for instance, the prevalence of any anxiety disorder is 12.3%, and for adolescents aged 13 to 18 years the prevalence is 11% (Costello, Egger, Copeland, Erkanli & Angold, 2011). Further, Kessler et al. (2005) report a median age of onset of 11 years for anxiety disorders. Thus, childhood and adolescence are the periods containing special risk to develop anxiety disorders (Beesdo, Knapp & Pine, 2009; Costello, Egger, & Angold, 2005).

There are huge costs every year for the health care system for the treatment of anxiety disorders (Olesen, Gustavsson, Svensson, Wittchen & Jönsson, 2012; Vos et al., 2012; Wittchen et al., 2011, Gustavsson et al., 2011; Farrell & Barrett, 2007; Greenberg et al., 1999; Turner, Beidel, Spaulding & Brown, 1996). This issue, moreover, does not take into account the suffering of the people affected and their families. Anxiety disorders reduce the quality of life dramatically and furthermore burden work and social relationships. In addition, it must be

considered that the widespread comorbidity with other anxiety disorders or other mental disorders is a very meaningful topic leading to further suffering and impairments (Costello et al., 2011; Wancata, Freidl & Fabrian, 2011). Children affected by anxiety disorders can be confronted with stigma, victimization and discrimination (Davis et al., 2017; Wright, Jorm & Mackinnon, 2011; Jorm & Wright, 2008), which means facing additional problems impairing a proper development. Christie et al. (1988) showed a far higher risk for drug use disorders in young adults following an earlier anxiety disorder. A very similar finding is reported by Merikangas et al. (1998). Alcohol and drug disorders almost independent of the degree of severity of substance use disorders were chronologically following the outbreak of anxiety disorders. An elevated risk for future psychological health problems like anxiety in adulthood, depression, substance misuse and abuse and attempts of suicide are also suggested in many studies (Gregory et al., 2007; Beesdo et al., 2007; Boden, Fergusson, & Horwood, 2007; Pine, Cohen, Gurley, Brook & Ma, 1998; Keller et al., 1992; Flament, Koby & Rapoport, 1990; Ferdinand & Verhulst, 1995; Feehan, McGee & Williams, 1993; Berg, Rapoport & Whitaker, 1989). There is a crucial challenge that we face in society: it is often not discovered if children or adolescents do have an anxiety disorder (e.g. Wancata, Windhaber, Bach & Meise, 2000; Wancata et al., 2011) or are at risk to develop an anxiety disorder and have a meaningful psychological stain.

In the context of fear learning the process of extinction of conditioned fear is essential because of its weighty meaning for therapeutical interventions especially concerning anxiety disorders (Waters, Theresiana, Neumann & Craske, 2017; Greco & Liberzon, 2016; Craske, Treanor, Conway, Zbozinek & Vervliet, 2014; Vervliet, Craske & Hermans, 2013). Roughly 40% of clinically anxious adolescents do not profit from exposure-based cognitive behavioral therapy (CBT), whereas about 60% of the adolescents show a reduction of their anxiety symptoms following a CBT. This result stresses the meaning of further research concerning extinction particularly in adolescents (Ryan, Zimmer-Gembeck, Neumann & Waters, 2019; Ginsburg et al., 2014).

Appreciably, a heightened trait anxiety seems to represent a risk factor for developing an anxiety disorder (Torrents-Rodas et al., 2013). Trait anxiety means an overall propensity to show a negative way of reacting when being confronted with a stressful situation (Wong & Lovibond, 2018; Gazendam et al., 2013; Chambers, Power & Durham, 2004; Jorm, Christensen, Henderson, Jacomb, Korten & Rodgers, 2000; Gershuny & Sher, 1998). Furthermore, as already mentioned above, associative fear learning is regarded to be the main

mechanism for the development of anxiety disorders (Gazendam et al., 2013). Therefore, it is relevant not only to have a look at samples with clinically relevant fears as has been done often in the past until now (i.e. Lissek et al., 2009; Lau et al., 2008), but to put the focus also on subclinical groups at risk for the development of anxiety disorders (Wong & Lovibond, 2018; Arnaudova, Krypotos, Effting, Kindt & Beckers, 2017; Torrents-Rodas et al., 2013; Gazendam et al., 2013).

Moreover, research indicates that anxiety sensitivity constitutes a risk factor for developing and maintaining anxiety disorders in minors (Evans et al., 2005). Anxiety sensitivity describes a permanent conviction that anxiety and its symptoms (for instance symptoms of the body) have dangerous psychological, corporal or social consequences, which exceed a pressing fear state or a pressing panic attack (Schneider, Adornetto, In-Albon, Federer, & Hensdiek, 2009; Silverman, Fleising, Rabian & Peterson, 1991; Reiss & McNally, 1985). Further, anxiety sensitivity can also be characterized briefly as follows: if someone believes that anxiety symptoms are followed by negative effects (Silverman et al., 1991).

Due to the shortage in studies and research dealing with underage samples especially comprising a wide age span regarding the development of fear learning, i.e. here fear conditioning, its generalization as well as its extinction specifically using the same paradigm, it is a main goal of this dissertation to contribute to this particular scientific field. For that the target is to show developmental stages from childhood via adolescence into the adulthood while considering every deviation and discrepancy in fear learning and its generalization as well as extinction in their meaning for maladaptive behavioral consequences like overgeneralization (e.g. in adolescents with anxiety disorders (El-Bar, Laufer, Yoran-Hegesh & Paz, 2017) and adult patients with panic disorder (Lissek et al., 2010).

1.1 Study goals and structure of the thesis

This propounded doctoral thesis investigates fear learning, fear generalization and fear extinction in children and adolescents aged 8-17 years by the use of a behavioral laboratory-assisted method with probands sitting in front of a monitor with fixed electrodes for psychophysiological measures. The studies included in this thesis aimed to have a closer look at the development between 8 and 17 years, thus there is a special focus on the timeline of age. Evidence suggests an enhanced generalization in healthy children compared to healthy adults (Schiele & Reinhard et al., 2016), thus, the current work aims at replicating this finding and to

determine when, i.e. at which age, the fear generalization gradient of children and youth assimilates to the one of healthy adults.

Crucially, potential influencing factors are examined at in this context. Research corroborates the meaning of trait anxiety concerning fear conditioning and also the generalization of conditioned fear presenting various findings (e.g. Boddez et al., 2012; Gazendam et al., 2013; Haaker et al., 2015; Dvir, Horovitz, Aderka & Shechner, 2019; El-Bar et al., 2017; Sep, Steenmeijer & Kennis, 2019; but see also: Torrents-Rodas et al., 2013), which consequently is relevant in the connection with the development of anxiety disorders (e.g. Lissek et al., 2005, 2010; Wong & Lovibond, 2018). Further, the impact of anxiety sensitivity on different fear learning processes is also of main interest due to its role as risk factor in the context of anxiety disorders in underage persons (Evans et al., 2005). Thus, the influence of trait anxiety and anxiety sensitivity on fear conditioning, its generalization and the extinction of conditioned fear will be analyzed. Sex will be controlled statistically regarding its potential influence. Notably, the same differential fear conditioning, generalization and extinction paradigm, which will be described in detail later in this thesis, was deployed consistently for all studies. The comparability of all results among each other shall be ensured by this because this is often not the case due to many different paradigms applied in research studies concerning various fear learning processes like fear acquisition, its generalization and extinction. In order to take the early onset of anxiety disorders into account the sample includes young children aged 8 years, who usually already show successful fear conditioning (Gao et al., 2010; Block, Sersen & Wortis, 1970), up to adolescents aged 17 years.

The first chapter of this thesis contains definitions regarding fear conditioning, fear generalization and fear extinction. Moreover, the theoretical context, background and the current state of research of the three defined processes in children and adolescents will be described. Additionally, a short outline of brain structures and pathways related to fear conditioning, its generalization and extinction will be given. Afterwards, an overview of the targets and hypotheses and the applied paradigm for all studies within this thesis will be introduced. The second chapter will comprise a study evaluating analyses related to fear conditioning, its generalization and extinction for the age span of childhood and adolescence (8 to 17 years) concerning a potentially modulatory effect of the probands' age. The next two chapters will present results out of analyses concerning the impact of trait anxiety (measured with the STAIC, see **1.4.2**) and anxiety sensitivity (measured with the CASI, see **1.4.2**) on fear conditioning, fear generalization and fear extinction. The analyses refer to behavioral -

subjective ratings - and psychophysiological data - skin conductance response (SCR). The final chapter will include a summary of the core outcomes and a discussion related to them. Limitations, an outlook and recommendations and ideas for future research will also be part of the last chapter.

1.2 Theoretical background of fear conditioning, fear generalization and fear extinction

1.2.1 Fear conditioning in children and adolescents

Classical fear-conditioning is an associative learning process through which a neutral conditioned stimulus (CS) (for example an image or a light) causes a fear reaction after being repeatedly coupled with an aversive unconditioned stimulus (US) (for example a loud scream or an electric shock) (Lissek et al., 2014b). Inborn defensive unconditioned responses (URs) (for example startle or electrodermal activity) are elicited (Kim & Richardson, 2010). Moreover, in differential fear conditioning one conditioned stimulus, the danger cue CS+, is reinforced by the US (unconditioned stimulus), whereas the other stimulus, the safety cue CS-, never precedes the US (Schiele & Reinhard et al., 2016). The reinforcement rate defines the likelihood that the US appears when the CS+ is displayed, for example a rate of 100% means that the CS+ and the US are paired in each case, whereas a partial reinforcement means a pairing in less cases (Lonsdorf et al., 2017). In this thesis cued conditioning is focused on, while contextual conditioning is not of relevance.

For fear conditioning the amygdala, which lays in the brain limbic circuit in the temporal lobe, is needed (Jovanovic, Nylocks & Gamwell, 2013; Phelps, 2006; LeDoux, 1998; LaBar, Gatenby, Gore, LeDoux & Phelps, 1998; Davis, 1990). The prefrontal cortex (PFC) with its medial, ventral and dorsolateral subregions is crucial especially for aware fear processing and the distinction between threatening and safe signals (Fullana et al., 2016; Lau et al., 2011). In particular, differential fear conditioning requires the insular cortex, which is also part of the fear circuit (Fullana et al., 2018; Fullana et al., 2016). Furthermore, the anterior cingulate (ACC), the hippocampus, the thalamus, the cerebellum, the striatum as well as sensorial cortices have been linked to fear conditioning, too.

Remarkably, there is a link between children and youths with anxiety disorders and a bigger size of the amygdala (Jovanovic et al., 2014; De Bellis et al., 2000) and stronger amygdala activation is often described in anxious individuals of all ages as well as in individuals at risk for anxiety (Blackford & Pine, 2012; Lissek, 2012; McClure et al., 2007). In addition, patients with anxiety disorders express a higher activity within the insular cortex throughout

fear conditioning as well as the processing of threat (Marin et al., 2017; Hofmann, Ellard & Siegle et al., 2012). This is only a small extract out of the broad research concerning fear conditioning to get a little insight into the brain structures involved.

In general, the many different past outcomes in this context might result from various CS-/US-types applied, wide-ranging methods conditioning paradigms were based on, distinct reinforcement rates and varying definitions for an effective fear conditioning (Shechner, Hong, Britton, Pine & Fox, 2014; Sehlmeyer et al., 2009).

Conditioned fear reactions can be measured in many different kinds. The self-report in form of subjective ratings like arousal, valence, contingency, and similar measures is very widespread (Schiele & Reinhard et al., 2016). Arousal and valence build two orthogonal dimensions, while all other emotional states are put together of different parts of the two affects and thus are arranged circularly in a circumplex-model (Feldman Barrett & Russell, 1999; Rothermund, & Eder, 2011; see **Figure 1.**). Both arousal, i.e. activation, and valence, i.e. pleasantness, are described as conscious states of perception with neurophysiological correlates (Feldman Barrett & Russell, 1999; Lang, Bradley & Cuthbert, 1997; Heilman, 1997). High arousal and low valence would result from aversive stimuli like the danger cue, whereas low arousal and high valence would be expressed after appetitive stimuli like the safety cue. Contingency represents the awareness - instructed or learned - of the US expectancy (Fullana et al., 2016), which has an enormous influence on the subjective ratings in a self-report. Furthermore, there are psychophysiological measures like the skin conductance response (SCR) or the heart rate (Gao et al., 2010; Schiele & Reinhard et al., 2016; McEchron, Tseng & Disterhoft, 2000). Skin conductance is classified as a nonspecific measurement of arousal (Lonsdorf et al., 2017; Glenn et al., 2012a). It undergoes a change in the electrical conductance of the skin due to a changing sweat gland activity. There are also fear reflexes that can be measured like the fear-potentiated startle (FPS), an elevated eye-blink reflex, which is valence-specific (Lonsdorf et al., 2017; Glenn et al., 2012a; Bradley, Cuthbert, & Lang, 1990). In their investigation Sevenster, Beckers & Kindt (2014) deduced that the fear-potentiated startle conditioning seems to be independent of, however, the SCR seems to be dependent on, conscious differential fear conditioning. Further, movement suppression or freezing is a very common measure for fearful behavior for example in rodents, fish but also primates (Tovote et al., 2016). Finally, the stress hormone cortisol is an example for endocrinal measures related to fear conditioning (Zorawski, Blanding, Kuhn, & LaBar, 2006). Hence, the application of various measurements for fear is possible to allow a more entire appraisal of fear conditioning

and the underlain operating principles (Graham, Yoon, Lee & Kim, 2009; Boddez et al., 2013). Although some important theoretical, but also methodological aspects must be considered. One aspect is that completely different dimensions of fear learning could be reflected by the different measurements. Another aspect is that during a parallel data recording a reciprocal interference could occur which could change or disturb or even cancel the experiment (Lonsdorf et al., 2017; Boddez et al., 2013), which seems not to be the case in this current work due to reasonable findings, which contribute to a greater picture in this scientific field.

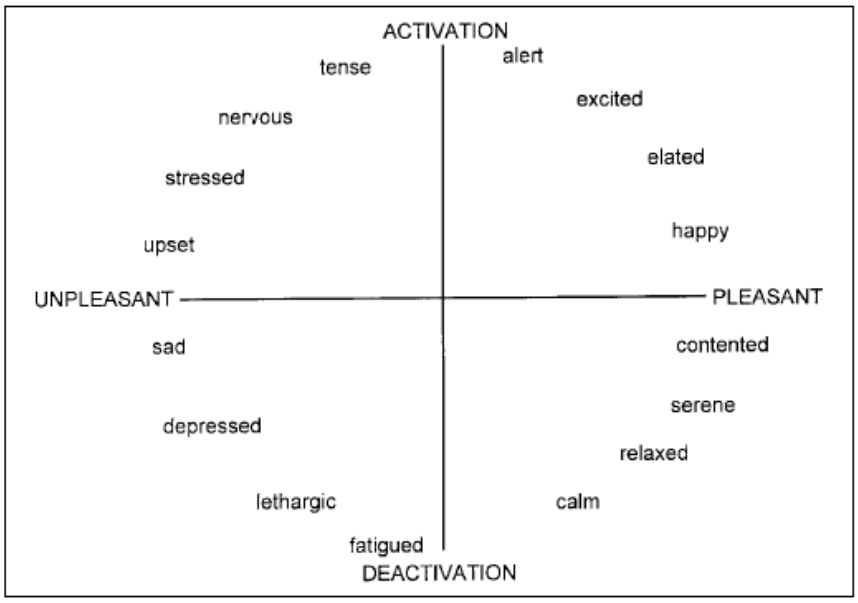


Figure 1. Circumplex-model with the two affects of arousal (activation – deactivation) and valence (pleasant – unpleasant). Adapted from Feldman Barrett and Russell (1998).

In this context it is of interest to mention to which occurrence fear conditioning in children can be traced back. It was back in 1920 when Watson and Rayner conducted their well-known psychological experiment called “little Albert”. The question of the ethical acceptance of this experiment will not be discussed here. The little boy was confronted again and again with a tremendously loud and unpleasant noise (US) simultaneously with a white rat. This procedure continued till the rat, i.e. a normally neutral stimulus, evoked fear in the absence of the US. This experiment was very meaningful because it demonstrated that fear conditioning is possible in humans in principle additionally to many different animals like monkeys, rabbits, rats, but also fish, fruit flies, snails and almost every category of animals which has been investigated (Graham et al., 2009). To date, this experiment for sure would not have passed any ethic committee, but there were some very important studies conducted in children and

adolescents concerning fear conditioning in the meantime. Due to ethical reasons it was not wanted to give electric shocks to children like it was the case for adults (i.e. Pittner, Kadosh & Lau, 2016; Sperl, Panitz, Hermann & Müller, 2016). Hence, there were different approaches to achieve fear conditioning in children by means of loud sounds, e.g. an auto horn (Block et al., 1970) or white noise in a tin can with metal jangling (Gao et al., 2010), also with electric shocks paired white lights (Morrow, Boring, Keough & Haesly, 1969), furthermore, via a linkage of geometric shapes with the noise of a three-pronged garden fork (Neumann et al., 2008a) or metal scrapping slate (Neumann et al., 2008b). Moreover, pictures of human faces with neutral, happy or angry expressions were connected with a neutral comment, a compliment or criticism (Haddad, Lissek, Pine & Lau, 2011) or knotted colored squares with white noise were used (Pattwell et al., 2012) or colored bells with an aversive alarm (Michalska et al., 2016; Shechner et al., 2015). In 2008 Lau and her colleagues created the "screaming lady" paradigm, where a fearful female face is combined with a loud female scream (together: US). In this respect, in various studies the effectivity of this paradigm, to trigger distinct fear reactions to the safety cue CS- and the danger cue CS+, was demonstrated (Den, Graham, Newall & Richardson, 2015; Glenn, Liebermann & Hajcak, 2012b; Lau et al., 2011, Glenn et al., 2012a).

Importantly, there is evidence that fear conditioning improves, i.e. a stronger CS-US association is formed, with increasing age. Block, Sersen and Wortis showed in 1970 that two- to four-year old children did not show conditioning effects, whereas four- to six-year old children already displayed conditioning effects in part and that six- to eleven-year old children demonstrated clearly fear conditioning. The outcomes of the investigation of Gao and colleagues (2010) go in line with these results evincing that discriminative fear conditioning grows with increasing age with a crucial stage at the ages of five to six years. Another important outcome dealing with fear conditioning in children and adolescents is that older children, i.e. adolescents, can differentiate better between danger and safety cues than younger ones (Michalska et al., 2016; Glenn et al., 2012a; Jovanovic et al., 2014). Lau and colleagues (2011) showed that adolescents expressed less differentiating skills concerning danger and safety cues than adults. This grown capability to discriminate with increased age persists into adult age and is related to different maturational patterns of neural activities throughout fear learning (Hartley & Lee, 2015; Lau et al., 2011; Gogtay et al., 2004).

Interestingly, a transformation of fears occurs in the course of the development for children, adolescents and adults. Whereas the childhood contains more concrete things in connection with fears, in the adolescence the issues related to fear become more and more

abstract (Lau et al., 2011; Weems & Costa, 2005; Gullone, 2000). In the course of the successive maturation stages the engagement of the subcortical parts of the brain like the hippocampus or the amygdala of the brain decreases while the use of the prefrontal parts gains growing weight. This is due to the fact that the subcortical regions ripen first, whereby the PFC structures ripen subsequently (Gogtay, 2004; Monk, 2008; Casey, Jones & Hare, 2008). Both take an active part in the process of fear learning (Lau et al., 2011).

Notably, there are hints that abnormalities in fear conditioning are involved in the development of anxiety disorders (e.g. Beckers et al., 2012). Britton et al. (2013) and also Waters, Henry and Neumann (2009) reported about higher fear reactions of anxious children compared to healthy ones regarding the danger, but also the safety cue at the same time. Consistently, Craske and colleagues (2008) observed similar conditioning effects for their sample containing healthy and anxious children in orienting responses (first interval responses (FIR, 1-4 seconds after CS onset: 1.part of SCR), higher orienting responses of anxious children towards both the CS+ and CS-, but no significant main effect of group), whereby during the acquisition the children with anxiety disorders showed both larger anticipatory responding (second interval responses (SIR, 4-7 seconds after CS onset: 2.part of the SCR) and larger responding to the timing of the US (third interval responses (TIR, 7-11 seconds after CS onset: 3.part of the SCR) towards the danger as well as the safety cue in comparison to healthy children (significant main effect of group). Whereas Lau et al. (2008) showed that the fear reactions towards the danger cue only were higher in anxious adolescents than in healthy ones. The investigation of Liberman, Lipp, Spence & March (2006) displayed stronger ratings of arousal regarding the danger cue after fear acquisition for healthy children, while there were no differences in the arousal ratings for anxious children possibly reflecting a poorer capability to discriminate between the presented stimuli CS- and CS+ after fear conditioning. These results suggest difficulties to inhibit exaggeratedly strong responses to understood and learned safety cues in anxious minors (Craske et al., 2008). Moreover, Craske et al. (2012) reported that youths expressing a stronger startle reaction towards a safe condition presented after an unpleasant stimulus had a significantly higher risk of experiencing an anxiety disorder onset hereafter. Pliszka, Hatch, Borcherding & Rogeness (1993) compared children with ADHD, children with ADHD comorbid with anxiety disorders and healthy controls with the aid of a discriminative conditioning paradigm, however, no differences between the three groups could be revealed. Waters and Pine (2016) did not find significant differences between their child groups of healthy controls, anxious responders (to cognitive behavioral therapy) and anxious non-

responders (to cognitive behavioral therapy) related to fear conditioning as reflected both in subjective ratings of arousal and valence and in the SCR (first interval responses (FIR) of SCR). Overall, there are not many studies addressing fear conditioning in healthy and/or in anxious children and adolescents. And as seen above outcomes are often very heterogeneous which might be due to several differences like applied methods and approaches, the overall small number of studies in children and adolescents, but also the age span looked at especially during growing up with changes concerning the created impact of used danger stimuli from childhood into adulthood (Pittner et al., 2016; Lonsdorf et al., 2017).

To date, there are only few studies dealing with the question how individuals differ in fear conditioning as a function of trait anxiety (i.e. in adults: Torrents-Rodas et al., 2013). A heightened trait anxiety is regarded as a relevant risk factor related to anxiety disorders (Torrents-Rodas et al., 2013). As seen above in the text associative fear learning is considered to play an important role for developing of anxiety disorders (Gazendam et al., 2013). It is crucial at this point to have an additional look at subclinical groups with an underlying risk to develop an anxiety disorder. There are only a few studies containing research particularly related to groups at risk so far and their outcomes concerning abnormal associative fear learning or fear conditioning in high trait anxious individuals have been inconsistent: Kadosh and colleagues (2015) reported about a non-discriminative startle regarding the safety and danger cues in high anxious adolescents (aged 12 to 17), however, different to former outcomes in adults, i.e. for both stimuli categories the startle was lowest for an unanticipated condition (US pseudo-randomly) and the largest startle concerning the condition without any US. Thus, there were differences with regard to different contingencies. Haaker et al. (2015) as well as Gazendam et al. (2013) both drew the conclusion that adult high trait anxious individuals are linked with deficient safety learning. Boddez et al. (2012) is in line with the latter proving to some extent the association between trait anxiety and a deficiency concerning selective fear learning in adults. Although Torrents-Rodas et al. (2013) provided evidence that there are no effects of trait anxiety in healthy adults related to a differential fear conditioning. In contrast there is a study conducted in adults from Indovina, Robbins, Nunez-Elizalde, Dunn, & Bishop (2011) implying an association between trait anxiety and even a better discrimination learning with a further study supporting this result, though with the important limitation that it was for contextual fear conditioning, and therefore, comparability to cue fear conditioning cannot be assured, but could give at least a hint in this context (Glotzbach-Schoon et al., 2013).

Finally and most importantly, there is a recent meta-analysis containing studies regarding fear conditioning processes in adolescents with diagnosed anxiety disorders and in their healthy counterparts. Some of the included studies are mentioned above in a more detailed manner. All in all, the main results indicated resembling discriminative fear conditioning responses, although the anxious adolescents expressed higher fear reactions to the danger as well as safety cue than the healthy ones. In addition, the outcomes for the adolescent sample with anxiety disorders were similar to the outcomes found in adults with anxiety disorders in preceding investigations (Dvir et al., 2019).

1.2.2 Fear generalization in children and adolescents

Fear generalization is a learning mechanism through which fear reactions expand to an area of stimuli being similar to the conditioned danger cue, but non-threatening (Lissek et al., 2010; Pavlov, 1927). Thus, in between the safety (CS-) and the danger cue (CS+), further stimuli can be found: they are a mixture of different proportions on a percentage basis between CS+ and CS-, so called morphs. Normally, there is a steady decline in generalization with decreasing resemblance of the shown stimulus to the danger cue (CS+) (Lissek et al., 2008). To present the extent of fear generalization, a fear generalization gradient or slope is used. The steeper the slope, the less fear is generalized in comparison to less steep generalization gradients (Schiele & Reinhard et al., 2016). There are also two numerical indices to express the extent of generalization in only one figure: the linear deviation score (LDS; Kaczkurkin et al., 2017; see p. 73 for an example) and the generalization index (GI; Lenaert et al., 2016; see p. 73 for an example). Generally, it seems that generalization of conditioned fear uses resembling neurocircuitry as involved in fear conditioning (like the ACC or the insula) and its regulation (like the vmPFC; Dymond, Dunsmoor, Vervliet, Roche & Hermans, 2015). Consistently with the outcomes above there is a neurobiological model of generalization of conditioned fear (Lissek et al., 2014a; Lissek, 2012) containing a dual-pathway hypothesis with the amygdala playing an important role relating to expressing and learning fear suggested by LeDoux (1996). From this perspective, possibly dangerous generalization stimuli, that are next to the danger cue, might be passed on straightforwardly from the sensory thalamus to the amygdala rerouting sensory cortex, and thus, quickly activating the display of a conditioned fear reaction via linkages with the insula, the brainstem and further regions (so called lower route: amygdala-based fear circuits with a “quick and dirty” route to a rapid fear reaction) contained in the manner fear is exhibited psychologically as well as physiologically. At the same time the

thalamus transmits sensorial data about the GS to the visual cortex (so called higher route, which is slower and longer). Moreover, the generalization of conditioned fear is mediated via the structure of the hippocampus, which in the "schematic matching" evaluates the overlapping between the pattern of activation within the brain, which represents the GS and the priorly encoded danger signal. If there is enough overlapping between a generalization signal and the danger signal, then the hippocampus triggers a procedure of pattern completion (that is generalization) including the reactivation of the neural representation of the conditioned stimulus, thus activating a conditioned reaction. Otherwise, if the overlapping is not enough, a procedure of pattern separation within the hippocampus is triggered, that results in activating the vmPFC, which as a consequence initiates a downregulation of the amygdala (Dymond et al., 2015; Lissek et al., 2014a). Taken together, in this model the generalization of conditioned fear represents an equilibrium between fear excitation (that is amygdala and insula) by means of pattern completion (generalization) and the inhibition of fear (that is vmPFC) by pattern separation (for more detailed information see Lissek et al. (2014a), Lissek (2012) and Dymond et al. (2015)). However, further research is needed regarding this model and its components. Indeed, the exact function of the amygdala during the generalization of conditioned fear persists not clarified due to the lack of prior investigations via fMRI displaying a robust activation of the amygdala towards GS morphs throughout the generalization part (Dymond et al., 2015).

Until now, there have been only few studies dealing with fear generalization in children and adolescents, especially, if compared to research connected to fear generalization in healthy adults as well as in patients suffering from different anxiety disorders. One of the first studies including fear generalization in children was the study from Glenn et al. (2012a), where 40 healthy children aged 8 to 13 participated. An adaption of the aversive conditioning paradigm from Lau et al. (2008) was applied with one generalization stimulus (GS), which was a blended morph of the safety and danger cue to equal parts. Measurements comprised physiological (fear-potentiated startle) and self-report data (fear ratings). There was a clear difference between younger and older children: whereas all children discriminated the danger from the safety cue as well in the phases of acquisition as in the phases of generalization of conditioned fear, the older children differentiated stronger between CS+ and CS-, and in addition, they gradated more differential diminishing between the stimuli CS+, GS and CS-. In younger children the gradation between the three stimuli in the generalization part was distinct regarding an overall smaller differentiation between CS+ and CS-, and furthermore, the smallest extent of the startle magnitude towards the GS and not CS- as in older children. This outcome for older children

reminded of similar results concerning fear generalization in adults (compare Lissek et al., 2008; 2010; Hajcak et al., 2009). Research in animals is consistent with the results above, indicating that rather complex facets of fear learning, like fear generalization of conditioned fear, develops far into adult age (Kim & Richardson, 2010; Rudy & Pugh, 1996; Rudy, 1993; Campbell & Haroutunian, 1983). Moreover, Lau et al. (2011) provided further support in human research, that the ability for higher complexity within fear learning grows from youth into adulthood.

Another study (Schiele & Reinhard et al., 2016) investigated fear generalization in healthy children aged 8 to 10 in comparison to healthy adults. An adaption of the aversive conditioning and generalization paradigm of Lau et al. (2008) was utilized, which corresponds to the one used in this work presenting three studies based on it. The main findings were a stronger fear generalization, i.e. an overgeneralization, expressed by healthy children in comparison to healthy adults as reflected by higher arousal ratings and higher SCR towards the generalization stimuli (GSs). Thus, the outcomes suggest that overgeneralization of conditioned fear might be a developmental pattern of fear learning. A related finding from animal research is of particular relevance here: Enlarged fear generalization of auditory conditioned fear could be detected in juvenile mice in comparison to mice of adult age (Ito, W., Pan, B.X., Yang, C., Thakur, S., Morozov, A., 2009).

In this context a further study shall be presented. Michalska and her colleagues (2016) analyzed fear learning and its generalization concerning shifts and variations during the development of children aged 5 to 10 years. The implemented fear conditioning paradigm contained a blue and a yellow cartoon bell as conditioned stimuli CS- and CS+ and a red cartoon bell linked with an aversive loud sound as unconditioned stimulus. Nine further blended cartoon bells lay in-between the blue and yellow cartoon bells in 10%-steps and served as generalization stimuli (GSs). SCR and subjective fear ratings were measured. There was a special methodological feature: the generalization took place within the extinction recall (see **1.2.3** for a definition) procedure three weeks after fear conditioning and extinction. Two of the core results were that older children discriminated stronger between the danger and safety cue compared to younger children and that generalization effects, i.e. increasing gradations from CS- to CS+, became significantly better with growing age of the children. In this study again, as already mentioned for the study of Glenn et al. (2012a), younger children expressed stronger reactions towards the safety cue CS- than for the generalization stimuli (GSs), which shared similarities with the danger cue CS+ to a varying extent.

Noteworthily, there is evidence that a stronger fear generalization is a characteristic feature in adult patients with different anxiety disorders (panic disorder (PD): Lissek et al., 2010; post-traumatic stress disorder (PTSD): Lissek & Grillon, 2012; generalized anxiety disorder (GAD): Lissek et al., 2014b; but see also: Tinoco-González et al., 2015; further: e.g. Lissek et al., 2008). Hence, overgeneralization of conditioned fear is seen as a conditioning correlative of anxiety disorders (Lissek et al., 2014a).

Furthermore, it is notable that Lenaert and colleagues (2014) found a relation between heightened reactions towards generalization stimuli (GSs), which were similar to the CS-, and a larger degree of anxiety at follow-up six month later in young healthy adults. Thus, this outcome implies that a pronounced fear generalization constitutes a risk factor for an elevated level of anxiety in future.

It is important to come back again to healthy participants, who show elevated trait anxiety, and thus reach a subclinical dimension. Again, there is only research mainly on fear generalization and anxious personality characteristics in adults. In that respect, the meta-analysis from Sep and colleagues (2019) demonstrated that there is a relation between anxious personality traits and fear generalization of conditioned fear reflected by a significant positive correlation, although it is only a small to medium sized effect. Thus, healthy adults with high anxious personality features are more prone to display a higher fear generalization to safe and novel stimuli. Possibly this sheds light on why they are more vulnerable to anxiety disorders.

Back again to the main focus on minors: A recent study from El-Bar and colleagues (2017) reported about overgeneralization in adolescents with anxiety disorders (aged 13 to 18 years) in comparison to healthy age-matched controls. Furthermore, the whole sample of anxious probands aged 9 to 18 years displayed worse perceptual discrimination skills after conditioning than healthy controls, who showed the awaited enhancement concerning the discrimination, and moreover, the anxious participants showed an overall enhanced generalization than controls. Additionally, adolescents with anxiety disorders (aged 13 to 18 years) generalized stronger than children with anxiety disorders (aged 9 to 12 years), while there was no significant difference between anxious and healthy children. In contrast healthy adolescents generalized less than anxious and healthy children. Summed up, with increasing age the extent of generalization grew in adolescent anxious participants, but decreased in adolescent healthy controls. Interestingly, male participants generalized more than female ones and discriminated less. In general, the extent of generalization was higher with a growing magnitude of anxiety and the discrimination declined.

1.2.3 Fear extinction in children and adolescents

Fear extinction refers to the presentation of the danger cue (CS+) without aversive reinforcement. Consequently, as time goes by a new association is built: the stimulus forecasts the lack of the aversive incident (Christianson et al., 2012). A fear reaction is not triggered anymore (Myers, Ressler & Davis, 2006; Norrholm et al., 2006; Phelps, Delgado, Nearing & LeDoux, 2004). Thus, while fear conditioning is related to learning that a particular signal stands for danger, during extinction one learns that a formerly harmful signal has gotten secure (Greco & Liberzon, 2016; Hartley & Lee, 2015; Jovanovic et al., 2013). Notably, the learning of extinction creates a novel memory rivalling with the former initial danger association, that leads to the inhibition of fear (Craske et al., 2014; Bouton, 2004). Even though there are studies suggesting a deletion concerning fear memory in some cases (Kim & Richardson, 2008; Monfils, Cowansage, Klann & LeDoux, 2009). The applied reinforcement rate used in the fear conditioning part can have an impact on the extinction: a higher reinforcement rate (i.e. 100%) leads to a quicker extinction than a smaller reinforcement rate (Phelps et al., 2004). So far, the within-session extinction, also called extinction training (new learning about CS/US contingency), has been described, which was conducted in the current work. However, there is also a between-session extinction, the so-called extinction recall or extinction test (need to activate the formerly learned memory of CS/US contingency a particular while subsequent to learning), which often takes place 24 hours after extinction training and can be characterized by strong context dependence (Jovanovic et al., 2013). There are different aspects like spontaneous recovery (just after some time passes), renewal (alteration within context) or reinstatement (re-exposition towards an aversive stimulus) connected with the extinction recall, that entailed the finding that there is no deletion of the original fear memory within the extinction training, but a substitution via new learning (Craske et al., 2014; Quirk, 2006; Bouton, 2004). The amygdala, the hippocampus and the ventromedial prefrontal cortex (vmPFC) are comprised in neurobiological substantiation of the extinction (Fullana et al., 2018; Phelps et al., 2004; Milad & Quirk, 2002). For extinction inhibitory learning seems to be crucial, whereby further processes like habituation are also probably taking part (Craske et al., 2014). Potentially, the vmPFC is meaningful for the inhibition of a conditioned fear reaction at the inception of the extinction (Greco & Liberzon, 2016). More precisely, there is evidence concerning neural processes fear extinction bases on, which goes in line with an inhibitory model: the amygdala seems to be affected by inhibition stemming from the medial prefrontal cortex (mPFC) as consequence of extinction learning (Craske et al., 2014).

Hence, when the fear reaction towards CS+ goes down, then the extinction training is effective (Dvir et al., 2019). More precisely, extinction is accompanied by declines of physiological reactions as well as self-report replies towards the danger cue reaching a similar degree as the safety cue (Ryan et al., 2019).

There have been quite different research outcomes presented in this context. For example, in two past studies the extinction training was successful both for children aged 8 to 11 years as well as for youths aged 13 to 17 years as reflected by all dependent measures like SCR and various subjective ratings as well as in addition the fear-potentiated startle (FPS) in the adolescents' group (Neumann et al., 2008a, 2008b). Furthermore, Waters and colleagues (2017) reported that regarding the US expectancy ratings towards the danger signal decreased significantly and did not differ significantly from the safety signal after one third of all trials for children, youths and adults. Though the age group of children generally displayed larger US expectancy ratings than youths and adults. Children showed a successful extinction learning of differential CS evaluations (valence), which was not achieved by the group of youths and adults. Additionally, the group of adolescents expressed more negative appraisal both towards the danger and safety cue compared to the group of adults. Another relevant study (Michalska et al., 2016) investigated various aspects of fear learning in three age groups: 5- and 6-, 7- and 8-, 9- and 10-year old children. The age groups did not differ concerning extinction training. Extinction was successful as reflected by SCR, however, the subjective ratings showed that the differential CS ratings were not extinguished, but importantly, the subjective ratings towards CS+ went significantly down (CS- declined slightly) comparing the end of the fear conditioning phase to after the extinction training. Moreover, Jovanovic and colleagues (2014) examined children aged 8 to 13 years, whereby no age-based differences emerged reflected by the SCR, the US expectancy ratings and the fear-potentiated startle (FPS). Further, for the SCR and the US expectancy there were no anxiety-related differences. Only for the FPS higher anxiety was associated with lower FPS responses.

On the contrary, a special meaning of the period of adolescence was found in the next animal and human studies: Pattwell and colleagues (2012) explored the extinction of conditioned fear from childhood into adolescence and adulthood in mice as well as in humans. Interestingly, the period of adolescence was characterized by a weakened extinction learning both in mice and humans in comparison to pre-adolescence and adult age. A paucity of synaptic plasticity within prefrontal cortical regions throughout youth might be linked with a numbed control over extinction learning of conditioned fear. A further study supports the above finding:

adolescent rats displayed declined extinction learning than younger rats, whose extinction learning resembled the one of adult rats (Kim, Li & Richardson, 2011). Noteworthily, there is an activation of neurons within the inhibitory area of the infralimbic cortex (IL) of the medial prefrontal cortex (mPFC) following extinction, however, only in preadolescent and adult rats, but not in the adolescent ones (Jovanovic et al., 2013; Kim et al., 2011). One might conclude that the diminished extinction resulted not from neural-based development, but from an attenuation of inhibitory circuits over the course of youth (Jovanovic et al., 2013). Possibly, there are alterations for the amygdala regarding synaptic inputs from the thalamus in this phase of life (Pan, Ito & Morozov, 2009) elucidating the dearth of extinction of conditioned fear (Jovanovic et al., 2013).

Considerably, retarded extinction is argued to be a decisive part in models basing on fear learning for the development of anxiety disorders and also for their persistence (Waters et al., 2009). Studies of Liberman et al. (2006), Craske et al. (2008) and Waters et al. (2009) indicate a delayed extinction in children with manifest anxiety disorders.

A recent meta-analysis is also of high relevance here. It was found that on the one hand the extinction patterns after a differential fear conditioning resembled each other for clinically anxious and not anxious adolescents. On the other hand, clinically anxious juvenile probands expressed stronger fear reactions towards both the danger and safety cue than their normally developing peers within the extinction training (Dvir et al., 2019). These outcomes go in line with the findings of two meta-analyses, which compared anxious and healthy adult probands (Duits et al., 2015; Lissek et al., 2005).

1.3 Aims and hypotheses

The main focus of the current dissertation is on fear learning, its generalization as well as extinction during the development from childhood via adolescence into adulthood. In addition, the impact of trait anxiety and anxiety sensitivity on fear learning, its generalization and extinction will be examined.

Infancy and young age bear the vulnerability for the development of an anxiety disorder as elucidated in detail above (see under **1.**). There is evidence that adolescent and adult patients with various anxiety disorders displayed overgeneralization of conditioned fear (e.g. El Bar et al., 2017; Lissek et al., 2010, 2014b; Lissek & Grillon, 2012). Interestingly, healthy children aged 8 to 10 years showed an overgeneralization of conditioned fear in contrast to healthy adults. Importantly, maturational differences between younger and older children with regard

to the prefrontal cortex might play a crucial role for the emergence of overgeneralization in younger healthy children (Tottenham & Gabard-Durnam, 2017; Vink, Derks, Hoogendam, Hillegers & Kahn, 2014; Decety, Michalska & Kinzler, 2012). The underlying mechanism for this phenomenon could be based on age-related perceptual variations. Thus, the question arises if and how fear generalization gradients alter during the course of childhood and adolescence up until adult age. Rephrased: Are there specific changes and if so, then at which age level during this time span exactly? The hypothesis is that there is a negative correlation between overgeneralization and age in minor participants.

Again, in contrast to research in adult age there are very few studies dealing with similarities and differences concerning fear generalization in children and adolescents with anxiety disorders in comparison to healthy children and adolescents. A comparison regarding fear generalization in healthy children and adolescents with a dimensional perspective on different aspects of anxiety would also be of great interest in this context.

So, another aim of this work was to examine fear learning and its generalization of conditioned fear as well as its extinction in a sample of children and adolescents between 8 and 17 years considering the modulatory effect of trait anxiety and anxiety sensitivity. The next hypothesis rests upon the above presented studies in adolescents and adults with enhanced trait anxiety or anxiety disorders (see under **1.**) and is as follows: the extent of fear generalization in children as well as adolescents is positively associated with the height of anxiety.

In terms of fear acquisition and extinction the expectation is that all ages show generally comparable robust effective learning effects, however, with overall higher fear reactions to both CS+ and CS- with a stronger extent of anxiety. This expectation is mainly based on the meta-analysis of Dvir and colleagues (2019) due to the fact that the observed sample consisted of healthy children and adolescents.

1.4 Fear conditioning, generalization and extinction paradigm

For all studies presented in the current work the same experimental paradigm was applied. Also, the whole way of proceeding was identical regarding the recruitment of the participants, the criteria of inclusion and exclusion, the measurement of the arousal, valence and contingency ratings, and the psychophysiological data (SCR), its data reduction and all the statistical calculations.

1.4.1 Sample

188 healthy children and adolescents were recruited from primary and secondary schools within the greater area of Wuerzburg as part of the collaborative research center SFB-TRR-58 subproject Z02 in the Department of Child and Adolescent Psychiatry. Nine children and adolescents had to be excluded from the analysis because they did not finalize the experiment due to a big stressful fear reaction - the probands communicated their wish to exit the experiment immediately - and 46 because of technical problems during the physiological recordings (mainly at the beginning of the study for instance due to various adaptions of the paradigm or no markers had been set by mistake, and due to further different problems during the physiological recordings). The final sample consisted of 133 children and adolescents (70 female) in the age range of 8 to 17 years (mean age: 12.27, SD: 2.82) for the (pre-)acquisition and generalization phases. There were no significant differences in the age groups regarding sex ($\chi^2(9) = 8.82$, $p = .454$, $\varphi = 0.26$, see **Table 1**.). All participants were native German speakers. A manifest or lifetime DSM-IV axis l disorder, ingestion of psychoactive medication, and an IQ < 85 determined by the German version of the Culture Fair Intelligence Test 2 (Weiss, 2006) were exclusion criteria. The SCR data could not be analyzed for one participant for the extinction part, that is why the final sample contained only 132 children and youths for the three extinction phases. The study was approved by the ethical committee of the Medical Faculty of the Julius-Maximilian-University of Würzburg (study numbers 211/16 and 106/10) and complied with the latest version of the declaration of Helsinki. All probands and also their parents gave written informed consent and every family was paid € 30 compensation for their participation.

Table 1. Age and sex distribution within the sample

age	male	female	N
8	9	4	13
9	8	8	16
10	7	8	15
11	7	7	14
12	9	6	15
13	5	3	8
14	4	11	15
15	5	9	14
16	5	10	15
17	4	4	8

1.4.2 Questionnaires

The children and adolescents of the sample had to fill in questionnaires during the whole procedure. One of it was the German version of the *Trait scale of the Stait-Trait Anxiety Inventory for Children (STAIC-T* from Spielberger, 1973; German version: STAIK-T Unnewehr, Joormann, Schneider & Margraf, 1992) for the estimation of the trait anxiety. The internal consistency is given with Cronbach's alpha of .81 (Schneider et al., 2009). During the STAIC the probands had to evaluate 20 assertions related to themselves in a self-report regarding trait anxiety on a three-point Likert scale: "almost never" = 1, "sometimes" = 2 and "often" = 3. An unweighted sum score without reversion of polarity can be calculated, while a score lies within the minimum of 20 and the maximum of 60. In their meta-analytic review Seligman, Ollendick, Langley and Baldacci (2004) show support for the capability of the STAIC to distinguish between children suffering from anxiety disorders and healthy children, which makes the STAIC very valuable.

Another questionnaire used was the *Children Anxiety Sensitivity Index (CASI),* which is a modification from the ASI by Peterson and Reiss (1987) and has 18 items (Silverman et al., 1991) and a high internal consistency (Cronbach's alpha ≥ .79, Schneider et al., 2009). The English version was translated into a German version *Kinder-Angstsensitivitätsindex (KASI)* by Schneider and Hensdiek in 1994 (Schneider et al., 2009), but has only 17 items because one item had not enough selectivity after the translation into German (Barkmann, Schulte-Markwort & Brähler, 2011). The answers were a self-report basis on a three-point Likert scale with "never" = 1, "sometimes" = 2 and "often" = 3 and build an unweighted sum score between 17 and 51 without polarity reversal.

1.4.3 Task

The "screaming lady paradigm" based on Lau et al. (2008) and adapted by Schiele & Reinhard et al. (2016) was used (see **Figure 2.**). The photos of two actresses showing a neutral facial expression (NimStim Face Stimulus Set; Tottenham et al., 2009) were used as danger cue CS+ or safety cue CS-. One of the two pictures was randomly chosen as danger cue CS+. The US combined a loud female scream (95 dB; International Affective Digital Sounds system) and a fearful facial expression of the same actress categorized as the danger cue CS+. Four generalization stimuli (GS) depicting gradual morphs from CS+ to CS- in 20%-steps (GS1-4) were created using the graphics software Sqirlz Morph Version 2.1 (Xiberpix, Solihull, UK).

For the presentation of the paradigm the software Presentation (Version 18.3, Neurobehavioral Systems, Inc., Albany, CA) was used.

The duration of the presentation of the CSs as well as the GSs was six seconds each. For the US the duration was one and a half seconds exactly after the end of the CS+. The intertrial intervals (ITI) varied between nine and twelve seconds with a presented white fixation cross pivotally on the monitor. The chronology of the presented stimuli was pseudo-randomized meaning that the same stimulus type never was displayed more often than two times subsequently.

The task contained four successive parts. The pre-acquisition (four CS- and four CS+, free of US), two identical acquisition phases (each phase: six CS- and six CS+, pairing of CS+ and US in five trials (83%)), two equal generalization phases (every phase: six CS- and six CS+ as well as six of each of the four GSs, pairing of CS+ and US in three trials (50%) aiming at a prevention of an early extinction) and the extinction containing three indiscriminate phases (six CS- and six CS+, no US). A pairing of CS- and the four GSs with the US never took place. The CS-US contingencies were not explained to the probands prior to the experiment.

Participants had the instruction to look inactively at photos of two female faces. Furthermore, an unpleasant noise would be presented from time to time. The participants were informed that it could happen to become frightened and scared and that the experiment could be ceased at all times.

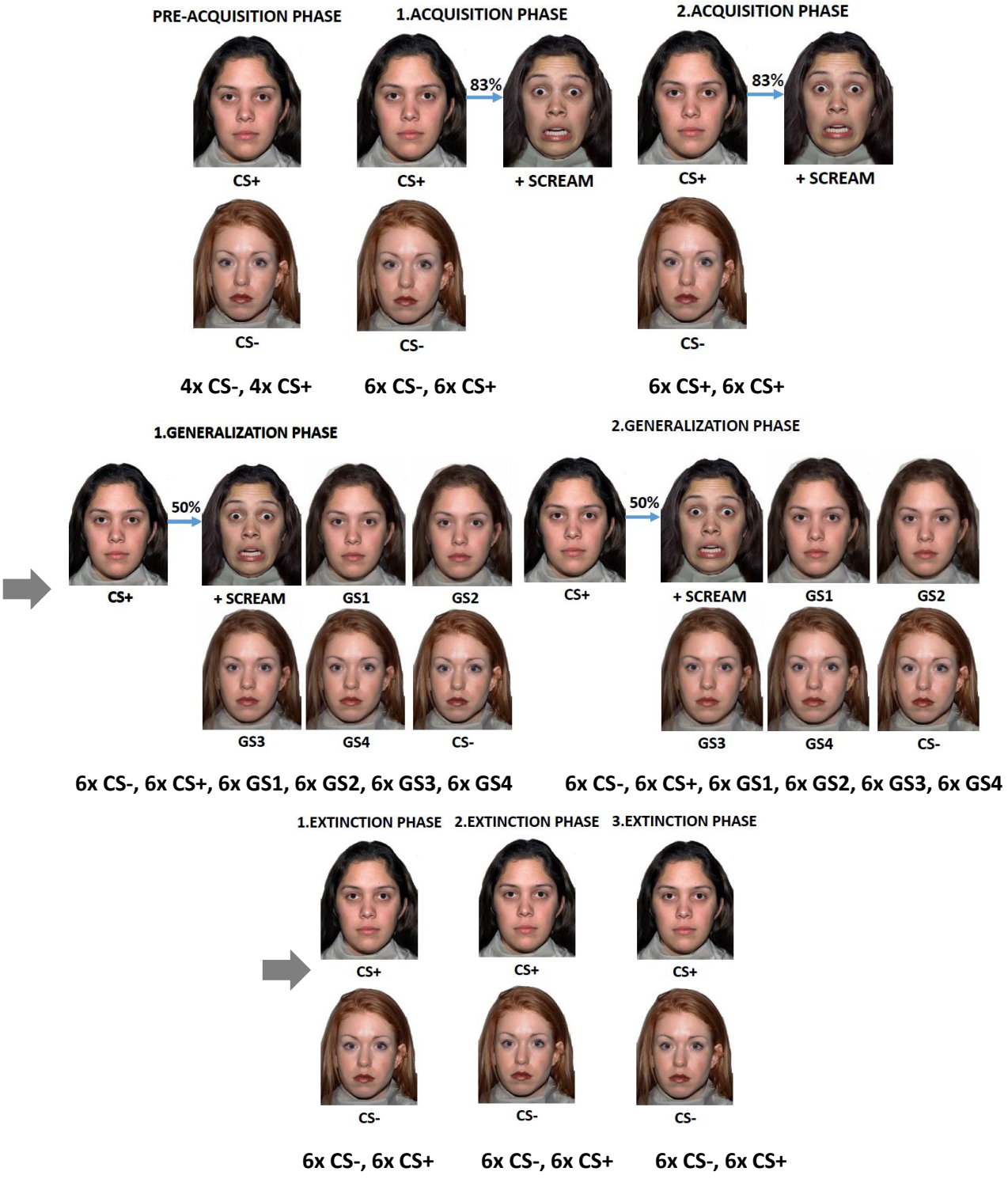


Figure 2. Schematic overview of the fear conditioning, generalization and extinction paradigm with a pre-acquisition phase being followed by two acquisition phases, which are followed by two generalization phases and at the end three extinction phases (based on Lau et al. (2008), as adapted by Schiele & Reinhard et al. (2016)).

1.4.4 Ratings

Each phase, that is the pre-acquisition phase, the two acquisition phases, the two generalization phases and the three extinction phases, was followed by ratings of arousal, valence and contingency, i.e. the US expectancy. Arousal was stated on a 9-point Likert scale with the scope from “very calm” (1) to “very arousing” (9). Valence was stated on a 9-point Likert scale with the scope from “very unpleasant” (1) to “very pleasant” (9). The contingency was measured on a scale from 0% to 100% in 10%-steps (here scaled from 1 to 11) reflecting the estimated likelihood of an unpleasant sound after the presentation of every stimulus.

1.4.5 Physiological recordings and data reduction

The skin conductance response (SCR) was recorded during the whole experiment. The Brainproducts V-Amp-16 and the Vision Recorder software (Brainproducts, Gilching, Germany) were utilized at a sampling rate of 1000 Hz. The analysis was done offline using the Vision Analyzer 2 software (Brainproducts, Gilching, Germany). The skin conductance was derived from the thenar and hypothenar eminences of the left palm of the hand with the aid of two Ag/AgCl electrodes. The amplifier provided a steady electricity of 0.5 V. A high cutoff filter of 1 Hz as well as a notch filter of 50 Hz were implemented for the SCR signal. The definition for the SCR was the base-to-peak difference in µS between the beginning of the response, i.e. from 900 to 4000 ms after stimulus onset, and the peak, i.e. from 2000 to 6000 ms after stimulus onset. The smallest reaction accepted for SCR was 0.02 µS. Smaller values were set to 0. SCR data was normalized in accordance with the procedure delineated by Dunsmoor, Prince, Murty, Kragel, & LaBar (2011) (see also Schiele & Reinhard et al., 2016).

1.4.6 Statistical analyses

For the statistical analyses, the software IBM SPSS (version 25, SPSS Inc., Chicago, IL) was used. 2 x 3 repeated-measures ANOVAs were applied for the purpose of proving learning effects on the basis of conditioning within the subjective ratings of arousal, valence, US expectancy and the objective measurements of the SCR. The within-subject factors were stimulus type, including CS- and CS+, and phase, comprising the pre-acquisition, the 1. acquisition and the 2. acquisition phase. Further, 6 x 2 repeated-measures ANOVAs were performed in order to investigate generalization effects. Once more stimulus type, i.e. CS-, CS+ and in addition GS1 - 4, as well as phase, with the 1. and 2. generalization phase, constituted the within-subject factors. With regard to the generalization gradients for all four dependent

variables (arousal, valence and US expectancy ratings and the SCR) trend analyses were executed to examine the course of the curve more precisely. Finally, 2 x 3 repeated-measures ANOVAs were also calculated in order to monitor if and to which extent the conditioning became extinguished at long last. In the 1. study age and sex were defined as covariates (sex as covariate of no interest), whereby in the 2. study the STAIC score and in the 3. study the CASI score were included as additional covariates (age and sex as covariates of no interest). The resulting modulatory effect of the particular covariate should be explored. When significant main or interaction effects existed, two-tailed Pearson correlations were built.

AN(C)OVAs were followed by post-hoc *t*-tests for significant interactions. Alpha was set at 0.05 and for all post-hoc *t*-tests the Bonferroni correction was applied where necessary. Greenhouse-Geisser corrections for non-sphericity were used where required, despite this, uncorrected degrees of freedom are presented for the sake of better readability. Corrected *p*-values and partial η^2 for significant results are stated.

2. Fear conditioning, its generalization and extinction in children and adolescents aged 8 to 17 years – the impact of age in underage probands

As already depicted quite detailed above, literature shows a successful fear conditioning for children from middle childhood (e.g. Gao et al., 2010) and adolescents (e.g. Schiele & Reinhard et al., 2016), which is comparable to results encountered in adults. That is why, in the first study of the current work, a robust and successful fear conditioning is expected for the whole sample. In respect of the generalization of conditioned fear, too little research has been done until now. Thus, it is aimed in this work to replicate and expand the results of one of the first studies, i.e. from Schiele, Reinhard and colleagues (2016), which included a huge sample of healthy children, looked at the process of fear generalization and compared it to a huge sample of healthy adults. There, the sample of children clearly expressed overgeneralization in comparison to the adult sample. Hence, the hypothesis is that overgeneralization is negatively correlated with the probands' age.

Like for fear conditioning, the expectation concerning its extinction is that children and adolescents show comparable outcomes to adults, i.e. a generally successful extinction training.

A part of the presented data in this chapter has been published in a research article in the journal *European Child & Adolescent Psychiatry* (Reinhard, Slyschak et al., 2021).

2.1 Results

In this chapter, the modulatory effect of the probands' age will be examined for fear learning with its different parts of fear acquisition, fear generalization and, also, its extinction (statistically controlled for sex as covariate of no interest, see Tables in the APPENDIX).

2.1.1 (Pre-)Acquisition phases

Subjective ratings: Regarding the ratings of arousal and the US expectancy, significant main effects of stimulus type (arousal: F (1,132) = 62.03, $p < .001$, $\eta^2 = .32$; US expectancy: F (1,132) = 36.09, $p < .001$, $\eta^2 = .22$) as well as phase (arousal: F (2,233) = 36.57, $p < .001$, $\eta^2 = .22$; US expectancy: F (2,220) = 8.21, $p = .001$, $\eta^2 = .06$) could be revealed and, furthermore, significant interaction effects of stimulus type x phase (arousal: F (2,245) = 24.89, $p < .001$, $\eta^2 = .16$; US expectancy: F (2,264) = 39.10, $p < .001$, $\eta^2 = .23$). Concerning the ratings of valence, a significant main effect of stimulus type (F (1,132) = 20.57, $p < .001$, $\eta^2 = .14$) as well as a significant interaction effect of stimulus x phase were observed (F (2,241) = 20.23, $p < .001$, $\eta^2 = .13$).

Thus, for the arousal ratings the danger cue CS+ was generally rated as more arousing than the safety cue CS-. Further, independent of the stimuli the two acquisition phases had higher arousal ratings compared to the pre-acquisition phase. And, the two-way interaction of stimulus type x phase means, that the difference between the arousal ratings concerning the two stimuli was distinct in the pre-acquisition phase, where both stimuli had quite similar arousal ratings, in comparison to both acquisition phases, where the CS+ was rated significantly higher than the CS-. The post hoc t-tests for the arousal ratings revealed no significant differences between CS- and CS+ after the pre-acquisition (t (132) = -0.43, $p = .669$), but there were significant differences between the stimuli after the 1. acquisition phase (t (132) = -7.11, $p < .001$) and, also, after the 2. acquisition phase (t (132) = -7.19, $p < .001$, see **Figure 3.**).

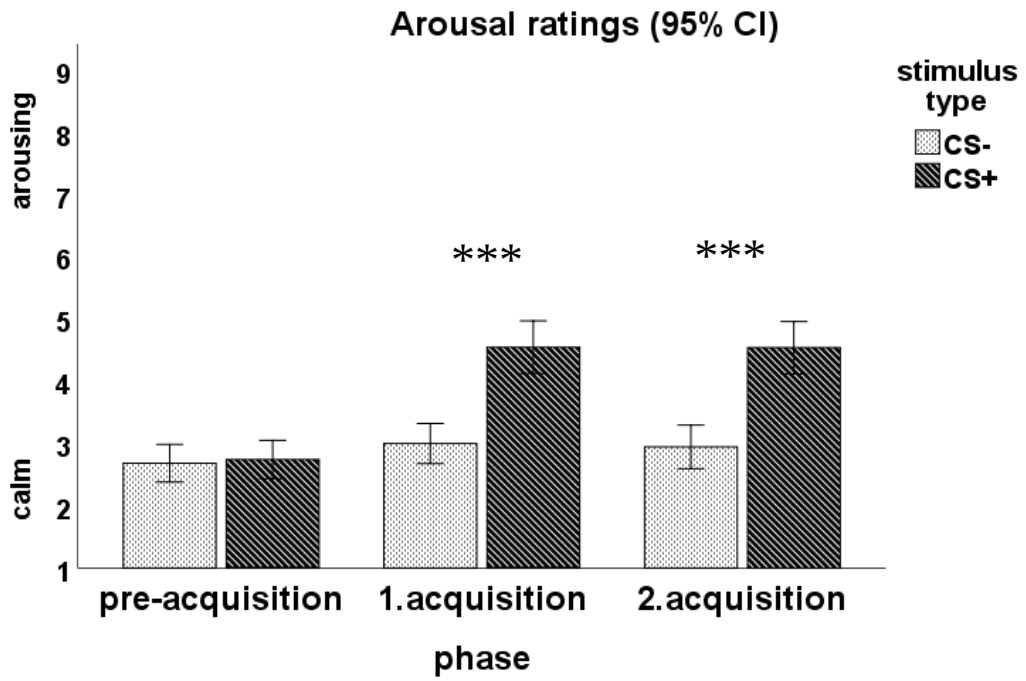


Figure 3. Arousal ratings (with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the pre-acquisition, the 1. acquisition (ACQ 1) and the 2. acquisition phase (ACQ 2). After ACQ 1 and ACQ 2, the discrimination concerning the stimulus types was apparent. ***$p < .001$

Regarding the valence ratings (see **Figure 4.**), the CS+ was evaluated less pleasant, i.e. with lower valence ratings, than the CS- and, first, there was no significant difference between the stimuli (pre-acquisition phase), but afterwards the valence ratings towards the CS+ were significantly smaller compared to the CS- (1. + 2. acquisition phases). Also, for the valence ratings the post hoc t-tests indicated, that there were no significant differences between the CS- and the CS+ post per-acquisition (t (132) = -1.43, p = .154), but similarly as for arousal and US expectancy, the differences between the stimuli were significant both after the 1. acquisition phase (t (132) = 3.82, $p < .001$) and after the 2. acquisition phase (t (132) = 5.79, $p < .001$, see **Figure 4.**).

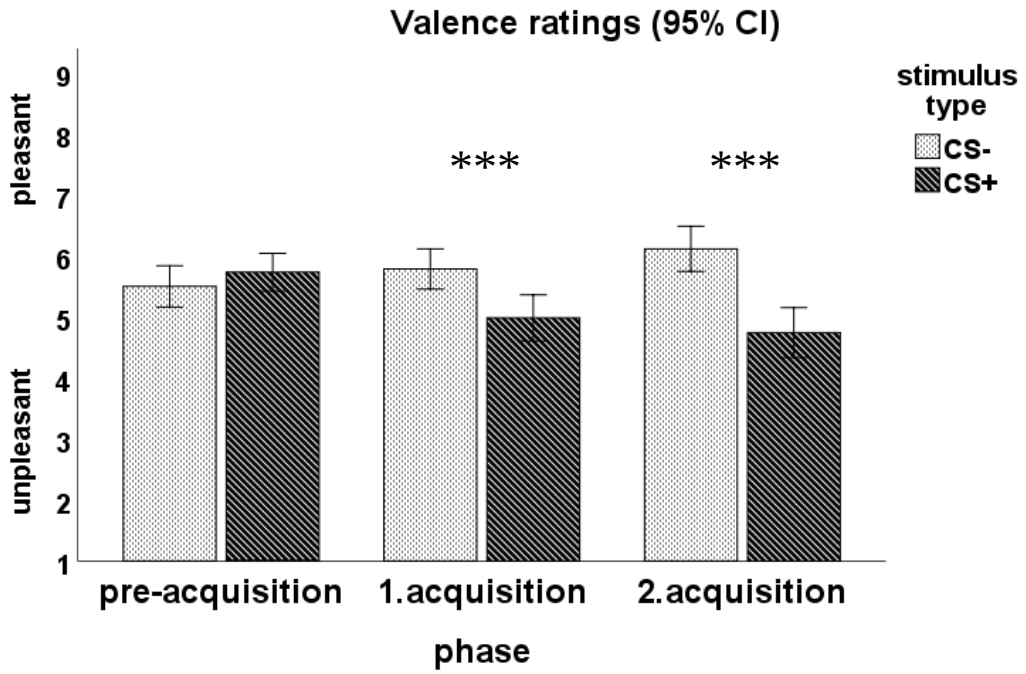


Figure 4. Valence ratings (with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the pre-acquisition, the 1. acquisition (ACQ 1) and the 2. acquisition phase (ACQ 2). After ACQ 1 and ACQ 2, the discrimination concerning the stimulus types was apparent. ***$p < .001$

Furthermore, the CS+ had higher US expectancy ratings than the CS- regardless of the phase and both acquisition phases comprised generally higher ratings than the pre-acquisition phase independent of the stimuli. The differentiation between both stimuli became significant in both acquisition phases in comparison to the pre-acquisition phase. Very similarly in respect of the US expectancy ratings, the post hoc t-tests displayed, like already for the arousal ratings, no significant differences between CS- and CS+ after the pre-acquisition phase (t (132) = -0.072, p = .942), but also for the US expectancy the stimuli were rated significantly different after the 1. acquisition phase (t (132) = -1.98, p = .05) and the 2. acquisition phase (t (132) = -9.04, $p < .001$, see **Figure 5.**).

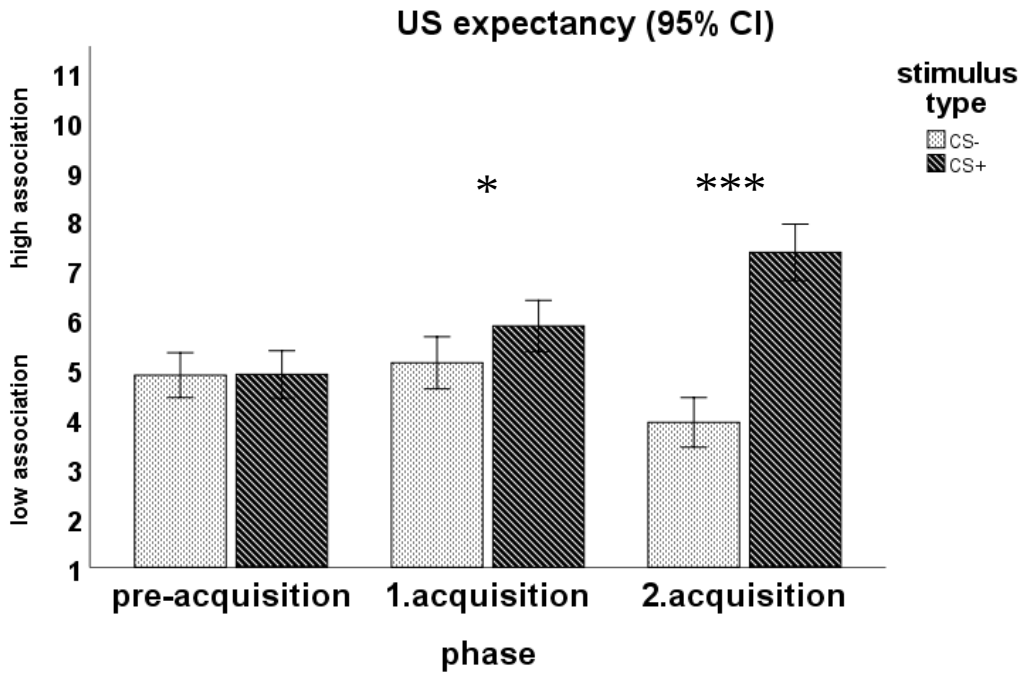


Figure 5. US expectancy ratings (with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the pre-acquisition, the 1. acquisition (ACQ 1) and the 2. acquisition phase (ACQ 2). After ACQ 1 and ACQ 2, the discrimination concerning the stimulus types was apparent. ***$p < .001$, *$p < .05$

Physiological reaction: Comparable to the subjective ratings, significant main effects of stimulus type (F (1,132) = 5.89, p = .017, $\eta 2$ = .04) as well as phase (F (2,237) = 5.21, p = .008, $\eta 2$ = .04) could be detected, however, the interaction effect of stimulus type x phase was not significant (F (2,240) = 1.76, p = .178, $\eta 2$ = .01). As a whole, the probands expressed higher SCR regarding the CS+ than towards the CS-. Altogether, the height of the psychophysiological arousal, regardless of the stimuli, was significantly higher in the 1. acquisition phase compared to the 2. acquisition phase ($M_{1.\text{ acquisition phase}}$ = 0.20, $SD_{1.\text{ acquisition phase}}$ = 0.14 vs. $M_{2.\text{ acquisition phase}}$ = 0.16, $SD_{2.\text{ acquisition phase}}$ = 0.14, t (132) = 3.83, p < .001, see **Figure 6.**). This result could point to a habituation effect.

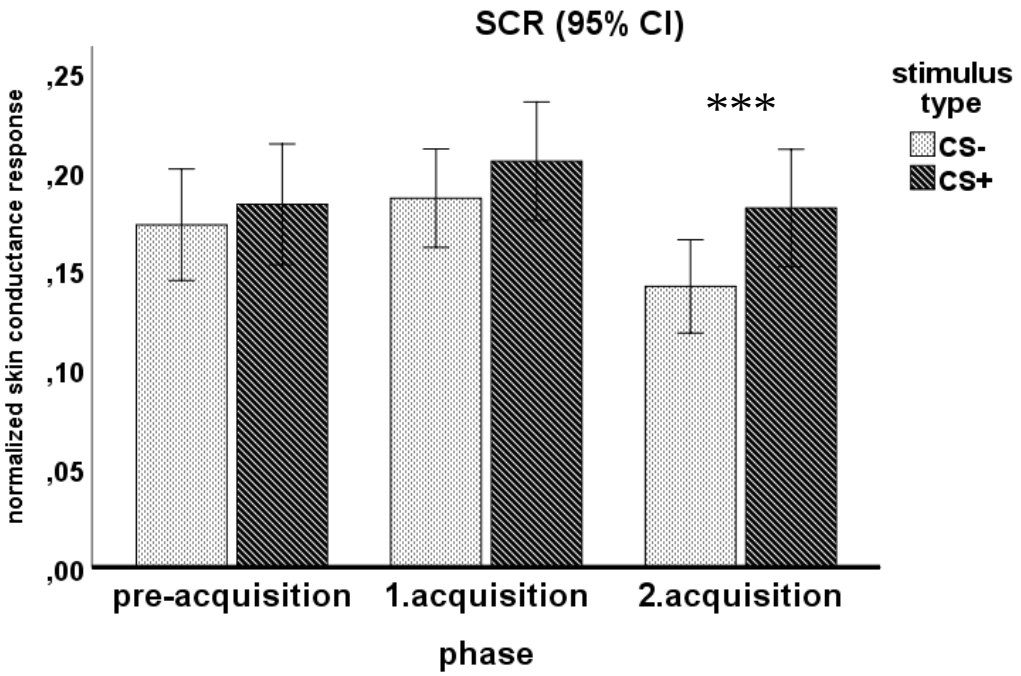


Figure 6. Skin conductance response (SCR, with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the pre-acquisition, the 1. acquisition (ACQ 1) and the 2. acquisition phase (ACQ 2). After ACQ 2, the discrimination concerning the stimulus types was apparent. ***$p < .001$

Taken together, the subjective ratings clearly displayed a successful fear conditioning, whereby the results for the psychophysiological reaction support this: By the 2. acquisition phase at the latest, the CS+ evoked significantly higher arousal and US expectancy ratings as well as SCR and, further, lower valence ratings, respectively.

Effects of age: The arousal ratings, the valence ratings, the US expectancy ratings and the SCR experienced some significant modulations by age (see **Table 2.**). A significant main effect of the covariate age was revealed for the arousal ratings (see **Table 2.**). A Pearson correlation was calculated between age and the arousal for the three phases together (r (131) = -0.21, p = .015): With growing age the arousal ratings were significantly lower for all three phases of pre-acquisition, the 1. and 2. acquisition phase, whereby the stimulus type did not play any role. As for arousal, also for the US expectancy ratings a significant main effect of the covariate age was detected (see **Table 2.**). The Pearson correlation between age and the US expectancy for the three phases together was significant and negative: r (131) = -0.30, p = .001. Thus, with growing age the probands showed lower ratings of US expectancy in every of the

three phases (pre-acquisition, 1. acquisition and 2. acquisition phase), independent of the stimulus type. Regarding the skin conductance response (SCR), like for the arousal and the US expectancy, there was a significant main effect of the covariate age (see **Table 2.**). Correlating age with the SCR of the three phases, a significant negative correlation was yielded: r (131) = -0.27, p = .002. Consequently, older participants expressed an overall lower SCR in all three phases (pre-acquisition, 1. acquisition and 2. acquisition phase), regardless of the stimulus type.

Table 2. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding age on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for sex as covariate of no interest)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,130) = 5.77, **p = .018**, η^2 = .04	F (1,130) = 1.26, p = .263, η^2 = .01	F (2,233) =4.87, **p = .011**, η^2 = .04	F (2,238) = 2.35, p = .103, η^2 = .02
Valence	F (1,130) = 2.02, p = .158, η^2 = .02	F (1,130) = 1.06, p = .306, η^2 = .01	F (2,229) = 0.47, p = .600, η^2 = .004	F (2,244) = 8.21, **p < .001**, η^2 = .06
US expectancy	F (1,130) = 11.31, **p = .001**, η^2 = .08	F (1,130) = 5.93, **p = .016**, η^2 = .04	F (2,219) = 3.29, **p = .047**, η^2 = .03	F (2,257) = 10.67, **p < .001**, η^2 = .08
SCR	F (1,130) = 9.85, **p =.002**, η^2 = .07	F (1,130) = 0.22, p = .639, η^2 = .002	F (2,234) = 0.26, p = .747, η^2 = .002	F (2,236) = 0.19, p = .804, η^2 = .001

Moreover, in this context Pearson correlations were created between age and such effects including the factor stimulus type (see **Table 2.**), pursuant to a method presented by Andreatta and colleagues (2020). Hence, for the valence ratings regarding the significant three-way interaction of stimulus x phase x age (F (2,244) = 8.21, p < .001, η^2 = .06, see **Table 2.**) a differential score was built, first, for the 1. acquisition phase, i.e. the safety cue CS- was subtracted from danger cue CS+ (ACQ 1[CS+ minus CS-]), and, then, also for the 2. acquisition phase (ACQ 2 [CS+ minus CS-]). Afterwards the differential score between the differential score of the 1. acquisition phase and the differential score of the 2. acquisition score was calculated (ACQ 2 [CS+ minus CS-] – ACQ 1 [CS+ minus CS-]). Further, a Pearson correlation was created between this latter differential score and age. A not significant positive correlation resulted (r (131) = 0.10, p = 0.277). Both Pearson correlations for the differential scores of the 1. acquisition phase (r (131) = 0.033, p = 0.705) and, also, for the 2. acquisition phase (r (131) = 0.117, p = 0.180) respectively with age did not reach significance neither.

Regarding the significant two-way interaction of stimulus type x age for the US expectancy (F (1,130) = 5.93, p = .016, η^2 = .04, see **Table 2.**), means of each stimulus, i.e. CS- and CS+, averaged over the 1. and 2. acquisition phases were built. Subsequently, the differential score was created through subtracting the mean of the safety cue CS- from the mean of the danger cue CS+. A significant positive correlation (r (131) = 0.23, p = .009) could be detected out of it and age, meaning that with growing age the differentiation between CS- and CS+ got better (see **Figure 7.**).

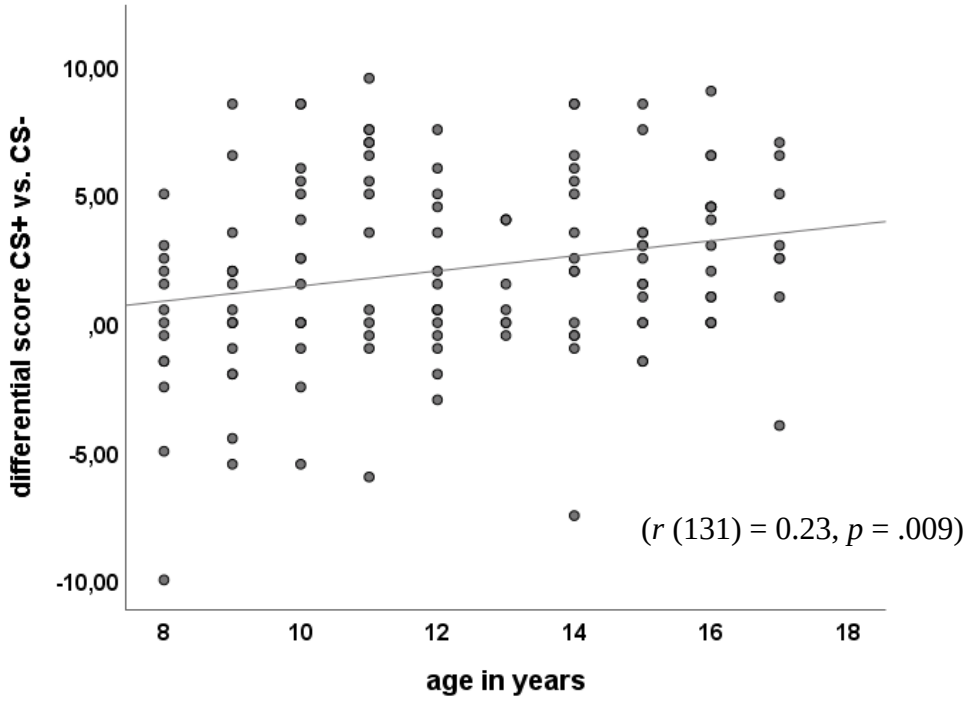


Figure 7. Correlation between age and the differential score between CS+ and CS-, whereby both stimulus types were averaged over the 1. and 2. acquisition phase, for US expectancy ratings. An enhanced discrimination between CS+ and CS- with an increasing age was indicated by the significant positive correlation.

Concerning the significant three-way interaction of stimulus type x phase x age for the US expectancy ratings (F (2,257) = 10.67, p < .001, η^2 = .08), another time, differential scores between the safety and danger cue were created for each of the two phases, i.e. for the 1. and 2. acquisition phase separately. Afterwards, the differential score of the 1. acquisition phase was subtracted from the differential score of the 2. acquisition score (ACQ 2 [CS+ minus CS-] – ACQ 1 [CS+ minus CS-]). A significant negative correlation (r (131) = -0.34, p < .001, see **Figure 8.**) emerged between the calculated differential score and age. This displays that with

growing age, the differentiation between CS- and CS+ of the US expectancy ratings decreased after the 2. acquisition phase in comparison to after the 1. acquisition phase or, vice versa, that with decreasing age the differentiation between CS- and CS+ of the US expectancy ratings grew after the 2. acquisition phase in comparison to after the 1. acquisition phase. In order to unravel these effects, the differential scores after every phase, i.e. the 1. and 2. acquisition phase, were correlated with age, revealing a significant positive correlation between age and the differential score of the 1. acquisition phase (r (131) = 0.38, $p < 0.001$, see **Figure 9.(a)**), however, not for the 2. acquisition phase (r (131) = 0.001, $p = .987$, see **Figure 9.(b)**). This indicates, that with increasing age the probands showed a larger differentiation between the CS- and CS+ after the 1. acquisition phase or, vice versa, with decreasing age the participants discriminated less between CS- and CS+ after the 1. acquisition phase, which was not the case anymore after the 2. acquisition phase.

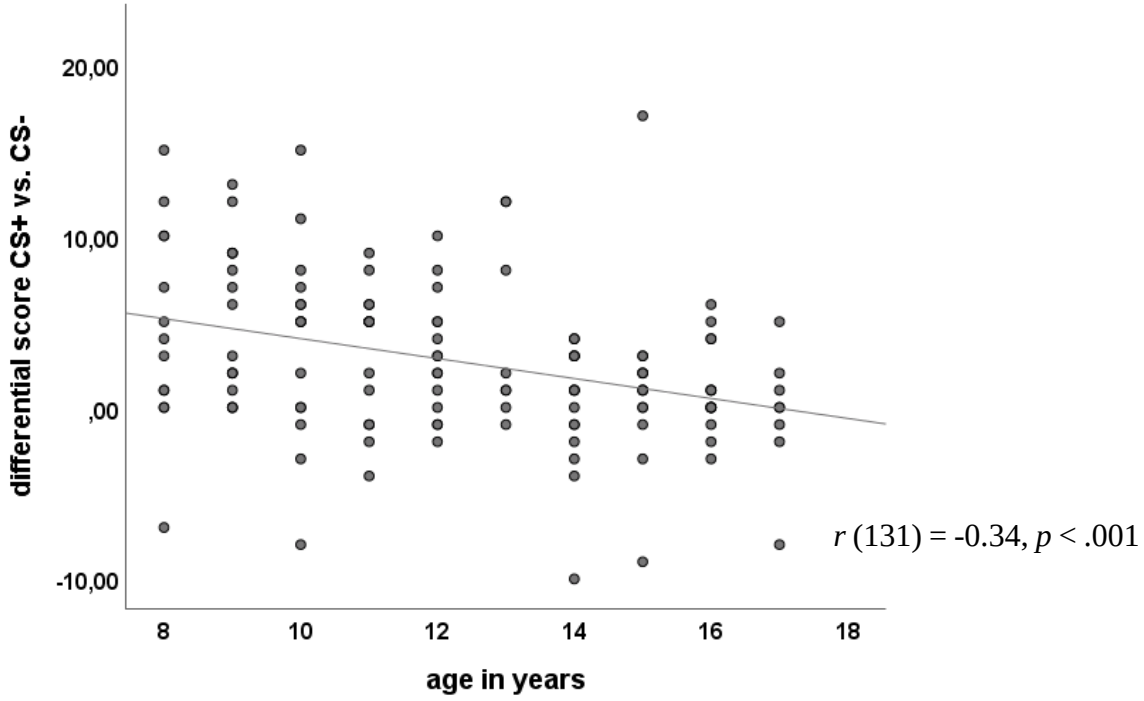
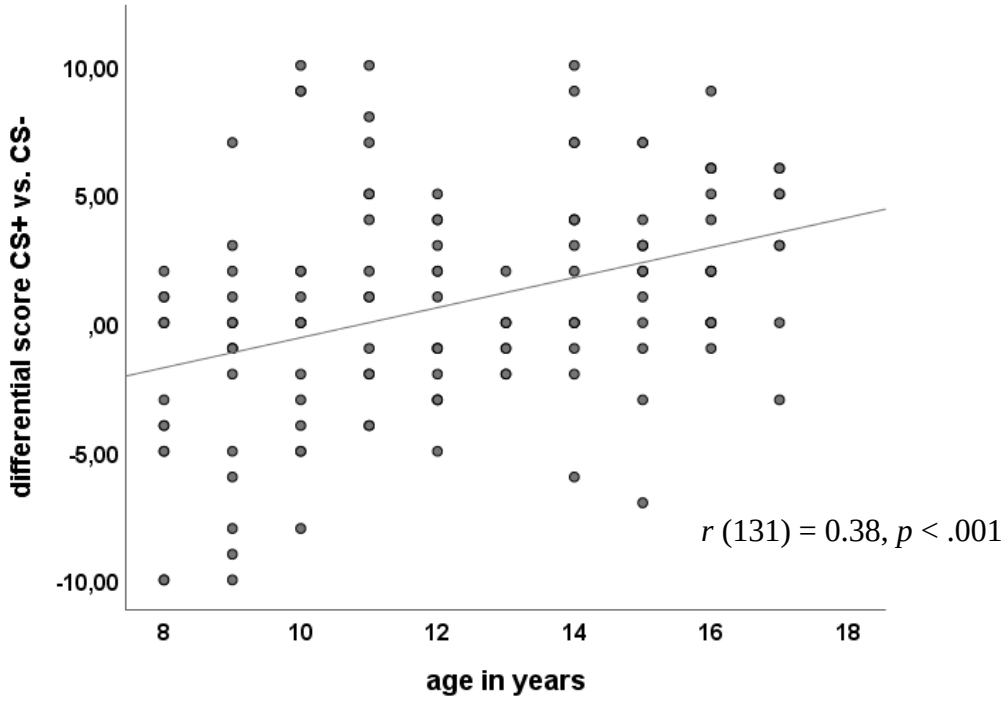


Figure 8. Correlation between age and the differential score of the two separate differential scores of each acquisition phase (ACQ 2 [CS+ minus CS-] – ACQ 1 [CS+ minus CS-]). The significant negative correlation indicates, that with growing age the discrimination between CS- and CS+ for the US expectancy ratings declined after the 2. acquisition phase (ACQ 2) compared to after the 1. acquisition phase (ACQ 1).

(a)



(b)

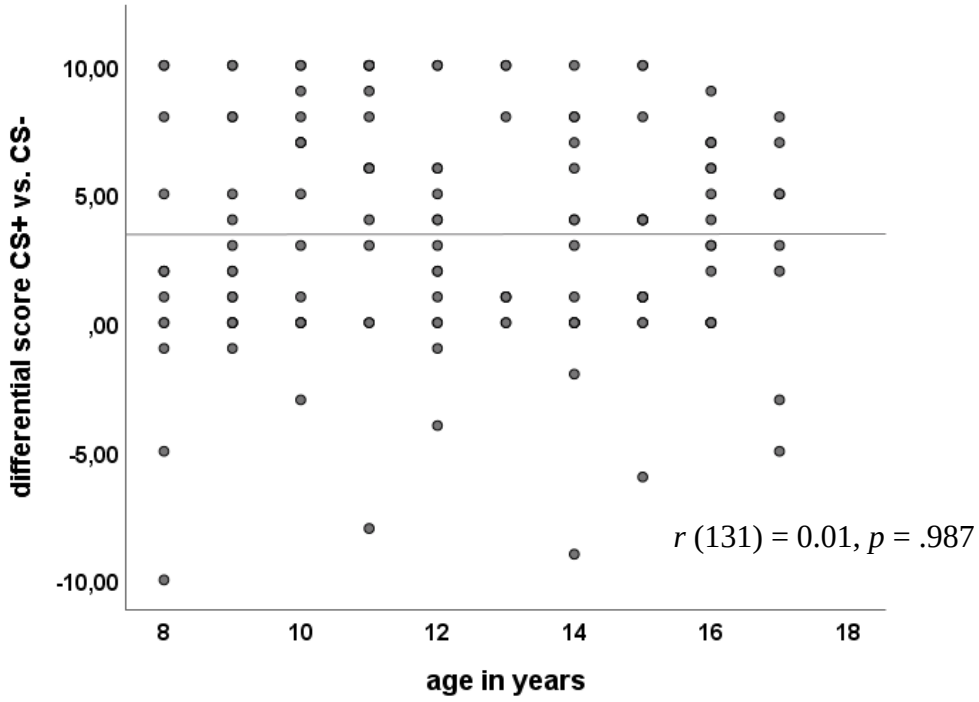
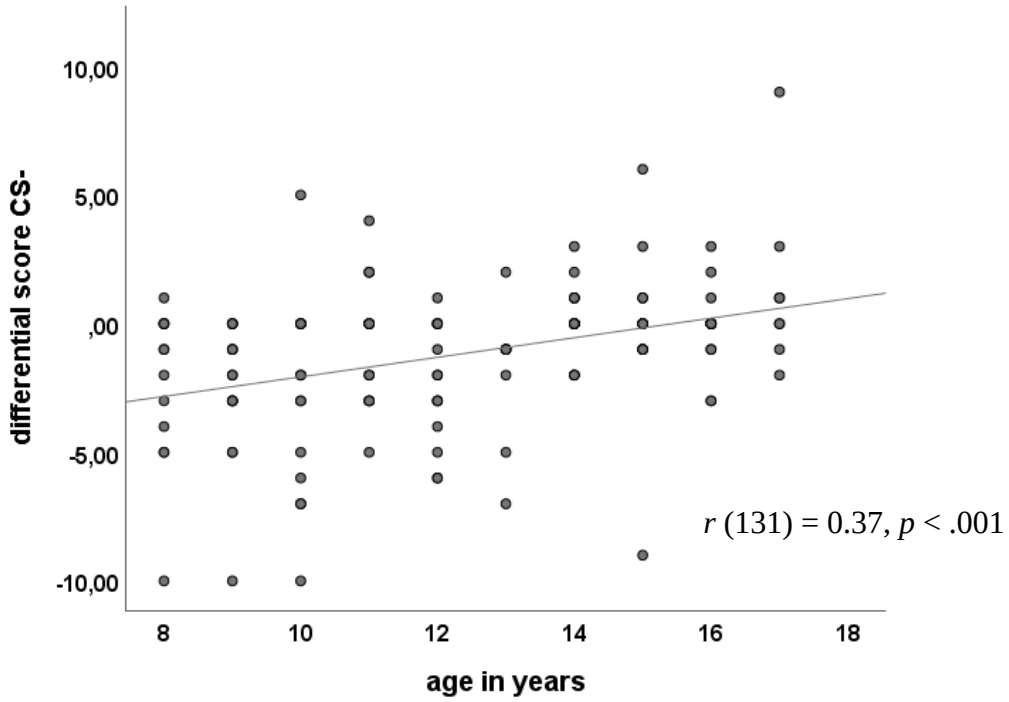


Figure 9. Correlations between age and differential scores between CS+ and CS- for US expectancy ratings for **(a)** the 1. acquisition phase (ACQ 1) and **(b)** the 2. acquisition phase (ACQ 2). A better differentiation between CS+ and CS- with increasing age after ACQ 1 is described by the significant positive correlation. No such significant correlation with age appeared after ACQ 2.

Further on, also for the US expectancy ratings a significant positive correlation turned up between age and the difference between the 1. and 2. acquisition phase for the safety cue CS- (r (131) = 0.37, p < .001, see **Figure 10.(a)**). Thus, with growing age the differentiation between the safety cue CS- between the 1. and 2. acquisition phase increased. This outcome suggests that the quicker recognition of the safety cue CS- as a secure stimulus seems to cause variations depending on age. For the danger cue CS+ a significant negative correlation was found (r (131) = -.18, p = .038, see **Figure 10.(b)**), which though did not survive Bonferroni correction.

(a)



(b)

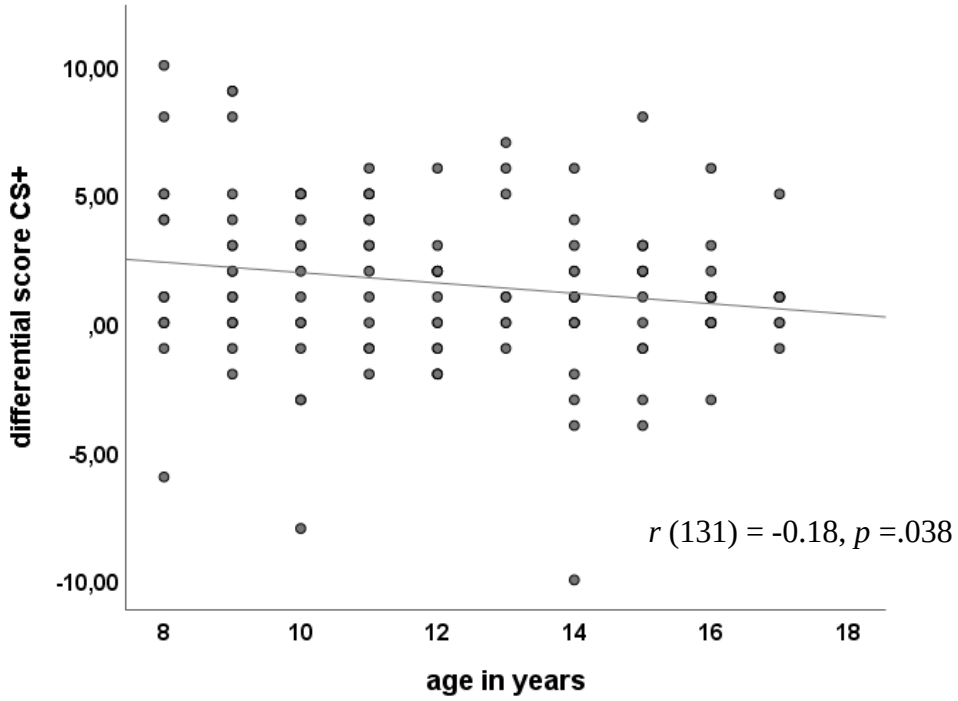


Figure 10. Correlation between age and the difference between the 1. acquisition phase (ACQ 1) and the 2. acquisition phase (ACQ 2) concerning **(a)** the safety cue CS- and **(b)** the danger cue CS+ for the US expectancy ratings. A better differentiation for CS- between ACQ 1 and ACQ 2 with increasing age is described by the significant positive correlation. The negative correlation for CS+ did not survive the Bonferroni correction.

Besides, for the arousal ratings a significant interaction of phase x age (F (2,233) = 4.87, p = .011, η^2 = .04) was observed. By means of Pearson correlations, analogous to the handling with interactions with stimulus type, between age and the arousal ratings of each phase, this interaction effect was looked at, in order to understand what it describes: With increasing age, the arousal ratings became generally smaller after the 1. and 2. acquisition phase (1. acquisition: r (131) = -0.21, p = .014; 2. acquisition: r (131) = -0.27, p = .002). No such variation based on age could be observed after the pre-acquisition phase (pre-acquisition: r (131) = -0.03, p = .724).

Additionally, there was a significant interaction of phase x age (F (2,219) = 3.29, p = .047, η^2 = .03) for the US expectancy ratings. As conducted for arousal, only for the US expectancy here, Pearson correlations were calculated between age and the US expectancy ratings of each phase to get an idea about the meaning of this interaction: With increasing age the participants expressed generally a smaller US expectancy after the pre-acquisition phase (r

(131) = -0.34, $p < .001$) and, also, after the 1. acquisition phase (r (131) = -0.25, $p = .004$). This effect, based on age, could not be detected anymore after the 2. acquisition phase (r (131) = -0.128, $p = .143$), i.e. there was no variation resulting from differing ages.

2.1.2 Generalization phases

Subjective ratings:

For the arousal ratings a significant main effect of stimulus type (F (3,446) = 34.30, $p < .001$, $\eta^2 = .21$) was observed displaying an uptrend from the safety cue CS- to the danger cue CS+. The probands rated the CS+ as significantly more arousing (t (132) = -8.00, $p < .001$) than the CS- (see **Figure 11.**). The participants generalized conditioned fear up to the both morphs GS1 and GS2 as these stimuli were rated as significantly more arousing (GS1: t (132) = -6.05, $p < .001$; GS2: t (132) = -3.57, $p = .001$) as compared to the safety cue CS- (see **Figure 11**.). No significant differences were found for the two morphs GS3 (t (132) = -1.91, $p = .058$) and GS4 (t (132) = -0.85, $p = .398$). The generalization gradient contained a significant linear (F (1,132) = 71.47, $p < .001$, $\eta^2 = .35$) and a quadratic trend (F (1,132) = 11.83, $p = .001$, $\eta^2 = .08$).

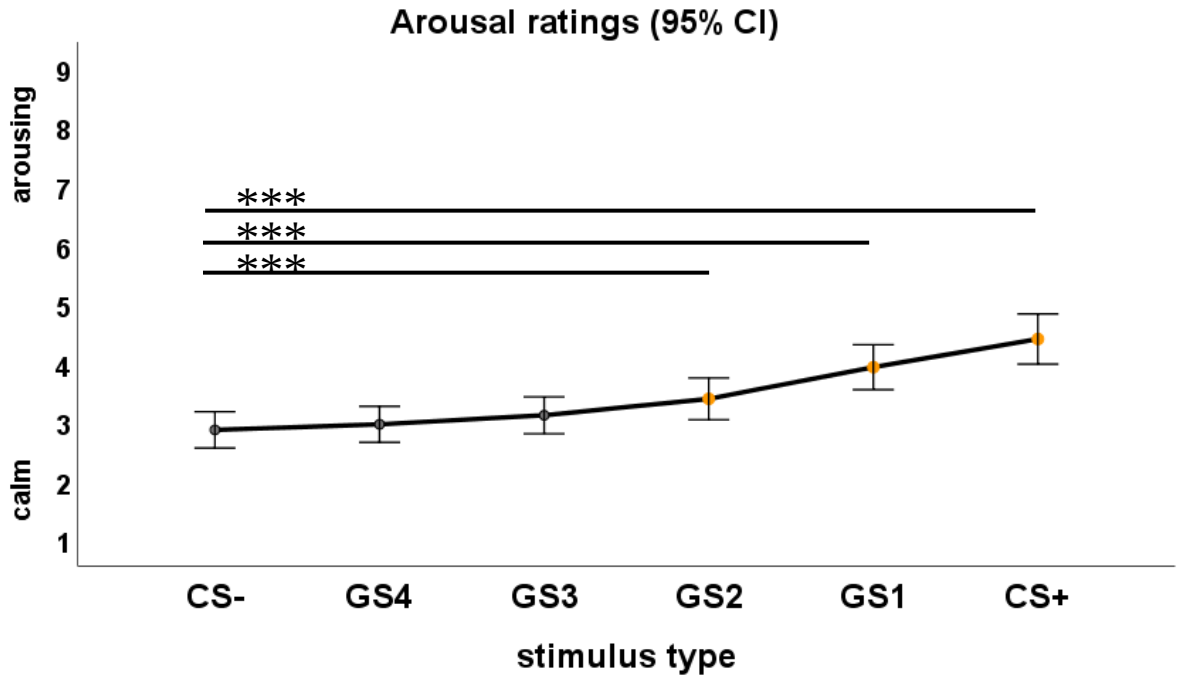


Figure 11. Generalization gradient for the arousal ratings (with confidence intervals (CI)) averaged over the 1. and 2. generalization phase. Extent of generalization (each stimulus (CS+ and GS1-GS4) compared to CS-) illustrated with orange dots. ***$p < .001$

In respect of the valence ratings, a significant main effect of stimulus type (F (3,397) = 31.72, p < .001, η^2 = .19) was revealed indicating a downtrend from CS- to CS+. The participants rated the danger cue as significantly more negative (t (132) = 7.25, p < .001) compared to the safety cue (see **Figure 12.**). The probands generalized conditioned fear up to GS1 and GS2 due to significantly smaller ratings regarding these stimuli (GS1: t (132) = 5.56, p < .001; GS2: t (132) = 3.00, p = .003) in comparison to the CS- (see **Figure 12.**). There were no significant differences for GS3 and GS4 (all p values ≥ .362). The generalization gradient combined a significant linear (F (1,132) = 57.46, p < .001, η^2 = .30) and a quadratic trend (F (1,132) = 16.26, p < .001, η^2 = .11).

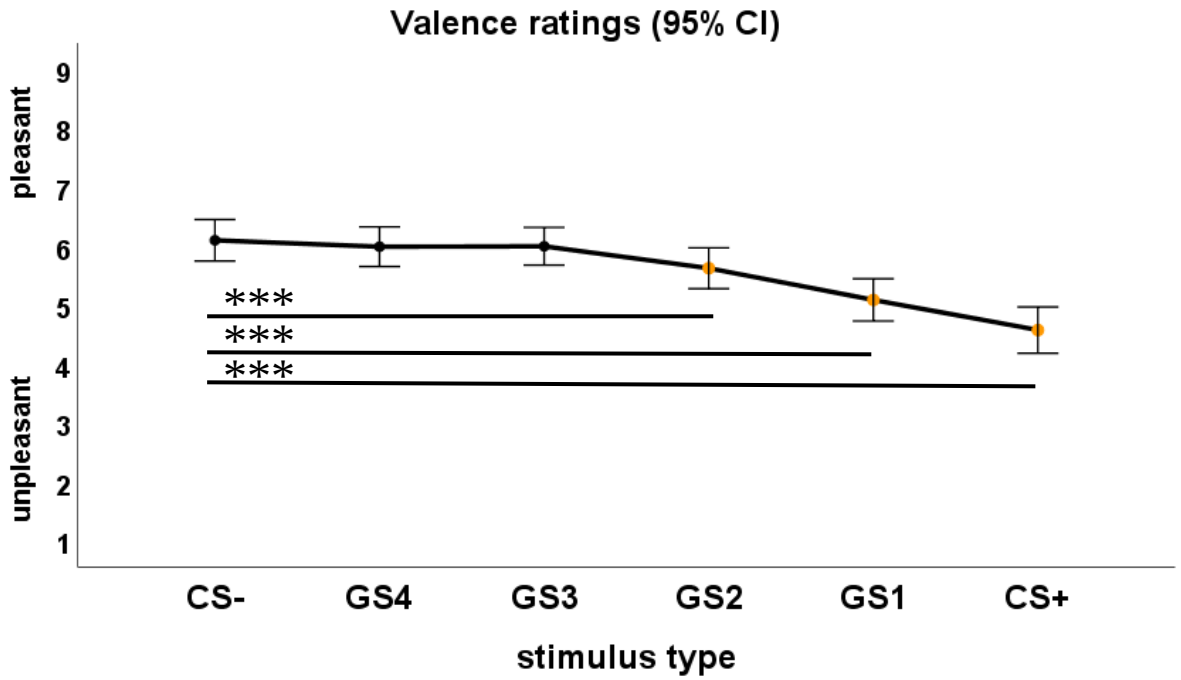


Figure 12. Generalization gradient for the valence ratings (with confidence intervals (CI)) averaged over the 1. and 2. generalization phase. Extent of generalization (each stimulus (CS+ and GS1-GS4) compared to CS-) illustrated with orange dots. ***p < .001

As for arousal, also for the US expectancy ratings, a significant main effect of stimulus type (F (3,350) = 91.35, p < .001, η^2 = .41) was found presenting an uptrend from the safety towards the danger cue. The participants showed higher US expectancy to the CS + (t (132) = -12.14, p < .001) than to the CS- (see **Figure 13.**). In Addition, the participants generalized conditioned fear, as for arousal and valence, up to GS1 and GS2 showing significantly higher US expectancy ratings (GS1: t (132) = -9.45, p < .001; GS2: t (132) = -4.68, p < .001) as relative

to the CS- (see **Figure 13.**). No significant differences were revealed for GS3 (t (132) = -2.11, p = .037, did not survive the Bonferroni correction) and GS4 (t (132) = -.18, p = .861). Furthermore, there was a significant main effect of phase (F (1,132) = 5.78, p = .018, η^2 = .04) and a significant interaction of stimulus type x phase (F (4,540) = 3.89, p = .004, η^2 = .03) for US expectancy. If comparing the 1. to the 2. generalization phase, it gets obvious that the participants rated the US expectancy mainly higher in the 1. phase. Regarding the significant two-way interaction of stimulus type x phase, there was a shift to a better discrimination between the stimulus types from the 1. to the 2. generalization phase as detected via post hoc t-tests (CS-: t (132) = 2.53, p = .013; GS4: t (132) = 2.68, p = .008; GS3: t (132) = 3.06, p = .003; GS2: t (132) = 1.73, p = .086; GS1: t (132) =0.88, p = .383; CS+: t (132) = -1.88, p = .062; see **Figure 14**.). Whereas for the safety cue CS- and all morphs GS1-4, the participants expressed a lower US expectancy, towards the danger cue CS+, they displayed a higher US expectancy, finally, in the 2. generalization phase compared to the 1. generalization phase. Statistical analyses yielded a significant linear (F (1,132) = 153.28, p < .001, η^2 = .54) and a quadratic trend (F (1,132) = 47.17, p < .001, η^2 = .26) concerning the generalization gradient.

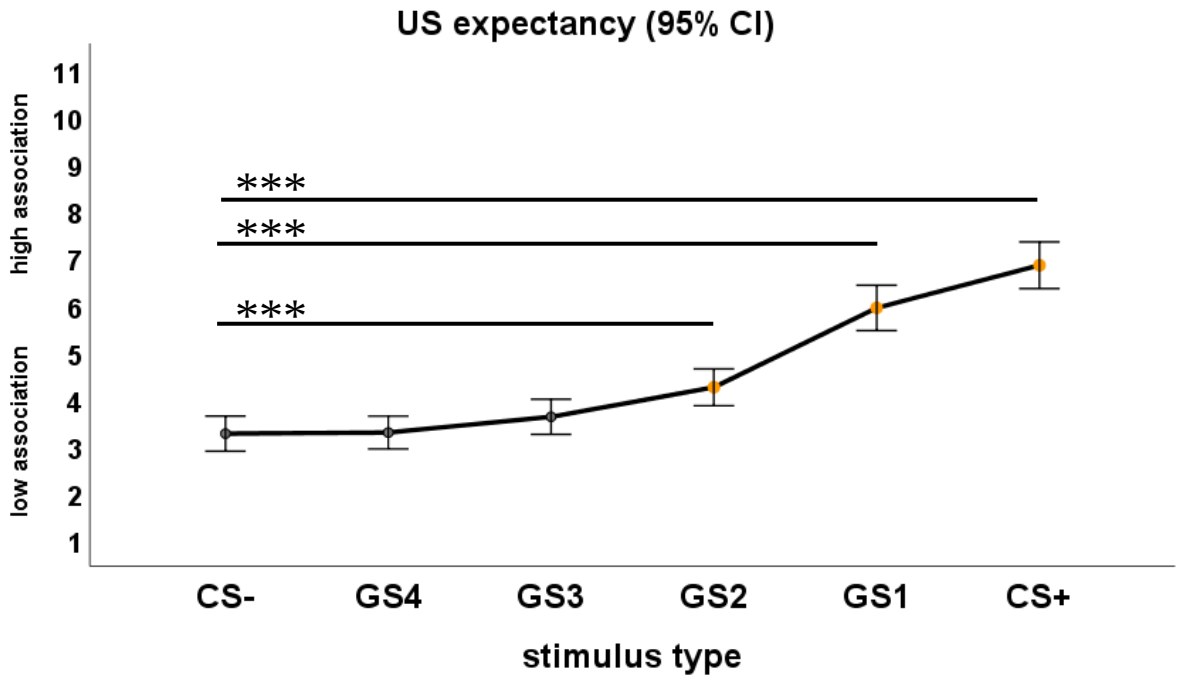


Figure 13. Generalization gradient for the US expectancy ratings (with confidence intervals (CI)) averaged over the 1. and 2. generalization phase. Extent of generalization (each stimulus (CS+ and GS1-GS4) compared to CS-) illustrated with orange dots. ***p < .001

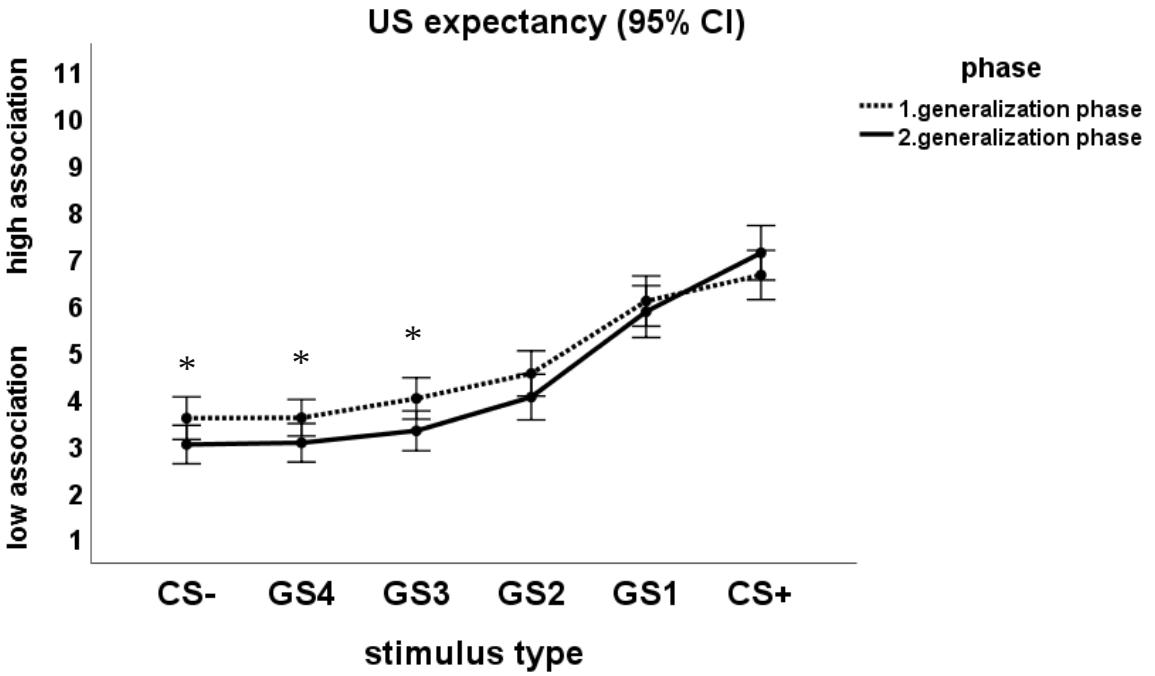


Figure 14. Generalization gradients for the US expectancy ratings (with confidence intervals (CI)) for the 1. and 2. generalization phase. A better discrimination between CS-, GS4, GS3, GS2, GS1 vs. CS+ arose for the entire sample after the 2. generalization phase. *$p < .025$ due to Bonferroni correction

Physiological reaction:

As for all subjective ratings, also, for the psychophysiological measure of SCR a significant main effect of stimulus type (F (3,442) = 6.23, $p < .001$, $\eta^2 = .05$) was observed. An uptrend from the CS- to the CS+ crystallized. Significant higher SCR was found towards the danger cue CS+ in comparison to the safety cue CS- (t (132) = -2.70, $p = .008$, see **Figure 15.**). Further, for the SCR there were no significant differences concerning GS1, GS2, GS3 and GS4 compared to CS- (GS1: t (132) = -1.86, $p = .066$, but all other p values ≥ .145, see **Figure 15.**). Moreover, a significant main effect of phase (F (1,132) = 9.07, $p = 0.003$, $\eta^2 = .06$) could be found, with overall higher SCR during the 2. generalization phase compared to the SCR during 1. generalization phase (post hoc t-tests: (CS-: t (132) = -1.44, $p = .152$; GS4: t (132) = -0.57, $p = .570$; GS3: t (132) = -2.74, $p = .007$; GS2: t (132) = -1.28, $p = .203$; GS1: t (132) = -1.72, $p = .087$; CS+: t (132) = -2.52, $p = .013$; see **Figure 16.**). Again as for the subjective ratings, there were a significant linear (F (1,132) = 11.58, $p = .001$, $\eta^2 = .08$) and a quadratic trend (F (1,132) = 9.35, $p = .003$, $\eta^2 = .07$) within the generalization gradient of the SCR.

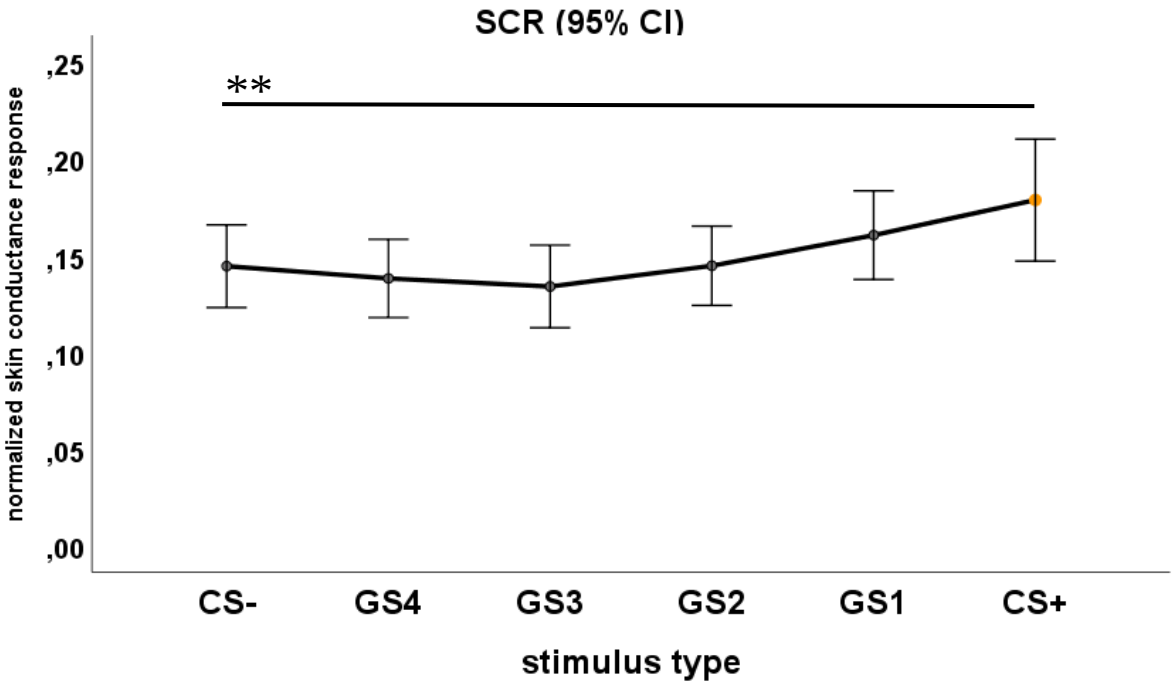


Figure 15. Generalization gradient for the skin conductance response (SCR, with confidence intervals (CI)) averaged over the 1. and 2. generalization phase. Extent of generalization (each stimulus (CS+ and GS1-GS4) compared to CS-) illustrated with orange dots. ***p* < .01

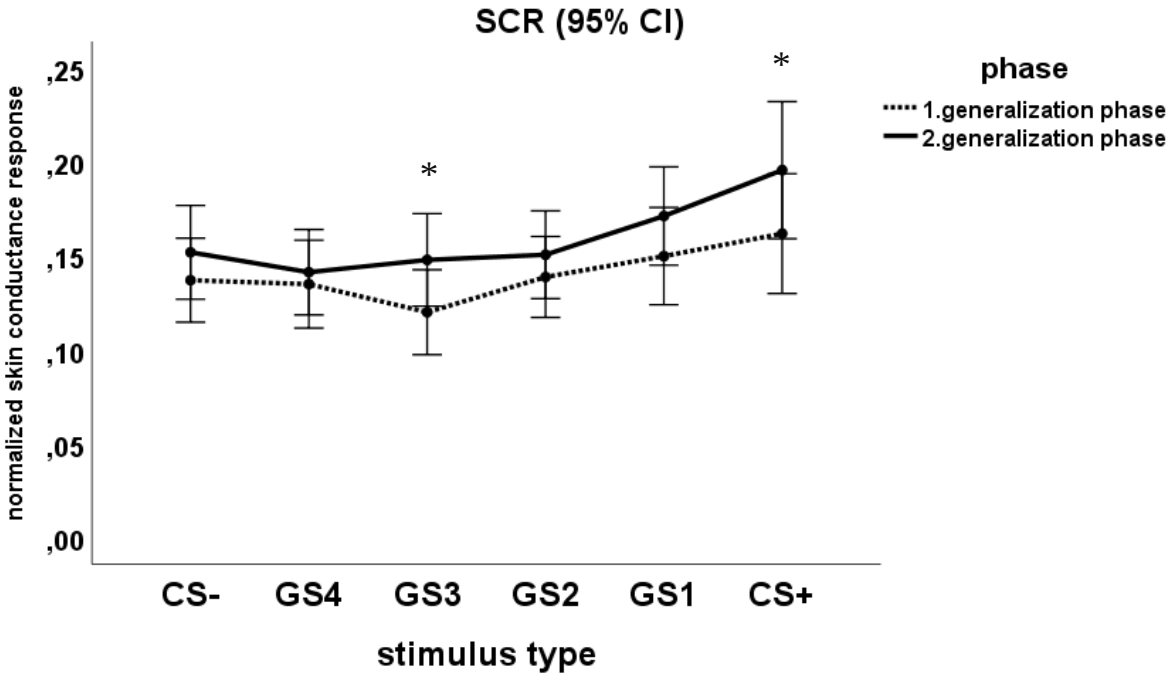


Figure 16. Generalization gradients for the skin conductance responses (SCR, with confidence intervals (CI)) for the 1. and 2. generalization phase. * $p < .025$ due to Bonferroni correction.

To sum it up, the subjective ratings of arousal, valence and US expectancy show a typical course of a generalization gradient of conditioned fear. This was less evident when looking at the generalization gradient based on SCR. Whereas for the subjective ratings fear was generalized up to the 2. morph GS2, counting from the danger cue CS+ (compare with **Figures 11.-13.**), for the SCR fear was generalized only towards CS+ (compare with **Figure 15.**). The fear generalization gradient included linear and quadratic trends for all four dependent variables. In addition, for the US expectancy ratings the degree of differentiation of the presented stimulus types improved from the 1. to the 2. generalization phase indicating an improvement of learning, i.e. a better discrimination of the stimulus types, within the whole sample.

Effects of age:

For the arousal ratings there was a significant main effect of the covariate age (F (1,130) = 12.04, p = .001, η^2 = .09). Thus, with increasing age the extent of the arousal ratings significantly decreased regardless of the stimulus and the phase, i.e. the participants expressed generally less excitement with higher age (r (131) = -0.29, p = .001). Concerning the generalization gradient neither a linear (F (1,130) = 3.79, p = .054, η^2 = .03) nor a quadratic trend (F (1,130) = 0.86, p = .355, η^2 = .01) could be detected anymore.

Also, in regard to the valence ratings a significant main effect of the covariate age (F (1,130) = 4.94, p = .028, η^2 = .04) was found. Hence, with growing age the valence ratings significantly increased independent of the stimulus and the phase, i.e. the probands showed generally a more pleasant state with higher age compared to younger participants (r (131) = 0.21, p = .016). A linear trend (F (1,130) = 6.75, p = .010, η^2 = .05), but no quadratic trend (F (1,130) = 0.01, p = .924, η^2 < .001) any longer, was contained in the generalization gradient.

For the US expectancy a significant main effect of the covariate age (F (1,130) = 14.97, p < .001, η^2 = .10) was revealed, too. Therefore, the older the probands were, the lower their stated ratings of US expectancy were, i.e. the less they expected an aversive noise in general independent of phase and stimuli (r (131) = -0.33, p < .001). Within the generalization gradient neither a linear (F (1,130) = 2.97, p = .087, η^2 = .02) nor a quadratic trend (F (1,130) = 0.85, p = .771, η^2 = .001) were present anymore.

Like for all subjective ratings, also for the amplitude of SCR there was a significant main effect of the covariate age (F (1,130) = 16.33, p < .001, η^2 = .11). With higher age the participants displayed an overall smaller SCR regardless of stimuli or phase (r (131) = -0.35, p

< .001). The generalization gradient comprised a linear trend (F (1,130) = 4.43, p = .037, η^2 = .03), however, no quadratic trend (F (1,130) = 1.03, p = .313, η^2 = .01) any longer.

Table 3. **Results of ANCOVAs for the 1. and 2. generalization phases.** Effects regarding age on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for sex as covariate of no interest)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,130) = 12.04, **p = .001**, η^2 = .09	F (3,439) = 0.86, p = .473, η^2 = .01	F (1,130) = 0.13, p = .718, η^2 = .001	F (5,585) = 1.72, p = .137, η^2 = .01
Valence	F (1,130) = 4.94, **p = .028**, η^2 = .04	F (3,388) = 0.71, p = .547, η^2 = .01	F (1,130) = 0.78, p = .378, η^2 = .01	F (5,617) = 0.96, p = .442, η^2 = .01
US expectancy	F (1,130) = 14.97, **p < .001**, η^2 = .10	F (3,343) = 0.61, p = .586, η^2 = .01	F (1,130) = 1.40, p = .239, η^2 = .01	F (4,532) = 1.97, p = .096, η^2 = .02
SCR	F (1,130) = 16.33, **p < .001**, η^2 = .11	F (3,435) = 0.42, p = .764, η^2 = .003	F (1,130) = 0.30, p = .585, η^2 = .002	F (5,599) = 0.29, p = .905, η^2 = .002

Additionally, a closer look shall be taken concerning the extent of generalization of conditioned fear and age. In accordance with a technique elucidated by Lenaert and colleagues (2016), a generalization index (GI) was created for every proband aiming at giving details about the individual extent of generalization of conditioned fear. Therefore, all US expectancy ratings of the morphs were added up and divided through the individual ratings of the danger cue CS+, i.e. GI = (GS1 + GS2 + GS3 + GS4) / CS+. It is interpreted as follows: With an increasing GI score the extent of generalization grows.

As the interaction effect of stimulus type x age was significant pursuant to the US expectancy ratings in the acquisition part, they, i.e. the US expectancy ratings, were explored exemplifying. A Pearson correlation was built between the GI score of the 1. generalization phase of the US expectancy and age, which was negative (r (131) = -0.19, p = .033, see **Figure 17.**). Thus, with increasing age, the GI score diminishes indicating a smaller extent of generalization, or, vice versa with decreasing age the GI score grows displaying a bigger extent of generalization. (2. generalization phase: r (131) = -0.167, p = .055; 1. + 2. generalization phases put together: r (131) = -0.169, p = .052).

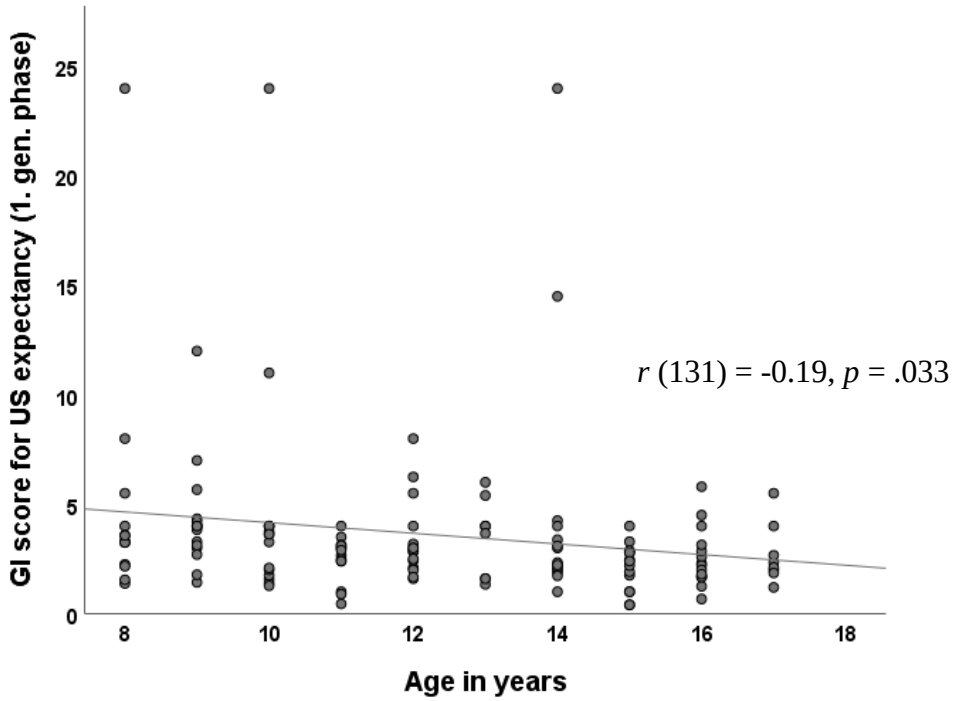


Figure 17. Correlation between age and the generalization index (GI) score calculated for the US expectancy ratings. With increasing age the fear generalization decreased as reflected by the significant negative correlation.

2.1.3 Extinction phases

Subjective ratings:

For arousal there were a significant main effect of stimulus type (F (1,132) = 14.30, p < .001, η^2 = .10) and a significant main effect of phase (F (2,247) = 13.14, p < .001, η^2 = .09), but they did not result in a significant interaction of stimulus type x phase (F (2,245) = 0.23, p = .782, η^2 < .00). So, the ratings for the CS+ were generally higher than for the CS- in every extinction phase as can be seen in **Figure 18.** (1. extinction phase: t (132) = -2.88, p = .005; 2. extinction phase: t (132) = -3.22, p = .002; 3. extinction phase: t (132) = -3.17, p = .002). And from phase to phase, the ratings for the safety and the danger cue, taken together, went down.

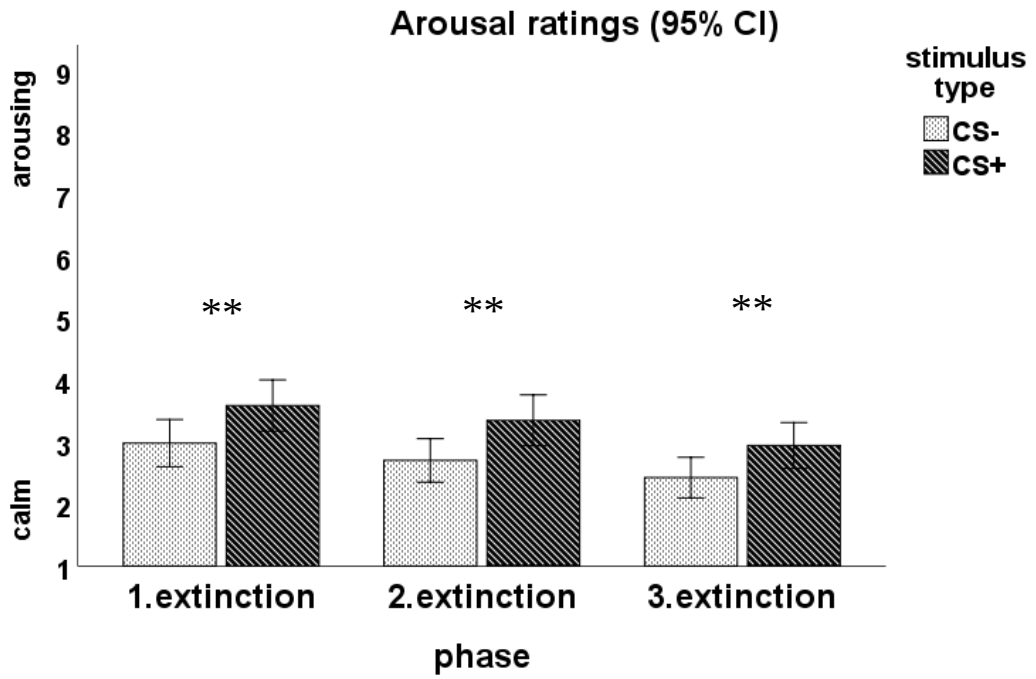


Figure 18. Arousal ratings (with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the 1., 2. and 3. extinction phase. **$p < .01$

In regard to valence, only a significant main effect of stimulus type (F (1,132) = 15.12, $p < .001$, $\eta^2 < .10$, see **Figure 19.**) could be detected with higher ratings towards the safety cue in comparison to the danger cue within each extinction phase (1. extinction phase: t (132) = 4.38, $p < .001$; 2. extinction phase: t (132) = 2.63, $p = .010$; 3. extinction phase: t (132) = 2.53, $p = .013$). Neither a significant main effect of phase (F (2,247) = 1.96, $p = .146$, $\eta^2 < .02$) nor a significant interaction effect of stimulus type x phase (F (2,239) = 2.05, $p = .136$, $\eta^2 = .02$) were yielded.

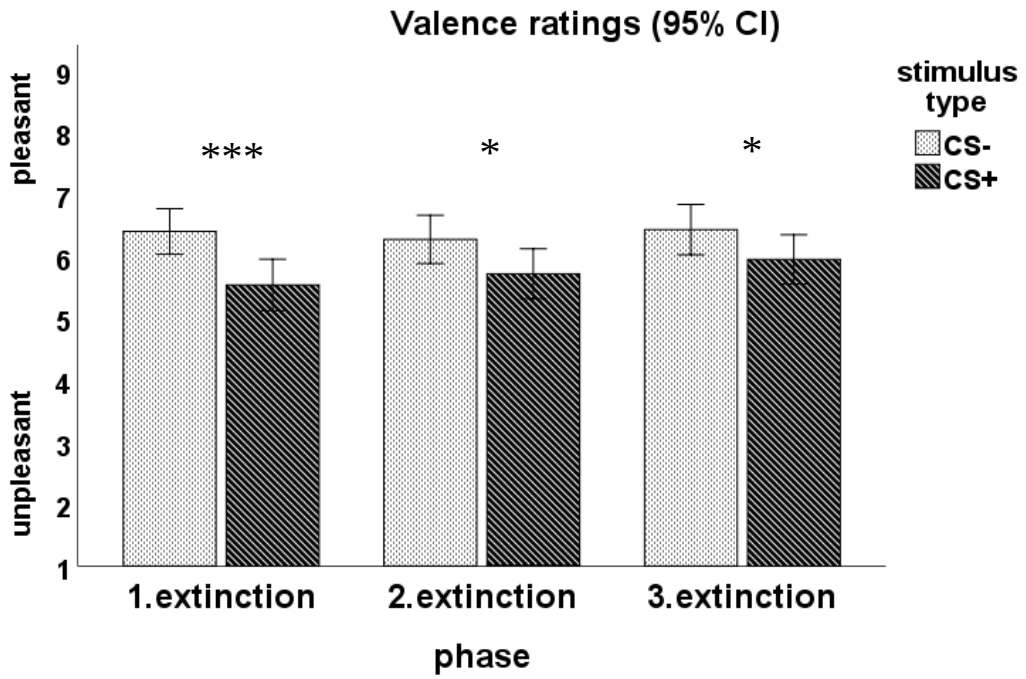


Figure 19. Valence ratings (with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the 1., 2. and 3. extinction phase. ***$p < .001$**;** *$p < .05$

Concerning the US expectancy, both a significant main effect of stimulus type (F (1,132) = 60.39, $p < .001$, $\eta^2 = .31$) and of phase (F (2,252) = 27.85, $p < .001$, $\eta^2 = .17$) were found resulting in a significant interaction of stimulus type x phase (F (2,255) = 6.63, $p = .002$, $\eta^2 = .05$). In general, the ratings for the danger cue were significantly higher compared to the safety cue in all extinction phases (1. extinction phase: t (132) = -7.89, $p < .001$, 2. extinction phase: t (132) = -6.01, $p < .001$, 3. extinction phase: t (132) = -5.38, $p < .001$, see **Figure 20.**). Furthermore, from the 1. extinction phase via the 2. extinction phase to the 3. extinction phase both ratings, i.e. CS- and CS+, fell, whereby the drop was stronger towards the CS+ than towards CS- (see **Figure 20.**).

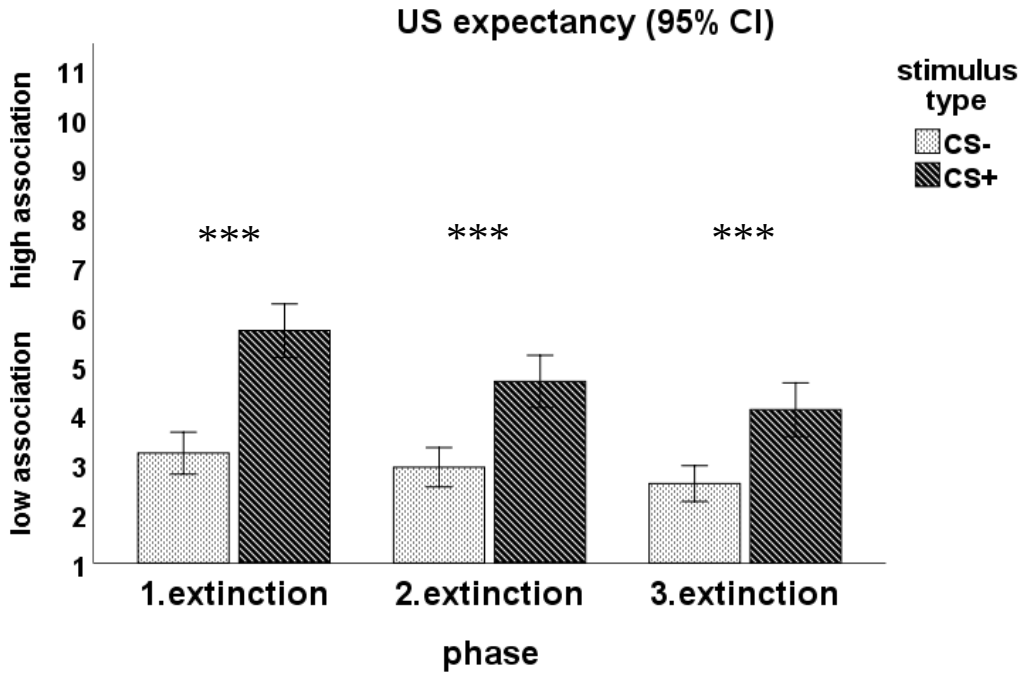


Figure 20. US expectancy ratings (with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the 1., 2. and 3. extinction phase. ***$p < .001$

Physiological reaction:

For the SCR a significant main effect of stimulus type (F (1,130) = 10.12, p = .002, η^2 < .07, see **Figure 21.**) was revealed reflecting an always stronger skin conductance response (SCR) regarding the CS+ compared to the CS- in every extinction phase (M_{CS+} = 0.14, SD_{CS+} = 0.01 vs. M_{CS-} = 0.12, SD_{CS-} = 0.01, t (130) = 3.18, p = .002). Neither a significant main effect of phase (F (2,260) = 0.64, p = .531, η^2 = .01) nor a significant interaction of stimulus type x phase (F (2,260) = 1.18, p = .309, η^2 = .01) could be observed.

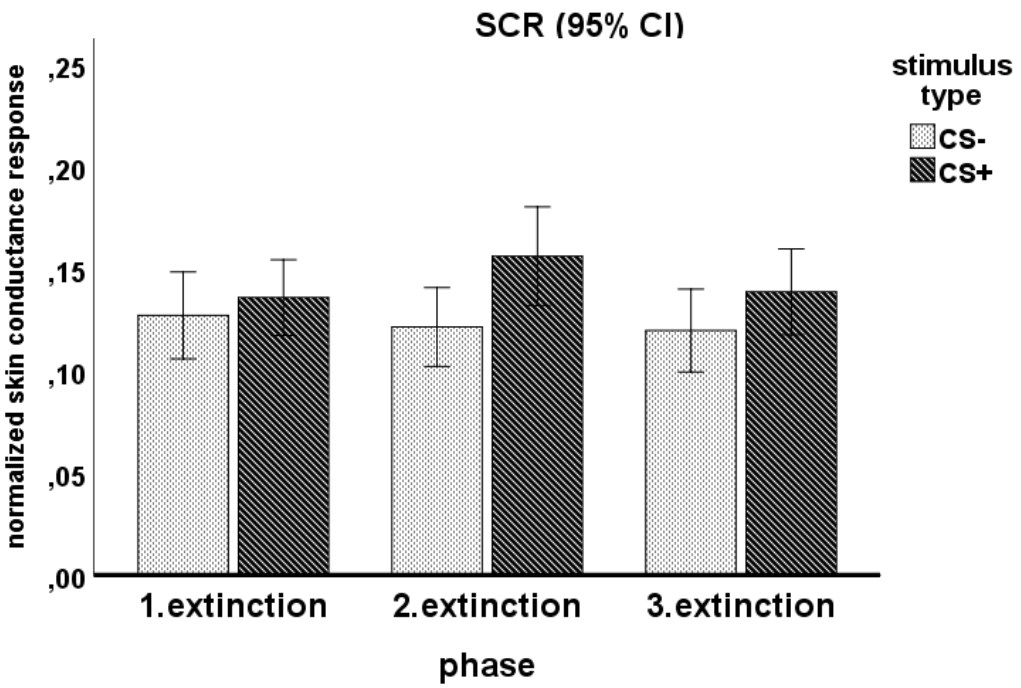


Figure 21. Skin conductance response (SCR, with confidence intervals (CI)) towards CS- (light bars) and CS+ (dark bars) after the 1., 2. and 3. extinction phase.

In total, the extinction was not successful. In fact, during all three extinction phases the participants distinguished significantly between the CS- and the CS+ regarding the arousal, valence as well as US expectancy ratings. Consistently, there was a significant main effect of stimulus type for the SCR, but its forms were not that strong in comparison with the subjective ratings. Further, the arousal and US expectancy ratings, independent of the stimulus type, decreased from phase to phase, although always maintaining the significant discrimination between the CS- and the CS+. In this special context, the drop for the US expectancy ratings from phase to phase was remarkably greater towards the CS+ than the CS-.

Table 4. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding age on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for sex as covariate of no interest)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,130) = 0.40, p = .528, η^2 = .003	F (1,130) = 2.39, p = .125, η^2 = .02	F (2,243) = 0.41, p = .649, η^2 = .003	F (2,241) = 1.22, p = .296, η^2 = .01
Valence	F (1,130) = 1.50, p = .223, η^2 = .01	F (1,130) = 5.65, **p = .019**, η^2 = .04	F (2,242) = 1.46, p = .234, η^2 = .01	F (2,235) = 0.52, p = .576, η^2 = .004
US expectancy	F (1,130) = 0.86, p = .356, η^2 = .01	F (1,130) = 0.21, p = .646, η^2 = .002	F (2,249) = 0.61, p = .539, η^2 = .01	F (2,249) = 2.39, p = .097, η^2 = .02
SCR	F (1,128) = 3.09, p = .081, η^2 = .02	F (1,128) = 0.49, p = .487, η^2 = .004	F (2,256) = 0.27, p = .765, η^2 = .002	F (2,256) = 0.85, p = .427, η^2 = .01

Effect of age:

For arousal there were no significant main effects of the covariate age nor significant interaction effects with age (see **Table 4.**).

A significant interaction effect of stimulus type x age (see **Table 4.**) was found regarding valence. Analogous to the two acquisition phases, a differential score was created between the CS+ and the CS-, whereby each stimulus type was averaged over the three extinction phases. Then, this differential score was correlated with age: a significant negative correlation resulted (r (131) = -0.25, p = .004). Thus, with growing age of the participants the differential score decreased (see **Figure 22.**). Additionally, a Pearson correlation between age and the CS+ was built, which was significant and negative (r (131) = -0.20, p = .024, see **Figure 23.**), however, the correlation for age and the CS- did not reach significance (r (131) = 0.09, p = .283, see **Figure 24.**), i.e. with increasing age the danger cue CS+ was rated less pleasant by the probands. As for the arousal and US expectancy ratings, also for the valence ratings no significant main effect of the covariate age nor further significant interaction effects with age could be observed (see **Table 4.**).

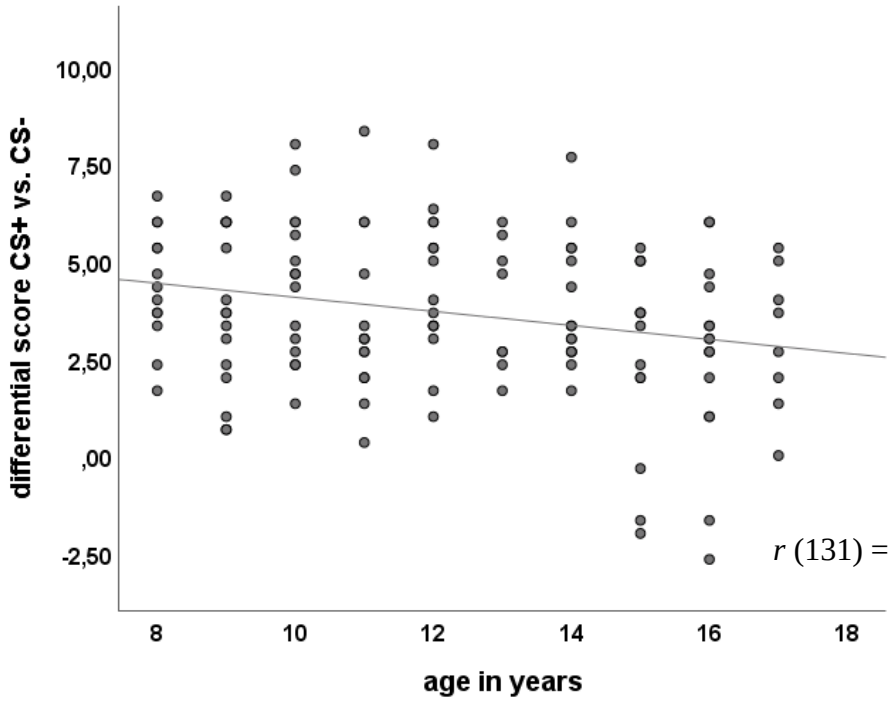


Figure 22. A Pearson correlation between age and the differential score between CS+ and CS- for the valence ratings (both stimulus types were averaged over the three extinction phases). The significant negative correlation indicates that the variation between CS+ and CS- diminished with increasing age.

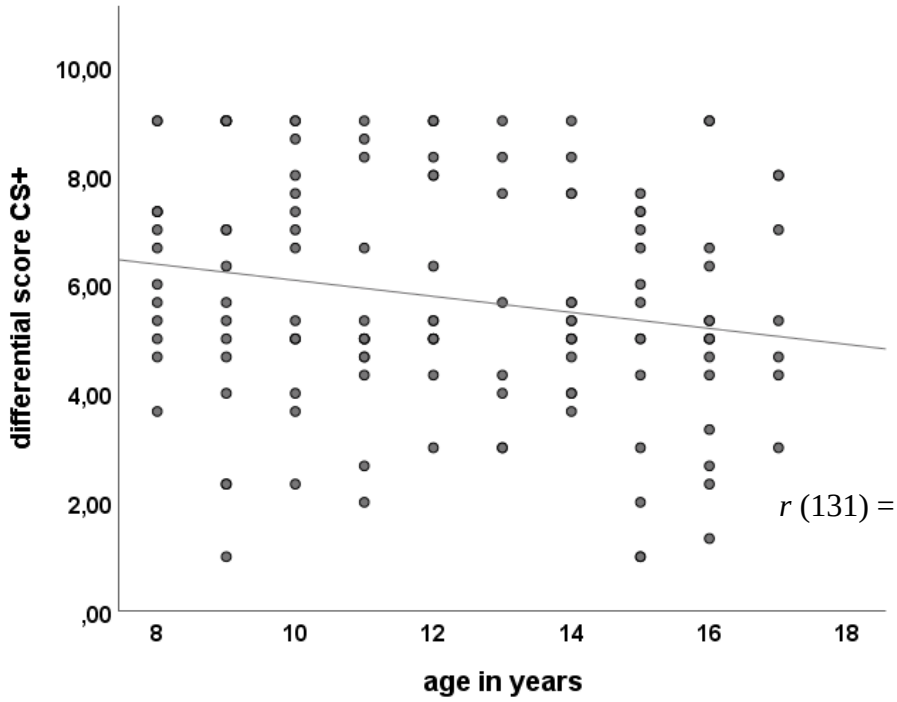


Figure 23. A Pearson correlation between age and the mean of the danger cue CS+, out of the averaged extinction phases, for the valence ratings.

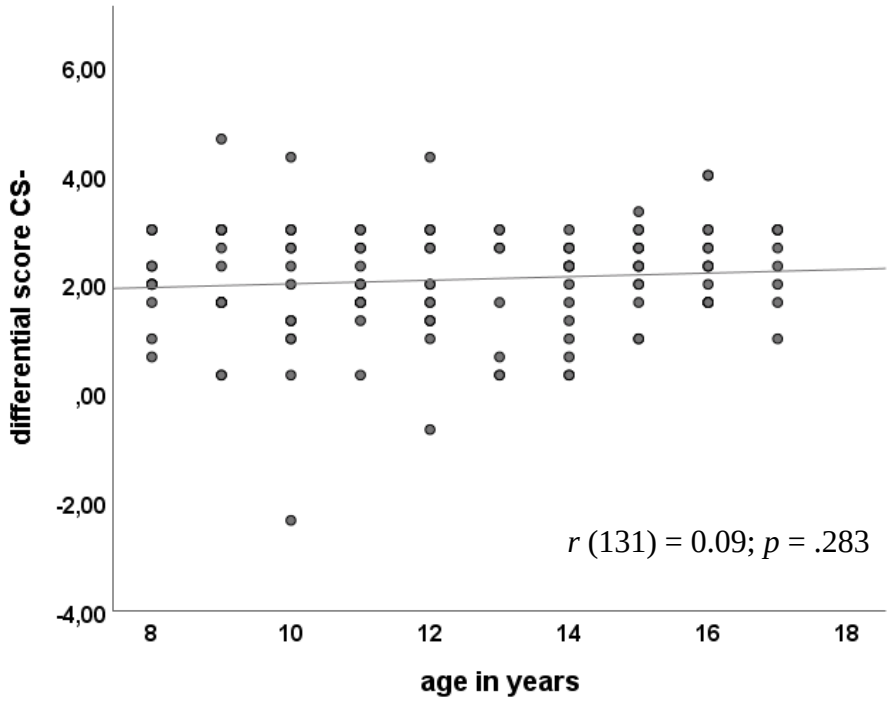


Figure 24. A Pearson correlation between age and the mean of the safety cue CS-, out of the averaged extinction phases, for the valence ratings.

As for arousal, also for the US expectancy ratings there were no significant main effects of the covariate age nor significant interaction effects with age (see **Table 4.**).

Physiological reaction:

Concerning the SCR, neither the main effect of the covariate age nor interaction effects with age were significant (see **Table 4.**).

3. Impact of trait anxiety in underage probands on fear conditioning, its generalization and extinction

As previously reported (see under **1.**), evidence for the role of trait anxiety, with regard to fear conditioning as well as for its generalization, is quite heterogenous. There are many studies evincing a connection between overgeneralization and anxiety disorders (e.g. in adolescents: El Bar et al., 2017; in adults: Lissek, et al., 2010) and, additionally, there is a recent meta-analysis providing support for such a positive linkage, when looking at the subclinical level of high trait anxiety in healthy adults (Sep et al., 2019). Moreover, in contrast to healthy underage probands, clinically anxious probands show an impairment of cue discrimination pointing to disrupted safety signal learning (in underage samples: Liberman et al., 2006; Waters

et al., 2009, Britton et al., 2013; in adult samples: Lissek et al., 2005, 2009; Duits et al., 2015), whereby trait anxiety could be even seen as a harbinger of anxiety disorders (Chambers et al., 2004).

Taking all these results into account, the hypothesis ergo states a positive correlation between high trait anxiety and an elevated generalization of conditioned fear, i.e. overgeneralization, in the sample. Thus, the observed association between subclinical levels of high anxious personality traits or even anxiety disorders and an enhanced generalization of conditioned fear shall also be determined in this minor sample.

For fear acquisition and extinction, an effective robust learning is expected with generally stronger fear reactions towards both the danger as well as the safety stimulus in high anxious probands. This hypothesis is mainly based on the outcomes of the meta-analysis of Dvir et al. (2019). Age and sex will be statistically considered (see further Tables in the APPENDIX) as covariates of no interest because there is evidence that girls have an elevated risk for clinically relevant anxiety (Lewinsohn, Gotlib, Lewinsohn, Seeley & Allen, 1998) and because the modulatory effect of age was already examined in the previous chapter (see under **2.**).

3.1 Results

In this part the impact of trait anxiety on fear acquisition, its generalization and extinction shall be investigated (statistically controlled for age and sex as covariates of no interest, see further Tables in the APPENDIX).

3.1.1 (Pre-)Acquisition phases

All main effects of the STAIC score as well as all interaction effects with the STAIC score are presented in **Table 5.** (statistically controlled for the covariates of no interest age and sex).

Table 5. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding the STAIC score on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for age and sex as covariates of no interest)

	main effect of STAIC	***stimulus type x STAIC***	***phase x STAIC***	***stimulus type x phase x STAIC***
arousal	F (1,129) = 1.19, p = .277, η^2 = .01	F (1,129) = 1.86, p = .175, η^2 = .01	F (2,233) = 2.58, p = .083, η^2 = .02	F (2,236) = 1.02, p = .355, η^2 = .01
valence	F (1,129) = 0.82, p = .336, η^2 = .01	F (1,129) = 0.18, p = .673, η^2 = .001	F (2,228) = 0.50, p = .584, η^2 = .004	F (2,241) = 1.11, p = .327, η^2 = .01
US expectancy	F (1,129) = 5.04, **p = .027**, η^2 = .04	F (1,129) = 0.001, p = .975, η^2 < .001	F (2,218) = 0.004, p = .992, η^2 < .001	F (2,255) = 1.26, p = .285, η^2 = .01
SCR	F (1,129) = 0.05, p = .817, η^2 < .001	F (1,129) = 4.68, **p = .032**, η^2 = .04	F (2,234) = 2.39, p = .099, η^2 = .02	F (2,236) = 1.82, p = .167, η^2 = .01

For the US expectancy ratings a significant main effect of the covariate STAIC score (F (1,129) = 5.04, p = .027, η^2 = .04) arose indicating a small positive association between higher STAIC scores and higher US expectancy ratings (r (131) = 0.06, p = .502, see **Figure 25.**).

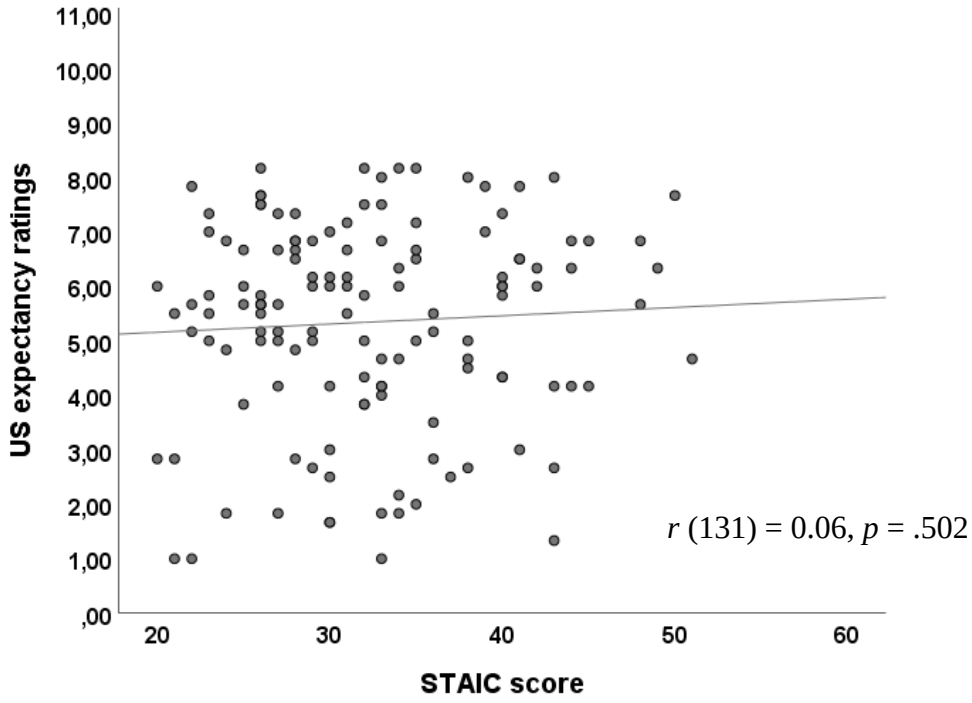


Figure 25. A Pearson correlation between the STAIC score and the US expectancy ratings averaged over the pre-acquisition, 1. and 2. acquisition phases. A small positive association between higher STAIC scores and higher US expectancy ratings is reflected by the positive correlation.

Moreover, a significant interaction of stimulus type x STAIC score (F (1,129) = 4.68, p = .032, η^2 = .04) could be found regarding the SCR. In order to understand this interaction, a differential score was built between the CS+ and the CS-, whereby each stimulus was averaged over the pre-acquisition, the 1. and the 2. acquisition phase. Then, this differential score was correlated with the STAIC score resulting in a negative, however, not significant correlation (r (131) = -0.13, p = .131, see **Figure 26.**). Hence, the discrimination between the danger and the safety cue decreased with a growing STAIC score. Looking at the CS+ and the CS- separately and correlating each stimulus with the STAIC score, two negative not significant correlations result: for the CS+ (r (131) = -0.14, p = .108) the SCR declined a little bit stronger with a growing STAIC score than for the CS- (r (131) = -0.05, p = .554). However, this effect is rather small.

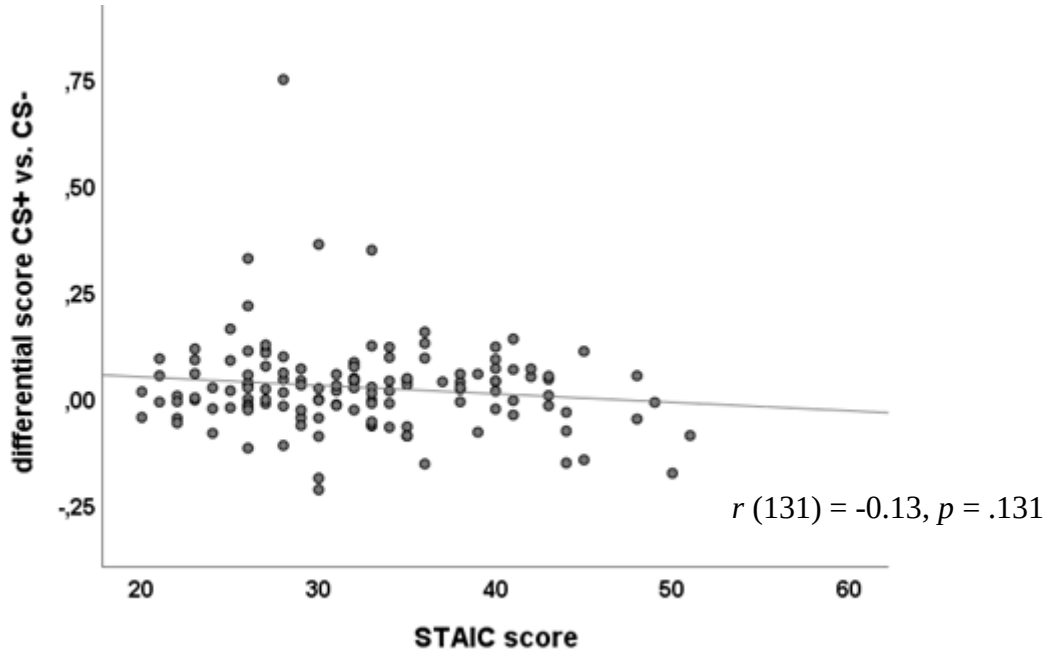


Figure 26. A Pearson correlation between the STAIC score and the differential score between CS+ and CS- for the SCR, whereby each stimulus type was averaged over the pre-acquisition, 1. and 2. acquisition phase. A smaller discrimination between CS+ and CS- with an increasing STAIC score is reflected by the negative correlation.

Neither other main effects of the STAIC score nor further interaction effects with the STAIC score reached significance (see **Table 5.**).

3.2.1 Generalization phases

During the generalization phases, neither significant main effects of the STAIC score nor significant interaction effects including the STAIC score emerged (see **Table 6.**). Moreover, for the arousal ratings neither a significant linear (F (1,129) = 2.46, p = .119, η^2 = .02) nor a quadratic trend (F (1,129) = 0.05, p = .827, η^2 < .001) were yielded for the generalization gradient. Concerning the valence ratings a significant linear (F (1,129) = 5.52, p = .020, η^2 = .04), however, no quadratic trend (F (1,129) = 0.35, p = .557, η^2 = .003) was comprised in the generalization gradient. Neither a significant linear (F (1,129) = 0.86, p = .355, η^2 = .01) nor a quadratic trend (F (1,129) = 1.86, p = .175, η^2= .01) existed relating to the generalization gradient in respect of the US expectancy ratings. Also, for the SCR the linear (F (1,129) = 2.60, p = .109, η^2 = .02) and the quadratic trend (F (1,129) = 1.70, p = .195, η^2 = .01) did not reach significance.

Table 6. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding the STAIC score on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for age and sex as covariates of no interest)

	main effect of STAIC	***stimulus type x STAIC***	***phase x STAIC***	***stimulus type x phase x STAIC***
arousal	F (1,129) = 1.19, p = .277, η^2 = .01	F (3,435) = 0.26, p = .873, η^2 = .002	F (1,129) = 0.81, p = .371, η^2 = .01	F (4,580) = 0.51, p = .750, η^2 = .004
valence	F (1,129) = 1.72, p = .192, η^2 = .01	F (3,383) = 0.77, p = .509, η^2 = .01	F (1,129) = 3.33, p = .070, η^2 = .03	F (5,612) = 0.53, p = .744, η^2 = .004
US expectancy	F (1,129) = 0.77, p = .382, η^2 = .01	F (3,338) = 1.19, p = .310, η^2 = .01	F (1,129) = 1.07, p = .304, η^2 = .01	F (4,529) = 0.67, p = .617, η^2 = .01
SCR	F (1,129) = 0.06, p = .815, η^2 < .001	F (3,430) = 0.57, p = .655, η^2 = .004	F (1,129) = 0.96, p = .328, η^2 = .01	F (5,595) = 0.42, p = .820, η^2 = .003

Purely explorative, as example and only to present and compare both aforementioned scores, that describe the extent of the generalization of conditioned fear, the linear deviation score (LDS, Kaczkurkin et al., 2017) and the generalization index (GI, Lenaert et al., 2016) are created in the following for the SCR.

The LDS is calculated as stated here: (CS- + CS+) / 2 – (GS4 + GS3 + GS2 + GS1) / 4. For the SCR higher values of the LDS represent less generalization, whereas lower values and values close to cero or already negative values stand for a larger extent of generalization.

Hence, with an increasing STAIC score, i.e. stronger trait anxiety, the LDS for the SCR of the 1. generalization phase decreased meaning that the extent of generalization grew (r (131) = -0.22, p = .012). There is support for this outcome, when looking at the GI (for details see p. 60): A growing STAIC score was accompanied by an increasing generalization index (GI, higher GI means higher extent of generalization) for the SCR in the 1. generalization phase indicating a higher extent of generalization (r (116) = 0.35, p < .001).

3.2.3 Extinction phases

Comparable to the generalization phases, also for the extinction phases neither significant main effects of the STAIC score nor significant interaction effects with the STAIC score appeared (see **Table 7.**).

Table 7. **Results of ANCOVAs for the 1., 2. and 3. extinction phases.** Effects regarding the STAIC score on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for age and sex as covariates of no interest)

	main effect of STAIC	***stimulus type x STAIC***	***phase x STAIC***	***stimulus type x phase x STAIC***
arousal	F (1,129) = 3.70, p = .057, η^2 = .03	F (1,129) = 0.40, p = .530, η^2 = .003	F (2,241) = 0.61, p = .532, η^2 = .01	F (2,239) = 0.39, p = .665, η^2 = .003
valence	F (1,129) = 1.31, p = .254, η^2 = .01	F (1,129) = 0.05, p = .832, η^2 < .001	F (2,240) = 1.60, p = .205, η^2 = .01	F (2,233) = 1.20, p = .300, η^2 = .01
US expectancy	F (1,129) = 0.10, p = .749, η^2 = .001	F (1,129) = 0.03, p = .854, η^2 < .001	F (2,258) = 0.08, p = .924, η^2 = .001	F (2,258) = 0.86, p = .424, η^2 = .01
SCR	F (1,127) = 0.02, p = .893, η^2 < .001	F (1,127) = 0.02, p = .893, η^2 < .001	F (2,254) = 1.32, p = .270, η^2 = .01	F (2,254) = 1.22, p = .297, η^2 = .01

4. Impact of anxiety sensitivity in underage probands on fear conditioning, its generalization and extinction

Of further interest is the impact of other self-report data, here specifically for anxiety sensitivity, on fear acquisition, its generalization and, also, the extinction training. Anxiety sensitivity means a constant belief that anxiety and related symptoms like bodily symptoms are followed by harmful physical, mental or social consequences, which go beyond acute fear or an acute panic attack (Schneider et al., 2009; Silverman et al., 1991; Reiss & McNally, 1985). A heightened anxiety sensitivity before the onset of an anxiety disorder is considered to be a vulnerability factor, especially, for the development of a panic disorder or agoraphobia (McNally, 2002; Ginsburg & Drake, 2002; Hayward, Killen, Kraemer & Taylor, 2000). The work of Evans et al. (2005) indicates that anxiety sensitivity is a risk factor for the development and maintenance of anxiety disorders in underage persons.

Hence, trait anxiety as well as anxiety sensitivity are important in connection with fear and anxiety, however, they represent different facets in this context. Importantly, it must be considered that there is a significant positive correlation between them. Different findings in the third and fourth chapter would reflect distinctive features of trait anxiety versus anxiety sensitivity. In general, there is not much research on anxiety sensitivity in fear learning processes like fear conditioning, generalization and extinction, especially, in an underage population up to the present. This investigation shall extend this field of research.

As for trait anxiety, the influence of age and sex was statistically considered (see further Tables in the APPENDIX) due to findings in the former chapter about the impact of age (see under **2.**) and, further, because girls have an enhanced risk for anxiety disorders (Lewinsohn et al., 1998).

4.1 Results

The following part describes the influence of anxiety sensitivity on fear acquisition, its generalization and extinction. In addition, the impact of age and sex was statistically considered as covariates of no interest (see further Tables in the APPENDIX).

4.1.1 (Pre-)Acquisition phases

In respect of the arousal ratings a significant main effect of the covariate CASI score (F (1,129) = 6.62, p = .011, η^2 = .05) could be revealed meaning that an increasing CASI score was accompanied by higher arousal ratings (r (131) = 0.18, p = .037). As for arousal, also for valence a significant main effect of the covariate CASI score (F (1,129) = 4.21, p = .042, η^2 = .03) arose with higher CASI scores being squired by declining ratings of valence (r (131) = -0.14, p = .112). For the US expectancy ratings, the main effect of the covariate CASI score (F (1,129) = 1.66, p = .200, η^2 = .01) was not significant. Also, for the SCR no significant main effect of the covariate CASI score (F (1,129) = 0.70, p = .406, η^2 = .01) existed.

Table 8. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding the CASI score on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for age and sex as covariates of no interest)

	main effect of CASI	***stimulus type x CASI***	***phase x CASI***	***stimulus type x phase x CASI***
Arousal	F (1,129) = 6.62, **p = .011**, η^2 = .05	F (1,129) = 0.17, p = .685, η^2 = .001	F (2,232) = 1.37, p = .255, η^2 = .01	F (2,235) = 0.99, p = .366, η^2 = .01
Valence	F (1,129) = 4.21, **p = .042**, η^2 = .03	F (1,129) = 0.003, p = .955, η^2 < .001	F (2,228) = 1.97, p = .147, η^2 = .02	F (2,241) = 0.38, p = .672, η^2 = .003
US expectancy	F (1,129) = 1.66, p = .200, η^2 = .01	F (1,129) = 0.06, p = .803, η^2 < .001	F (2,217) = 1.82, p = .170, η^2 = .01	F (2,254) = 2.37, p = .097, η^2 = .02
SCR	F (1,129) = 0.70, p = .406, η^2 = .01	F (1,129) = 1.17, p = .282, η^2 = .01	F (2,233) = 0.78, p = .448, η^2 = .01	F (2,234) = 0.25, p = .754, η^2 = .002

4.1.2 Generalization phases

For arousal a significant main effect of the covariate CASI score (F (1,129) = 9.25, p = .003, η^2 = .07) was revealed. Consequently, probands with higher CASI scores showed an overall stronger arousal compared to probands with lower CASI scores (r (131) = 0.21, p = .018). Neither a significant linear (F (1,129) = 0.39, p = .534, η^2 = .003) nor a quadratic trend (F (1,129) = 0.54, p = .466, η^2 = .004) determined the generalization gradient.

Regarding the valence ratings a significant main effect of the covariate CASI score (F (1,129) = 9.35, p = .003, η^2 = .07) was detected with decreasing valence ratings, i.e. a smaller extent of pleasantness, when the CASI score, i.e. the anxiety sensitivity, got larger (r (131) = -0.21, p = .017). The generalization gradient comprised a significant linear trend ((F (1,129) = 4.09, p = .045, η^2= .03), but no quadratic one (F (1,129) = 1.53, p = .218, η^2 = .01).

Moreover, a significant interaction of phase x CASI score (F (1,129) = 6.05, p = .015, η^2 = .05) was found, whereby a growing CASI score was accompanied by higher ratings of US expectancy (r (131) = 0.22, p = .012) in the 1. generalization phase, however, not in the 2. generalization phase (r (131) = 0.04, p = .660). As for arousal and valence, also for the US expectancy a significant main effect of the covariate CASI score (F (1,129) = 5.68, p = .019, η^2 = .04) was observed with higher US expectancy ratings for probands characterized by higher CASI scores (r (131) = 0.14, p = .108). Neither a significant linear (F (1,129) = 0.04, p = .835, η^2 < 0.001) nor a quadratic trend (F (1,129) = 1.92, p = .168, η^2 = .02) marked the generalization gradient.

Unlike for the subjective ratings, there was no significant main effect of the covariate CASI score (F (1,129) = 0.28, p = .600, η^2 < .01) concerning the SCR. There were neither a significant linear (F (1,129) = 0.29, p = .593, η^2 = .002) nor a quadratic trend (F (1,129) = 0.05, p = .827, η^2 < .001) within the generalization gradient.

Taken together, with an increasing CASI score the arousal and the US expectancy ratings grew, while the valence ratings went down, respectively. However, such an effect could not be observed for the SCR.

Table 9. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding the CASI score on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for age and sex as covariates of no interest)

	main effect of CASI	***stimulus type x CASI***	***phase x CASI***	***stimulus type x phase x CASI***
Arousal	F (1,129) = 9.25, **p = .003**, η^2 = .07	F (3,437) = 1.47, p = .217, η^2 = .01	F (1,129) = 0.03, p = .856, η^2 < .001	F (4,580) = 1.16, p = .326, η^2 = .01
Valence	F (1,129) = 9.35, **p = .003**, η^2 = .07	F (3,381) = 1.16, p = .325, η^2 = .01	F (1,129) = 1.62, p = .206, η^2 = .01	F (5,610) = 1.32, p = .255, η^2 = .01
US expectancy	F (1,129) = 5.68, **p = .019**, η^2 = .04	F (3,340) = 1.60, p = .196, η^2 = .01	F (1,129) = 6.05, **p = .015**, η^2 = .05	F (4,528) = 2.02, p = .089, η^2 = .02
SCR	F (1,129) = 0.28, p = .600, η^2 = .002	F (3,434) = 0.83, p = .491, η^2 = .01	F (1,129) = 0.16, p = .687, η^2 = .001	F (5,596) = 1.14, p = .338, η^2 = .01

4.1.3 Extinction phases

A significant main effect of the covariate CASI score (F (1,129) = 9.42, p = .003, η^2 = .07) could be revealed meaning that a growing CASI score was squired by a stronger arousal (r (131) = 0.26, p = .002). For valence a significant interaction of phase x CASI score (F (2,238) = 4.03, p = .022, η^2 = .03) could be detected indicating that with an increasing CASI score in the 1. extinction phase (r (131) = -0.07, p= .420) the valence went slightly down, in contrast to the 2. extinction phase (r (131) = 0.07, p = .441), where the valence increased to some extent, and the 3. extinction phase (r (131) = 0.05, p = .567), where it increased slightly less compared to the 2. extinction phase. Further, there was a three-way significant interaction of stimulus type x phase x CASI score (F (2,235) = 3.21, p = .047, η^2 = .02). In order to be consistent with the way of interpreting a three-way interaction, a differential score (CS+ minus CS-) was calculated for each extinction phase. Afterwards, a correlation was created between every differential score and the CASI score. The participants expressed a slowly growing differential score for the valence with higher CASI scores in the 1. extinction phase (r (130) = 0.04, p = .648), whereas this changed in the 2. extinction phase (r (130) = -0.02, p = .850), where the differential score became smaller and, afterwards, in the 3. extinction phase (r (130) = -0.13, p = .129) even smaller. There was no significant main effect of the covariate CASI score (F (1,129) = 0.29, p = .593, η^2 < .01). Regarding the US expectancy ratings no significant main effect nor interaction effects concerning the CASI score were found. In respect of the SCR, a significant three-way interaction of stimulus type x phase x CASI (F (2,254) = 3.76, p = .025, η^2 = .03) was revealed.

With a higher CASI score the probands expressed a declining differential score (CS+ minus CS-) of the SCR in the 2. extinction phase (r (131) = -0.24, p = .005), but neither in the 1. (r (131) = 0.08, p = .391) nor in the 3. extinction phase (r (131) = 0.02, p = .795).

As already for the fear conditioning and the fear generalization part, also for the extinction part higher CASI scores were associated with higher arousal ratings. For the other three dependent variables no such associations could be observed (see also **Table 10.**).

Table 10. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding the CASI score on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (statistically controlled for age and sex as covariates of no interest)

	main effect of CASI	***stimulus type x CASI***	***phase x CASI***	***stimulus type x phase x CASI***
Arousal	F (1,129) = 9.42, **p = .003**, η^2 = .07	F (1,129) = 0.35, p = .557, η^2 = .003	F (2,241) = 0.38, p = .669, η^2 = .003	F (2,238) = 0.77, p = .455, η^2 = .01
Valence	F (1,129) = 0.29, p = .593, η^2 = .002	F (1,129) = 0.02, p = .888, η^2 < .001	F (2,238) = 4.03, **p = .022**, η^2 = .03	F (2,235) = 3.21, **p = .047**, η^2 = .02
US expectancy	F (1,129) = 0.32, p = .575, η^2 = .002	F (1,129) = 0.37, p = .542, η^2 = .003	F (2,258) = 0.17, p = .848, η^2 = .001	F (2,258) = 1.29, p = .276, η^2 = .01
SCR	F (1,127) = 0.24, p = .623, η^2 = .002	F (1,127) = 1.47, p = .227, η^2 = .01	F (2,254) = 0.003, p = .997, η^2 < .001	F (2,254) = 3.76, **p = .025**, η^2 = .03

5. General discussion

5.1 Main findings

Different processes in the context of fear learning like fear conditioning and its generalization as well as fear unlearning like the extinction of conditioned fear evolutionarily are very adaptive for living beings to be able to respond rapidly and adequately to environmental changes, especially when facing potential danger (Ahrens et al., 2016; LeDoux, 2003). Thus, survival is more likely (Vervliet et al., 2013). The above mentioned (un-)learning mechanisms, implemented in an experimental paradigm, help to examine fundamental procedures of fear (un-)learning and especially classical fear conditioning seems to fit very well as a model for the process of acquiring pathological fear (Mineka & Zinbarg, 2006). Thereby, developmental

changes based on maturation of different brain areas seem to be crucial. Whereas the amygdala as part of the limbic subcortical region is fully developed at an early stage in life, the PFC needs far more time to reach its mature state and full functionality (Tottenham & Gabard-Durnam, 2017; Vink et al., 2014; Decety et al., 2012). From an evolutionary perspective this might explain the enhanced generalization of conditioned fear found in very young healthy children compared to healthy adults. This overgeneralization of stimuli resembling the danger cue might protect children lacking life experience enforcing therewith more cautiousness regarding their conduct particularly in unknown surroundings. Since at young age in life the environment is full of uncertainness and very much has to be learned for future life compared to adult age (Tottenham & Gabard-Durnam, 2017). Step by step experience with various situations in life grows and with increasing age via youth into adult age fear generalization gradually declines (Schiele & Reinhard et al., 2016). Anomalies in the different mechanisms of fear learning as well as unlearning can cause impairments regarding the skill of flexible adaptability in new challenging surroundings. Hence, inappropriate and unsuitable fear reactions could result reflected by for example an enhanced fear acquisition, overgeneralization or a not achieved extinction of conditioned fear. The question from which level on anxiety patients depart from healthy counterparts concerning fear learning led to the consideration that elevated acquisition and generalization effects, defects regarding inhibition processes and resistance to extinction might be potential factors (Ahrens et al., 2016; Duits et al., 2015; Briscione, Jovanovic & Norrholm, 2014; Lissek et al., 2005). Lissek and colleagues (2010, 2014b, 2012) found an association between overgeneralization and diagnosed anxiety disorders in adults like the panic disorder (PD), the generalized anxiety disorder (GAD) and also the post-traumatic stress disorder (PTSD), whereas Ahrens et al. (2016) detected deviations regarding fear reactions towards conditioned and generalized threat cues in social anxiety disorder (SAD), although not a large overgeneralization as distinguishing feature, but a generalization of heart rate reactions (fear bradycardia). In addition, comparable results of overgeneralization were detected for youths with anxiety disorders compared to healthy counterparts (El-Bar et al., 2017). Furthermore, overgeneralization in young adulthood has shown a relation to a stronger extent of anxiety six month later at the follow-up examination (Lenaert et al., 2014). These findings inevitably lead to the question whether overgeneralization of conditioned fear in childhood, which does not decline via youth into adult age, might result in maladaptive behavioral outcomes and forward the development of anxiety disorders. Waters and colleagues (2009) indicate an impaired inhibition of reactions towards safety stimuli as well as a delayed and

impeded extinction as learning procedures playing potentially a role for the development of anxiety disorders in young age. Liberman and colleagues (2006) also point to a delay concerning the extinction of conditioned fear in children with anxiety disorders, whereby there is further support for this finding from Craske and colleagues (2008).

The present doctoral thesis had the target to contribute to a better understanding of aberrant procedures in the context of fear learning as well as unlearning as a transdiagnostic characteristic of psychopathology in anxiety disorders.

First of all, this present thesis aimed to explore the effects of age on fear conditioning, its generalization and as well as its extinction. Therefore, it was of particular interest to focus on generalization of conditioned fear to examine trajectories during the development in the context of fear learning. Moreover, the potential impact of trait anxiety on the one hand and of anxiety sensitivity on the other hand on fear conditioning, its generalization and also its extinction was explored. One main goal of these conducted studies was to contribute to the scientific field by replicating previous research outcomes as well as expanding and advancing them and, furthermore, hopefully foster linkages to new therapeutic and preventive concepts in the context of anxiety disorders. To achieve the goal of this thesis, 133 healthy children and adolescents aged 8 to 17 years fulfilled a discriminative fear, generalization and extinction paradigm, meanwhile measuring arousal, valence and US expectancy ratings and, further, the skin conductance responses, which can be considered as a physiological index of arousal. Besides that, the probands had to complete the questionnaires STAIC and CASI in order to determine the levels of trait anxiety and anxiety sensitivity in the presented sample of healthy minors. All statistical analyses controlled for effects of sex (as covariate of no interest, results see in the tables in the APPENDIX).

The following subchapter contains the core findings of the presented work, which will be outlined and discussed especially in the context of their influence on the different fear learning processes, which in turn could be possible promoting aspects in the development as well as the maintenance of anxiety disorders.

The acquisition of conditioned fear, i.e. fear conditioning, was overall successful as reflected by higher arousal and US expectancy ratings as well as SCR and lower valence ratings, respectively, towards the danger cue CS+ in comparison to the safety cue CS-. This states a clear and supportive replication of former investigations including the same fear conditioning and generalization task in a sample of children and youths (Glenn et al., 2012a; Lau et al., 2008; Schiele & Reinhard et al., 2016). Hence, healthy children and adolescents display a successful

and stable fear conditioning comparable to healthy adults. Interestingly, the participants‘ age played an important role reflected by significant main effects of arousal and US expectancy ratings as well as SCR, however, not for the valence ratings. Thus, the older the probands were the less excitement was expressed by them and the smaller their ratings of likelihood for an aversive noise in general and, further, the lower the SCR they exhibited. These results could be illustrated with a kind of parallel shift towards smaller arousal and less US expectancy as well as smaller SCR with increasing age. Notably, these findings are in line with the results reported by Silvers et al. (2017), which indicate that children show overall stronger responses towards aversive as well as neutral stimulus types reflected both by their subjective reports and reactions within the amygdala in comparison to youths. This is also consistent with the following previous finding: Fearfulness and fear intensity decrease with age (Gullone & King, 1997; Gullone, 2000; King et al. 1989). Additionally, this supports the evolutionary view described more detailed above, that children should display a more cautious behaviour due to their lack of life experience in various surroundings in order to enhance their survivability. Moreover, the age mattered regarding the SCR amplitudes insofar, that the older the underage participants were the smaller the psychophysiological reactions were they exhibited, which is in line with former research (e.g. Lau et al., 2011; El-Sheikh, Keiley & Hinnant, 2010; El-Sheikh, 2007; Janes, Hesselbrock & Stern, 1978; overview of resembling continuing development of the electrodermal activity, i.e. a decrease for young to higher adult ages: see Mertens, 2016).

Moreover, as research literature (e.g. Michalska et al., 2016; Glenn et al., 2012a; Lau et al., 2011; Gao et al., 2010) states, also the findings of this work demonstrate, that the ability to discriminate between CS+ and CS- improves with increasing age from childhood into advanced youth, as indexed by the US expectancy ratings at least. More precisely, the older the probands were the better they differentiated between CS+ and CS- already until the end of the 1. acquisition phase compared to younger probands. Although after the 2. acquisition phase no such discrepancy could be detected any longer. This means that the younger probands required more time for discrimination learning, but reached a comparable discrimination learning outcome as the older probands, but only until the end of the 2. acquisition phase, which is very similar to what Waters et al. (2017) found: comparable successful discrimination learning outcome, but the children needed far more trials than the youths and adults. Back again to the current work: Consequently, with increasing age the probands displayed quicker a better discrimination between the danger and the safety cue for the US expectancy ratings. Moreover, adolescent participants acquired the knowledge about the forecasting property of CS- about

safety and the forecasting property of CS+ about danger quicker than younger participants, i.e. with growing age the probands learned quicker the meaning connected with the signal as secure or not. This superior and quicker learning procedure was reflected by a smaller generalization index (GI) score indicating a decline of the extent of generalization of conditioned fear for older probands.

Finally, there were two interesting different observations made for the arousal and the US expectancy ratings. Concerning the ratings of arousal, first, no differences linked to age were found in the pre-acquisition phase, however, then the ratings revealed that after the 1. as well as the 2. acquisition phase arousal decreased with growing age of the participants. Whereas in regard to the US expectancy ratings, first, a difference linked to age existed already after the pre-acquisition as well as the 1. acquisition phase. More accurately, first, the older probands expressed overall lower US expectancy ratings than younger ones, whereby after the 2. acquisition phase no variations due to age could be detected anymore. Again, these two findings fit with the evolutionary perspective: Younger children displayed higher arousal for a longer time than youths, whose arousal decreased more rapidly due to more experience in life, and younger children generally estimated the probability of risk, i.e. US expectancy, as higher from the beginning, however, after enough trials their learning outcome, as reflected by the US expectancy, was comparable to the one expressed by youths. Both findings state good strategies enhancing survivability.

Besides, an evident generalization was expressed by the subjective ratings, i.e. the evaluations towards the generalization stimuli, however, the amplitudes of the electrodermal reactions did not display a significant generalization effect. Significant linear and, additionally, significant quadratic effects were detected within trend analyses for both the subjective ratings and the SCR. Especially, the outcome of the quadratic effects fits with prior observations in samples of healthy adult probands (Schiele & Reinhard et al., 2016; Lissek et al., 2010). Considering the fact that the psychophysiological measures were recorded non-stop, when the underage participants accomplished the paradigm, in contrast to the subjective ratings, which were gathered after every single phase of the paradigm, it is not unusual that deviations, when comparing the results of the subjective ratings to the results of the psychophysiological reactions, could have emerged. Hence, one and the same stimulus can cause variations concerning automatically expressed physiological reactions compared to the cognitive evaluation of it (Lonsdorf et al., 2017; LeDoux, 2014; Boddez et al., 2013; Öhman, Carlsson, Lundqvist & Ingvar, 2007). Considerably, Lonsdorf et al. (2017) mention a paper of Lovibond

and Shanks (2002), where they recommend evaluating also subjective ratings of US expectancy after every trial and not after an entire phase to have a higher reliability and validity, however, this could possibly interfere with the experimental procedure of learning.

Regarding the extent of generalization, which is typically indicated by the pairwise comparison between the danger cue CS+ and each of the four morphs GS1-GS4 vs. the safety cue CS-, it was evident up to the second morph GS2, when counting from the danger cue CS+ via the first morph GS1 for the subjective ratings. Both morphs, i.e. GS1 and GS2, exhibited predominantly very similar features like the danger cue CS+ itself and induced stronger negative reactions, i.e. a larger fear response, in comparison to the safety cue CS-. The other two morphs GS3 and GS4 contained more features from the safety cue CS- and were followed by ratings resembling the ones towards the CS-. For the psychophysiological measure of SCR the extent of generalization was by far not that pronounced compared to the subjective ratings. Only the danger cue CS+ evoked significantly higher responses in comparison to the safety cue CS-. As already elaborated above, discrapancies between subjective (that is ratings) and more objective measures (that is SCR for example) are not unusual (e.g. Lonsdorf et al., 2017; LeDoux, 2014; Boddez et al., 2013; Öhman et al., 2007).

Comprehensibly and expectably, independent of the probands‘ age the learning performance, indexed by the US expectancy ratings, improved for the whole sample after the 2. generalization phase compared to the ratings after the 1. generalization phase. This means more detailed that the entire sample showed an increased discrimination between all five secure stimuli and the danger signal, i.e. the safety signal as well as all four morphs were rated with even lower US expectancy than the danger signal, which was rated with even higher US expectancy, after the 2. generalization phase. This extent of differentiation was not yet achieved after the 1. generalization phase.

Consistently with the (pre-)acquisition phases, statistical anlyses showed a clear impact of the probands‘ age both on the subjective ratings and the psychophysiological reactions for the generalization phases. Main effects for arousal, valence and US expectancy ratings as well as for the SCR showed that with increasing age the probands in general reacted less strong regardless of the stimulus type compared to younger probands. Again, the picture of a kind of parallel shift is very helpful: with growing age the generalization gradients move downward towards smaller arousal and US expectancy ratings as well as lower SCR and upward towards higher valence ratings, respectively. In the generalization part the age effect was additionally reflected by the valence ratings, which was not the case for the (pre-)acquisition part. Also here

the results are consistent with the findings of Silvers and colleagues (2017), Gullone & King (1997), Gullone (2000) and King et al. (1989) as already elaborated above for the (pre-) acquisition. In this context it must be taken thoroughly into consideration that within the examined age span of healthy children and youths a crucial and decisive bias could have an effect. The development of anxiety disorders begins normally in childhood age and a median onset of 11, 13 and 15 years has been suggested (Kessler et al., 2005; Beesdo, Pine, Lieb & Wittchen, 2010; Christie et al., 1988), i.e. at a time point during the first half of adolescense. This possibly has already led to an exclusion of adolescents with a diagnosed anxietey disorder, so that the youths included in the sample were more „healthy“ than the younger children within the sample, who might have been excluded due to a diagnosis of an anxiety disorder just some years later.

Research in animals presents a similar influence of age on generalization (Ito et al., 2009; Rudy & Pugh, 1996; Campbell & Haroutunian, 1983) as found for the US expectancy ratings in this thesis, i.e. a decline of the extent of fear generalization with increasing age. In addition Schiele & Reinhard et al. (2016) found a clear difference concerning the generalization gradients of young children aged 8 to 10 years, who exhibited a recognisable overgeneralization compared to adult probands as reflected by the arousal ratings and the SCR. Potential reasons that the impact of the age became visible only regarding the US expectancy ratings, but neither for the arousal and valence ratings nor for the SCR, could have been the broad age span selected and, additionally, the small statistical power. Moreover, in accordance with Lonsdorf et al. (2017) the US expectancy ratings are more associated with cognitive comprehension and not primarily with reacting to fear. In contrast, arousal and valence ratings represent subjective evaluations. Arousal stands for the intensity of fear, which could be low or high or somewhere in between. Valence stands for the quality of the reaction, which could be negative in case of an aversive stimulation like for example after a danger signal or positive in case of an appetitive stimulation like for example after a safetey signal. As a consequence, the US expectancy ratings display rather the cognitive development with respect to contingency awareness to a greater extent compared to the ratings of arousal and valence. This finding, which is evident only for the US expetancy ratings, means that there seems to be an improvement during the development in the sense of an enhanced differentiation between the different stimulus types and a decline concerning the extent of generalization of conditioned fear in accordance with animal as well as human research data as mentioned above. The maturation of the prefrontal cortex (PFC) might play a decisive role regarding the inhibition of fear responses towards signals, which

have never been linked to danger, i.e. in this case the secure stimulus types CS- and GS1-GS4. Thus, contingency awareness, concluded from the US expectancy ratings, is correlated with age in the course of the process of fear learning and more specifically the process of the generalization of conditioned fear.

Interestingly, for the SCR there was a kind of a parallel shift from the 1. to the 2. generalization phase with overall higher elctrodermal reactions within the 2. generalization phase in comparison to the 1. generalization phase. Strikingly, this result contradicts the first supposed expectation of a possible habituation effect. Maybe the four new morphs triggered a kind of delayed novelty effect, which affected all stimuli because the new morphs could have been realized not before the 2. generalization phase in a clear manner. Thus, resulting only then in a better differentiation between the secure stimuli, i.e. the safety cue and the four morphs, and the danger cue, whereby the SCR towards CS+ was significantly higher than towards CS-, but only in the 2. generalization phase (see **Figure 16.).** The novelty effect describes that humans tend to express the strongest stress reaction when they are confronted with a possibly harmful event for the first time, whereby the stress reaction declines whith fading newness (Gravetter & Forzano, 2015). A recent study suggested that diminished SCR might constitute the consequence of the paling of the novelty effect (Rutten & Geerts, 2020), whereas here in the current work the heightened SCR maybe reflects the fully unfolded newness within the 2. generalization phase.

The extinction training did not bring the expected deletion of the discrimination between the safety and the danger cue neither as indexed by the subjectve ratings nor by the SCR. The subjective ratings demonstrated that throughout all three extinction phases the differentiation between the safety and the danger signal was clearly still preserved. For the SCR the main effect of the stimulus type could also been detected for the extinction phases, however, it was not that pronounced compared to the arousal, valence and US expectancy ratings. Additionally, for the arousal and the US expectancy ratings a generell decline regardless of the stimulus type was revealed, although still containing the discrimination between CS+ and CS-from phase to phase. In particular, the described drop of the US expectancy ratings towards both stimulus types was notably stronger towards CS+ than CS-. Thus in sum, the extinction was not successful. Various reasons could have played a decisive role for this outcome. First, one reason could be the length of the extinction training, i.e. that it was just not long and extensive enough. Each of the three extinction phases included six times the safety cue and further six times the danger cue. Maybe the presentation of every stimulus type only six times was insufficient per phase. The studies

of Glenn and colleagues (2012a) as well as of Schiele and Reinhard and colleagues (2016) used the same paradigm, but did not report about extinction. While the study of Lau and colleagues (2008) implemented the same paradigm including an extinction training. However, it contained only 30 trials divided into 6 (3 x CS+; 3 x CS-) at the end of the first day of the experiment following a preacquisition and conditioning part and further 24 (12 x CS+; 12 x CS-) on the second day. Consistently, also in this study an extinction was not achieved with still constant discrimination between the CS+ and the CS-. The authors argued that in this context especially the partial reinforcement could have played a crucial role inasmuch as not 100% of all danger stimuli CS+ were linked with the female scream (US) and that is why it is possible that the probands did not bring CS+ together with safeness although no US was presented within the entire extinction training. Lau and colleagues (2008) used a reinforcement rate of 75% and in the current work it was 82% during acquisition, which was reduced to 50% during generalization. Potentially, the probands did not perceive a big difference between the 25% of the danger cues not being connected with US during acquisition and the latter complete absence of the US after CS+ during the extinction training. This could be in an analogous manner for the current thesis looking at the extinction training after the generalization with only 50% of CS+ being linked with US.

Interestingly, one modulating effect of age concerning the participants‘ valence ratings could be found for the extinction phases. With increasing age the probands‘ valence ratings towards CS- and CS+ differed less than for younger probands for the extinction part, i.e. averaged over the three phases of the extinction. Unraveling this effect it becomes obvious that it is based on the decline of the valence ratings towards CS+ with growing age, however, not towards CS-. This means that older participants expressed smaller valence ratings, which means less pleasentness, towards the CS+ compared to the younger ones, whereas the valence ratings towards CS- were similar for all ages. Here, one possible reason for the variation between younger and older probands could be a better memorized learning about the connection between CS+ and the aversive noise, which was conditioned within the acquisition part and maintained during the generalization part, resulting in a less pleasant evaluation of the CS+ from the beginning of the extinction expressed by the adolescents.

So far, this part of the thesis contributes to the scientific discourse and field of research on fear learning with its different aspects. One core finding is that there is a correlation between the extent of fear generalization and age within a time range, which bears high risk for developing anxiety disorders (i.e. Kessler et al., 2005; Beesdo et al., 2010; Christie et al., 1988).

Although it must be considered in this context that the development of anxiety disorders is based on highly intricate processes and, in addition, on various numerous factors, which interact among each other. Hence, this scientific field requires far more research including catamnestic and longitudinal follow-up investigations taking into account e.g. the neurobiological fear circuits, which might play a mediating role concerning fear generalization during the development beginning with young age via youth into adult age. Also, the impact of changes concerning gonodal hormones in particular must be considered, especially, when puberty is reached as well as potential consequences of hormonal contraceptives (e.g. hormonal contraceptives: Lonsdorf et al., 2015; gonadal hormones: Maeng & Milad, 2015; Lebron-Milad & Milad, 2012; Milad et al., 2010).

In the second experiment, the influence of trait anxiety, reflected by the STAIC score (*STAIC-T* from Spielberger, 1973; German version: STAIK-T Unnewehr, Joormann, Schneider, & Margraf, 1992), was investigated in the same sample as described above, i.e. in healthy participants aged 8 to 17 years. Again, subjective ratings of arousal, valence and the US expectancy as well as the psychophysiological measure of the SCR were utilized. The hypothesis regarding heightened responses with a stronger trait anxiety got support merely by some hints displayed by only one of four dependent measures, namely the US expectancy. The further dependent measures, i.e. the arousal and valence ratings and the SCR, fit with the findings of Torrents-Rodas and colleagues (2013), where no effects of trait anxiety could be revealed concerning fear conditioning. For the US expectancy ratings in the preacquisition and the two acquisition phases a significant main effect of the STAIC score was observed, however, not for the other subjective ratings nor for the psychophysiological measure of the SCR. Thus, with a growing trait anxiety the probands rated the US expectancy higher, i.e. they estimated an aversive noise to emerge with a higher likelihood than probands with lower trait anxiety. This result can be illustrated with a kind of parallel shift of the ratings with increasing trait anxiety. Only the finding for this dependent variable supported the hypothesis of stronger fear responses being connected with higher trait anxiety. Interestingly and as already mentioned, this was only the case for the US expectancy, which has more to do with the recognition on a cognitive level than reacting to fear (Lonsdorf et al., 2017). Thus, one possible explanation is, that here the probands with higher trait anxiety could just have put the better-safe-than-sorry strategy to use. This is no contradiction to all the other dependent measures: neither the subjective perception and expression of arousal and valence nor the psychophysiological

measure of SCR have to be affected by the rather rational choice of the better-safe-than-sorry strategy.

Furthermore, a smaller discrimination ability could be revealed for higher STAIC scores as reflected by the SCR, but none of the subjective ratings showed support for this finding. More precisely, the SCR towards the danger signal declined slightly stronger than the SCR towards the safety signal with an increasing STAIC score. This outcome finds support through the study reported by Kadosh and colleagues (2015), where no discriminative learning in high anxious youths was observed as indexed by the fear-potentiated startle. As already mentioned above variations, in respect of the SCR as an unconscious and automatic psychophysiological reaction compared to an evaluation on a conscious and cognitive level concerning the same stimuli can emerge (Lonsdorf et al., 2017; LeDoux, 2014; Boddez et al., 2013; Öhman et al., 2007).

Importantly, there was no support for the hypothesis stating a positive association between the extent of trait anxiety and the generalization of conditioned fear. Neither for the generalization phases nor for the extinction phases significant main or interaction effects involving the STAIC score could be detected. Hence, the generalization gradients were not influenced by the extent of trait anxiety with the exception of the trends, which did not reach significance anymore (only the linear trend for the valence ratings remained significant). This findings regarding fear generalization go in line with previous results reported by Torrents-Rodas et al. (2013), where no effect of trait anxiety could be detected in a sample of healthy adults. Thus, there was no support concerning the hypotheses concerning fear generalization nor regarding fear extinction. Interestingly, Wong & Lovibond (2020) found no variations due to trait anxiety in fear generalization to new type of generalization stimuli (GSs), which obviously were part of the secure or the menacing section, measured by SCR and shock expectancy ratings. Although the main outcome was that probands with high trait anxiety expressed stronger generalized fear towards the GSs, which suited in both sections, compared to probands with low trait anxiety if the GSs contained ambiguous threat values. The authors explained that this is not a result of a higher probability of probands with high trait anxiety to discern ambiguous features as being part of the menacing section, but that they overvalue the menace when the degree of menace is ambiguous. Hence, the ambiguity of menace has a modulatory effect of trait anxiety on categorical fear generalization.

Moreover, the impact of anxiety sensitivity as indexed by the CASI score (Schneider et al., 2009) was explored in a third experiment, whereby the same sample was looked at as already

presented for the first and second experiment. The same dependent measures of subjective ratings and the psychophysiological measure of SCR were examined. Likewise, the hypotheses were set in an analogous manner to the ones for trait anxiety. Significant main effects were found concerning the arousal as well the valence ratings for the preacquisition and both acquisition phases. Hence, with stronger anxiety sensitivity, reflected by growing CASI scores, the probands rated arousal higher and valence lower, respectively. This observation is traceable considering the subjectivity of the exhibited feelings. Anxiety sensitivity is very connected with bodily sensations, which makes subjective ratings expressing stronger fear responses, i.e. a more excited state and a less pleasent state, absolutely plausible. Hence, the hypothesis about an association between higher fear reactions and higher anxiety levels is more fulfilled for anxiety sensitivity than for trait anxiety. However, there is no common dependent variable for trait anxiety and anxiety sensitivity supporting the hypothesis. In contrast to trait anxiety, which was supported by US expectancy in favour of the hypothesis, for anxiety sensitivity the other two subjective variables, i.e. the arousal and valence ratings, speak in favour of the hypothesis. Though two further variables did not support this hypothesis: Neither for the US expectancy ratings, reflecting a rather cognitive comprehension outcome, nor for the SCR, reflecting physiological arousal, significant main effects could be detected. These findings are not contradictive considering the findings for the different subjective ratings because the US expectancy does not depict a fear reaction like arousal and valence do in a subjective manner and for the SCR the unconsciousness and automatic mode must be seen. As already delineated above, such variations regarding the outcomes resulting from different ways of measurement are not uncommon (i.e. Londsdorf et al., 2017; LeDoux, 2014; Boddez et al., 2013; Öhman et al., 2007). In sum, this hypothesis is partly confirmed by study data.

Whereby the previously mentioned effects, which were in favour of the hypothesis about an association between higher anxiety levels and higher fear responses, were supported by the findings for the generalization phases. There, even for all three subjective ratings, i.e. the rather subjective feelings (arousal and valence) as well as the aspect of cognitive comprehension (US expectancy), main effects of the CASI score emerged, meaning that higher CASI levels were accompanied by larger arousal as well as US expectancy ratings and smaller valence ratings, respectively. However, this finding still was not reflected by the pyshiological arousal, i.e. the SCR. This additional significant increase of the US expectancy ratings along with stronger anxiety sensitivity in the generalization part, contrary to the (pre-)acquisition part, could be explained in this way: the statistical power might be too small or the considered age span too

wide, affecting the results for the first three phases of the paradigm and, possibly, the probands needed longer to grasp the relation between the CS+ and CS- as reflected by the US expectancy ratings, but accomplished it during the generalization phases and used the better-safe-than-sorry strategy. Taken together, the hypothesis suggesting a positive correlation between anxiety sensitivity and overgeneralization was not true for the fear generalization: It must be stressed that the extent of the generalization remained similar for all probands regardless of the level of anxiety sensitivity, only the intensity of the fear reactions was higher for stronger anxiety sensitivity levels, which can be illustrated by a kind of parallel shift: upward for the arousal and the US expectancy ratings and downward for the valence ratings, respectively. An overgeneralization could not be observed.

Interestingly, after the 1. generalization phase the US expectancy ratings were generally higher for stronger anxiety sensibility regardless of the stimulus type, whereas this effect did not appear after the 2. generalization phase. Thus, first participants who exhibited a stronger anxiety sensitivity, reflected by a higher CASI score, showed higher US expectancy ratings, but only in the 1. generalization phase. Then, for the 2. generalization phase no such variation due to the extent of anxiety sensitivity showed up, finally resulting in a comparable learning outcome independent of the height of the CASI score.

As for trait anxiety, also for anxiety sensitivity the trend analyses showed only one significant linear trend, namely for the generalization gradient of the valence ratings, but no other trends concerning the further dependent variables reached significance.

For the three extinction phases only for the arousal ratings a main effect of the CASI score could be found, indicating that higher arousal ratings were accompanied by stronger anxiety sensitivity. Hence, higher levels of the expressed arousal were associated with stonger extents of anxiety sensitivity throughout the whole experiment. In contrast to the (pre-) acquisition and generalization parts, during the extinction the valence ratings were not influenced by the height of anxiety sensitivity. Whereas the US expectancy ratings were not affected by the extent of the anxiety sensitivity neither during the (pre-)acquisition nor the extinction phases, this was different for the generalization phases. There, stronger anxiety sensitivity was linked with higher ratings. Summing it up, these outcomes can be described best as a kind of parallel shift always, when there was an association between the level of anxiety sensitivity and the height of fear reactions. For the arousal ratings, there was a kind of parallel shift towards stronger fear responses with an increasing CASI score in every single phase of the experiment. Furthermore, for the valence the kind of parallel shift went towards lower

valence ratings with higher CASI scores in the (pre)acquisition and generalization parts, however, not during the extinction training. Concerning the US expectancy ratings the kind of parallel shift moved towards higher US expectancy with growing anxiety sensitivity, though only during generalization.

Moreover, regarding the valence ratings the differentiation between CS+ and CS- was first larger for the probands with higher anxiety sensitivity, whereas after the 2. and even more after the 3. extinction phase the probands with stronger anxiety sensitivity discriminated less between the safety and the former danger signal, compared to the probands with lower anxiety sensitivity. Thus, exhibited on the level of the subjective feeling of pleasentness towards the safety and the former danger cue, the expected outcome of an approximation of the ratings and consequently a decreasing discrimination between the stimulus types showed up. This could not be detected for the other two subjective ratings. This finding for the valence ratings could be a first hint that highly anxiety sensitive probands learned better and also faster maybe due to stronger attention processes in more threatening situations, what led to an earlier beginning of extinction of fear than in less anxiety sensitive probands.

Besides, when looking at the SCR there is an observation of a decline of the discrimination between CS+ and CS- with a growing anxiety sensitivity, but this is only evident in the 2. extinction phase. This could be seen as quite in line with the valence ratings as a first hint in probands with a stronger extent of anxiety sensitivity for a better and faster learning of the new lacking association between the danger signal and the aversive female scream resulting in a decreasing differentiation between both stimulus types, i.e. the safety and the former danger cue.

In conclusion, for trait anxiety and anxiety sensitivity different findings emerged. This underpins the different single features of anxiety that they represent, indexed by their different scores, defined in their inventories. Consequently, anxiety sensitivity with its bodily component seems to influence fear learning procedures to a stronger extent than trait anxiety.

5.2 Conclusions

To sum it up, further research is important due to all the further questions, which still cannot be answered, in this context. Although there are noteworthy findings contributed by the current thesis: First, age focusing on a range from 8 to 17 years has an impact on fear learning insofar as the findings indicate overall decreasing fear reactions with growing age of the probands. All stimuli types, independent of their sort, were affected by the diminished reactions

of the older probands comparable to kind of parallel shifts depending on the probands‘ age. Further, the discrimination ability, which was reflected by the US expectancy ratings, got better with growing age, illustrating that older probands overgeneralized less compared to younger ones. Consequently, the outcome suggests enhanced fear generalization to be a developmental correlate in the context of fear learning. Although it must be stressed very clearly at this point, that there is no causality reflected by the finding, but merely a negative association between age and fear generalization. As a result, the question still cannot be answered unequivocally, whether enhanced generalization of conditioned fear facilitates the development of anxiety disorders or vice versa. Second, trait anxiety seems not to affect fear learning processes like fear acquisition, its generalization or extinction. Third, anxiety sensitivity plays a noteworthily role in the context of all fear learning procedures, looked at in this current thesis. The level of anxiety sensitivity was associated with the height of the fear responses comparable to kind of parallel shifts, depending on the extent of the anxiety sensitivity.

5.3 Limitations

There are some methodical limitations, among others, which should be mentioned regarding the presented work. It was a cross sectional study, which always provides only information about one specific moment. However, it also can bring relevant data. Although, in general and especially in developmental contexts, longitudinal studies should preferably be envisaged. Particularly because of the wide age range, a higher statistical power aiming to achieve a higher replicability in psychological research (Maxwell, Lau & Howard, 2015) and, thus, a bigger number of participants would have been more desirable and appropriate. Furthermore, the age span between 8 and 17 years includes the crucial onset of puberty with its hormonal, as already mentioned above, and other bodily changes, which could play a decisive role for fear learning and should be considered in further research more specifically.

Moreover, another aspect, that could have had an influence, is the choice of the stimulus type itself, which were faces of young adult females. Here, the potential impact of an adaptation to juvenile faces of both sexes within the paradigm would be of justified interest. Additionally, also the social aspect of human faces could have a further effect, especially for probands with social anxiety. An adjustment using for example geometric shapes without any social connotation could be a conceivable option like already implemented in adult anxiety patients (e.g. Lissek et al., 2010). In conclusion, differences concerning the reaction towards the stimuli by reason of age of the presented faces (as stimuli) or the type of stimuli cannot be ruled out,

although the screaming lady paradigm has been applied repetitively in some variations for all age groups from childhood via adolescence into adulthood (e.g. Schiele & Reinhard et al., 2016; Ahrens et al., 2016; Lau et al., 2008, 2011; Glenn et al., 2012a; Haddad, Xu, Raeder & Lau, 2013).

Noteworthily and as already elaborated above, the collection of subjective ratings took place only at the end of each phase and not throughout the experiment, which in contrast was the case for the measurement of the electrodermal activity (EDA, here SCR). An expansion to a more continuous way (for example trial-by-trial) for the gathering of the subjective ratings would enable a better examination of the precise course of the fear learning procedure straightly linked to fear conditioning, its generalization or extinction, whereas it would have to be proven that the continuous method does not influence the fear learning process itself (Lonsdorf et al., 2017; Lovibond & Shanks, 2002). Also, it would be meaningful to look at fear learning processes separately for both sexes, i.e. girls and boys, to have more detailed information about developmental differences and courses within one certain sex in order to adapt potential therapeutic or preventive measures appropriately. Of further interest are also genetic aspects that have impact on the versatility within fear learning processes, whereby there are first findings presented by Reinhard and colleagues (2019). Here, more studies including genetic aspects for the purpose of replication and further insights are necessary. Furthermore, fMRI studies would be valuable in this context as well.

5.4 Outlook, clinical implications and considerations and thoughts for future research

In the context of fear learning attentional processes, for example captured via eye tracking, should be considered very carefully because they might have a crucial influence. Dudeney, Sharpe and Hunt (2015) reported for example in their meta-analysis about a significantly larger attentional bias towards signals associated with menace in clinically anxious children than in their healthy counterparts. Furthermore, this bias seemed to be moderated by age, namely that the extent to which anxious and healthy children differed grew with higher age. The authors explained that all of the younger children showed a bias towards signals associated with menace in comparison to neutral signals, however, with increasing age the bias declined in healthy children, while in anxious children the bias remained.

The startle probe as fear specific measure in contrast to the SCR (Glenn et al., 2012a) would be also of interest in this context, however, it must be considered that its implementation would change the paradigm and its resulting findings substantially (Sjouwerman, Niehaus,

Kuhn & Lonsdorf, 2016). It must be taken into account that instructions given concerning awareness also have a meaningful effect on learning procedures (Weidemann, Satkunarajah & Lovibond, 2016) and hence their absence or presence must be implemented consistently.

Moreover, healthy, subclinical and also clinical samples of all ages should be compared in the context of fear learning and its different processes. Noticeably, still there is far more research in adult healthy, subclinical and clinical samples, which might have ethical reasons for the conduct as well as general acceptance of such experimental scientific work, where children and adolescents are going to be scared on purpose. Here, not only parents prefer to choose not to participate in order not to traumatize their healthy child in the worst case and, especially not to worsen the situation, if the child already suffers from a anxiety disorder. Thus, it is extremely important to build a good contact based on trust and confidence and to really take time to inform the families with children about the crucial meaning of this scientific field, particularly for preventive and new and more personalized therapeutic measures. Questions and doubts of the families have to be taken very seriously and have to constitute the highest priority in order to convince families to support this research and have a good as well as safe feeling to participate and contribute to new more targeted preventive and therapeutic ways in the field of anxiety research, which is a relevant topic already since childhood, as seen more detailed above. Furthermore, the role of comorbidities within anxiety disorders, which can vary in number and type(s), should be explored more thoroughly regarding their impact on fear learning procedures.

There are already promising findings, which deserve full consideration for future therapeutic measures: Shore, Kadosh, Lommen, Cooper & Lau (2017) demonstrated in a youth sample that subjective fear evaluations could be reduced significantly towards the danger as well as saftey cue, which were acquired during fear conditioning, via a cognitive reappraisal training in comparison to the controls post extinction. During this training the probands examined alternative and harmless interpretations related to the danger cue (i.e. scream). Another very promising finding about one possibility to reduce the generalization of conditioned fear effectively is presented by Feng and colleagues (2017) via the induction of positive emotions in healthy adults. This finding opens a new dimension for therapeutic interventions, although facing further questions of how to induce positive emotions experimentally and in daily life reliably, which can be a very individual issue, and how to enable anxious individuals to maintain positive emotional states or even better to create positive emotions themselves. Hughes and Kendall (2008) found quite supportive results, when they investigated the impact of a positive emotional condition on how children with a manifest

anxiety disorder would interpret an ambiguous menacing signal. Clinically anxious children displayed a negative bias interpreting menace, while this was not the case when they had positive emotions. Consequently, the question emerges whether further research based on these outcomes also is true for anxious adult and adolescent probands reducing their degree of overgeneralization or whether the extent of fear responses, like in this current work the level expressed by probands with higher anxiety sensitivity, could be relocated downwards to similar levels like probands with lower anxiety sensitivity.

To conclude, the scientific research concerning developmental aspects affecting the generalization of conditioned fear has to be expanded by far, that is it must be looked more detailed and precisely at the course from childhood via adolescence into adulthood in large and representative healthy, subclinical and clinical anxious samples of all ages. Especially replication studies are what is most needed now in order to prove the previous findings to be right and promising or wrong giving new directions for scientific experimental research.

Despite the enormous gain of insights and recognitions concerning psychological disorders within the last century, the comprehension of their constituents and procedures contained is still inchoate. Often psychological disorders are mainly diagnosed due to specific symptoms and obvious features of a particular disease, whereof a prescription of drug treatment or/and psychotherapy results usually. This process is based on two substantial diagnostic manuals: the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, use mainly in the USA) and the International Classification of Diseases (ICD-11, international use). Both are established and important for nationwide health, clinical diagnostic analysis, service performance as well as use in scientific work (Clark, Cuthbert, Lewis-Fernández, Narrow and Reed, 2017). Compared with these two the Research Domain Criteria (RDoC), founded by the National Institute of Mental Health (NIHM), were created in order to integrate neuroscience and basic behavioural science for a more profound comprehension of psychological disorders. This NIHM research domain criteria matrix includes six main domains of human operability, i.e. negative and positive valence, cognitive systems, systems for social process, arousal/modulatory systems and sensorimotor systems. Every domain embraces some behavioral elements or constructs. These constructs are examined on a continuum of typical/healthy to atypical/pathological functioning, whereby placed into the influential context of the individuals‘ sociocultural environment and neurodevelopment. Measuring constructs is possible via classes of variables or units of analysis: genes, molecules, cells, circuits, physiology, behavior and self-reports. The presented RDoC matrix was conceptualized in order

to develop further and make progress by means of repeatedly new joining research outcomes consequently being followed by modifications integrating the latest research results and building new and/or revised constructs as well as domains (Clark et al., 2017; retrieved from https://www.nimh.nih.gov/research/research-funded-by-nimh/rdoc/about-doc.shtml). Hence, RDoC aims at the creation of a scientific fundament for neuroscience-based diagnostic schemes in the future, which enable and foster more concise treatment purposes via the incorporation of decisive neural circuits. As a result RDoC will strengthen and ameliorate translational research (Sanislow, Ferrante, Pacheco, Rudorfer & Morris, 2019).

Moreover, computer-based neuroscience provides encouraging and auspicious approaches for data-supported and incorporating techniques potentially making it possible to delineate various phases of one disease, i.e. the gradual beginning vs. the full clinical picture. The accuracy, specificity as well as sensitivity of diagnostic means could benefit from this. In contrast, science in psychiatry normally relies upon one operating principle, based frequently on a linear causal model (Sanislow et al., 2019). These three presented systems, that is the ICD-11, the DSM-5 and the RDoC, are characterized by some resembling as well as completely different parts, but all of them aim at the diminution of the sorrows and impairments connected with psychological disorders (Clark et al., 2017).

This current thesis aimed at shedding additional light on crucial questions related to fear learning processes and related influencing factors contributing to the development of anxiety disorders in children and youths. Since the onset of anxiety disorders is usually in childhood, focusing on this decisive age span is of enormous importance - not only for understanding these processes from a developmental point of view, but also in the context of targeted prevention. Although this thesis could contribute to gaining more insight into these fundamental processes, there surely remain open questions - especially in underage samples - which need to be addressed by future research.

References:

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. http://dx.doi.org/10.1016/j.janxdis.2016.10.003

Andreatta, M., Neueder, D., Herzog, K., Genheimer, H., Schiele M.A., Deckert, J., Domschke, K., Reif, A., Wieser, M.J. & Pauli, P. (2020). Generalization of Conditioned Contextual Anxiety and the Modulatory Effects of Anxiety Sensitivity. *Neurotherapeutics 17*, 1239–1252. https://doi.org/10.1007/s13311-020-00831-8

Arnaudova, I. Krypotos, A.-M., Effting, M., Kindt, M. & Beckers, T. (2017). Fearing shades of grey: individual differences in fear responding towards generalisation stimuli. *Cognition and Emotion, 31*(6), 1181-1196. https://doi.org/10.1080/02699931.2016.1204990

Barkmann, C., Schulte-Markwort, M. & Brähler, E. (2011). Klinisch-psychiatrische Ratingskalen für das Kindes- und Jugendalter. Hogrefe Verlag, Göttingen.

Barlow, D.H., 2002. Anxiety and Its Disorders: The Nature and Treatment of Anxiety and Panic, 2nd ed. Guilford Press, New York.

Blackford, J.U., & Pine, D.S. (2012). Neural substrates of childhood anxiety disorders: a review of neuroimaging findings. *Child and Adolescent Psychiatric Clinics of North America, 21*(3), 501-525. http://doi.org/10.1016/j.chc.2012.05.002

Beckers, T., Krypotos, A.-M., Boddez, Y., Effting, M. & Kindt, M. (2012). What's wrong with fear conditioning? *Biological Psychology*, *92*(1), 90-96. https://doi.org/10.1016/j.biopsycho.2011.12.015

Beesdo, K., Bittner, A., Pine, D. S., Stein, M. B., Höfler, M., Lieb, R. & Wittchen, H.-U. (2007). Incidence of social anxiety disorder and the consistent risk for secondary depression in the first three decades of life. *Archives of General Psychiatry, 64*, 903–912. http://doi.org/10.1001/archpsyc.64.8.903

Beesdo, K., Knapp, S. & Pine, D.S. (2009). Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. *Psychiatric Clinics of North America, 32*(3), 483-524. http://doi.org/10.1016/j.psc.2009.06.002

Beesdo, K., Pine, D.S., Lieb, R. & Wittchen, H.-U. (2010). Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Archives of General Psychiatry, 67*(1), 47-57. http://doi.org/10.1001/archgenpsychiatry.2009.177

Berg, C.Z., Rapoport, J.L. & Whitaker, A. (1989). Childhood obsessive compulsive disorder: a two-year prospective study of a community sample. *Journal of the American Academy of Child and Adolescent Psychiatry, 28*(4), 528–533. https://doi.org/10.1097/00004583-198907000-00010

Bittner, A., Egger, H.L., Erkanli, A., Costello, E.J., Foley, D.L. & Angold, A. (2007). What do childhood anxiety disorders predict? *Journal of Child Psychology and Psychiatry, 48*(12), 1174-1183. http://doi.org/10.1111/j.1469-7610.2007.01812.x

Block, J.D., Sersen, E.A. & Wortis, J. (1970). Cardiac classical conditioning and reversal in mongoloid, encephalopathic, and normal child. *Child Development, 41*(3), 771–785. http://doi.org/10.2307/1127223

Boddez, Y., Baeyens, F., Luyten, L., Vansteenwegen, D., Hermans, D., & Beckers, T. (2013). Rating data are underrated: Validity of US expectancy in human fear conditioning. *Journal of Behavior Therapy and Experimental Psychiatry*, *44*, 201-206. http://dx.doi.org/10.1016 /j.jbt ep.2012.08.003

Boddez, Y., Vervliet, B., Baeyens, F., Lauwers, S., Hermans, D. & Beckers, T. (2012). Expectancy bias in a selective conditioning procedure: trait anxiety increases the threat value of a blocked stimulus. *Journal of Behavior Therapy and Experimental Psychiatry 43*, 832–837. https://doi.org/10.1016/j.jbtep.2011.11.005

Boden, J. M., Fergusson, D. M., & Horwood, L. J. (2007). Anxiety disorders and suicidal behaviours in adolescence and young adulthood: Findings from a longitudinal study. *Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences, 37*, 431–440. http://doi.org/10.1017/S0033291706009147

Bouton, M.E. (2004). Context and behavioral processes in extinction. *Learning & Memory, 11*, 485-494. http://doi.org/10.1101/lm.78804

Briscione, M.A., Jovanovic, T. & Norrholm, S.D. (2014). Conditioned fear associated phenotypes as robust, translational indices of trauma-, stressor-, and anxiety-related behaviors. Frontiers in Psychiatry, 5(88), 1-9. https://doi.org/10.3389/fpsyt.2014.00088

Britton, J.C., Grillon, C., Lissek, S., Norcross, M., Szuhany, K.L., Chen, G., Ernst, M., Nelson, E.E., Leibenluft, E., Shechner, T. & Pine D.S. (2013). Response to learned threat: An fMRI study in adolescent and adult anxiety. *American Journal of Psychiatry, 170*(10), 1198–1204. https://doi.org/10.1176/appi.ajp.2013.12050651

Campbell, B.A. & Haroutunian, V. (1983). Perceptual sharpening in the developing rat. *Journal of Comparative Psychology, 97*(1), 3–11. https://doi.org/10.1037/0735-7036.97.1.3

Casey, B.J., Jones, R.M. & Hare T.A. (2008). The Adolescent Brain, *Annals of the New York Academy of Sciences, 1124*(1), 111-126. https://doi.org/10.1196/annals.1440.010

Chambers, J.A., Power, K.G. & Durham, R.C. (2004). The relationship between trait vulnerability and anxiety and depressive diagnoses at long-term follow-up of Generalized Anxiety Disorder. *Journal of Anxiety Disoerders, 18*(5), 587-607. https://doi.org/10.1016/j.janxdis.2003.09.001

Christianson, J.P., Fernando, A.B.P., Kazama, A.M., Jovanovic, T., Ostroff, L.E. & Sangha, S. (2012). Inhibition of Fear by Learned Safety Signals: A Mini-Symposium Review. *The Journal of Neuroscience, 32*(41), 14118-14124. https://doi.org/10.1523/JNEUROSCI.3340-12.2012

Christie, K.A., Burke, J.D., Jr., Regier, D.A., Rae, D.S., Boyd, J.H. & Locke, B.Z. (1988). Epidemiologic evidence for early onset of mental disorders and higher risk of drug abuse in young adults. *American Journal of Psychiatry, 145*(8), 971-975. https://doi.org/10.1176/ajp.145.8.971

Clark, L.A., Cuthbert, B., Lewis-Fernández, R., Narrow, W.E. & Reed, G.M. (2017). Three Approaches to Understanding and Classifying Mental Disorder: *ICD-11, DSM-5*, and the National Institute of Mental Health's Research Domain Criteria (RDoC). *Psychological Science in the Public Interest, 18*(2), 72– 145. https://doi.org/10.1177/1529100617727266

Costello, E.J., Egger, H.L. & Angold, A. (2005). The developmental epidemiology of anxiety disorders: Phenomenology, prevalence, and comorbidity. *Child and Adolescents Psychiatric Clinics of North America, 14*(4), 631-648. https://doi.org/10.1016/j.chc.2005.06.003

Costello, E.J., Egger, H.L., Copeland, W., Erkanli, A. & Angold, A. (2011). Anxiety Disorders in Children and Adolescents, Second edition. http://doi.org/0.1017/CBO9780511994920.004

Craske, M.G., Treanor, M., Conway, C., Zbozinek, T. & Vervliet, B. (2014). Maximizing Exposure Therapy: An Inhibitory Learning Approach. *Behaviour Research and Therapy, 58,* 10-23. http://doi.org/10.1016/j.brat.2014.04.006.

Craske, M.G., Waters, A.M., Bergman, R.L., Naliboff, B., Lipp, O.V., Negoro, H., & Ornitz, E.M. (2008). Is aversive learning a marker of risk for anxiety disorders in children? *Behaviour Research and Therapy, 46*(8), 954–967. https://doi.org/10.1016/j.brat.2008.04.011

Craske, M.G., Wolitzky-Taylor, K.B., Mineka, S., Zinbarg, R., Waters, A.M., Vrshek-Schallhorn, S., Epstein, A., Naliboff, B., & Ornitz, E. (2012). Elevated responding to safe conditions as a specific risk factor for anxiety versus depressive disorders: Evidence from a longitudinal investigation. *Journal of Abnormal Psychology, 121*(2), 315–324. https://doi.org/10.1037/a0025738

Davis, M. (1990). Animal models of anxiety based on classical conditioning: the conditioned emotional response (CER) and the fear-potentiated startle effect. *Pharmacology & Therapeutics, 47*(2), 147–165. https://doi.org/10.1016/0163-7258(90)90084-F

Davis, T.E., Castagna, P., Shaheen, G. & Reuther, E.T. (2017) Anxiety Disorders. In: Matson J. (eds) Handbook of Social Behavior and Skills in Children. Autism and Child Psychopathology Series. Springer, Cham. http://doi.org/10.1007/978-3-319-64592-6_16

De Bellis, M.D., Casey, B.J., Dahl, R.E., Birmaher, B., Williamson, D.E., Thomas, K.M. & Ryan, N.D. (2000). A pilot study of amygdala volumes in pediatric generalized anxiety disorder. *Biological Psychiatry, 48*(1), 51–57. https://doi.org/10.1016/S0006-3223(00)00835-0

Decety, J., Michalska, K.J. & Kinzler, K.D. (2012). The contribution of emotion and cognition to moral sensitivity: a neurodevelopmental study. *Cerebral Cortex, 22*(1), 209–20. https://doi.org/10.1093/cercor/bhr111

Den, M.L., Graham, B.M., Newall, C. & Richardson, R. (2015). Teens that fear screams: A comparison of fear conditioning, extinction, and reinstatement in adolescents and adults. *Developmental Psychobiology, 57*(7), 818-832. https://doi.org/10.1002/dev.21330

Drake, K.L. & Ginsburg, G.S. (2012). Family Factors in the Development, Treatment, and Prevention of Childhood Anxiety Disorders. *Clinical Child and Family Psychology Review, 15,* 144-162. http://doi.org/10.1007/s10567-011-0109-0

Dudeney, J., Sharpe, L. & Hunt, C. (2015). Attentional bias towards threatening stimuli in children with anxiety: A meta-analysis. *Clinical Psychology Review, 40*, 66-75. http://doi.org /10.1016/j.cpr.2015.05.007

Dunsmoor, J.E. & Paz, R. (2015). Fear Generalization and Anxiety: Behavioral and Neural Mechanisms. *Biological Psychiatry*, *78*(5), 336-343. https://doi.org/10.1016/j.biopsych.2015.04.010

Dunsmoor, J.E., Prince, S. E., Murty, V. P., Kragel, P. A., & LaBar, K. S. (2011). Neurobehavioral mechanisms of human fear generalization. *NeuroImage*, *55*(4), 1878–1888. http://doi.org/10.1016/j.neuroimage.2011.01.041

Duits, P., Cath, D.C., Lissek, S., Hox, J.J., Hamm, A.O., Engelhard, I.M., van den Hout, M.A. & Baas, J.M.P. (2015). Updated meta-analysis of classical fear conditioning in the anxiety disorders. *Depression and Anxiety*, *32*(4), 239-253. https://doi.org/10.1002/da.22353

Dvir, M., Horovitz, O., Aderka, I.M. & Shechner, T. (2019). Fear conditioning and extinction in anxious and non-anxious youth: A meta-analysis. Behaviour Research and Therapy, 120, 1-7. https://doi.org/10.1016/j.brat.2019.103431

Dymond, S., Dunsmoor, J.E., Vervliet, B., Roche, B. & Hermans, D. (2015). Fear Generalization in Humans: Systematic Review and Implications for Anxiety Disorder Research, *Behavior Therapy*, *46*(5), 561-582. https://doi.org/10.1016/j.beth.2014.10.001

El-Bar, N., Laufer, O., Yoran-Hegesh, R. & Paz, R. (2017). Over-generalization in youth with anxiety disorders. *Social Neuroscience*, *12*(1), 76-85. http://dx.doi.org/10.1080/17470919.2016.1167123

El-Sheikh M. (2007). Children's skin conductance level and reactivity: Are these measures stable over time and across tasks? *Developmental Psychobiology*, *49*(2), 180–186. https://doi.org/10.1002/dev.20171

El-Sheikh, M., Keiley, M., & Hinnant, J.B. (2010). Developmental Trajectories of Skin Conductance Level in Middle Childhood: Sex, Race, and Externalizing Behavior problems as Predictors of Growth. *Biological Psychology*, *83*(2), 116-124. http://doi.org/10.1016/j.biopsycho.2009.11.009

Evans, D.L., Foa, E.B., Gur, R.E., Hendin, H., O'Brien, C.P., Seligman, M.E.P. & Walsh, B.T. (2005). *Treating and preventing adolescent mental health disorders: What we know and what we don't know, a research agenda for improving the mental health of our youth.* Oxford: University Press.

Farrell, L.J. & Barrett, P.M. (2007). Prevention of Childhood Emotional Disorders: Reducing the Burden of Suffering Associated with Anxiety and Depression. *Child and Adolescent Mental Health, 12*(2), 58-65. http://doi.org/10.1111/j.1475-3588.2006.00430.x

Feehan, M., McGee, R. & Williams, S.M. (1993). Mental health disorders from age 15 to age 18 years. *Journal of the American Academy of Child and Adolescent Psychiatry, 32*(6), 1118–1126. https://doi.org/10.1097/00004583-199311000-00003

Feldman Barrett, L., & Russell, J.A. (1998). Independence and bipolarity in the structure of current affect. *Journal of Personality and Social Psychology, 74,* 967–984. https://doi.org/10.1037/0022-3514.74.4.967

Feldman Barrett, L. & Russell, J.A. (1999). The Structure of Current Affect: Controversies and Emerging Consensus. *Current Directions in Psychological Science, 8*(1), 10-14. http://doi.org/10.1111/1467-8721.00003

Feng, B., Xu, L., Zhang, W., Chen, T., Wang, W. & Zheng, X. (2017). The inhibitory effect of positive emotions on fear generalization, *Acta Psychologica Sinica, 49*(3), 317-328. http://doi.org/10.3724/SP.J.1041.2017.00317

Ferdinand, R.F. & Verhulst, F.C. (1995). Psychopathology from adolescence into young adulthood: an 8 year follow-up study. *American Journal of Psychiatry, 152*(11), 1586–1594. https://doi.org/10.1176/ajp.152.11.1586

Flament, M.F., Koby, E. & Rapoport, J.L. (1990). Childhood obsessive-compulsive disorder: a prospective follow-up study. *Journal of Child Psychology and Psychiatry, 31* (3), 363–380. https://doi.org/10.1111/j.1469-7610.1990.tb01575.x

Frijda, N.H. (1986). *The Emotions*. Cambridge University Press, Cambridge, England.

Fullana, M.A., Albajes-Eizagirre, A., Soriano-Mas, C., Vervliet, B., Cardoner, N., Benet, O., Radua, J. & Harrison, B.J. (2018). Fear extinction in the human brain: A meta-analysis of fMRI studies in healthy participants. *Neuroscience & Biobehavioral Reviews, 88,* 16-25. https://doi.org/10.1016/j.neubiorev.2018.03.002

Fullana, M.A., Harrison, B. J., Soriano-Mas, C., Vervliet, B., Cardoner, N., Avila-Parcet, A., & Radua, J. (2016). Neural signatures of human fear conditioning: an updated and extended meta-analysis of fMRI studies. *Mol Psychiatry*, *21*(4), 500-508. http://doi.org/10.1038/mp.2015.88

Gao, Y., Raine, A., Venables, P.H., Dawson, M.E. & Mednick, S.A. (2010). The development of skin conductance fear conditioning in children from ages 3 to 8 years. *Developmental Science*, *13*(1), 201-212. https://doi.org/10.1111/j.1467-7687.2009.00874.x

Gazendam, F.J., Kamphuis, J.H. & Kindt, M. (2013). Deficient safety learning characterizes high trait anxious individuals. *Biological Psychology*, *92*, 342– 352. https://doi.org/10.1016/j.biopsycho.2012.11.006

Gershuny, B.S. & Sher, K.J. (1998). The relation between personality and anxiety: Findings from a 3-year prospective study. *Journal of Abnormal Psychology*, *107*(2), 252–262. https://doi.org/10.1037/0021-843X.107.2.252

Ginsburg, G.S., Becker, E.M., Keeton, C.P., Sakolsky, D., Piacentini, J., Albano, A.M., Compton, S.N., Iyengar, S., Sullivan, K., Caporino, N., Peris, T., Birmaher, B., Rynn, M., March, J. & Kendall, P.C. (2014). Naturalistic Follow-up of Youths Treated for Pediatric Anxiety Disorders. *JAMA* Psychiatry. *71*(3), 310–318. http://doi.org/10.1001/jamapsychiatry.2013.4186

Ginsburg, G.S. & Drake, K.L. (2002). Anxiety sensitivity and panic attack symptomatology among low-income African-American adolescents. *Journal of Anxiety Disorders*, *16*, 83-96. https://doi.org/10.1016/S0887-6185(01)00092-5

Glenn, C.R., Klein, D.N., Lissek, S., Britton, J.C., Pine, D.S., & Hajcak, G. (2012a). The development of fear learning and generalization in 8–13 year-olds. *Developmental Psychobiology*, *54*, 675–684. https://doi.org/10.1002/dev.20616

Glenn, C.R., Lieberman, L., Hajcak, G. (2012b). Comparing electric shock and a fearful screaming face as unconditioned stimuli for fear learning. *International Journal of Psychophysiology*, *86*(3), 214–219. https://doi.org/10.1016/j.ijpsycho.2012.09.006

Glotzbach-Schoon, E., Tadda, R., Andreatta, M., Tröger, C., Ewald, H., Grillon, C., Pauli, P., & Mühlberger, A. (2013). Enhanced discrimination between threatening and safe contexts in high-anxious individuals. *Biological Psycholology*, *93*(1), 159–166. http://doi.org/10.1016/j.biopsycho.2013.01.011

Gogtay, N., Giedd, J.N., Lusk, L., Hayashi, K.M., Greenstein, D., Vaituzis, A.C., Nugent, T.F. III, Herman, D.H., Clasen, L.S., Toga, A.W., Rapoport, J.L. & Thompson, P.M. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences of the United States of America, 101*(21), 8174-8179. https://doi.org/10.1073/pnas.0402680101

Graham, L.K., Yoon, T., Lee, H.J. & Kim, J.J. (2009). Strain and sex differences in fear conditioning: 22 kHz ultrasonic vocalizations and freezing in rats. *Psychology & Neuroscience, 2*(2), 219 – 225. http://doi.org/10.3922/j.psns.2009.2.015

Gravetter, F.J. & Forzano, L.-A.B. (2015). *Research Methods for the Behavioral Sciences*. Cengage Learning.

Greco, J.A. & Liberzon, I. (2016). Neuroimaging of Fear-Associated Learning. *Neuropsychopharmacology Reviews, 41*(1), 320–334. https://doi.org/10.1038/npp.2015.255

Greenberg, P.E., Sisitsky, T., Kessler, R.C., Finkelstein, S.N., Berndt, E.R., Davidson, J.R.T., Ballenger, J.C. & Fyer, A.J. (1999). The economic burden of anxiety disorders in the 1990s. *Journal of Clinical Psychiatry*, *60*(7), 427–435. https://doi.org/10.4088/jcp.v60n0702

Gregory, A.M., Caspi, A., Moffitt, T.E., Koenen, K., Eley, T.C. & Poulton, R. (2007). Juvenile mental health histories of adults with anxiety disorders. *The American Journal of Psychiatry, 164*(2), 301–308. https://doi.org/10.1176/appi.ajp.164.2.301

Grillon, C. & Morgan III, C.A. (1999). Fear-potentiated startle conditioning to explicit and contextual cues in Gulf War veterans with posttraumatic stress disorder. *Journal of Abnormal Psychology, 108*(1), 134–142. https://doi.org/10.1037/0021-843X.108.1.134.

Gullone, E. & King, N.J. (1997). Three-year follow-up of normal fear in children and adolescents aged 7 to 18 years. *British Journal of Developmental Psychology, 15*, 97-111. https://doi.org/10.1111/j.2044-835X.1997.tb00727.x

Gullone, E. (2000). The development of normal fear: a century of research. *Clinical Psychology Review*,*20*(4), 429-451. https://doi.org/10.1016/S0272-7358(99)00034-3

Gustavsson, A., Svensson, M., Jacobi, F., Allgulander, C., Alonso, J., Beghi, E., Dodel, R., Ekman, M., Faravelli, C., Fratiglioni, L., Gannon, B., Jones, D.H., Jennum P. Jordanova, A., Jonsson, L., Karampampa, K., Knapp, M., Kobelt, G., Kurth, T., Lieb, R. et al. (2011). Cost of disorders of the brain in Europe 2010. *European Neuropsychopharmacology, 21*(10), 718-779. https://doi.org/10.1016/j.euroneuro.2011.08.008

Haaker, J., Lonsdorf, T.B., Schümann, D., Menz, M., Brassen, S., Bunzeck, N., Gamer, M. & R. Kalisch (2015). Deficient inhibitory processing in trait anxiety: Evidence from context-dependent fear learing, extinction recall and renewal. *Biological Psychology, 111*, 65-72. https://doi.org/10.1016/j.biopsycho.2015.07.010

Haddad, A.D.M., Lissek, S., Pine, D.S. & Lau, J.Y. (2011). How do social fears in adolescence develop? Fear conditioning shapes attention orienting to social threat cues. *Cognition & Emotion, 25*(6), 1139–1147. https://doi.org/10.1080/02699931.2010.524193

Haddad, A.D.M., Xu, M., Raeder, S. & Lau, J.Y.F. (2013). Measuring the role of conditioning and stimulus generalisation in common fears and worries. *Cognition and Emotion, 27*(5), 914-922. http://doi.org/10.1080/02699931.2012.747428

Hajcak, G., Castille, C., Olvet, D.M., Dunning, J.P., Roohi, J. & Hatchwell, E. (2009). Genetic variation in brain-derived neurotrophic factor and human fear conditioning. *Genes, Brain and Behavior, 8*(1), 80-85. https://doi.org/10.1111/j.1601-183X.2008.00447.x

Hartley, C.A. & Lee, F.S. (2015). Sensitive Periods in Affective Development: Nonlinear Maturation of Fear Learning. *Neuropsychopharmacology, 40*, 50–60. https://doi.org/10.1038/npp.2014.179

Hayward, C., Killen, J.D., Kraemer, H.C. & Taylor, C.B. (2000). Predictors of panic attacks in adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*, 207-214. https://doi.org/10.1097/00004583-200002000-00021

Heilman, K.M. (1997). The neurobiology of emotional experience. *Journal of Neuropsychiatry and Clinical Neurosciences, 9*(3), 439–448. https://doi.org/10.1176/jnp.9.3.439

Hofmann, S.G., Ellard, K.K. & Siegle, G.J. (2012). Neurobiological correlates of cognitions in fear and anxiety: a cognitive-neurobiological information-processing model. *Cognition and Emotion, 26*(2), 282-299. http://doi.org/10.1080/02699931.2011.579414

Hughes, A.A. & Kendall, P.C. (2008). Effect of a positive emotional state on interpretation bias for threat in children with anxiety disorders. *Emotion, 8*(3), 414-418. https://doi.org/10.1037/1528-3542.8.3.414

Indovina, I., Robbins, T.W., Nunez-Elizalde, A.O., Dunn, B.D. & Bishop, S.J. (2011). Fear-conditioning mechanisms associated with trait vulnerability to anxiety in humans. *Neuron, 69*, 563–571. https://doi.org/10.1016/j.neuron.2010.12.034

Ito, W., Pan, B.X., Yang, C., Thakur, S. & Morozov, A. (2009). Enhanced generalization of auditory conditioned fear in juvenile mice. *Learning & Memory, 16*, 187-192. http://doi.org/10.1101/lm.1190809

Janes, C.L., Hesselbrock, V. & Stern, J.A. (1978). Parental psychopathology, age and race as related to electrodermal activity in children. *Psychophysiology, 15*(1), 24-34. https://doi.org/10.1111/j.1469-8986.1978.tb01329.x

Jorm, A.F., Christensen, H., Henderson, A.S., Jacomb, P.A., Korten, A.E., & Rodgers, B. (2000). Predicting anxiety and depression from personality: Is there a synergistic effect of neuroticism and extraversion? *Journal of Abnormal Psychology, 109*(1), 145–149. https://doi.org/10.1037/0021-843X.109.1.145

Jorm, A.F. & Wright, A. (2008). Influences on young people's stigmatising attitudes towards peers with mental disorders: National survey of young Australians and their parents. *British Journal of Psychiatry, 192*(2), 144-149. http://doi.org/10.1192/bjp.bp.107.039404

Jovanovic, T., Nylocks, K.M., Gamwell, K.L., Smith, A., Davis, T.A., Norrholm, S.D. & Bradley, B. (2014). Development of fear acquisition and extinction in children: effects of age and anxiety. *Neurobiology of Learning and Memory, 113*, 135-142. http://doi.org/10.1016/j.nlm.2013.10.016

Jovanovic, T., Nylocks, K.M. & Gamwell, K.L. (2013). Translational neuroscience measures of fear conditioning across development: applications to high-risk children and adolescents. *Biology of Mood & Anxiety Disorders, 3*(17), 1-11. https://doi.org/10.1186/2045-5380-3-17

Kaczkurkin, A.N., Burton, P.C., Chazin, S.M., Manbeck, A.B., Espensen-Sturges, T., Cooper, S.E., Sponheim, S.R. & Lissek, S. (2017). Neural Substrates of Overgeneralized Conditioned Fear in PTSD. *American Journal of Psychiatry, 174*(2), 125-134. https://doi.org/10.1176/appi.ajp.2016.15121549

Kadosh, K.C., Haddad, A.D.M., Heathcote, L.C., Murphy, R.A. Pine, D.S. & Lau, J.Y.F. (2015). High trait anxiety during adolescence interferes with discriminatory context learning. *Neurobiology of Learning and Memory, 123*, 50-57. https://doi.org/10.1016/j.nlm.2015.05.002

Keller, M.B., Lavori, P.W., Wunder, J., Beardslee, W.R., Schwartz, C.E. & Roth, J. (1992). Chronic course of anxiety disorders in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 31*(4), 595–599. https://doi.org/10.1097/00004583-199207000-00003

Kessler, R.C., Berglund, P., Demler, O., Jin, R., Merikangas, K.R. & Walters, E.E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry, 62*(6), 593-602. http://doi.org/10.1001/archpsyc.62.6.593

King, N.J., Ollier, K., Iacuone, R., Schuster, S., Bays, K., Gullone, E. & Ollendick, T.H. (1989). Child and adolescent fears: An Australian cross-sectional study using the Revised Fear Survey Schedule for Children. *Journal* of *Child Psychology and Psychiatry*, *30*(5), 775-784. https://doi.org/10.1111/j.1469-7610.1989.tb00789.x

Kim, J.H., Li & S., Richardson, R. (2011). Immunohistochemical analyses of long-term extinction of conditioned fear in adolescent rats. *Cerebral Cortex, 21*, 530–538. https://doi.org/10.1093/cercor/bhq116

Kim, J.H. & Richardson, R. (2010). New Findings on Extinction of Conditioned Fear Early in Development: Theoretical and Clinical Implications. *Biological Psychiatry, 67*, 297-303. http://doi.org.10.1016/j.biopsych.2009.09.003

Kim, J.H. & Richardson, R. (2008). The effect of temporary amygdala inactivation on extinction and reextinction of fear in the developing Rat: unlearning as a potential mechanism for extinction early in development. *Journal of Neuroscience, 28*, 1282–1290. https://doi.org/10.1523/JNEUROSCI.4736-07.2008

LaBar, K.S., Gatenby, J.C., Gore, J.C., LeDoux, J.E. & Phelps, E.A. (1998). Human Amygdala Activation during Conditioned Fear Acquisition and Extinction: a Mixed-Trial fMRI Study. *Neuron, 20*(5), 937-945. https://doi.org/10.1016/S0896-6273(00)80475-4

Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (1997). Motivated attention: Affect, activation, and action. In Lang, P.J., Simons, R.F. & Balaban, M.T. (Eds.), *Attention and orienting: Sensory and motivational processes* (pp. 97–136). Hillsdale, NJ: Erlbaum.

Lau, J.Y., Britton, J.C., Nelson, E.E., Angold, A., Ernst, M., Goldwin, M., Grillon, C., Leibenluft, E., Lissek, S., Norcross, M., Shiffrin, N. & Pine, D.S. (2011). Distinct neural signatures of threat learning in adolescents and adults. *Proceedings of the National Academy of Sciences of the United States of America, 108,* 4500–4505. https://doi.org/10.1073/pnas.1005494108

Lau, J.Y., Lissek, S., Nelson, E.E., Lee, Y., Roberson-Nay, R., Poeth, K., Jenness, J., Ernst, M., Grillon, C. & Pine, D.S. (2008). Fear conditioning in adolescents with anxiety disorders: results from a novel experimental paradigm. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*, 94–102. https://doi.org/10.1097/chi.0b01e31815a5f01

Lebron-Milad, K. & Milad, M.R. (2012). Sex differences, gonadal hormones and the fear extinction network: implications for anxiety disorders. *Biology of Mood & Anxiety Disorders, 2*(3), 1-12. https://doi.org/10.1186/2045-5380-2-3

LeDoux, J.E. (2014). Coming to terms with fear. *Proceedings of the National Academy of Sciences of the United States of America, 111(8*), 2871-2878. https://doi.org/10.1073/pnas.1400335111

LeDoux, J. (2003). The emotional brain, fear, and the amygdala. *Cellular and Molecular Neurobiology*, *23*(4–5), 727–738. https://doi.org/10.1023/A:1025048802629

LeDoux, J.E. (1996). *The emotional brain: The mysterious underpinnings of emotional life.* New York: Simon & Schuster.

LeDoux, J. (1998). The Neural Circuits Underlying Anxiety and Fear. Fear and the brain: where have we been, and where are we going? *Biological Psychiatry, 44*(12), 1229-1238. https://doi.org/10.1016/S0006-3223(98)00282-0

Lenaert, B., van de Ven, V., Kaas, A.L. & Vlaeyen, J.W.S. (2016). Generalization on the Basis of Prior Experience Is Predicted by Individual Differences in Working Memory. *Behavior Therapy, 47*, 130-140. https://doi.org/10.1016/j.beth.2015.10.001

Lenaert, B., Boddez, Y., Griffith, J.W., Vervliet, B., Schruers, K. & Hermans, D. (2014). Aversive learning and generalization predict subclinical levels of anxiety: A six-month longitudinal study. *Journal of Anxiety Disorders, 28*(8), 747-753. https://doi.org/10.1016/j.janxdis.2014.09.006

Lewinsohn, P.M., Gotlib, I.H., Lewinsohn, M., Seeley, J.R., & Allen, N.B. (1998). Gender differences in anxiety disorders and anxiety symptoms in adolescents. *Journal of Abnormal Psychology, 107*(1), 109–117. https://doi.org/10.1037/0021-843X.107.1.109

Liberman, L.C., Lipp, O.V., Spence, S.H. & March, S. (2006). Evidence for retarded extinction of aversive learning in anxious children. *Behaviour Research and Therapy, 44*(10), 1491–1502. https://doi.org/10.1016/j.brat.2005.11.004

Lindsay, D. S. (2015). Replication in psychological science. *Psychological Science, 26*(12), 1827–1832. http://doi.org/10.1177/0956797615616374

Lissek, S., Biggs, A.L., Rabin, S.J., Cornwell, B.R., Alvarez, R.P., Pine, D.S. & Grillon, C. (2008). Generalization of conditioned fear-potentiated startle in humans: experimental validation and clinical relevance. *Behaviour Research and Therapy, 46*(5), 678-87. http://doi.org/10.1016/j.brat.2008.02.005.

Lissek, S., Bradford, D.E., Alvarez, R.P., Burton, P., Espensen-Sturges, T., Reynolds, R.C. & Grillon, C. (2014a). Neural substrates of classically conditioned fear-generalization in humans: a parametric fMRI study. *Social Cognitive and Affective Neuroscience, 9*(8), 1134-1142. https://doi.org/10.1093/scan/nst096

Lissek, S., & Grillon C., (2012). Learning Models of PTSD. In J. G. Beck, & D. M. Sloan, (Eds.), *The Oxford handbook of traumatic stress disorders* (pp. 175–190). New York: Oxford University Press. https://doi.org/10.1093/oxfordhb/9780195399066.013.0013

Lissek, S., Kaczkurkin, A. N., Rabin, S., Geraci, M., Pine, D. S. & Grillon, C. (2014b). Generalized anxiety disorder is associated with overgeneralization of classically conditioned fear. *Biological Psychiatry, 75*, 909–915. https://doi.org/10.1016/j.biopsych.2013.07.025

Lissek, S., Powers, A.S., McClure, E.B., Phelps, E.A., Woldehawariat, G., Grillon, C. & Pine, D.S. (2005). Classical fear conditioning in the anxiety disorders: a meta-analysis. *Behaviour Research and Therapy, 43*, 1391–1424. https://doi.org/10.1016/j.brat.2004.10.007

Lissek, S., Rabin, S., Heller, R.E., Lukenbaugh, D., Geraci, M., Pine, D.S., & Grillon, C. (2010). Overgeneralization of conditioned fear as a pathogenic marker of panic disorder. *American Journal of Psychiatry, 167*(1), 47–55. https://doi.org/10.1176/appi.ajp.2009.09030410

Lissek, S., Rabin, S.J., McDowell, D.J., Dvir, S., Bradford, D.E., Geraci, M., Pine, D.S. & Grillon, C. (2009). Impaired Discriminative Fear-Conditioning Resulting from Elevated Fear-Responding to Learned Safety Cues Among Individuals with Panic Disorder. *Behaviour Research and Therapy, 47*(2), 111–118. http://doi.org/10.1016/j.brat.2008.10.017.

Lissek, S. (2012). Toward an account of clinical anxiety predicated on basic, neurally mapped mechanisms of pavlovian fear-learning: the case for conditioned overgeneralization. *Depression and Anxiety, 29*(4), 257-263. http://doi.org/10.1002/da.21922

Lonsdorf, T.B., Menza, M.M., Andreatta, M., Fullana, M.A., Golkarf, A., Haaker, J., Heitland, I., Hermann, A., Kuhn, M., Kruse, O., Meir Drexler, S., Meulders, A., Nees, F., Pittig, A., Richter, J., Römero, S., Shiban, Y., Schmitz, A., Straube, B., … Merz, C.J. (2017). Don't fear 'fear conditioning': Methodological considerations for the design and analysis of studies on human fear acquisition, extinction, and return of fear. *Neuroscience and Biobehavioral Reviews,* 77, 247–285. http://dx.doi.org/10.1016/j.neubiorev.2017.02.026

Lonsdorf, T.B., Haaker, J., Schümann, D., Sommer, T., Bayer, J., Brassen, S., Bunzeck, N., Gamer, M. & Kalisch, R. (2015). Sex differences in conditioned stimulus discrimination during context-dependent fear learning and its retrieval in humans: the role of biological sex, contraceptives and menstrual cycle phases. *Journal of Psychiatry & Neuroscience, 40*(6), 368-375. http://doi.org/10.1503/140336

Lovibond, P.F. & Shanks, D.R. (2002). The role of awareness in Pavlovian conditioning: empirical evidence and theoretical implications. *Journal of Experimental Psychology: Animal Behavior Processes, 28*, 3-26. http://org.doi/10.1037//0097-7403.28.1.3

Maeng, L.Y. & Milad, M.R. (2015). Sex Differences in Anxiety Disorders: Interactions between Fear, Stress, and Gonadal Hormones. *Hormones and Behavior, 76*, 106–117. http://doi.org/10.1016/j.yhbeh.2015.04.002

Marin, M.F., Zsido, R.G., Song, H., Lasko, N.B., Killgore, W.D.S., Rauch, S.L., Simon, N.M. & Milad, M.R. (2017). Skin Conductance Responses and Neural Activations During Fear Conditioning and Extinction Recall Across Anxiety Disorders. *JAMA Psychiatry*. http://doi.org/10.1001/jamapsychiatry.2017.0329

Maxwell, S.E., Lau, M.Y. & Howard, G.S. (2015). Is Psychology Suffering From a Replication Crisis? What Does "Failure to Replicate" Really Mean? *American Psychologist, 70*(6), 487-498. http://dx.doi.org/10.1037/a0039400

McClure, E.B., Monk, C.S., Nelson, E.E., Parrish, J.M., Adler, A., Blair, R.J.R., Fromm, S., Charney, D.S., Leibenluft, E., Ernst, M. & Pine, D.S. (2007). Abnormal attention modulation of fear circuit function in pediatric generalized anxiety disorder. *Archives of General Psychiatry, 64*(1), 97-106. http://doi.org/10.1001/ archpsyc.64.1.97

McEchron, M.D., Tseng, W. & Disterhoft, J.F. (2000). Neurotoxic Lesions of the Dorsal Hippocampus Disrupt Auditory-Cued Trace Heart Rate (Fear) Conditioning in Rabbits. *Hippocampus, 10*, 739–751. https://doi.org/10.1002/1098-1063(2000)10:6<739::AID-HIPO1011>3.0.CO;2-I

McNally, R.J. (2002). Anxiety sensitivity and panic disorder. *Biological Psychiatry, 52*, 938-946. https://doi.org/10.1016/S0006-3223(02)01475-0

Merikangas, K.R., Mehta, R.L., Molnar, B.E., Walters, E.E., Swendsen, J.D., Aguilar-Gaziola, S., Bijl, R., Borges, G., Caraveo-Anduaga, J.J., Dewit, D.J., Kolody, B., Vega, W.A., Wittchen, H.-U. & Kessler, R.C. (1998). Comorbidity of substance use disorders with mood and anxiety disorders: results of the international consortium in psychiatric epidemiology. *Addictive Behaviors, 23*(6), 893-907. https://doi.org/10.1016/S0306-4603(98)00076-8

Mertens, R. (2016). *Aussagekraft der elektrodermalen Aktivität in Laborexperimenten mit Schwerpunkt Lärm – Literaturstudie zu wichtigen Einflussfaktoren und gesundheitlichen Implikationen* – (Medical Doctoral Dissertation). Heinrich-Heine-University Düsseldorf.

Michalska, K.J., Shechner, T., Hong, M., Britton, J.C., Leibenluft, E., Pine, D.S. & Fox, N.A. (2016). A developmental analysis of threat/safety learning and extinction recall during middle childhood. *Journal of Experimental Child Psychology, 146*, 95-105. https://doi.org/10.1016/j.jecp.2016.01.008

Milad, M.R., Zeidan, M.A., Contero, A., Pitman, R.K., Klibanski, A., Rauch, S.L. & Goldstein, J.M. (2010). The influence of gonadal hormones on conditioned fear extinction in healthy humans. *Neuroscience, 168*(3), 652–658. http://doi.org/10.1016/j.neuroscience. 2010.04.030.

Milad, M.R. & Quirk, G.J. (2002). Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature, 420*, 70–74. https://doi.org/10.1038/nature01138

Mineka, S. & Zinbarg, R. (2006). A Contemporary Learning Theory Perspective on the Etiology of Anxiety Disorders. *American Psychologist, 61*(1), 10-26. https://doi.org/10.1016/j.cpr.2004.04.003

Monfils, M.H., Cowansage, K.K., Klann, E. & LeDoux, J.E. (2009). Extinction-reconsolidation boundaries: key to persistent attenuation of fear memories. *Science, 324*(5929), 951–955. http://doi.org/10.1126/science.1167975

Monk, C.S. (2008). The development of emotion-related neural circuitry in health and psychopathology. *Development and Psychopathology, 20*, 1231-1250. http://doi.org/10.1017/S095457940800059X

Morrow, M.C., Boring, F.W., Keough, T.E. & Haesly, R.R. (1969). Differential GSR conditioning as a function of age. *Developmental Psychology, 1*(4), 299–302. https://doi.org/10.1037/h0027688

Muroff J. & Ross A. (2011) Social Disability and Impairment in Childhood Anxiety. In: McKay D. & Storch E. (eds) *Handbook of Child and Adolescent Anxiety Disorders*. Springer, New York, NY. https://doi.org/10.1007/978-1-4419-7784-7_31

Myers, K.M., Ressler, K.J. & Davis, M. (2006). Different mechanisms of fear extinction dependent on length of time since fear acquisition. *Learning & Memory, 13,* 216–223. http://doi.org/10.1101/lm.119806

Neumann, D.L., Waters, A.M. & Westbury, H. (2008a). The use of an unpleasant sound as the unconditional stimulus in aversive Pavlovian conditioning experiments that involve children and adolescent participants. *Behavior Research Methods, 40*(2), 622–625. https://doi.org/10.3758/BRM.40.2.622.

Neumann, D.L., Waters, A.M., Westbury, H. & Henry, J. (2008b). The use of an unpleasant sound unconditional stimulus in an aversive conditioning procedure with 8- to 11-year-old children. *Biological Psychology, 79*(3), 337–342. https://doi.org/10.1016/j.biopsycho. 2008.08.005.

Norrholm, S.D., Jovanovic, T., Vervliet, B., Myers, K.M., Davis, M., Rothbaum, B.O. & Duncan, E.J. (2006). Conditioned fear extinction and reinstatement in a human fear-potentiated startle paradigm. *Learning & Memory, 13*, 681–685. http://doi.org/10.1101/lm.393906

Öhman, A., Carlsson, K., Lundqvist, D. & Ingvar, M. (2007). On the unconscious subcortical origin of human fear. *Physiology & Behavior, 92*(1), 180-185. https://doi.org/10.1016/j.physbeh.2007.05.057

Öhman, A. (2008). Fear and anxiety: Overlaps and dissociations. In M. Lewis, J. M. Haviland-Jones, & L. F. Barrett (Eds.), *Handbook of emotions* (3rd ed.). New York: Guilford Press.

Öhman, A. (2009). Of snakes and faces: An evolutionary perspective on the psychology of fear. *Scandinavian Journal of Psychology, 50*, 543–552. http://doi.org/10.1111/j.1467-9450.2009.00784.x

Olesen, J., Gustavsson, A., Svensson, M., Wittchen, H.-U. & Jönsson, B. (2012). The economic cost of brain disorders in Europe. *European Journal of Neurology, 19*, 155–162. http://doi.org/10.1111/j.1468-1331.2011.03590.x

Pan, B.X., Ito, W. & Morozov, A. (2009). Divergence between thalamic and cortical inputs to lateral amygdala during juvenile–adult transition in mice. *Biological Psychiatry, 66,* 964–971. https://doi.org/10.1016/j.biopsych.2009.07.006

Pattwell, S.S., Duhoux, S., Hartley, C.A., Johnson, D.C., Jing, D., Elliott, M.D., Ruberry, E.J., Powers, A., Mehta, N., Yang, R.R., Soliman, F., Glatt, C.E., Casey, B.J., Ninan, I. & Lee, F.S. (2012). Altered fear learning across development in both mouse and human. *Proceedings of the National Academy of Sciences of the United States of America, 109*(40), 16318–16323. https://doi.org/10.1073/pnas.1206834109

Pavlov, I.P. (1927). *Conditioned reflexes*. Oxford: University Press.

Phelps, E.A. (2006). Emotion and cognition: insights from studies of the human amygdala. *Annual Review of Psychology, 57*, 27-53. http://doi.org/10.1146/annurev.psych.56. 091103.070234

Phelps, E.A., Delgado, M.R., Nearing, K.I. & LeDoux, J.E. (2004). Extinction learning in humans: role of the amygdala and vmPFC. *Neuron, 43*, 897–905. https://doi.org/10.1016/j.neuron.2004.08.042

Pine, D.S., Cohen, P., Gurley, D., Brook, J. & Ma, Y. (1998). The risk for early adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry, 55*(1), 56–64. http://doi.org/10.1001/archpsyc.55.1.56

Pittner, K., Kadosh, K.C., & Lau, J.Y.F. (2016). *Child and adolescent anxiety: Does fear conditioning play a role?* In R. A. Murphy & R. C. Honey (Eds.), *Wiley handbooks in cognitive neuroscience. The Wiley handbook on the cognitive neuroscience of learning* (p. 468–488). Wiley-Blackwell. https://doi.org/10.1002/9781118650813.ch18

Pliszka, S.R., Hatch, J.P., Borcherding, S.H. & Rogeness, G.A. (1993). Classical conditioning in children with attention deficit hyperactivity disorder (ADHD) and anxiety disorders: A test of Quay's model. *Journal of Abnormal Child Psychology, 21*(4), 411–423. https://doi.org/10.1007/BF01261601

Quirk, G.J. (2006). Extinction: new excitement for an old phenomenon. *Biological Psychiatry, 60,* 317–318. https://doi.org/10.1016/j.biopsych.2006.05.023

Reinhard, J. (2017). *Developmental Aspects of Fear Learning and Fear Generalization* (Doctoral Dissertation, Medical Psychology). University Hospital of Würzburg.

Reinhard, J., Drepper, C., Weber, H., Schiele, M.A., Kneer, K., Mittermeier, A., Frey, L., Reif, A., Pauli, P., Domschke K., Deckert, J. & Romanos, M. (2020). European Child & Adolescent Psychiatry, 29, 1301-1310. https://doi.org/10.1007/s00787-019-01458-7

Reinhard, J., Slyschak, A., Schiele, M.A., Andreatta, M., Kneer, K., Reif, A., Domschke, K., Gamer, M., Pauli, P., Deckert, J. & Romanos, M. (2021). Fear conditioning and stimulus generalization in association with age in children and adolescents. *European Child & Adolescent Psychiatry*. https://doi.org/10.1007/s00787-021-01797-4

Reiss, S. & McNally, R.J. (1985). The expectancy model of fear. In S. Reiss & R.R. Bootzin (Eds.), *Theoretical Issues in Behavior Therapy* (pp. 107-121). New York: Academic Press.

Rothermund, K., & Eder, A.B. (2011). *Motivation und Emotion*. Wiesbaden: VS Verlag für Sozialwissenschaften. Retrieved from https://link.springer.com/content/pdf/10.1007/978-3-531-93420-4.pdf

Rudy, J.W. (1993). Contextual conditioning and auditory cue conditioning dissociate during development. *Behavioral Neuroscience, 107*(5), 887–891. https://doi.org/10.1037/0735-7044.107.5.887

Rudy, J.W. & Pugh, C.R. (1996). A comparison of contextual and generalized auditory-cue fear conditioning: evidence for similar memory processes. *Behavioral Neuroscience, 110*(6), 1299-1308. https://doi.org/10.1037/0735-7044.110.6.1299

Rutten, I. & Geerts, D. (2020). Better Because It's New: The Impact of Perceived Novelty on the Added Value of Mid-Air Haptic Feedback. *CHI '20: Proceedings of the 2020 CHI Conference on Human Factors in Computing Systems, paper 539*, 1-13. https://doi.org/10.1145/3313831.3376668

Ryan, K.M., Zimmer-Gembeck, M.J., Neumann, D.L. & Waters, A.M. (2019). The need for standards in the design of differential fear conditioning and extinction experiments in youth: A systematic review and recommendations for research on anxiety. *Behaviour Research and Therapy, 112*, 42-62. https://doi.org/10.1016/j.brat.2018.11.009

Sanislow, C.A., Ferrante, M., Pacheco, J., Rudorfer, M.V. & Morris, S.E. (2019). Advancing Translational Research Using NIMH Research Domain Criteria and Computational Methods. *Neuron, 101*, 779-782. https://doi.org/10.1016/j.neuron.2019.02.024

Schiele, M.A., Reinhard, J., Reif, A., Domschke, K., Romanos, M., Deckert, J. & Pauli, P. (2016). Developmental aspects of fear: Comparing the acquisition and generalization of conditioned fear in children and adults. *Developmental Psychobiology, 58*(4), 471-481. https://doi.org/10.1002/dev.21393

Schneider, S., Adornetto, C., In-Albon, T., Federer, M. & Hensdiek, M. (2009). Psychometrische Eigenschaften und Normierung der deutschen Version des Childhood Anxiety Sensitivity Index (CASI). *Zeitschrift für Klinische Psychologie und Psychotherapie, 38*(3), 175-180. http://doi.org/10.1026/1616-3443.38.3.175

Sehlmeyer C., Schöning S., Zwitserlood P., Pfleiderer B., Kircher T., Arolt V. & Konrad, C. (2009). Human fear conditioning and extinction in neuroimaging: A systematic review. *PLOS ONE, 4*(6): e5865. http://doi.org/10.1371/journal.pone.0005865

Seligman, L.D., Ollendick, T.H., Langley, A.K. & Baldacci, H.B. (2004). The Utility of Measures of Child and Adolescent Anxiety: A Meta-Analytic Review of the Revised Children's Manifest Anxiety Scale, the State–Trait Anxiety Inventory for Children, and the Child Behavior Checklist. *Journal of Clinical Child and Adolescent Psychology, 33*(3), 557-565. http://dx.doi.org/10.1207/s15374424jccp3303_13

Sep, M.S.C., Steenmeijer, A. & Kennis, M. (2019). The relation between anxious personality traits and fear generalization in healthy subjects: A systematic review and meta-analysis. Neuroscience & Biobehavioral Reviews, 107, 320-328. https://doi.org/10.1016/j.neubiorev.2019.09.029

Sevenster, D., Beckers, T. & Kindt, M. (2014). Fear conditioning of SCR but not the startle reflex requires conscious dicrimination of threat and safety. *Frontiers in Behavioral Neuroscience, 8*(32), 1-9. http://dx.doi.org/10.3389/fnbeh.2014.00032

Shechner, T., Britton, J.C., Ronkin, E.G., Jarcho, J.M., Mash, J.A., Michalska, K.J., Leibenluft, E. & Pine, D.S. (2015). Fear Conditioning and Extinction in Anxious and Nonanxious Youth and Adults: Examining a Novel Developmentally Appropriate Fear-Conditioning Task. *Depression and Anxiety, 32*(4), 277-88. http://doi.org/10.1002/da.22318

Shechner, T., Hong, M., Britton, J.C., Pine, D.S. & Fox, N.A. (2014). Fear conditioning and extinction across development: evidence from human studies and animal models. *Biological Psychology, 100*, 1-12. http://doi.org/10.1016/j.biopsycho.2014.04.001

Shibagaki, M., Sakamoto, M. & Furuya, T. (1994). Age differences in characteristics of the attention process of electrodermal activity during auditory stimulation. *Perceptual and Motor Skills, 79*, 403-410. https://doi.org/10.2466/pms.1994.79.1.403

Shore, T., Kadosh, K.C., Lommen, M., Cooper, M. & Lau, J.Y.F. (2017). Investigating the effectiveness of brief cognitive reappraisal training to reduce fear in adolescents. *Cognition and Emotion, 31*(4), 806-815. http://dx.doi.org/10.1080/02699931.2016.1159542

Silverman, W.K., Fleising, W., Rabian, B. & Peterson, R.A. (1991). Childhood anxiety sensitivity index. *Journal of Clinical Child Psychology, 20*, 162-168. https://doi.org/10.1207/s15374424jccp2002_7

Silvers, J.A., Insel, C., Powers, A., Franz, P., Helion, C., Martin, R., Weber, J., Mischel, W., Casey, B.J. & Ochsner, K.N. (2017). The transition from childhood to adolescence is marked by general decrease in amygdala reactivity and affect-specific ventral-to-dorsal shift in medial prefrontal recruitment. *Developmental Cognitive Neuroscience, 25*, 128-137. https://doi.org/10.1016/j.dcn.2016.06.005

Simonsohn, U. (2016). Small telescopes: Detectability and the evaluation of replication results. *Psychological Science, 26*(5), 559–569. http://doi.org/10.1177/0956797614567341

Sjouwerman, R., Niehaus, J., Kuhn, M. & Lonsdorf, T.B. (2016). Don't startle me – Interference of startle probe presentations and intermittent ratings with fear acquisition. *Psychophysiology, 53*, 1889–1899. http://doi.org/10.1111/psyp.12761

Sperl, M.F.J., Panitz, C., Hermann, C. & Müller, E.M. (2016). A pragmatic comparison of noise burst and electric shock unconditioned stimuli for fear conditioning research with many trials. *Psychophysiology, 53*, 1352-1365. http://doi.org/10.1111/psyp.12677

Spielberger, C.D. (1973). *STAIC. Preliminary manual for the state-trait anxiety inventory for children.* Palo Alto: Consulting Psychologists Press.

Stroebe, W. & Strack, F. (2014). The alleged crisis and the illusion of exact replication. *Psychological Science, 9*(1), 59–71. http://doi.org/10.1177/1745691613514450

Tinoco-González, D., Fullana, M.A., Torrents-Rodas, D., Bonillo, A., Vervliet, B., Blasco, M.J. & Torrubia, R. (2015). Conditioned Fear Acquisition and Generalization in Generalized Anxiety Disorder. *Behavior Therapy, 46*(5), 627-639. http://doi.org/10.1016/j.beth.2014.12.004

Torrents-Rodas, D., Fullana, M.A., Bonillo, A., Caseras, X., Andión, O. & Torrubia, R. (2013). No effect of trait anxiety on differential fear conditioning or fear generalization. *Biological Psychology, 92*(2), 185-190. https://doi.org/10.1016/j.biopsycho.2012.10.006

Tottenham, N. & Gabard-Drunam, L.J. (2017). The developing amygdala: a student of the world and a teacher of the cortex. *Current Opinion in Psychology, 17,* 55-60. http://doi.org/10.1016/j.copsyc.2017.06.012

Tottenham, N., Tanaka, J.W., Leon, A.C., McCarry, T., Nurse, M., Hare, T.A., Marcus, D.J., Westerlund, A., Casey, B.J. & Nelson, C. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research, 168,* 242–249. https://doi.org/10.1016/j.psychres.2008.05.006

Tovote, P., Esposito, M.S., Botta, P., Chaudun, F., Fadok, J.P., Markovic, M., Wolff, S.B.E., Ramakrishnan, C., Fenno, L., Deisseroth, K., Herry, C., Arber, S. & Lüthi, A. (2016). Midbrain circuits for defensive behaviour. *Nature, 534,* 206-211. http://doi.org/10.1038/nature17996

Turner, S.M., Beidel, D.C., Spaulding, S.A. & Brown, J. (1996). The practice of behavior therapy: A national survey of cost and methods. *Behavior Therapist, 18*(1), 1-4.

Unnewehr, S., Joormann, S., Schneider, S., & Margraf, J. (1992). *Deutsche Übersetzung des State-Trait Anxiety Inventory for Children*. Unveröffentlichtes Manuskript an der Philipps-Universität Marburg.

van Meurs, B., Wiggert, N., Wicker, I. & Lissek, S. (2014). Maladaptive Behavioral Consequences of Conditioned Fear-Generalization: A Pronounced, Yet Sparsely Studied, Feature of Anxiety Pathology. *Behaviour Research and Therapy, 57*, 29-37. http://doi.org/10.1016/j.brat.2014.03.009

Vervliet, B., Craske, M.G. & Hermans, D. (2013). Fear Extinction and Relapse: State of the Art. *Annual Review of Clinical Psychology, 9*(1), 215-248. https://doi.org/10.1146/annurev-clinpsy-050212-185542

Vink M., Derks, J.M., Hoogendam, J.M., Hillegers, M. & Kahn, R.S. (2014). Functional differences in emotion processing during adolescence and early adulthood. *NeuroImage, 91,* 70–6. https://doi.org/10.1016/j.neuroimage.2014.01.035

Vos, T., Flaxman, A.D., Naghavi, M., Lozano, R., Michaud, C., Ezzati, M., Shibuya, K., Salomon, J.A., Abdalla, S., Aboyans, V., Abraham, J., Ackerman, I., Aggarwal, R., Ahn, S.Y., Ali, M.K., Alvarado, M., Anderson, H.R., Anderson, L.M., Andrews, K.G. & Atkinson, C. … et al. (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet, 380*(9859), 2163–2196. http://doi.org/10.1016/S0140-6736(12)61729-2

Wancata, J., Freidl, M. & Fabrian, F. (2011). Epidemiologie der Angsstörungen. *Journal für Neurologie, Neurochirurgie und Psychiatrie, 12*(4), 332-335. Retrieved from https://www.kup.at/kup/pdf/ 10175.pdf

Wancata, J., Windhaber, J., Bach, M. & Meise, U. (2000). Recognition of psychiatric disorders in nonpsychiatric hospital wards. *Journal of Psychosomatic Research, 48*(2), 149-155. https://doi.org/10.1016/S0022-3999(99)00098-7

Waters, A.M., Henry, J. & Neumann, D.L. (2009). Aversive Pavlovian conditioning in childhood anxiety disorders: Impaired response inhibition and resistance to extinction. *Journal of Abnormal Psychology, 118*(2), 311–321. https://doi.org/10.1037/a0015635

Waters, A.M. & Pine, D.S. (2016). Evaluating differences in Pavlovian fear acquisition and extinction as predictors of outcome from cognitive behavioral therapy for anxious children. *The Journal of Child Psychology and Psychiatry, 57*(7), 869-876. https://doi.org/10.1111/jcpp.12522

Waters, A.M., Theresiana, C., Neumann, D.L. & Craske, M.G. (2017). Developmental differences in aversive conditioning, extinction, and reinstatement: A study with children, adolescents, and adults. *Journal of Experimental Child Psychology, 159*, 263–278. http://doi. org/10.1016/j.jecp.2017.02.012

Watson, J.B. & Rayner, R. (1920). Conditioned emotional reactions. *Journal of Experimental Psychology, 3*, 1–14. https://doi.org/10.1037/h0069608

Weems, C.F. & Costa, N.M. (2005). Developmental Differences in the Expression of Childhood Anxiety Symptoms and Fears. *Journal of the American Academy of Child & Adolescent Psychiatry, 44*(7), 656-663. https://doi.org/10.1097/01.chi.0000162583.25829.4b

Weidemann, G., Satkunarajah, M. & Lovibond, P.F. (2016). I think, therefore eyeblink: The importance of contingency awareness in conditioning. *Psychological Science, 27*(4), 467–475. http://doi.org/10.1177/0956797615625973

Weiss, R.H. (2006). *Grundintelligenztest Skala 2 - Revision (CFT 20-R, Culture Fair Intelligence Test 20-R-Scale 2)*. Hogrefe, Göttingen.

Wittchen, H.-U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M. Jönsson, B., Olesen, J., Allgulander, C., Alonso, J., Faravelli, C., Fratiglioni, L., Jennum, P., Lieb, R., Maercker, A., van Os, J., Preisig, M., Salvador-Carulla, L., Simon, R. & Steinhausen, H.-C. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European Neuropsychopharmacology, 21*(9), 655-679. http://doi.org/10.1016/j.euroneuro.2011.07.018

Wong, A.H.K., & Lovibond, P.F. (2020). Breakfast or bakery? The role of categorical ambiguity in overgeneralization of learned fear in trait anxiety. *Emotion.* Advance online publication. https://doi.org/10.1037/emo0000739

Wong, A.H.K. & Lovibond, P.F. (2018). Excessive generalization of conditioned fear in trait anxious individuals under ambiguity. *Behaviour Research and Therapy, 107*, 53-63. https://doi.org/10.1016/j.brat.2018.05.012

Woodward, L.J. & Fergusson, D.M. (2001). Life course outcomes of young people with anxiety disorders in adolescence. *American Academy of Child and Adolescent Psychiatry, 40*(9), 1086-1093. https://doi.org/10.1097/00004583-200109000-00018

Wright, A., Jorm, A.F. & Mackinnon, A.J. (2011). Labeling of mental disorders and stigma in young people. Social Science & Medicine, 73(4), 498-506. https://doi.org/10.1016/j.socscimed.2011.06.015

Zorawski, M., Blanding, N.Q., Kuhn, C.M. & LaBar, K.S. (2006). Effects of stress and sex on acquisition and consolidation of human fear conditioning. *Learning & Memory, 13*, 441–450. http://doi.org/10.1101/lm.189106

APPENDIX

1. Tables

1.1 Results with no covariates

Table A1. Results of ANOVAs for the pre-acquisition, 1. acquisition and 2. acquisition phases. Main effects of stimulus type as well as phase and further their interaction effects on arousal, valence and US expectancy ratings and also on skin conductance response (SCR)

	stimulus type	***phase***	***stimulus type x phase***
Arousal	F (1,132) = 62.03,	F (2,233) = 36.57,	F (2,245) = 24.89,
	$\mathbf{p < .001}$, η^2 = .32	$\mathbf{p < .001}$, η^2 = .22	$\mathbf{p < .001}$, η^2 = .16
Valence	F (1,132) = 20.57,	F (2,232) = 1.65	F (2,241) = 20.23,
	$\mathbf{p < .001}$, η^2 = .14	p = .198, η^2 = .01	$\mathbf{p < .001}$, η^2 = .13
US expectancy	F (1,132) = 36.09,	F (2,220) = 8.21,	F (2,264) = 39.10,
	$\mathbf{p < .001}$, η^2 = .22	$\mathbf{p = .001}$, η^2 = .06	$\mathbf{p < .001}$, η^2 = .23
SCR	F (1,132) = 5.89,	F (2,237) = 5.21,	F (2,240) = 1.76,
	$\mathbf{p = .017}$, η^2 = .04	$\mathbf{p = .008}$, η^2 = .04	p = .178, η^2 = .01

Table A2. Results of ANOVAs for the 1. and 2. generalization phases. Main effects of stimuli and phase and also their interaction effects of arousal, valence and US expectancy as well as the skin conductance response (SCR)

	stimulus type	***phase***	***stimulus type x phase***
Arousal	F (4,446) = 34.30,	F (1,132) = 0.001,	F (5,593) = 0.13,
	$\mathbf{p < .001}$, η^2 = .21	p = .979, η^2 < .001	p = .979, η^2 < .001
Valence	F (3,397) = 31.72,	F (1,132) = 0.15,	F (5,629) = 1.47,
	$\mathbf{p < .001}$, η^2 = .19	p = .698, η^2 < .001	p = .199, η^2 = .01
US Expectancy	F (3,350) = 91.35,	F (1,132) = 5.78,	F (4,540) = 3.89,
	$\mathbf{p < .001}$, η^2 = .41	$\mathbf{p = .018}$, η^2 = .04	$\mathbf{p = .004}$, η^2 = .03
SCR	F (3,442) = 6.23,	F (1,132) = 9.07,	F (5,606) = 1.05,
	$\mathbf{p < .001}$, η^2 = .05	$\mathbf{p = .003}$, η^2 = .06	p = .383, η^2 = .01

Table A3. Results of ANOVAs for the three extinction phases. Main effects of stimuli and phase and also their interaction effects of arousal, valence and US expectancy as well as the skin conductance response (SCR)

	stimuli type	***phase***	***stimuli type x phase***
Arousal	F (1,132) = 14.30, **p < .001**, η^2 = .10	F (2,247) = 13.14, **p < .001**, η^2 = .09	F (2,245) = 0.23, p = .782, η^2 = .002
Valence	F (1,132) = 15.12, **p < .001**, η^2 = .10	F (2,247) = 1.96, p = .146, η^2 = .02	F (2,239) = 2.05, p = .136, η^2 = .02
US Expectancy	F (1,132) = 60.39, **p < .001**, η^2 = .31	F (2,252) = 27.85, **p < .001**, η^2 = .17;	F (2,255) = 6.63, **p = .002**, η^2 = .05
SCR	F (1,130) = 10.12, **p = .002**, η^2 = .07	F (2,260) = 0.64, p = .531, η^2 = .01	F (2,260) = 1.18, p = .309, η^2 = .01

1.2 Results with covariate of no interest: sex (and age as covariate of special interest)

Table A4. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,130) = 0.006, p = .938, η^2 < .001	F (1,130) = 0.20, p = .655, η^2 = .002	F (2,233) =0.84, p = .423, η^2 = .01	F (2,238) = 1.26, p = .283, η^2 = .01
Valence	F (1,130) = 1.48, p = .226, η^2 = .01	F (1,130) = 4.57, **p = .034**, η^2 = .03	F (2,229) = 0.42, p = .635, η^2 = .003	F (2,244) = 0.64, p = .520, η^2 = .01
US expectancy	F (1,130) = 0.91, p = .341, η^2 = .01	F (1,130) = 0.57, p = .453, η^2 = .004	F (2,219) = 0.62, p = .515, η^2 = .01	F (2,257) = 1.16, p = .315, η^2 = .01
SCR	F (1,130) = 0.08, p =.778, η^2 = .001	F (1,130) = 1.15, p = .286, η^2 = .01	F (2,234) = 0.68, p = .495, η^2 = .01	F (2,236) = 0.46, p = .614, η^2 = .004

Table A5. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,130) = 0.17, p = .684, η^2 = .001	F (3,439) = 1.49, p = .213, η^2 = .01	F (1,130) =0.17, p = .681, η^2 = .001	F (5,585) = 0.95, p = .439, η^2 = .01
Valence	F (1,130) = 1.30, p = .256, η^2 = .01	F (3,388) = 0.59, p = .624, η^2 = .004	F (1,130) = 0.08, p = .776, η^2 = .001	F (5,617) = 0.91, p =.473, η^2 = .01
US expectancy	F (1,130) = 0.06, p = .804, η^2 < .001	F (3,343) = 1.46, p = .230, η^2 = .01	F (1,130) = 0.89, p = .347, η^2 = .01	F (4,533) = 0.47, p =.759, η^2 = .004
SCR	F (1,130) = 0.97, p =.327, η^2 = .007	F (3,435) = 2.22, p = .078, η^2 = .02	F (1,130) = 0.09, p = .769, η^2 = .001	F (5,599) = 1.41, p = .222, η^2 = .01

Table A6. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,130) = 1.50, p = .223, η^2 = .01	F (1,130) = 1.11, p = .294, η^2 = .01	F (2,243) =0.16, p = .843, η^2 = .001	F (2,241) = 0.14, p = .859, η^2 = .001
Valence	F (1,130) = 1.00, p = .319, η^2 = .01	F (1,130) = 0.04, p = .839, η^2 < .001	F (2,242) = 2.95, p = .058, η^2 = .02	F (2,235) = 0.09, p = .898, η^2 = .001
US expectancy	F (1,130) = 0.25, p = .620, η^2 = .002	F (1,130) = 1.39, p = .241, η^2 = .01	F (2,249) = 1.35, p = .262, η^2 = .01	F (2,249) = 1.15, p = .318, η^2 = .01
SCR	F (1,128) = 1.82, p =.180, η^2 = .01	F (1,128) = 1.28, p = .260, η^2 = .01	F (2,256) = 1.43, p = .240, η^2 = .01	F (2,256) = 0.20, p = .817, η^2 = .002

1.3 Results with covariates of no interest: sex and age (STAIC as covariate of special interest, see chapter 3.)

1.3.1 Results for the covariate: age

Table A7. **Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases.** Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: STAIC, age and sex)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,129) = 6.83, **p = .010**, η^2 = .05	F (1,129) = 0.49, p = .486, η^2 = .004	F (2,233) =2.89, p = .063, η^2 = .02	F (2,236) = 1.42, p = .245, η^2 = .01
Valence	F (1,129) = 2.61, p = .109, η^2 = .02	F (1,129) = 0.75, p = .389, η^2 = .01	F (2,228) = 0.69, p = .483, η^2 = .01	F (2,241) = 7.11, **p = .001**, η^2 = .05
US expectancy	F (1,129) = 15.26, **p < .001**, η^2 = .11	F (1,129) = 5.47, **p = .021**, η^2 = .04	F (2,218) = 3.06, p = .058, η^2 = .02	F (2,255) = 8.01, **p < .001**, η^2 = .06
SCR	F (1,129) = 8.63, **p =.004**, η^2 = .06	F (1,129) = 1.13, p = .289, η^2 = .01	F (2,234) = 0.02, p = .978, η^2 < .001	F (2,236) = 0.38, p = .667, η^2 = .003

Table A8. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: STAIC, age and sex)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,129) = 13.25, **p < .001**, η^2 = .09	F (3,435) = 0.73, p = .548, η^2 = .01	F (1,129) =0.36, p = .550, η^2 = .003	F (5,580) = 1.81, p = .116, η^2 = .01
Valence	F (1,129) = 6.28, **p = .013**, η^2 = .05	F (3,383) = 0.56, p = .637, η^2 = .004	F (1,129) = 0.12, p = .731, η^2 = .001	F (5,612) = 0.90, p =.479, η^2 = .01
US expectancy	F (1,129) = 15.66, **p < .001**, η^2 = .11	F (3,338) = 0.76, p = .500, η^2 = .01	F (1,129) = 0.72, p = .398, η^2 = .01	F (4,529) = 1.33, p =.257, η^2 = .01
SCR	F (1,129) = 14.43, **p < .001**, η^2 = .10	F (3,430) = 0.43, p = .755, η^2 = .003	F (1,129) = 0.06, p = .802, η^2 < .001	F (5,595) = 0.27, p = .918, η^2 = .002

Table A9. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: STAIC, age and sex)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,129) = 1.33, p = .251, η^2 = .01	F (1,129) = 2.74, p = .100, η^2 = .02	F (2,241) =0.61, p = .536, η^2 = .01	F (2,239) = 1.34, p = .263, η^2 = .01
Valence	F (1,129) = 2.24, p = .137, η^2 = .02	F (1,129) = 5.45, **p = .021**, η^2 = .04	F (2,240) = 2.05, p = .135, η^2 = .02	F (2,233) = 0.99, p = .367, η^2 = .01
US expectancy	F (1,129) = 0.63, p = .428, η^2 = .01	F (1,129) = 0.15, p = .698, η^2 = .001	F (2,258) = 0.45, p = .631, η^2 = .003	F (2,258) = 1.57, p = .211, η^2 = .01
SCR	F (1,127) = 2.66, p =.105, η^2 = .02	F (1,127) = 0.49, p = .484, η^2 = .004	F (2,254) = 0.70, p = .497, η^2 = .01	F (2,254) = 0.31, p = .737, η^2 = .002

1.3.2 Results for the covariate: sex

Table A10. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: STAIC, age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,129) = 0.12, p = .731, η^2 = .001	F (1,129) = 0.01, p = .923, η^2 < .001	F (2,233) =0.26, p = .746, η^2 = .002	F (2,236) = 0.74, p = .469, η^2 = .01
Valence	F (1,129) = 1.97, p = .163, η^2 = .02	F (1,129) = 4.70, **p = .032**, η^2 = .04	F (2,228) = 0.58, p = .540, η^2 = .004	F (2,241) = 0.80, p = .443, η^2 = .01
US expectancy	F (1,129) = 2.24, p = .137 η^2 = .02	F (1,129) = 0.52, p = .474, η^2 = .004	F (2,218) = 0.59, p = .526, η^2 = .01	F (2,255) = 0.65, p = .522, η^2 = .01
SCR	F (1,129) = 0.05, p =.830, η^2 < .001	F (1,129) = 2.52, p = .115, η^2 = .02	F (2,234) = 0.19, p = .802, η^2 = .002	F (2,236) = 0.94, p = .387, η^2 = .01

Table A11. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: STAIC, age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,129) = 0.02, p = .900, η^2 < .001	F (3,435) = 1.27, p = .284, η^2 = .01	F (1,129) =0.39, p = .536, η^2 = .003	F (5,580) = 0.96, p = .436, η^2 = .01
Valence	F (1,129) = 2.06, p = .154, η^2 = .02	F (3,383) = 0.76, p = .514, η^2 = .01	F (1,129) = 0.03, p = .863, η^2 < .001	F (5,612) = 0.75, p =.579, η^2 = .01
US expectancy	F (1,129) = 0.21, p = .648, η^2 = .002	F (3,338) = 1.44, p = .235, η^2 = .01	F (1,129) = 1.37, p = .244, η^2 = .01	F (4,529) = 0.58, p =.684, η^2 = .004
SCR	F (1,129) = 0.80, p =.374, η^2 = .01	F (3,430) = 1.79, p = .142, η^2 = .01	F (1,129) = 0.002, p = .966, η^2 < .001	F (5,595) = 1.06, p = .380, η^2 = .01

Table A12. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: STAIC, age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,129) = 0.52, p = .471, η^2 = .004	F (1,129) = 1.38, p = .242, η^2 = .01	F (2,241) =0.28, p = .738, η^2 = .002	F (2,239) = 0.07, p = .925, η^2 = .001
Valence	F (1,129) = 1.57, p = .212, η^2 = .01	F (1,129) = 0.02, p = .886, η^2 < .001	F (2,240) = 3.22, **p = .045**, η^2 = .02	F (2,233) = 0.28, p = .736, η^2 = .002
US expectancy	F (1,129) = 0.31, p = .577, η^2 = .002	F (1,129) = 1.19, p = .277, η^2 = .01	F (2,258) = 1.38, p = .254, η^2 = .01	F (2,258) = 1.53, p = .218, η^2 = .01
SCR	F (1,127) = 1.59, p =.209, η^2 = .01	F (1,127) = 1.11, p = .295, η^2 = .01	F (2,254) = 0.74, p = .478, η^2 = .01	F (2,254) = 0.10, p = .905, η^2 = .001

1.3 Results with covariates of no interest: sex and age (CASI as covariate of special interest, see chapter 4.)

1.4.1 Results for the covariate: age

Table A13. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: CASI, age and sex)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,129) = 7.60, **p = .007**, η^2 = .06	F (1,129) = 1.12, p = .291, η^2 = .01	F (2,232) =4.18, **p = .020**, η^2 = .03	F (2,235) = 1.95, p = .149, η^2 = .02
Valence	F (1,129) = 2.83, p = .095, η^2 = .02	F (1,129) = 1.05, p = .308, η^2 = .01	F (2,228) = 0.73, p = .467, η^2 = .01	F (2,241) = 7.98, **p = .001**, η^2 = .06
US expectancy	F (1,129) = 12.29, **p = .001**, η^2 = .09	F (1,129) = 5.65, **p = .019**, η^2 = .04	F (2,217) = 2.82, p = .071, η^2 = .02	F (2,254) = 9.40, **p < .001**, η^2 = .07
SCR	F (1,129) = 10.34, **p =.002**, η^2 = .07	F (1,129) = 0.36, p = .548, η^2 = .003	F (2,233) = 0.16, p = .833, η^2 = .001	F (2,234) = 0.24, p = .775, η^2 = .002

Table A14. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: CASI, age and sex)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,129) = 15.46, **p < .001**, η^2 = .11	F (3,437) = 0.90, p = .449, η^2 = .01	F (1,129) =0.15, p = .704, η^2 = .001	F (4,580) = 1.76, p = .127, η^2 = .01
Valence	F (1,129) = 7.06, **p = .009**, η^2 = .05	F (3,381) = 0.62, p = .598, η^2 = .01	F (1,129) = 0.52, p = .473, η^2 = .004	F (5,610) = 1.05, p =.387, η^2 = .01
US expectancy	F (1,129) = 17.69, **p < .001**, η^2 = .12	F (3,340) = 0.58, p = .604, η^2 = .01	F (1,129) = 0.79, p = .376, η^2 = .01	F (4,528) = 1.72, p =.142, η^2 = .01
SCR	F (1,129) = 16.51, **p < .001**, η^2 = .11	F (3,434) = 0.54, p = .678, η^2 = .004	F (1,129) = 0.24, p = .624, η^2 = .002	F (5,596) = 0.30, p = .902, η^2 = .002

Table A15. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: CASI, age and sex)

	main effect of age	***stimulus type x age***	***phase x age***	***stimulus type x phase x age***
Arousal	F (1,129) = 1.07, p = .304, η^2 = .01	F (1,129) = 2.12, p = .148, η^2 = .02	F (2,241) =0.31, p = .717, η^2 = .002	F (2,238) = 1.05, p = .347, η^2 = .01
Valence	F (1,129) = 1.63, p = .204, η^2 = .01	F (1,129) = 5.44, **p = .021**, η^2 = .04	F (2,238) = 1.93, p = .151, η^2 = .02	F (2,235) = 0.82, p = .430, η^2 = .01
US expectancy	F (1,129) = 0.72, p = .399, η^2 = .01	F (1,129) = 0.14, p = .705, η^2 = .001	F (2,258) = 0.53, p = .591, η^2 = .004	F (2,258) = 1.94, p = .146, η^2 = .02
SCR	F (1,127) = 3.25, p =.074, η^2 = .03	F (1,127) = 0.73, p = .396, η^2 = .01	F (2,254) = 0.27, p = .764, η^2 = .002	F (2,254) = 0.48, p = .620, η^2 = .004

1.4.2 Results for the covariate: sex

Table A16. Results of ANCOVAs for the pre-acquisition, 1. and 2. acquisition phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: CASI, age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,129) = 0.16, p = .692, η^2 = .001	F (1,129) = 0.15, p = .696, η^2 = .001	F (2,232) =0.61, p = .530, η^2 = .01	F (2,235) = 1.01, p = .360, η^2 = .01
Valence	F (1,129) = 2.18, p = .142, η^2 = .02	F (1,129) = 4.43, **p = .037**, η^2 = .03	F (2,228) = 0.64, p = .510, η^2 = .01	F (2,241) = 0.69, p = .493, η^2 = .01
US expectancy	F (1,129) = 1.23, p = .269, η^2 = .01	F (1,129) = 0.60, p = .440, η^2 = .01	F (2,217) = 0.45, p = .604, η^2 = .03	F (2,254) = 0.88, p = .413, η^2 = .01
SCR	F (1,129) = 1.47, p =.702, η^2 = .001	F (1,129) = 1.43, p = .233, η^2 = .01	F (2,233) = 0.51, p = .582, η^2 = .004	F (2,234) = 0.53, p = .571, η^2 = .004

Table A17. Results of ANCOVAs for the 1. and 2. generalization phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: CASI, age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,129) = 0.002, p = .968, η^2 < .001	F (3,437) = 1.19, p = .314, η^2 = .01	F (1,129) =0.19, p = .668, η^2 = .001	F (4,580) = 1.11, p = .353, η^2 = .01
Valence	F (1,129) = 2.40, p = .124, η^2 = .02	F (3,381) = 0.61, p = .605, η^2 = .01	F (1,129) = 0.02, p = .900, η^2 < .001	F (5,610) = 0.74, p =.584, η^2 = .01
US expectancy	F (1,129) = 0.30, p = .586, η^2 = .002	F (3,340) = 1.33, p = .266, η^2 = .01	F (1,129) = 1.59, p = .210, η^2 = .01	F (4,528) = 0.68, p =.613, η^2 = .01
SCR	F (1,129) = 1.08, p =.301, η^2 = .01	F (3,434) = 2.37, p = .063, η^2 = .02	F (1,129) = 0.06, p = .810, η^2 < .001	F (5,596) = 1.20, p = .308, η^2 = .01

Table A18. Results of ANCOVAs for the 1., 2. and 3. extinction phases. Effects regarding sex on arousal, valence and US expectancy ratings and also on skin conductance response (SCR) (with covariates: CASI, age and sex)

	main effect of sex	***stimulus type x sex***	***phase x sex***	***stimulus type x phase x sex***
Arousal	F (1,129) = 0.76, p = .384, η^2 = .01	F (1,129) = 0.94, p = .334, η^2 = .01	F (2,241) =0.10, p = .894, η^2 = .001	F (2,238) = 0.18, p = .823, η^2 = .001
Valence	F (1,129) = 1.12, p = .293, η^2 = .01	F (1,129) = 0.05, p = .828, η^2 < .001	F (2,238) = 3.35, **p = .040**, η^2 = .03	F (2,235) = 0.19, p = .804, η^2 = .001
US expectancy	F (1,129) = 0.32, p = .575, η^2 = .002	F (1,129) = 1.19, p = .278, η^2 = .01	F (2,258) = 1.42, p = .243, η^2 = .01	F (2,258) = 1.35, p = .261, η^2 = .01
SCR	F (1,127) = 1.96, p =.164, η^2 = .02	F (1,127) = 0.93, p = .337, η^2 = .01	F (2,254) = 1.38, p = .253, η^2 = .01	F (2,254) = 0.07, p = .932, η^2 = .001

2. Flyer for the advertising of the study and the recruitment of participants

Liebe Eltern,
liebe Kinder und Jugendliche,

im Kindes- und Jugendalter sind Angsterkrankungen die häufigsten psychischen Erkrankungen. Wir wollen herausfinden, wie Angsterkrankungen entstehen und wie sie verhindert werden können.

Wir würden uns sehr freuen, wenn Ihre Familie unser Anliegen unterstützen würde.

Hinweise

Welche Untersuchungen werden bei allen Teilnehmern durchgeführt?

- wir führen eine Aufgabe am Computer durch, welche die Mechanismen der Angstentstehung untersucht
- wir bitten die Kinder und Jugendlichen Fragebögen auszufüllen
- wir führen eine Blutentnahme (oder alternativ Speichelprobe) durch, um zu untersuchen, inwiefern Erbfaktoren bei der Entstehung von Ängsten eine Rolle spielen

Alle Untersuchungen sind ungefährlich und es wurden von der Ethikkommission keine ethischen Bedenken erhoben.

Die Dauer beträgt ca. 3 Stunden.

Jeder erhält pauschal eine Aufwandsentschädigung von 20 Euro.

Warum sollen wir teilnehmen?

Bislang existiert weltweit keine vergleichbar große und aufwändige Studie, die darauf abzielt, die Entstehung von Angsterkrankungen bereits im Kindesalter zu entschlüsseln. Durch Ihre Bereitschaft an dieser Studie teilzunehmen, leistet Ihre Familie einen wichtigen Beitrag, um Angsterkrankungen besser zu verstehen und dadurch langfristig Angsterkrankungen vorzubeugen und Betroffenen zu helfen.
Herzlichen Dank für Ihr Interesse und Ihre Hilfe!

Wer kann teilnehmen?

Kinder und Jugendliche zwischen 8 und 17 Jahren mit einer Angsterkrankung.

Möchten Sie mehr Informationen zur Studie haben?

Gerne nehmen wir unverbindlich mit Ihnen Kontakt auf! Bitte füllen Sie dazu das nachfolgende Formular aus und schicken Sie es uns zu. Gerne können Sie auch per E-Mail Kontakt mit uns aufnehmen.

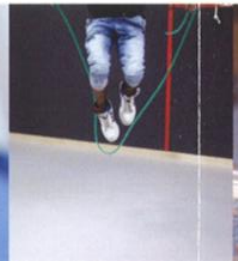
Kontakt

Universitätsklinikum Würzburg
Zentrum für Psychische Gesundheit
Klinik für Kinder- und Jugendpsychiatrie,
Psychosomatik und Psychotherapie
Margarete-Höppel-Platz 1 (ehemals Füchsleinstrasse 15)
97080 Würzburg

Frau Brandstetter, Frau Mowat und Frau Reinhard
E-Mail: KJ_Angst@ukw.de

www.ukw.de/kjppp



3. Informed consent form and sign-up sheet for the study

3.1 Informed consent form and sign-up sheet for children

Universitätsklinikum Würzburg

Zentrum für Psychische Gesundheit

Klinik und Poliklinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie
Direktor: Prof. Dr. med. Marcel Romanos

Klinik und Poliklinik für Kinder- und Jugendpsychiatrie,
Psychosomatik und Psychotherapie · Füchsleinstr. 15 · 97080 Würzburg

STUDIENINFORMATION

FÜR MINDERJÄHRIGE STUDIENTEILNEHMER

Furchtgeneralisierung und ihre Modifikation durch Aufmerksamkeitsprozesse bei Kindern und Jugendlichen im Alter von 8 bis 17 Jahren

WARUM WIRD DIESE STUDIE GEMACHT?

Viele Kinder, die zu uns ins Krankenhaus kommen, haben Angst vor bestimmten Situationen und sind dadurch sehr belastet. Manche trauen sich nicht vor anderen zu sprechen oder haben große Angst vor Hunden; wieder andere haben so viel Angst, dass sie nicht mehr in die Schule gehen wollen. Wir sind Wissenschaftler an der Universitätsklinik und wir wissen bereits, dass Ängste zum Teil angeboren sind, aber es ist auch wichtig, was die Kinder vorher erlebt haben. Nun möchten wir herausfinden, wie diese Ängste entstehen und wollen dadurch neue Ideen sammeln, wie wir diese Ängste besser behandeln können.
Dabei kannst Du uns helfen!

WAS WIRD IN DIESER STUDIE GEMACHT?

Wir stellen zunächst Dir und Deinen Eltern/Sorgeberechtigten einige Fragen, weil wir wissen wollen, wie es Dir geht und welche Dinge Dir vielleicht Angst machen können.
Danach machen wir einen Test, mit dem wir herausfinden wollen, wie Angsterkrankungen entstehen. Der Test ist aber ungefährlich und Du wirst dadurch nicht ängstlicher werden als vorher. Während der eigentlichen Untersuchung zeigen wir Dir auf einem Computerbildschirm Fotografien mit Gesichtern. Manchmal zeigen wir dir die Gesichter mit einem ängstlichen Gesichtsausdruck. Manchmal hörst Du dann auch über einen Kopfhörer ein unangenehmes lautes Geräusch. Das ist zwar kurz unangenehm, aber gar nicht gefährlich.
Zwischendurch wirst Du kleine Aufgaben von uns bekommen, die aber nicht schwierig sind und die wir dir gut erklären. Während der Untersuchung messen wir mit kleinen Knöpfen, wie Dein Körper während dem Test reagiert. Außerdem misst eine kleine Kamera während der Untersuchung deine Augenbewegungen. Alle Fragebögen und die Untersuchung dauern zusammen nicht mehr als zwei Stunden.
Um zu untersuchen, welchen Einfluss die Vererbung auf die Entstehung von Ängsten hat, möchten wir Dir eine kleine Menge Blut abnehmen (ca. 2,5 Esslöffel). Dies wird nur von Personen gemacht, die das gelernt haben.

Klinik und Poliklinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie
Füchsleinstr. 15
97080 Würzburg
Anstalt des Öffentlichen Rechts

Tel.: (0931) 201 -
Fax: (0931) 201 - 78040
www.kjp.ukw.de

ZEP Zentrum für Psychische Gesundheit

KJPPP Klinik und Poliklinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie

WAS HABE ICH DAVON, BEI DER STUDIE MITZUMACHEN?

Du selbst wirst nichts davon haben, wenn Du an der Studie teilnimmst. Du hilfst uns aber dabei, besser nachzuvollziehen, wie Ängste entstehen und dadurch kann dann in Zukunft möglicherweise Menschen mit Angsterkrankungen besser geholfen werden. Als Aufwandsentschädigung zahlen wir 30 Euro.

IST DIE TEILNAHME AN DER STUDIE GEFÄHRLICH?

Beim Blutabnehmen kann es an der Einstichstelle zu einem blauen Fleck kommen oder sich die Einstichstelle entzünden. Man kann auch ein falsches Blutgefäß treffen. Diese Probleme passieren aber, wenn man vorschriftsmäßig Blut abnimmt, extrem selten.

WAS PASSIERT MIT DEN DATEN?

Alle Informationen, die wir von Dir und Deiner Familie bekommen, werden streng vertraulich behandelt. Wir stellen sicher, dass keine Unbefugten an diese Informationen gelangen können. Bevor wir die Daten auswerten, werden die Informationen, die Blutprobe und die Ergebnisse aus den Tests mit einer speziellen Zahl beschriftet und ohne Deinen Namen weiterverwendet. Hierbei beachten wir, dass die Gesetze zum Datenschutz (Art. 23 BayDSG) eingehalten werden.

WAS WÜRDE PASSIEREN, WENN ICH DOCH NICHT MEHR AN DER STUDIE TEILNEHMEN WILL?

Die Teilnahme an dieser Studie ist völlig freiwillig. Du kannst jederzeit und ohne sagen zu müssen, warum, aufhören.

AN WEN KANN ICH MICH BEI FRAGEN WENDEN?

Wenn Du Fragen hast kannst Du Dich an den Studienleiter oder die Ärztin/Wissenschaftler(in)/der Arzt, der Dir die Studie erklärt hat, wenden. Eine **Kopie dieser Information** hast Du erhalten.

KONTAKTDATEN DER STUDIENLEITUNG:

Univ.-Prof. Dr. med. Marcel Romanos,
Direktor der Klinik und Poliklinik für Kinder- und Jugendpsychiatrie,
Psychosomatik und Psychotherapie, Universitätsklinikum Würzburg
Margarete-Höppel-Platz 1 (ehemals Füchsleinstr. 15,) 97080 Würzburg
Tel. 0931 / 201 – 78010

Wir möchten Dich darauf hinweisen, dass Dir nach Art. 15 und Art. 16 der EU-Datenschutzgrundverordnung (EU-DSGVO) ein Auskunfts- und Berichtigungsrecht sowie ein Recht auf Löschung (Art. 17), Einschränkung der Verarbeitung (Art. 18) und Widerspruch gegen die Verarbeitung (Art. 21) zusteht.
Im Falle eines Widerrufs kannst Du grundsätzlich entscheiden, ob Deine Daten und Proben gelöscht bzw. vernichtet werden sollen oder ob sie in anonymisierter Form für weitere Forschungsvorhaben verwendet werden dürfen. Die Rechtmäßigkeit der Verarbeitungen bis zum Zeitpunkt des Widerrufes bleibt davon unberührt, das heißt, dass die Daten, die vor Deinem Widerspruch gesammelt wurden, weiter für die Forschung verwendet werden dürfen. Möchtest Du eines dieser Rechte in Anspruch nehmen, wende Dich bitte mit deinen Eltern an die Studienleitung (s.o.).
Bei Anliegen zur Datenverarbeitung und zur Einhaltung der datenschutzrechtlichen Anforderungen kannst Du Dich an den Datenschutzbeauftragten des Universitätsklinikums Würzburg wenden (Datenschutzbeauftragter des Universitätsklinikums Würzburg, Josef-Schneider-Straße 2, 97080 Würzburg, Telephon: 0931/201-55485, Email: datenschutz@ukw.de).
Außerdem hast Du das Recht, Beschwerde bei der/den Datenschutz-Aufsichtsbehörde/n einzulegen, wenn Du der Ansicht bist, dass die Verarbeitung der Dich betreffenden personenbezogenen Daten gegen die DSGVO verstößt. Dies ergibt sich aus Art. 77 DSGVO. Datenschutzrechtliche Beschwerden können an den Bayerischen Landesbeauftragte für den Datenschutz (BayLfD) gerichtet werden (Postfach 22 12 19, 80502 München, Telephon: 089/212672-0, Email: poststelle@datenschutzbayern.de). Die Beschwerde bei der Aufsichtsbehörde kann formlos erfolgen.
Verantwortliche Stelle für die Datenverarbeitung: Universitätsklinikum Würzburg, Anstalt des öffentlichen Rechts, Josef-Schneider-Straße 2, 97080 Würzburg, Deutschland, Tel.: 0931 201 0

Vielen Dank für Dein Interesse und Deine Teilnahme!

Durch meine Unterschrift bestätige ich:

Man hat mir erklärt, dass bei dieser Studie verschiedene Fragen gestellt werden, ich an einem Computertest mitmache, gemessen wird, wie mein Körper in bestimmten Situationen reagiert und dass mir Blut abgenommen wird. Mir werden auch Gesichter mit einem ängstlichen Gesichtsausdruck gezeigt. Manchmal werde ich auch ein lautes Geräusch hören, was unangenehm sein kann.

Damit bin ich einverstanden.

Ich habe mir lange genug überlegt, ob ich mitmachen will und durfte Fragen stellen, wenn ich etwas nicht verstanden habe. Ich weiß, dass ich jederzeit aufhören darf.

Ich bin einverstanden damit, dass die Informationen in dieser Studie ohne meinen Namen aufgezeichnet, in Computern gespeichert und ausgewertet werden. Mir ist bekannt, dass ich meine Einwilligung jederzeit ohne Angaben von Gründen und ohne Nachteile jederzeit mit Wirkung für die Zukunft widerrufen kann. Ich weiß, dass die Untersuchung wissenschaftlichen Zwecken dient, und bin einverstanden, dass die gewonnenen Daten für wissenschaftliche Veröffentlichungen und Forschung verwendet werden. Ich stimme der Speicherung/Lagerung und Nutzung der Daten/Proben gemäß den geltenden Datenschutzbedingungen zu. Auch diese Einwilligung kann ich jederzeit widerrufen.

Name und Unterschrift des teilnehmenden Kindes:

.....	.....	.....
Name	Datum	Unterschrift

Name und Unterschrift des aufklärenden Mitarbeiters:

.....	.....	.....
Name	Datum	Unterschrift

3.2 Informed consent form and sign-up sheet for parents

Universitätsklinikum Würzburg

Zentrum für Psychische Gesundheit

Klinik und Poliklinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie
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Psychosomatik und Psychotherapie · Füchsleinstr. 15 · 97080 Würzburg

STUDIENINFORMATION

FÜR ELTERN/SORGEBERECHTIGTE VON TEILNEHMENDEN KINDERN UND JUGENDLICHEN

Furchtgeneralisierung und ihre Modifikation durch Aufmerksamkeitsprozesse bei Kindern und Jugendlichen im Alter von 8 bis 17 Jahren

Sehr geehrte Eltern, sehr geehrte Sorgeberechtigte,

vielen Dank für Ihr Interesse an unserer Studie. Wir möchten Sie bitten, uns durch die Teilnahme Ihres Kindes an einer wissenschaftlichen Studie zur Untersuchung der Entstehung von Angst zu unterstützen.

SINN UND ZWECK DER UNTERSUCHUNG

In unserem Krankenhaus behandeln und erforschen wir Erkrankungen von Kindern und Jugendlichen, die für die Betroffenen und ihre Familien oft sehr belastend und im Alltagsleben einschränkend sind. Angsterkrankungen gehören zu den häufigsten psychischen Störungen im Kindes- und Jugendalter und bleiben unbehandelt oftmals im Erwachsenenalter bestehen bzw. führen zu weiteren psychischen Erkrankungen, wie beispielsweise zu depressiven Erkrankungen. Um das Auftreten von Angsterkrankungen zu verhindern bzw. sie noch wirksamer behandeln zu können, ist es notwendig, die Entstehung und den Verlauf von Angst und Angsterkrankungen besser zu verstehen.
Heute wissen wir, dass für die Entstehung von Angsterkrankungen sowohl genetische Faktoren als auch Lebenserfahrungen eine Rolle spielen. Außerdem wissen wir, dass Furcht erlernt werden kann, indem sich Erfahrungen von Furcht und Angst in bestimmten Situationen „generalisieren“, das heißt, sich auf andere Situationen ausweiten. Mit Hilfe der medizinisch-genetischen Erforschung dieser Ursachen versuchen wir, Einblicke in die Entstehung und den Verlauf der Erkrankung zu erhalten und so zu der Entwicklung einer effizienteren Therapie und Prävention beizutragen. Auf lange Sicht erhoffen wir uns die biologischen und psychologischen Mechanismen von Angsterkrankungen besser zu verstehen. Zudem soll der Einfluss von genetischen Faktoren auf mögliche Entstehungsmechanismen bei Ängsten untersucht werden. Wir wollen auch untersuchen, ob sich erlernte Furcht vor einem Reiz auf ähnliche Reize überträgt („Generalisierung“) und wie sich diese Generalisierung wieder umkehren oder verhindern lässt. Weiterhin soll untersucht werden, welche Rolle die Aufmerksamkeitslenkung bei der Generalisierung spielt.

Klinik und Poliklinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie
Füchsleinstr. 15
97080 Würzburg
Anstalt des Öffentlichen Rechts

Tel.: (0931) 201 - 0
Fax: (0931) 201 - 78040
www.kjp.ukw.de

WELCHE UNTERSUCHUNGEN SOLLEN DURCHGEFÜHRT WERDEN, WENN ICH EINER TEILNAHME MEINES KINDES AN DER STUDIE ZUSTIMME?

Zuerst werden Sie und Ihr Kind gebeten, Fragen zu Ängstlichkeit und Stimmung zu beantworten. Während der Untersuchung soll Ihr Kind dann Fotographien betrachten, die über einen Computerbildschirm präsentiert werden. In regelmäßigen Abständen wird Ihr Kind zu den Bildern befragt. Diese zeigen weibliche Personen mit neutralem Gesichtsausdruck. Ab und an wird zusätzlich ein ängstlicher Gesichtsausdruck gezeigt. In bestimmten Abständen wird über einen Kopfhörer ein unangenehmes lautes Geräusch dargeboten. Dieses kann einen Augenblick lang unangenehme Gefühle sowie Erregungsgefühle auslösen, ist jedoch weder körperlich noch psychologisch für Ihr Kind gefährlich. Während der Untersuchung wird ihr Kind auch Fotografien verschiedener neutraler Gesichter und Tiergesichter sehen. Hier ist dann die Aufgabe zu entscheiden, ob die Gesichter identisch sind. Während der Untersuchung möchten wir über auf die Haut aufgeklebte Elektroden kontinuierlich die Schweißdrüsenaktivität (Hautleitfähigkeit), Blinzelreflex (Startle) und Herzrate als physiologische Maße erheben. Die Messung der Hautleitfähigkeit erfolgt über 2 kleine Klebeelektroden an der linken Hand, der Blinzelreflex wird über zwei Klebeelektroden unter dem linken Auge und die Herzrate über 3 EKG-Elektroden auf dem Brustkorb abgeleitet. In einer kurzen zusätzlichen Aufgabe werden Ihrem Kind gleichzeitig zwei Gesichter mit neutralem und/oder ängstlichem Gesichtsausdruck gezeigt. Anschließend folgt ein Symbol an einer Stelle, an der vorher eines der beiden Gesichter präsentiert wurde. Aufgabe ist es, so schnell wie möglich eine Taste zu drücken, sobald das Symbol erscheint.
Während der gesamten Untersuchung registriert ein spezielles Gerät die Augenbewegungen Ihres Kindes. Dafür werden auf dem Tisch vor Ihrem Kind eine Hochgeschwindigkeitskamera und eine Infrarotbeleuchtung platziert. Die Augen werden während der Messung mit infrarotem Licht beleuchtet und über die Kamera aufgenommen. Das Videobild wird jedoch nicht gespeichert, sondern lediglich Ihre Pupillengröße sowie die Orte, die Ihr Kind auf dem Monitor anschaut. Vor dem eigentlichen Beginn des Experiments wird Ihr Kind gebeten, verschiedene Positionen auf dem Bildschirm zu fixieren. Dadurch wird das Gerät individuell eingestellt. Während des Experiments kann Ihr Kind die Augen frei bewegen. Das Gerät zur Messung der Augenbewegungen wurde speziell für diese Art von Untersuchungen konstruiert und ist weltweit in vielen Laboren im Einsatz. Die Messung ist vollkommen sicher und es existieren keine bekannten Nebenwirkungen.
Die Untersuchung dauert insgesamt nicht mehr als 120 Minuten.

Um die genetischen Variationen untersuchen zu können, benötigen wir von Ihrem Kind eine geringe Menge Blut (ca. 2,5 Esslöffel). Die Blutentnahme erfolgt unter sterilen Bedingungen, wie sie auch der Hausarzt bei einer Routineuntersuchung durchführt. Die Blutentnahme erfolgt durch medizinisch qualifiziertes Personal (Ärzte, oder durch sie supervidierte Medizin-Doktoranden). Durch spezielle Labormethoden (z.B. Anlage permanenter Zelllinien) ist es möglich, die Blutzellen zu vermehren und so wiederholt zu untersuchen, ohne dass erneut Blut abgenommen werden muss. Die Zellen werden tief gefroren und in flüssigem Stickstoff aufbewahrt. Bei Bedarf werden die Zellen aufgetaut und stehen dann zur erneuten Untersuchung, z.B. neu bekannt gewordener Genvarianten, zur Verfügung. Die Untersuchungen im Labor der Klinik und Poliklinik für

Psychiatrie, Psychosomatik und Psychotherapie oder eines beauftragten Labors sind ausschließlich zur Feststellung von Genvarianten bestimmt.

WAS SIND DIE VORTEILE FÜR MEIN KIND, WENN ES AN DIESER STUDIE TEILNIMMT?

Diese Untersuchung wird keinen direkten Nutzen für Ihr Kind haben, da individuelle Ergebnisse nicht weitergegeben werden. Durch Ihre Bereitschaft, an dieser Studie teilzunehmen, leistet Ihre Familie jedoch einen sehr wichtigen Beitrag zu einem besseren Verständnis psychischer Funktionen und Erkrankungen. Auch wenn wir nicht davon ausgehen können, dass die Ergebnisse in kürzester Zeit zur Entwicklung von neuen Therapien (medikamentös und psychotherapeutisch) führen, erhoffen wir uns erhebliche Vorteile für viele Patienten mit Angststörungen, da wir nur durch die Aufklärung der Entstehungswege von Ängsten Fortschritte in der Therapie erzielen können.
Als pauschale Aufwandsentschädigung erhält jede Familie 30 Euro.

ERGEBEN SICH IRGENDWELCHE RISIKEN FÜR MEIN KIND?

Alle Ableitungen sind vollkommen schmerzfrei und beinhalten keinerlei Risiko. Die Messungen sind nicht-invasiv, d.h. sie sind nicht mit einem Einschnitt oder dem Einführen von Geräten oder Nadeln in den Körper verbunden. Das über Kopfhörer präsentierte Geräusch mit einem Schallpegel von 95 Dezibel kann unangenehm sein, ist aber ebenfalls mit keinem Risiko verbunden. Jedes Kind erhält am Ende der Untersuchung ein sogenanntes Extinktionstraining, d.h. die möglicherweise erlernte Furcht vor dem Gesicht einer Person auf einer Fotografie wird wieder „gelöscht".
Die Risiken der Blutentnahme sind identisch mit denen einer Routineblutabnahme: lokale Infektion („bakterielle Entzündung, Vereiterung") und Fehlpunktion einer Schlagader. Beide Risiken sind bei sachgemäßer Durchführung extrem selten.

WIE WIRD MIT ZUFALLSBEFUNDEN UMGEGANGEN?

Sie werden mit dieser Aufklärung darüber informiert, dass im Rahmen dieser Forschungsstudie kein Arzt-Patient-Verhältnis besteht. In dieser Forschungsstudie wird keine klinische Diagnostik durchgeführt, da die Forschungsstudie ausschließlich auf wissenschaftlichen Erkenntnisgewinn und nicht auf die Entdeckung von Auffälligkeiten abzielt.

WERDEN DIE DATEN VERTRAULICH BEHANDELT?

Wir unterliegen der Schweigepflicht. Alle Informationen, die wir von Ihrer Familie bekommen, werden streng vertraulich behandelt. Alle persönlichen Daten wie z. B. Name und Adresse werden streng getrennt von den Fragebögen, den Ergebnissen der genetischen Tests sowie den Ergebnissen der Generalisierungsuntersuchung aufbewahrt. Es werden alle technischen und organisatorischen Maßnahmen getroffen, damit keine Unbefugten an persönliche Informationen gelangen können. Alle medizinischen Informationen werden vor der Verwendung für wissenschaftliche Analysen pseudonymisiert (Fachbegriff:

„Pseudonymisierung“ gemäß § 3 Abs, 6a Bundesdatenschutzgesetz). Dies bedeutet, dass die Fragebögen, die Aufzeichnungen der physiologischen Messungen aus dem Generalisierungstest, die Blutprobe und die genetischen Testergebnisse mit einem speziellen Zahlencode versehen werden, wenn sie zur Analyse geschickt werden. Persönliche Daten werden den Wissenschaftlern, die die wissenschaftlichen Analysen ausführen, nicht offen gelegt und ein direkter Rückgriff auf Ihre Person ist somit ausgeschlossen. Bei der Erhebung, Speicherung und Analyse der Daten bzw. Proben ist der Datenschutz entsprechend den geltenden Datenschutzgesetzen bzw. allen einschlägigen rechtlichen Anforderungen zum Datenschutz auf jeden Fall gewährleistet.
Veröffentlicht werden die Daten in anonymer Form als Sammeldatensatz in wissenschaftlichen Journalen.

WAS WÜRDE PASSIEREN, WENN ICH ODER MEIN KIND DIE STUDIE ABBRECHEN WOLLTE?

Die Teilnahme an dieser Studie ist absolut freiwillig. Sie und Ihr Kind können selbstverständlich jederzeit und natürlich auch ohne Angabe von Gründen von der Teilnahme zurücktreten. Wir werden dann alle bis dahin erfassten Studienunterlagen und Blutproben von Ihnen sofort vernichten.
Für den Fall, dass Sie Ihre Einwilligung nicht zurückziehen, werden alle Informationen und die DNS so lange aufbewahrt und analysiert, wie sie einen wertvollen Beitrag für die Erforschung der biologischen und umweltbedingten Grundlagen psychischer und neurologischer Erkrankungen liefern. Wir werden Ihre Daten also erst dann vernichten, wenn sie nicht mehr zu einem weiteren Wissensgewinn in diesem Forschungsbereich beitragen können, spätestens jedoch nach 10 Jahren.

AN WEN KANN ICH MICH BEI FRAGEN WENDEN?

Bei Rückfragen stehen Ihnen die verantwortlichen Studienleiter oder die/der aufklärende Arzt/Ärztin/Wissenschaftler(in) gerne zur Verfügung.

KONTAKTDATEN DER STUDIENLEITUNG:

Univ.-Prof. Dr. med. Marcel Romanos,
Direktor der Klinik und Poliklinik für Kinder- und Jugendpsychiatrie,
Psychosomatik und Psychotherapie, Universitätsklinikum Würzburg
Margarete-Höppel-Platz 1 (ehemals Füchsleinstr. 15,) 97080 Würzburg
Tel. 0931 / 201 – 78010

Wir möchten Sie darauf hinweisen, dass Ihnen nach Art. 15 und Art. 16 der EU-Datenschutzgrundverordnung (EU-DSGVO) ein Auskunfts- und Berichtigungsrecht sowie ein Recht auf Löschung (Art. 17), Einschränkung der Verarbeitung (Art. 18) und Widerspruch gegen die Verarbeitung (Art. 21) zusteht. Im Falle eines Widerrufs können Sie grundsätzlich entscheiden, ob Ihre Daten und Proben gelöscht bzw. vernichtet werden sollen oder ob sie in anonymisierter Form für weitere Forschungsvorhaben

verwendet werden dürfen. Die Rechtmäßigkeit der Verarbeitungen bis zum Zeitpunkt des Widerrufes bleibt davon unberührt. Möchten Sie eines dieser Rechte in Anspruch nehmen, wenden Sie sich bitte an die Studienleitung (s.o.). Bei Anliegen zur Datenverarbeitung und zur Einhaltung der datenschutzrechtlichen Anforderungen können Sie sich an den Datenschutzbeauftragten des Universitätsklinikums Würzburg wenden (Datenschutzbeauf-tragter des Universitätsklinikums Würzburg, Josef-Schneider-Straße 2, 97080 Würzburg, Telephon: 0931/201-55485, Email: datenschutz@ukw.de).
Außerdem haben Sie das Recht, Beschwerde bei der/den Datenschutz-Aufsichtsbehörde/n einzu-legen, wenn Sie der Ansicht sind, dass die Verarbeitung der Sie betreffenden personenbezogenen Daten gegen die DSGVO verstößt. Dies ergibt sich aus Art. 77 DSGVO. Datenschutzrechtliche Beschwerden können an den Bayerischen Landesbeauftragte für den Datenschutz (BayLfD) ge-richtet werden (Postfach 22 12 19, 80502 München, Telephon: 089/212672-0, Email: poststel-le@datenschutzbayern.de). Die Beschwerde bei der Aufsichtsbehörde kann formlos erfolgen.

VERANTWORTLICHE STELLE FÜR DIE DATENVERARBEITUNG

Universitätsklinikum Würzburg, Anstalt des öffentlichen Rechts, Josef-Schneider-Straße 2, 97080 Würzburg, Deutschland, Tel.: 0931 201 0

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 Nachteile Ihr Einverständnis rückgängig machen. Eine Kopie dieser Information wird Ihnen ausgehändigt.

Vielen Dank für Ihr Interesse und Ihre Teilnahme!

Durch meine Unterschrift bestätige ich:

Ich bin über die geplante Untersuchung eingehend und ausreichend unterrichtet worden. Ich konnte Fragen stellen, die Informationen dazu habe ich inhaltlich verstanden. Ich habe keine weiteren Fragen, fühle mich ausreichend informiert und willige hiermit nach ausreichender Bedenkzeit freiwillig in die Untersuchung wie oben beschrieben ein. Ich wurde darauf hingewiesen, dass ich jederzeit von dieser Untersuchung zurücktreten kann, ohne dass mir oder meinem Kind dadurch ein Nachteil entsteht.

Ich erkläre mich freiwillig mit der Datenerhebung einverstanden. Über mögliche Risiken wurde ich aufgeklärt. Ich weiß, dass es nicht möglich ist, Informationen über individuelle Untersuchungsergebnisse zu erhalten. Ich weiß, dass die Untersuchung wissenschaftlichen Zwecken dient und die gewonnenen Daten eventuell für wissenschaftliche Veröffentlichungen verwendet werden. Ich stimme der Speicherung/Lagerung und Nutzung der Daten/Proben gemäß den geltenden Datenschutzbedingungen zu. Auch diese Einwilligung kann ich jederzeit widerrufen.

Veröffentlicht werden die Daten in jedem Fall in anonymer Form als Sammeldatensatz in wissenschaftlichen Journalen.

Mir ist bekannt, dass ich meine Einwilligung jederzeit ohne Angaben von Gründen und ohne Nachteile jederzeit mit Wirkung für die Zukunft widerrufen kann.

Name des teilnehmenden Kindes: .....

Name und Unterschrift der Erziehungsberechtigten:

1) ....
Name Datum Unterschrift

2) ....
Name Datum Unterschrift

Name und Unterschrift des aufklärenden Mitarbeiters:

....

Ergänzende Information für Studienteilnehmer gemäß Europäischer Datenschutz-Grundverordnung[1]

für bereits laufende medizinische Forschungsvorhaben (Start vor 25.05.2018)

Furchtgeneralisierung und ihre Modifikation durch Aufmerksamkeitsprozesse bei Kindern und Jugendlichen im Alter von 8 bis 17 Jahren

Ethikvotum: 211/16

Sehr geehrte/r Studienteilnehmer/in,

aufgrund des Wirksamwerdens der Europäischen Datenschutz-Grundverordnung (**DSGVO**) zum 25. Mai 2018 ändern sich die Datenschutzvorschriften in Europa. Auch für bereits laufende medizinische Forschungsvorhaben (im Folgenden klinische Studien genannt) ergeben sich dadurch neue Anforderungen an die Verarbeitung personenbezogener Daten.

Wenn Sie bereits Teilnehmer/in einer klinischen Studie sind, wurden Sie in der jeweiligen Patienteninformation/Einwilligungserklärung bereits über die Aspekte zum Datenschutz informiert und haben dem schriftlich zugestimmt. Dies beinhaltet z. B. Informationen über die Erfassung, Speicherung und Weiterleitung Ihrer personenbezogenen Daten sowie Ihre diesbezüglichen Rechte. Auch als mögliche/r neue/r Studienteilnehmer/in erhalten Sie diese Informationen im Rahmen des Aufklärungsgesprächs durch den Sie aufklärenden Wissenschaftler und in der schriftlichen Patienteninformation/Einwilligungserklärung zur klinischen Studie.

Der in der Patienteninformation/Einwilligungserklärung zu der jeweiligen klinischen Studie beschriebene Umgang mit Ihren Daten gilt weiterhin.

Zusätzlich werden Sie hiermit über die in der DSGVO festgelegten Rechte informiert:

Rechtsgrundlage
Die Rechtsgrundlagen zur Verarbeitung der Sie betreffenden personenbezogenen Daten bilden bei klinischen Studien Ihre freiwillige schriftliche Einwilligung gemäß DSGVO sowie die Deklaration von Helsinki (Erklärung des Weltärztebundes zu den ethischen Grundsätzen für die medizinische Forschung am Menschen) und die Leitlinie für Gute Klinische Praxis. Bei klinischen Prüfungen mit Arzneimitteln ist zusätzlich das Arzneimittelgesetz und bei klinischen Prüfungen mit Medizinprodukten entsprechend das Medizinproduktegesetz anzuwenden. Zeitgleich mit der DSGVO treten in Deutschland das überarbeitete Bundesdatenschutzgesetz (BDSG-neu) und landesdatenschutzrechtliche Regelungen in Kraft.

Bezüglich Ihrer Daten haben Sie folgende Rechte:

Einwilligung zur Verarbeitung personenbezogener Daten und Recht auf Widerruf der Einwilligung
Die Verarbeitung Ihrer personenbezogenen Daten ist nur mit Ihrer Einwilligung rechtmäßig. Sie haben das Recht, Ihre Einwilligung zur Verarbeitung personenbezogener Daten jederzeit zu widerrufen. Es dürfen jedoch die bis zu diesem Zeitpunkt erhobenen Daten durch die in der Patienteninformation/Einwilligungserklärung zu der jeweiligen klinischen Studie genannten Stellen verarbeitet werden.

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1 Verordnung (EU) 2016/679 des Europäischen Parlaments und des Rates vom 27. April 2016 zum Schutz natürlicher Personen bei der Verarbeitung personenbezogener Daten, zum freien Datenverkehr und zur Aufhebung der Richtlinie 95/46/EG (Datenschutz-Grundverordnung)

Recht auf Auskunft
Sie haben das Recht auf Auskunft über die Sie betreffenden personenbezogenen Daten, die im Rahmen der klinischen Studie erhoben, verarbeitet oder ggf. an Dritte übermittelt werden.

Recht auf Berichtigung
Sie haben das Recht, Sie betreffende unrichtige personenbezogene Daten berichtigen zu lassen.

Recht auf Löschung
Sie haben das Recht auf Löschung Sie betreffender personenbezogener Daten, z. B. wenn diese Daten für den Zweck, für den sie erhoben wurden, nicht mehr notwendig sind und der Löschung keine gesetzlichen Aufbewahrungsfristen entgegen stehen.

Recht auf Einschränkung der Verarbeitung
Unter bestimmten Voraussetzungen haben Sie das Recht auf Einschränkung der Verarbeitung zu verlangen, d. h. die Daten dürfen nur gespeichert, nicht verarbeitet werden. Dies müssen Sie beantragen. Wenden Sie sich hierzu bitte an die Studienleitung (s.u.).

Recht auf Datenübertragbarkeit
Sie haben das Recht, die Sie betreffenden personenbezogenen Daten, die Sie dem Verantwortlichen für die klinische Studie bereitgestellt haben, zu erhalten. Damit können Sie beantragen, dass diese Daten entweder Ihnen oder, soweit technisch möglich, einer anderen von Ihnen benannten Stelle übermittelt werden.

Widerspruchsrecht
Sie haben das Recht, jederzeit gegen konkrete Entscheidungen oder Maßnahmen zur Verarbeitung der Sie betreffenden personenbezogenen Daten Widerspruch einzulegen. Eine Verarbeitung findet anschließend grundsätzlich nicht mehr statt, es sei denn, die Verarbeitung ist gesetzlich weiterhin gefordert (wie beispielsweise in § 40 Abs. 2a S. 2 Nr. 3 AMG).

Möchten Sie eines dieser Rechte in Anspruch nehmen, wenden Sie sich bitte an die Studienleitung. Außerdem haben Sie das **Recht, Beschwerde bei der/den Datenschutzaufsichtsbehörde/n einzulegen,** wenn Sie der Ansicht sind, dass die Verarbeitung der Sie betreffenden personenbezogenen Daten gegen die DSGVO verstößt.

Kontaktdaten der Studienleitung:

Prof. Dr. med. Marcel Romanos
Direktor der Klinik und Poliklinik für Kinder- und Jugendpsychiatrie,
Psychosomatik und Psychotherapie,
ZEP, Universitätsklinikum Würzburg
Margarete-Höppel-Platz 1 (ehemals Füchsleinstr. 15)
97080 Würzburg

Verantwortliche Stellen für die Datenverarbeitung:

Universitätsklinikum Würzburg, Anstalt des öffentlichen Rechts, Josef-Schneider-Straße 2, 97080 Würzburg, Deutschland, Tel.: 0049 - 931 201 0

Kontaktdaten des Datenschutzbeauftragten am Studienzentrum:

Datenschutzbeauftragte/r des Studienzentrums:

Datenschutzbeauftragter des Universitätsklinikums Würzburg, Josef-Schneider-Straße 2, 97080 Würzburg, Telephon: 0931/201-55485, Email: datenschutz@ukw.de.

Außerdem haben Sie das Recht auf Beschwerde bei einer Aufsichtsbehörde, wenn Sie der Ansicht sind, dass die Verarbeitung Ihrer Daten datenschutzrechtlich nicht zulässig ist. Dies ergibt sich aus Art. 77 DSGVO. Die Beschwerde bei der Aufsichtsbehörde kann formlos erfolgen. Für das UKW ist dies der Bayerische Landesbeauftragte für den Datenschutz (BayLfD), Postfach 22 12 19, 80502 München, Telephon: 089/212672-0, Email: poststelle@datenschutzbayern.de

Hiermit bestätige ich, dass ich über die Änderungen der Europäischen Datenschutz-Grundverordnung informiert wurde und diese akzeptiere.

Name, Vorname: _____

Ort, Datum: _____

Unterschrift: _____

4. Questionnaires

4.1 STAIC-Trait

STAIC

Im folgenden Fragebogen findest Du eine Reihe von Feststellungen, die Mädchen und Jungen benutzen, um sich selbst zu beschreiben. Lies Dir jede Feststellung durch und entscheiden Sie, ob sie fast nie, oder manchmal oder oft auf Dich zutrifft. Kreuze dann bitte für jede Feststellung das entsprechende Kästchen an.

Es gibt keine richtigen oder falschen Antworten. Überlege bitte nicht zu lange und denke daran, diejenige Antwort auszuwählen, die am besten beschreibt, wie Du Dich im Allgemeinen fühlst.

1. Ich habe Angst, Fehler zu machen	☐ fast nie	☐ manchmal	☐ oft
2. Mir ist zum weinen zumute	☐ fast nie	☐ manchmal	☐ oft
3. Ich fühle mich unglücklich	☐ fast nie	☐ manchmal	☐ oft
4. Es fällt mir schwer, mich zu entscheiden	☐ fast nie	☐ manchmal	☐ oft
5. Es fällt mir schwer, meine Probleme anzupacken	☐ fast nie	☐ manchmal	☐ oft
6. Ich mache mir zuviel Sorgen	☐ fast nie	☐ manchmal	☐ oft
7. Zu Hause rege ich mich auf	☐ fast nie	☐ manchmal	☐ oft
8. Ich bin schüchtern	☐ fast nie	☐ manchmal	☐ oft
9. Ich bin beunruhigt	☐ fast nie	☐ manchmal	☐ oft
10. Unwichtige Gedanken gehen mir durch den Kopf und stören mich	☐ fast nie	☐ manchmal	☐ oft
11. Ich mache mir Sorgen über die Schule	☐ fast nie	☐ manchmal	☐ oft
12. Ich habe Schwierigkeiten zu entscheiden, was ich tun soll	☐ fast nie	☐ manchmal	☐ oft
13. Ich merke, dass mein Herz schneller schlägt	☐ fast nie	☐ manchmal	☐ oft
14. Ich fürchte mich heimlich	☐ fast nie	☐ manchmal	☐ oft
15. Ich mache mir Sorgen um meine Eltern	☐ fast nie	☐ manchmal	☐ oft
16. Ich bekomme feuchte Hände	☐ fast nie	☐ manchmal	☐ oft
17. Ich mache mir Sorgen über Dinge, die passieren könnten	☐ fast nie	☐ manchmal	☐ oft
18. Es fällt mir schwer, abends einzuschlafen	☐ fast nie	☐ manchmal	☐ oft
19. Ich habe ein komisches Gefühl im Magen	☐ fast nie	☐ manchmal	☐ oft
20. Ich grübele darüber nach, was andere Personen von mir denken	☐ fast nie	☐ manchmal	☐ oft

4.2 CASI

KU/CASI

Auf dieser und auf der folgenden Seite findest du eine Reihe von Gefühlen und Gedanken, die Jungen und Mädchen haben können. Bitte lies diese Gefühle und Gedanken aufmerksam durch und mach ein Kreuz in das Kästchen, das auf Dich zutrifft. Dabei gibt es keine richtigen oder falschen Antworten, es geht nur darum, jeweils das Wort anzukreuzen, das Dich am besten beschreibt.

	gar nicht	manchmal	häufig
1. Ich möchte nicht, dass andere Menschen es merken, wenn ich mich ängstlich fühle.	θ	θ	θ
2. Wenn ich mich nicht auf meine Schulaufgaben konzentrieren kann, fürchte ich, dass ich verrückt werden könnte.	θ	θ	θ
3. Es macht mir Angst, wenn ich mich zittrig fühle.	θ	θ	θ
4. Es macht mir Angst, wenn ich mich so fühle, als ob ich in Ohnmacht falle.	θ	θ	θ
5. Es ist wichtig für mich, meine Gefühle unter Kontrolle zu haben.	θ	θ	θ
6. Es macht mir Angst, wenn mein Herz schnell schlägt.	θ	θ	θ
7. Es ist mir peinlich, wenn mein Magen knurrt (Geräusche macht).	θ	θ	θ
8. Es macht mir Angst, wenn ich mich so fühle, als ob ich mich übergeben muss.	θ	θ	θ
9. Wenn ich merke, dass mein H erz schnell schlägt, fürchte ich, dass etwas mit mir nicht in Ordnung sein könnte.	θ	θ	θ
10. Es macht mir Angst, wenn ich Schwierigkeiten habe, Luft zu bekommen.	θ	θ	θ
11. Wenn ich Bauchschmerzen habe, fürchte ich, dass ich richtig krank sein könnte.	θ	θ	θ

	gar nicht	manchmal	häufig
12. Es macht mir Angst, wenn ich nicht auf meine Schulaufgaben konzentrieren kann.	θ	θ	θ
13. Andere Kinder können es merken, wenn ich mich ängstlich fühle.	θ	θ	θ
14. Ungewöhnliche Körpergefühle machen mir Angst.	θ	θ	θ
15. Wenn ich Angst habe, fürchte ich, verrückt zu werden.	θ	θ	θ
16. Es macht mir Angst, wenn ich mich nervös fühle.	θ	θ	θ
17. Ich mag es nicht, meine Gefühle zu zeigen.	θ	θ	θ
18. Komische Gefühle in meinem Körper machen mir Angst.	θ	θ	θ

5. PUBLICATION LIST

5.1 Publication in peer-reviewed journals

Reinhard, J.#, **Slyschak, A**.#, Schiele, M.A., Andreatta, M., Kneer, K., Reif, A., Domschke, K., Gamer, M., Pauli, P., Deckert, J. & Romanos, M. (2021). Fear conditioning and stimulus generalization in association with age in children and adolescents. *European Child & Adolescent Psychiatry*.
# Equal contribution

Kneer, K., Reinhard, J., Ziegler, C., **Slyschak, A.**, Schiele, M.A., Vietz, M., Peters, K., Meisenzahl, E.M., Pauli, P., Reif, A., Deckert, J., Romanos, M., Domschke, K. & Neufang, S. (2020). Serotonergic influence on depressive symptoms and trait anxiety is mediated by negative life events and frontal activation in children and adolescents. *European Child & Adolescent Psychiatry*, *29*, 691-706.

Reinhard, J., Schiele, M.A., Schuler, M., **Slyschak, A.**, Kneer, K., Reif, A., Domschke, K., Pauli, P., Deckert, J. & Romanos, M. (under review). Fear learning and generalization in children: The modulatory effects of anxiety traits. *PLoS one.*

5.2 Published poster abstracts

Slyschak, A., Reinhard, J., Reif, A., Deckert, J., Domschke, K., Pauli, P., Romanos, M. (2017). Conditioned fear generalization and discrimination learning in children and adolescents. *9th European Meeting of Human Fear Conditioning (EMHFC)*, Jesteburg, Germany

Slyschak, A., Reinhard, J., Reif, A., Deckert, J., Domschke, K., Pauli, P., Romanos, M. (2017). Conditioned fear generalization and discrimination learning in children and adolescents. *Center of Mental Health Scientific Conference*, Würzburg, Germany

Slyschak, A., Reinhard, J., Reif, A., Deckert, J., Domschke, K., Pauli, P., Romanos, M. (2017). Conditioned fear generalization and discrimination learning in children and adolescents. *2nd International Summer School on Emotional Learning and Memory in Health and Psychopathology*, Leuven, Belgium

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Domschke, K., Romanos, M. (2018). Fear generalization in children and adolescents: a cross-sectional study across ages. *10th European Meeting on Human Fear Conditioning in Würzburg (EMHFC)*, Cardiff, Wales

Herzog, K., Andreatta, M., **Slyschak, A.**, Schiele, M.A., Deckert, J., Romanos, M., Domschke, K., Pauli, P. (2018). (De-)Generalization of Conditioned Fear in Healthy Adults and Children. *SFB Retreat*, Brixen, Austria

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2019). *11th European Meeting on Human Fear Conditioning (EMHFC)*, Würzburg, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2019). Generalization of conditioned fear in children and adolescents: a cross sectional study. *Center for Mental Health Scientific Conference*, Würzburg, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Domschke, K., Romanos, M. (2018). Generalization of conditioned fear in children and adolescents: a cross sectional study across age. *Research Conference of the DGKJP e.V.*, Tübingen, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Domschke, K., Romanos, M. (2019). Generalization of conditioned fear in children and adolescents: a cross sectional study across age (8-17 years). *XXXVI. DGKJP Congress*, Mannheim, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2019). Generalization of conditioned fear in children and adolescents: a cross sectional study across age. *International Congress of the World Association for Stress Related and Anxiety Disorders (WASAD)*, Würzburg, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2019). Generalization of conditioned fear in children and adolescents: a cross sectional study across age. *Conference of the Society for Anxiety Research (GAF)*, Würzburg, Germany

Mowat, K., Brandstetter, L., Mittermeier, A., Reinhard, J., **Slyschak, A.**, Gamer, M., Romanos, M. (2019). Generalization of conditioned fear in children and adolescents with an anxiety disorder. *Conference of the Society for Anxiety Research (GAF)*, Würzburg, Germany

Brandstetter, L., Mowat, K., Reinhard, J., **Slyschak, A.**, Deckert, J., Pauli, P., Domschke, K., Romanos, M. (2019) Fear conditioning and extinction in children and adolescents with an anxiety disorder. *Conference of the Society for Anxiety Research (GAF)*, Würzburg, Germany

Mittermeier, A., Frey, L. (shared authorship)* , Daub, J., **Slyschak, A.**, Reinhard, J., Romanos, M. (2017). Fear generalization in children and adolescents with internalizing and externalizing disorders. *9th European Meeting of Human Fear Conditioning (EMHFC)*, Jesteburg, Germany

Brandstetter, L., Mowat, K., Reinhard, J., **Slyschak, A.**, Rösler, L., Gamer, M., Pauli, P., Romanos, M. (2019). Generalization of conditioned fear in children and adolescents with anxiety disorders. *11th European Meeting on Human Fear Conditioning (EMHFC)*, Würzburg, Germany

5.3 Published talk abstracts

Slyschak, A., Reinhard, J., Reif, A., Deckert, J., Domschke, K., Pauli, P., Romanos, M. (2017). Conditioned fear generalization and discrimination learning in children and adolescents. *International Congress of the World Association for Stress Related and Anxiety Disorders (WASAD)*, Würzburg, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2017). (De-)generalization of conditioned fear (catamnesis). *Summer School on Small Molecules, Big Emotions - Neuronal circuitry of emotions and its malfunctioning disease*, Marktbreit, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2018). Generalization of conditioned fear in children and adolescents. *Summer School on Cutting Edge - Trend-setting Techniques and Topics in Brain Research*, Marktbreit, Germany

Slyschak, A., Reinhard, J., Deckert, J., Pauli, P., Gamer, M., Domschke, K., Romanos, M. (2018). Fear generalization in children and adolescents: a cross-sectional study across ages, *Center for Mental Health Scientific Conference*, Würzburg, Germany

6. Curriculum Vitae

7. Activities and Funding

May 2017 - Oct 2018 Mentee in **SCIENTIA Mentoring program** for female PhD students and PostDocs (offer at Julius-Maximilians-University in Würzburg, Germany)

2017 **Travel Fellowship** from the Graduate School of Life Sciences (GSLS) for:
Sep 2017 2nd International Summer School on "Emotional Learning and Memory in Health and Psychopathology" in Leuven, Belgium

2018 **Travel Fellowship** from the Graduate School of Life Sciences (GSLS) for:
Apr 2018 10th European Meeting on Human Fear Conditioning in Würzburg (EMHFC) in Cardiff, Wales, United Kingdom

_____ _____

Place, Date Signature

Affidavit

I hereby confirm that my thesis entitled “Fear conditioning, its generalization and extinction in children and adolescents under consideration of trait anxiety and anxiety sensitivity” 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 „Furchtkonditionierung, ihre Generalisierung und Extinktion bei Kindern und Jugendlichen unter Berücksichtigung von Ängstlichkeit und Angstsensitivität“ eigenständig, d.h. insbesondere selbständig 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 Prüfungsverfahren vorgelegen hat.

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Ort, Datum Unterschrift