

# EMHFC 2023

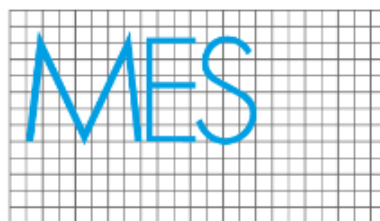


May 22<sup>nd</sup> – 24<sup>th</sup> 2023  
Salzburg, Austria

14<sup>th</sup> European Meeting of Human Fear Conditioning



© Photo by Michael Liedlgruber



FORSCHUNGSSYSTEME GMBH  
Lösungen für neurowissenschaftliche  
Anwendungen





# General Information

## Websites

<https://emhfc.blogs.uni-hamburg.de/>

<https://www.plus.ac.at/psychologie/oep/emhfc-2023/>

## Format of symposia

90 min for 5 talks, talk duration max. 14 min, Q&A max. 2min, final Q&A panel: ca. 10min

## Format of posters

Portrait format (upright), max. 90 cm wide, max. 140 cm high;  
recommended is A0 size (84,1 × 118,9 cm)

## Format of Salzburg outing

Taking bus to the inner city, different guided tours with about N=20, depending on weather conditions;  
a detailed description and doodle will follow

## Format of lunches and dinners

Different options incl. vegetarian;  
a detailed description and doodle will follow

# Programme Overview

## Monday, May 22

12:30 - 13:45	Arrival, Registration, & Light Lunch Buffet
13:45 - 14:00	Welcome Note
14:00 - 15:30	Symposium 1: Highlight of Human Fear Conditioning Research: Scientific Advances and Clinical Applications
15:30 - 16:30	Keynote Lecture by Karin Roelofs: The relevance of considering parasympathetic as well as sympathetic threat states
16:30 - 17:00	Coffee Break
17:00 - 18:30	Symposium 2: The Neuroscience of Fear Conditioning
18:30 - 19:00	Break
19:00 - 20:30	Dinner
20:30 - 22:30	Poster Session 1 & Drinks

## Tuesday, May 23

07:00 - 09:00	Breakfast
09:00 - 10:30	Symposium 3: Generalization of Fear Conditioning and Extinction
10:30 - 11:00	Coffee break
11:00 - 12:30	Symposium 4: Conceptual Advances in Human Fear Conditioning
12:30 - 13:30	Lunch
13:30 - 14:30	EMHFC General Assembly & Coffee
14:30 - 19:00	Salzburg Outing
19:00 - 20:30	Dinner
20:30 - 22:30	Poster Session 2 & Drinks

## Wednesday, May 24

07:00 - 09:00	Breakfast
09:00 - 10:30	Symposium 5: Behavioural Avoidance in Fear Conditioning
10:30 - 11:00	Coffee Break
11:00 - 12:30	Symposium 6: Neuroscientific Advances & Data Sharing Initiatives
12:30 - 12:45	Poster Awards & Farewell
12:30 - 13:45	Light Lunch Buffet or Lunch Package to Go

# Symposia – Day 1

## Symposium 1

### Highlights of Human Fear Conditioning Research: Scientific Advances and Clinical Applications

Chair: Christian Merz

	<b>Presenter</b>	<b>University/Lab</b>	<b>Title</b>
1	Anastasia Chalkia	Leuven/ Beckers	Disrupting emotional associative memories through instructions to forget
2	Valerie Jentsch	Bochum/ Merz, Wolf	The impact of physical exercise on extinction memory consolidation
3	Marta Andreatta	Würzburg & Rotterdam/ Andreatta	How long-lasting are the effects of stress on fear memories?
4	Matthias Sperl	Giessen/ Hermann	Imagery-based fear conditioning: a learning model for social anxiety?
5	Caroline Kwee	Utrecht/ Baas	Prediction of exposure therapy outcome by latent fear learning trajectories

## Symposium 2

### The Neuroscience of Fear Conditioning

Chair: Joke Baas

	<b>Presenter</b>	<b>University/Lab</b>	<b>Title</b>
1	Anne Willems	Leuven/ Vervliet	The pleasure of absent danger: fMRI evidence for reward prediction error-like processing of absent danger
2	Victor Spoormaker	MPI Munich/ Spoormaker	Hippocampal reactivity to aversive films predicts intrusion distress and is independent of pattern separation
3	Bálint Kincses	Essen/ Bingel & Spisak	Resting brain connectivity signature of pain-related learning
4	Lisa Wirz	Nijmegen & Bochum/ Hermans & Wolf	Temporal dynamics of threat-associated memory accuracy versus generalization

## **Symposium 3** **Generalization of Fear Conditioning and Extinction**

**Chair: Bram Vervliet**

	<b>Presenter</b>	<b>University/Lab</b>	<b>Title</b>
1	Tom Beckers	Leuven/ Beckers	“Implanting” fear in the human mind: false threat memories support fear generalization
2	Armin Zlomuzica	Bochum/ Zlomuzica	Generalization of exposure effects to untreated stimuli
3	Celine Samaey	Leuven/ van Winkel	Childhood adversity is associated with increased fear generalization in adolescents
4	Katharina Hutterer	Würzburg/ Erhardt-Lehmann	Predictive power of experimental fear conditioning and generalization measures on longitudinal changes in negative affect during the COVID-19 pandemic
5	Jonas Zaman	Leuven & Hasselt/ Beckers & Zaman	Multiple pathways to widespread fears: Disentangling idiosyncratic fear generalization mechanisms using computational modelling

## **Symposium 4** **Conceptual Advances in Human Fear Conditioning**

**Chair: Thomas Agren**

	<b>Presenter</b>	<b>University/Lab</b>	<b>Title</b>
1	Olivier de Vries	Amsterdam/ van Ast/Kindt	Threat conditioning and episodic memory: towards an integrated account of emotional associative learning
2	Sarah Danböck	Salzburg/ Wilhelm	Beyond analogue fear conditioning paradigms: the complex interplay between dissociation and other conditioned responses to trauma scripts in individuals with posttraumatic stress disorder
3	Tina Lonsdorf/ Alina Koppold	Hamburg-Eppendorf/ Lonsdorf	How adverse childhood experiences get under the skin: a systematic review, integration and methodological discussion on threat and reward learning mechanisms
4	Ondrej Zika	MPI Berlin/ Schuck	Trait anxiety is associated with increased reliance on context during Pavlovian learning
5	María Quintero	Málaga/ López	Occasional reinforced extinction as a method for relapse prevention: A critical review and future directions

## **Symposium 5 Behavioural Avoidance in Fear Conditioning**

**Chair: Andre Pittig**

	<b>Presenter</b>	<b>University/Lab</b>	<b>Title</b>
1	Pauline Dibbets	Maastricht/ Dibbets	Half the shock, half the avoidance?
2	Ann Meulders	Maastricht/ Meulders	Exploring strategies to prevent return of pain-related avoidance behaviour after successful extinction with response prevention
3	Xaver Fuchs	Salzburg/ Heed	Avoiding movement or space? Disentangling the roles of movement-related vs. spatial cues in learned movement avoidance
4	Felix Klaassen	Nijmegen/ Roelofs	The neurocomputational link between bradycardia and approach-avoidance decision-making under threat
5	Anneloes Hulsman	Nijmegen/ Roelofs	Mechanisms underlying costly fearful avoidance in patients with affective disorders

## **Symposium 6 Neuroscientific Advances & Data Sharing Initiatives**

**Chair: Tomer Shechner**

	<b>Presenter</b>	<b>University/Lab</b>	<b>Title</b>
1	Valentina Jelinčić	Leuven/ von Leupoldt	Investigating the effects of threat and safety cues on the perception and neural processing of unpleasant tactile stimuli
2	Gil Shner-Livne	Haifa/ Shechner	The effects of age and trait anxiety on Pavlovian threat acquisition and extinction: An ERP study comparing adolescents and adults
3	Raul Andero	Barcelona/ Andero	The neurokinin 3 receptor system and fear modulation in both mice and humans
4	Mana Ehlers	Hamburg- Eppendorf/ Lonsdorf	FEAR BASE – a curated, dynamically growing database and living analyses of publicly available fear conditioning data
5	Miguel Fullana	Barcelona/ Fullana	Unravelling fear learning ENIGMAS by sharing data

# Poster Session – Day 1

## Poster Session 1: Stress, Neuroscience, Clinical Populations, & Interventions

	Presenter	University/Lab	Title
1	Christian Merz	Bochum/ Wolf&Merz	The influence of stress on context-dependent reinstatement
2	Lianne Wolsink	Bochum/ Wolf	The impact of pre-extinction stress vs. exercise on contextual retrieval and generalization
3	Jaël Caviola	Bochum/ Wolf&Merz	Non-genomic and genomic cortisol effects on the return of fear after contextual extinction generalization
4	Fatemeh Yavari	Dortmund/ Nitsche	Involvement of neocortical areas in context-dependent fear extinction
5	Javier Schneider	Bochum/ Axmacher	Polygenic prediction of fear conditioning learning mediated by brain connectivity in the human extinction network
6	Zohar Klein	Haifa/ Shechner	Neural correlates of avoidance learning and threat extinction
7	Kim Marie Sobania	Hamburg/ Riesel	Neural correlates of fear learning processes in EEG
8	Stephan Miedl	Salzburg/ Wilhelm	Neural response to trauma-film and pain stimulation and their association with the formation of audio-visual and pain intrusions
9	Elena Andres	Nijmegen& Donders/ Roelofs	The role of cortico-spinal networks in defensive responses to threat
10	Hannes Per Carsten	Hamburg/ Riesel	Startle responses and event-related potentials during threat anticipation in patients with anxiety spectrum disorders
11	Sonia Betti	Bologna/ di Pellegrino	Dissociable acquisition of conditioned fear responses by the motor and autonomic systems
12	Alexander Hauck	Saarbrücken/ Michael	Effects of adjuvant glucose on the extinction of fear - results of two placebo-controlled studies
13	Sylvia Papalini	Leuven/ Vervliet	Overnight fasting facilitates safety learning by changing the neurophysiological response to reward (relief) Prediction Errors
14	Madelaine Müller	Hamburg-Eppen- dorf/Haaker	Nicotine reduces discrimination between threat and safety by reduction of hippocampal activations
15	Christoph Szeska	Potsdam/ Weymar	From the lab to the clinic: translating promoted fear extinction by non-invasive vagus nerve stimulation to exposure-based treatment in phobic individuals
16	Simone Battaglia	Bologna/ di Pellegrino	Low-frequency rTMS of the prefrontal cortex disrupts threat memory consolidation in humans
17	Steven Klein	Saarbrücken/ Michael	Devaluation of threat memory or associated neutral cues through bilateral eye movement
18	Annalisa Lipp	Bochum/ Zlomuzica	The effects of verbal instructions on fear extinction and extinction retrieval in patients with anxiety disorders and healthy controls
19	Jarosław Michałowski	Warsaw/ Michałowski	Efficacy and treatment stability of imaginal exposure and imagery rescripting: a randomized control trial
20	Maren Klingelhöfer- Jens	Hamburg-Eppendorf/ Lonsdorf	The long shadows of early experiences: evaluating the link between childhood maltreatment and psychopathology using a fear conditioning and generalization paradigm
21	Anna Wester	Leuven/ Vervliet	Establishing a potent reward for counterconditioning
22	Bram Vervliet	Leuven/ Vervliet	Impaired action-safety learning and excessive relief during avoidance in patients with anxiety disorders



# Poster Session – Day 2

## Poster Session 2: Approach/Avoidance, Pain, Uncertainty, & Generalization

	Presenter	University/Lab	Title
1	Bram Vervliet	Leuven/ Vervliet	Subjective relief as a proxy for predictor error dynamics in avoidance learning
2	Menghuan Chen	Würzburg/ Pittig	Psychophysiological responses in active vs. passive approach-avoidance conflict decision task
3	Alexandros Kastrinogiannis	Hamburg-Eppen-dorf/ Lonsdorf	Navigating the approach-avoidance matrix: exploring individual differences in a novel virtual reality foraging task
4	Andre Pittig	Erlangen-Nürnberg & Göttingen/ Pittig	The impact of experimentally controlled degrees of safety behaviour on protection from fear extinction
5	Arlinda Gashi	Salzburg/ Wilhelm	Confronting fear after trauma? The impact of avoidance on intrusive memories in a trauma-film fear conditioning paradigm
6	Lu Leng	Leuven/ Vervliet	No joy - why bother? Higher anhedonia relates to reduced pleasure from and motivation for threat avoidance
7	Francesco Tortora	Würzburg/ Andreatta	How does the interplay between conjunctive and elemental context representation guide avoidance behaviour?
8	Juliane Boschet-Lange	Würzburg/ Pittig	Temporal dynamics of costly avoidance in anxiety disorders
9	Valentina Glück	Würzburg/ Pittig	No elevated persistence of extensively trained avoidance in participants with anxiety disorders in an outcome devaluation study
10	Alex Wong	Rotterdam/ Wieser	The degree of safety behaviours to a safety stimulus predicts development of threat beliefs
11	Naomi Carpentier	Leuven/ Raes	Optimizing extinction with approach behaviour
12	Marcelo Malbec	Rotterdam/ Wieser	Uncertainties about the role of Intolerance of Uncertainty in fear extinction
13	Alina Koppold	Hamburg-Eppen-dorf/ Lonsdorf	Uncovering individual freezing-like behaviour in relation to threat proximity in the context of threat and uncertainty
14	Michalina Dudziak	Leuven/ Beckers	In and out of control: the impact of having and losing control over threat on the acquisition and extinction of conditioned fear
15	Lea Busch	Duisburg-Essen/ Bingel	Mechanisms of appetitive and aversive pain-related learning in health and chronic back pain
16	Sabrina Hetteger	Salzburg/ Wilhelm	Pre-traumatic risk factors for the development of classically conditioned pain intrusions: A fear- and pain-conditioning trauma-analogue study
17	Ena Alcan	Marburg/ Pané-Farré	Observational fear learning of interoceptive threat
18	Edgar Nazareus	Hildesheim/ Richter	Individual differences in generalizing fear extinction learning across the spectrum of trait anxiety
19	Leonie Rumpf	Hamburg-Eppen-dorf/ Haaker	Perceptual similarities increase the generalisation of fear
20	Paula Engelke	Würzburg/ Pittig&Pauli	Does variability make a difference? Return of fear after extinction learning with perceptually similar generalization stimuli
21	Jessica Reinhart	Würzburg/ Reiter	Dynamics of fear-generalization processes and their predictive value for the development of anxiety-related psychopathology in adolescents
22	Asimina Aslanidou	Rotterdam/ Wieser	Increased generalized threat expectations in threatening contexts

# Keynote Lecture by Karin Roelofs

## The relevance of considering parasympathetic as well as sympathetic threat states

*Donders Institute for Brain, Cognition and Behavior & Behavioral Science Institute, Radboud University, Nijmegen*

In the face of threat, psychophysiological reactions by the autonomic nervous system (ANS) are important for learning and action preparation. The ANS generates both sympathetic and parasympathetic arousal but those responses are typically not distinguished in the threat conditioning literature. Additionally, whereas human studies traditionally rely on sympathetic outcome measures, such as skin conductance, the animal literature predominantly uses freezing observations, often associated with parasympathetic dominance. Is that a problem? In my talk I will show that states of sympathetic versus parasympathetic dominance in the anticipation of threat are associated with distinct behavioral and cognitive consequences. For instance, freezing-related parasympathetic heart rate deceleration is associated with action preparation, approach-avoidance decision making and improved perception. Additionally, I will provide preliminary evidence indicating that sympathetic versus parasympathetic dominance during threat conditioning is associated with distinct predictions for anxiety. In light of these findings, I'll argue that we should take parasympathetic as well as sympathetic states into account when studying threat reactions in healthy and clinical populations.

### Short bio

Karin Roelofs is Professor of Experimental Psychopathology at Radboud University (Behavioural Science Institute-BSI) and chair of the Affective Neuroscience group at the Donders Institute for Brain Cognition and Behaviour (DI). After obtaining her Masters' Degrees in Neuropsychology and in Clinical Psychology, she obtained her PhD in psychology with the highest distinction at the RU under the supervision of Prof Hoogduin and Prof Gaalman (2002). Part of her studies she spent at the National Institutes of Health (NIH, USA) working with Prof P. Brouwers. From 2001-2011 she worked as assistant and associate professor, respectively, at Leiden University. Thereafter she moved to the Radboud University where she started the [EPAN](#) group "Experimental Psychopathology and Affective Neuroscience" at the [BSI](#) and the Donders Centre for Cognitive Neuroimaging ([DCCN](#)).

With her group she studies the neuroendocrine mechanisms underlying stress-vulnerability and resilience in health and psychopathology. With a clear focus on neurocognitive mechanisms of defensive stress-responses, she uses various brain imaging (fMRI, MEG) techniques, combined with neural stimulation (TMS, cTBS, tACS) or pharmacological interventions during emotional control and decision-making tasks. Next, to test their role in resilience, she applies the neurocognitively grounded paradigms in longitudinal samples, including a developmental sample from the Nijmegen Longitudinal Study (NLS) a large police cohort from the Police-In-Action (PIA) study and patients with affective disorders from the ERC-DARE2APPROACH study.

Karin Roelofs is member of the Royal Netherlands Academy of Arts and Sciences ([KNAW](#)) and the Academia Europaea (AE). As vice-president of the Association for ERC Grantees ([AERG](#)) she is committed to fundamental science in Europe. She is also chair of the International Resilience Alliance ([INTRESA](#)). Karin Roelofs received an ERC-starting (NEURODEFENSE) and an ERC-consolidator grant (DARE2APPROACH) as well as several national grants including an NWO-VICI. Additionally, she is involved in several research consortia, including Horizon2020 (DYNAMORE) and NWO-Crossover (NTENSE) consortia. In 2020 Roelofs was awarded the prestigious [Evens Science Prize, an international prize for cognitive neuroscience with societal relevance](#), for her contributions to the field of stress-resilience research.

### Related publications

**Roelofs K.** Dayan, P. (2022). Freezing revisited: Coordinated autonomic and central optimization of threat coping. *Nature Reviews Neuroscience* 23, 568–580.

Skora L, Livermore J, **Roelofs K** (2022). The functional role of cardiac activity in perception and action. *Neuroscience and Biobehavioral Reviews*, 137, 104655.

Kalisch R, ea, **Roelofs K**, ea, Kleim (2017). International Resilience Alliance (intresa Resilience Consortium). 2017. The resilience framework as a strategy to combat stress-related disorders. *Nature Human Behavior*. 1-7.

Schipper P, ea **Roelofs K**, Henckens MJAG, Homberg JR. (2019). The association between serotonin transporter availability and the neural correlates of fear bradycardia. *Proc Natl Acad Sci USA (PNAS)*. 116(51):25941-25947.

**Roelofs, K.** (2017). Freeze for Action. Neurobiological mechanisms in animal and human freezing. *Philos Trans R Soc Lond B Biol Sci*. 372(1718). pii: 20160206.

# Abstracts – Symposium 1

Highlights of Human Fear Conditioning Research: Scientific Advances and Clinical Applications

22<sup>nd</sup> May, 14:00 - 15:30

## 1. Disrupting emotional associative memories through instructions to forget

Anastasia Chalkia<sup>1</sup>, Michelle Craske<sup>2</sup>, & Tom Beckers<sup>1</sup>

<sup>1</sup>Centre for the Psychology of Learning and Experimental Psychopathology, KU Leuven | <sup>2</sup>Anxiety and Depression Research Center, UCLA

Empirical work spanning over 50 years has repeatedly demonstrated that declarative memory encoding is sensitive to disruption, as participants can be cued to intentionally “forget” information before it is stored using a directed forgetting manipulation. Recently, original research from our lab has revealed that directed forgetting may also be successfully applied to interfere with the encoding of emotional associative memories acquired through fear conditioning. To that end, we developed a novel fear conditioning procedure where simple line drawings were displayed one at a time, and half of them were paired with a mild electric shock US (CS+), while the other half were not (CS-). An acoustic forget cue was presented after half of all the CS+ and CS- trials, indicating that those trials were to be forgotten. SCR was included as an index of physiological fear responding and declarative memory retention was probed with free recall and recognition tasks. Across a series of proof-of-concept experiments, participants recalled and recognized fewer of the items that were followed by the forget cue (referred to as the directed forgetting effect). Most importantly, subjects developed weaker SCR in response to CS+ items that were instructed to be forgotten. I will report on those early experiments, as well as a series of follow-up experiments where we manipulated certain aspects of our procedure in order to replicate and confirm our original observations. Taken together, our results provide robust evidence in favor of a disruption of the encoding of emotional associative memories through instructions to forget.

Keywords: *fear conditioning, directed forgetting, associative memory*

## 2. The impact of physical exercise on extinction memory consolidation

Valerie L. Jentsch, Oliver T. Wolf, & Christian J. Merz

*Ruhr University Bochum, Bochum, Germany*

Extinction learning represents a major mechanism of exposure therapy, a technique in cognitive-behavioural psychotherapy commonly used for the treatment of anxiety disorders. However, despite its general effectiveness nonresponse and relapse still pose challenges for the long-term success of these interventions. Physical exercise improves learning and memory and appears also to enhance extinction processes, rendering it a promising candidate for augmenting the efficacy of exposure-based treatments. In this study, 60 healthy men underwent a differential fear conditioning paradigm with fear acquisition on day one and fear extinction on day two followed by an exercise or resting control intervention. On the third day, retrieval and reinstatement were tested including two additional but perceptually similar stimuli to explore the generalization of exercise effects. Significant increases in heart rate, salivary alpha amylase, and cortisol in the exercise but not in the control group indicated successful exercise manipulation. Contrary to our expectations, exercise did not enhance but rather impaired extinction memory retrieval, evidenced by significantly stronger differential skin conductance responses (SCR) and pupil dilation (PD) in the exercise relative to the control group. Notably, although conditioned fear responses were successfully acquired, they did not completely extinguish, explaining why exercise might have boosted fear memory consolidation instead. Stronger differential SCR and PD towards the novel stimuli furthermore suggest that the exercise-induced memory enhancement also generalized to perceptually similar stimuli. Our findings indicate that physical exercise can facilitate the

retrievability and generalization of extinction memories, but presumably only when extinction has been successful in the first place.

### 3. How long-lasting are the effects of stress on fear memories?

Christopher M. Klinke<sup>1,2</sup>, Maren D. Lange<sup>1,2</sup>, & Marta Andreatta<sup>1,2</sup>

<sup>1</sup>Erasmus University Rotterdam (EUR, the Netherlands) | <sup>2</sup>University of Wuerzburg (JMU, Germany)

Individuals, stressed days prior fear acquisition, show persistent defensive responses, which suggests that their extinction learning was impaired. It remains to clarify whether such stress-induced impairment of fear extinction has long-lasting effects. We tested fear and extinction memories in 110 participants, who underwent either the socially evaluated cold pressure test (SECPT) or a sham protocol on Day1. All participants underwent a fear acquisition on Day2 and a fear extinction on Day3. Half of the participants were tested 24 hours after extinction (Day4), while the other half 2 weeks later (Day17). Two visual stimuli were presented as conditioned stimuli and a mildly painful electric shock as unconditioned stimulus (US). US was delivered only during fear acquisition at the offset of CS+ but not at the offset of CS-. Successful fear acquisition was indicated by higher fear and US-expectancy ratings as well as startle potentiation to CS+ vs. CS-. All participants reduced their conditioned defensive responses during extinction. Spontaneous recovery of the verbal defensive responses was evident in those participants tested two weeks after extinction but not in those tested one day later. Stress seems to boost spontaneous recovery two weeks after extinction as startle responses of the stressed participants were potentiated, while no startle potentiation was observed in the other groups. In sum, stress may strengthen fear memories, thereby facilitating the spontaneous recovery of conditioned defensive responses.

Keywords: *stress, return of fear, psychophysiology*

### 4. Imagery-based fear conditioning: A learning model for social anxiety?

Matthias F. J. Sperl<sup>1</sup>, Lena Moench<sup>1</sup>, Erik M. Mueller<sup>2</sup>, & Christiane Hermann<sup>1</sup>

<sup>1</sup>University of Giessen (Germany), Department of Psychology, Clinical Psychology and Psychotherapy | <sup>2</sup>University of Marburg (Germany), Department of Psychology, Personality Psychology and Assessment

Aversive learning experiences are important factors in the etiology and maintenance of Social Anxiety Disorder. A central mechanism is classical conditioning, whereby a conditioned stimulus (CS) is paired with an unpleasant stimulus (US). Negative learning experiences (e.g., social rejection) are paired with environmental stimuli, which subsequently elicit threat and contribute to avoidance of social situations. However, many patients cannot explicitly recall a specific unpleasant learning experience. The question arises whether aversive imagery can also be paired with specific environmental stimuli. To investigate the influence of unpleasant and pleasant imaginations on social conditioning processes, we developed a novel imagery-based paradigm and validated it in healthy participants. During acquisition, three neutral faces (CS) were paired with an unpleasant, pleasant, or neutral socially relevant imagination. To measure the conditioned response, activity of facial mimic muscles was recorded using electromyography (EMG). Processing of unpleasant stimuli is typically associated with increased activity of the M. corrugator supercilii (frowning), whereas activity of the M. zygomaticus major (pulling up the corners of the mouth when smiling) is associated with pleasant stimuli. As expected, faces paired with a socially relevant unpleasant imagination elicited stronger corrugator activity. Conversely, faces paired with a pleasant imagination elicited stronger zygomaticus activity. Presentation of the faces was accompanied by the corresponding EMG activity, even when no imagination was to be performed at all. Our results show successful conditioning with imagined social stimuli, which was captured by mimic facial muscles. Social anxiety can be learned through imagination, opening perspectives for innovative imagery-based therapeutic approaches.

Keywords: *social anxiety, imagery, facial muscles*

## 5. Prediction of exposure therapy outcome by latent fear learning trajectories

Caroline M. B. Kwee<sup>1,2</sup>, Puck Duits<sup>2</sup>, Neeltje M. Batelaan<sup>3</sup>, Danielle, C. Cath<sup>4,5</sup>, & Johanna M. P. Baas<sup>1</sup>

<sup>1</sup>*Department of Experimental Psychology and Helmholtz Institute, Utrecht University, Utrecht, the Netherlands* | <sup>2</sup>*Altrecht Academic Anxiety Center, Utrecht, the Netherlands* | <sup>3</sup>*Department of Psychiatry, Amsterdam Public Health Research Institute, VU University Medical Centre and GGZ inGeest, Amsterdam, the Netherlands* | <sup>4</sup>*University of Groningen, University Medical Centre Groningen, Groningen, the Netherlands* | <sup>5</sup>*GGZ Drenthe, department of specialist trainings, Assen, the Netherlands*

Although in general, exposure therapy is an effective treatment for anxiety disorders, approximately one third of patients do not respond satisfactorily. Moreover, deterioration should be also taken into account as a possible outcome. These instances of treatment failure are unacceptable, given that exposure therapy is often experienced as burdensome. Naturally, predictors of treatment (non)response have been a topic of considerable interest. Associations between clinical status and fear learning have been identified in previous work, and preliminary evidence exists for fear learning trajectories predicting treatment outcome after exposure therapy. In this previous study, participants received instructions about stimulus-threat associations during fear acquisition and extinction phases. We investigated whether treatment outcome could also be predicted by fear learning trajectories when these instructions were not provided. Results from latent class growth analyses (means of the latent intercept and slope factors) on the previous sample (n=194) were used to classify patients with social anxiety disorder (n=19) and panic disorder with agoraphobia (n=24) from a new sample to latent fear learning trajectories. We evaluated in the previous sample competing hypotheses using the Bayes factor: Whether learning trajectories based on fear and shock expectancy alone, or in combination, were associated with treatment outcome. Hypotheses with the most support in the data were then evaluated in the new sample, who received highly protocolized exposure therapy. Our findings may elucidate which type(s) of fear learning should receive attention to optimize exposure treatment outcomes in currently treatment refractory patients.

*Keywords: fear extinction, safety learning, treatment outcome*

# Abstracts – Symposium 2

The Neuroscience of Fear Conditioning

22<sup>nd</sup> May, 17:00 - 18:30

## 1. The pleasure of absent danger: fMRI evidence for reward prediction error-like processing of absent danger

Anne L. Willems<sup>1,2</sup>, Lukas Van Oudenhove<sup>2,3</sup>, & Bram Vervliet<sup>1,2</sup>

<sup>1</sup>Laboratory of Biological Psychology, KU Leuven, Belgium | <sup>2</sup>Leuven Brain Institute, KU Leuven, Belgium | <sup>3</sup>Laboratory for Brain-Gut Axis Studies (LaBGAS), Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Belgium

Accumulating evidence supports that unexpected absence of danger drives the learning of safety via reward prediction error (PE)-like signaling in the dopaminergic reward circuit. But how aversive expectations can transform “nothing”, the mere omission of danger, into a rewarding event is not yet clear. Here, I will present the results of two fMRI experiments in which we tried to answer this question. Using the Expectancy Violation Assessment (EVA) task, we investigated neural and emotional processing of threat omissions in greater detail. In this task, participants received trial-by-trial instructions on the probability (0% to 100%) and intensity (weak, moderate, strong) of a potentially painful electrical stimulation. But, in reality the stimulation was omitted in most of the trials allowing us to assess subjective (relief pleasantness), physiological and neural reactions to the omissions. The first study (N = 31) showed that unexpected omissions of threat triggered reward-PE like activations in the ventral tegmental area (VTA)/substantia nigra (SN) that were furthermore modulated by self-reported relief. The second study (N = 60) zoomed in on a potential role of the endogenous opioid system in triggering these activations, given its close link to both pain and reward processing. Participants received either Naltrexone (mu-opioid receptor antagonist) or placebo, one hour before they completed the task. Preliminary results will be presented during the talk. Together, these studies provide new insights in how omissions of threat and the associated relief are processed in the brain, and how they are modulated by aversive expectations and endogenous opioid activity.

Keywords: *prediction error, pharmacology, fMRI*

## 2. Hippocampal reactivity to aversive films predicts intrusion distress and is independent of pattern separation

Dorothee Pöhlchen<sup>1,2</sup>, Janina Gordon<sup>1</sup>, Marthe Priouret<sup>1</sup>, Andy Brendler<sup>1</sup>, Michael Czisch<sup>3</sup>, Frank H. Wilhelm<sup>4</sup>, Philipp G. Saemann<sup>3</sup>, Monika Schönauer<sup>5</sup>, & Victor I. Spoormaker<sup>1</sup>

<sup>1</sup>Department of Translational Research in Psychiatry, Max Planck Institute of Psychiatry, Munich, Germany | <sup>2</sup>International Max Planck Research School for Translational Psychiatry (IMPRS-TP), Max Planck Institute of Psychiatry, Munich, Germany | <sup>3</sup>Max Planck Institute of Psychiatry, Munich, Germany | <sup>4</sup>Division of Clinical Psychology and Psychopathology, Department of Psychology, Paris Lodron University Salzburg, Salzburg, Austria | <sup>5</sup>Institut für Psychologie, Albert-Ludwigs-Universität Freiburg, Germany

Posttraumatic stress disorder (PTSD) can be conceptualized as a memory disorder with symptoms of intrusive, vivid memories as well as contextual memory deficits of traumatic experiences. The hippocampus is assumed to play a major role in this pathological memory formation due to its involvement in episodic memory. It is unclear, however, which hippocampal mechanisms contribute to PTSD memory symptoms. Hippocampal pattern separation may promote adaptive mnemonic processes such as binding of the trauma memory to its respective context. Deficits in hippocampal pattern separation could thereby underly pathological memory formation. To investigate the hippocampal role in predicting memory symptoms, we compared healthy female participants with low and high “lure discrimination ability” (a behavioral proxy for hippocampal pattern separation) with regard to their neural and pupillary response profiles during a conditioned-intrusion induction paradigm applying short film clips on severe interpersonal violence. We were specifically interested

in relating fear-related hippocampal response strength and representational similarity in hippocampal subfields to reported intrusion distress and contextual memory deficits. An expected stress-induced hippocampal deactivation was observed in response to aversive films. Critically, weaker hippocampal deactivation predicted intrusion distress. Neither behavioral lure discrimination nor neural pattern separation in hippocampal subfields were associated with individual differences in hippocampal deactivation. Instead, the extent of hippocampal deactivation was correlated with pupil dilations, a proxy for noradrenergic signaling. Results support a hippocampal role in intrusion formation, that was not driven by the cognitive mechanism of pattern separation but may result from a hippocampal involvement in autonomic stress reactivity.

Keywords: *intrusions, hippocampus, pattern separation*

### 3. Resting brain connectivity signature of pain-related learning

Balint Kincses<sup>1</sup>, Frederik Schlitt<sup>1</sup>, Robert Pawlik<sup>2</sup>, Katharina Schmidt<sup>1</sup>, Dagmar Timmann<sup>1</sup>, Sigrid Elsenbruch<sup>2</sup>, Katarina Forkmann<sup>1</sup>, Ulrike Bingel<sup>1</sup>, & Tamas Spisak<sup>1,3</sup>

<sup>1</sup>Department of Neurology & Center of Translational Neuro- and Behavioural Sciences, University Medicine Essen, University Duisburg-Essen | <sup>2</sup>Department of Medical Psychology and Medical Sociology, Faculty of Medicine, Ruhr University Bochum, Bochum, Germany | <sup>3</sup>Institute for Diagnostic and Interventional Radiology and Neuroradiology, Essen University Hospital, Essen, Germany

Individuals show considerable differences in aversive learning in which both psychological and biological factors play a role. Here, we investigated the potential of resting state connectivity to predict such individual differences. Participants (n=99) performed a differential conditioning paradigm with pain and unpleasant tone as unconditioned and neutral geometrical figures as conditioned stimuli. Individual differential valence change of pain and tone cues were recorded during acquisition and used as our target in the model discovery phase. Resting state fMRI was acquired before the conditioning paradigm and individual functional connectivity matrices were used as predictive brain features. After model discovery on a sample of n=25, we fixed and preregistered our fMRI pre-processing pipeline and the finalized model to be used in the external validation phase. The conditioning paradigm resulted in increased pain-cue valence ratings in both the discovery and the external validation samples. The predicted values of our model on the discovery and the external validation sample significantly correlated with the observed values ( $r=0.72$ ,  $p<0.01$ ;  $r=0.34$ ,  $p=0.019$ , respectively). Model predictions were specific to pain and captured both the emotional and the cognitive aspect of learning (i.e., valence and contingency). The most important connections of the model are between regions that are well known to play a role in pain-related learning, in particular the amygdala, cerebellum, and insula. The proposed model can be considered as a robust and objective brain-based measure of pain related learning with broad implications in basic and translational research.

Keywords: *resting state fMRI, pain related learning, multivariate prediction*

### 4. Temporal dynamics of threat-associated memory accuracy versus generalization

Lisa Wirz<sup>1,2</sup>, Alessio Proposito<sup>1,2</sup>, Anika Pützer<sup>2</sup>, Benno Roozendaal<sup>1</sup>, Oliver T. Wolf<sup>2</sup>, Erno Hermans<sup>1</sup>

<sup>1</sup>Donders Institute for Brain, Cognition and Behaviour, Radboud university medical center, Nijmegen, The Netherlands; <sup>2</sup>Department of Cognitive Psychology, Ruhr-University Bochum, Bochum, Germany

There is ongoing debate on how memory representations in the brain change over time, and how this may be different for fear memories. Using a fear conditioning paradigm with 2 categories (CS+/CS-: animals/objects), 2 spatial contexts as occasion setters (threat and safe), and 2 different test intervals (1 day vs. 21 days), we investigated long-term changes in fear memory quality. Participants (27 female, 26 male) completed fear acquisition, and a fear retrieval and item (CS+, CS- items) memory recognition test after 1d (N=26) or 21d (N=27). Item recognition memory performance ( $d'$ ) was higher for CS+ vs. CS- items ( $p=.03$ ), and lower after 21d vs. 1d ( $p<.001$ ). This memory performance decrease over time was caused by a lower hit rate for CS- items ( $p<.001$ ), whereas for CS+ items, the false alarm rate was higher ( $p=.03$ ). This is in line with a more liberal

response bias for CS+ vs. CS- items after 21d ( $p=.02$ ). The fMRI data showed stronger vmPFC activation for CS+ false alarms vs. hits after 21d vs. 1d (cluster pFWE-corr=.003) during the item memory recognition test, suggesting that more generalized memories for CS+ items over time more strongly recruit the vmPFC. In sum, over time, memory strength decreases for safe stimuli (CS-), whereas memory specificity decreases for threat stimuli (CS+). This suggest that for threat compared to safe memories, the time-dependent incorporation into neocortical networks is accelerated, resulting in more generalized memories.

Key words: *Fear memory generalization, systems consolidation, fMRI*



# Abstracts – Symposium 3

## Generalization of Fear Conditioning and Extinction

23<sup>rd</sup> May, 09:00 - 10:30

### 1. “Implanting” fear in the human mind: false threat memories support fear generalization

Jianqin Wang<sup>1</sup>, Emma Biggs<sup>2,3,4</sup>, Henry Otgaar<sup>3</sup>, & Tom Beckers<sup>4</sup>

<sup>1</sup>Fudan University | <sup>2</sup>Stanford University | <sup>3</sup>Maastricht University | <sup>4</sup>KU Leuven

Could the emergence of false episodic threat memories, through known processes of false memory formation, be a cognitive mechanism of fear generalization? Here we introduce a new fear generalization paradigm that combines the Deese-Roediger/ McDermott false memory procedure with a trial-unique fear conditioning task. Using this paradigm, in four experiments, we successfully created false memories of past fear experiences, where participants falsely remembered a non-presented lure item predicting threat. False threat memories led participants to avoid the lure items; the more false threat memories they reported for the critical lures, the more they exhibited avoidance to these items. Critically, the extent of avoidance to these critical lures went over and beyond the mere effect of category generalization. We thus identified false memory formation as a potential mechanism for fear generalization, further supporting the important function of episodic memory in human fear learning and expression.

Keywords: *fear conditioning, false memory, generalization*

### 2. Generalization of exposure effects to untreated stimuli

Armin Zlomuzica

*Department of Behavioral and Clinical Neuroscience, Mental Health Research and Treatment Center, Ruhr-University Bochum*

Exposure is considered as the most effective intervention to attenuate exaggerated fear. The extent to which exposure treatment effects can generalize to fears not targeted during treatment remains elusive. In a series of recent studies, we demonstrated that a generalization of therapeutic effects during exposure is possible across stimuli which belong to the same category yet differ perceptually from each other. Subjects with fear of spiders and cockroaches who underwent an exposure for one phobic stimulus (spiders), whereas the other phobic stimulus (cockroaches) was left untreated, exhibited attenuated fear to both spiders and cockroaches. We further showed that exposure treatment generalization can be observed for untreated stimuli which do not share any perceptual resemblance with treated stimuli and belong to a different fear category. Findings from our studies indicate that exposure might entail beneficial effects which go beyond the observed reductions in fear and avoidance related to the treatment stimuli. Future research aimed to identify the decisive factors underlying exposure treatment generalization might help to expand the generalization effect permanently to any given type of fear.

### 3. Childhood adversity is associated with increased fear generalization in adolescents

Celine Samaey<sup>1</sup>, Aleksandra Lecei<sup>1</sup>, & Ruud van Winkel<sup>1,2</sup>

<sup>1</sup>Center for Clinical Psychiatry, Department of Neurosciences, KU Leuven | <sup>2</sup>University Psychiatric Center (UPC), KU Leuven

Childhood adversity is associated with increased risk of almost all types of psychopathology, making it a major transdiagnostic risk factor. Altered threat-related information processing has been put forward as a potential process underlying this association between childhood adversity and psychopathology, with previous research providing support for altered fear conditioning, i.e., lower distinction between threat and safety cues, in both children and adults exposed to childhood

adversity, as well as increased fear generalization in young adults. To investigate whether childhood adversity is associated with increased fear generalization during adolescence, we applied a fear conditioning and generalization paradigm in 119 adolescents between 12 and 16 years of age (mean age = 13.95). 63 adolescents were exposed to childhood adversity, defined as child maltreatment, sexual victimization, indirect victimization, physical and emotional neglect, and severe peer victimization. Fear conditioning was assessed through trial-by-trial US expectancy ratings and fear-potentiated startle responses. Additionally, we included a sequential perceptual discrimination task following the fear conditioning paradigm. Results showed that childhood adversity is associated with (1) reduced threat-safety differentiation during fear acquisition, and (2) increased fear generalization in both boys and girls, albeit to a different extent. This overgeneralization of fear could not be attributed to group differences in perceptual discrimination abilities. The results from this study will be discussed in light of the existing literature.

Keywords: *childhood adversity, fear generalization, adolescence*

#### **4. Predictive power of experimental fear conditioning and generalization measures on longitudinal changes in negative affect during the COVID-19 pandemic**

Katharina Hutterer<sup>1</sup>, Celina Imholze<sup>2</sup>, Dominik Gall<sup>2</sup>, Udo Dannlowski<sup>3</sup>, Katharina Domschke<sup>4,5</sup>, Elisabeth E. Leehr<sup>3</sup>, Ulrike Lueken<sup>6</sup>, Tina B. Lonsdorf<sup>7</sup>, Andreas Reif<sup>8</sup>, Karoline Rosenkranz<sup>7</sup>, Miriam A. Schiele<sup>4</sup>, Peter Zwanzger<sup>9,10</sup>, Paul Pauli<sup>2</sup>, & Matthias Gamer<sup>2</sup>

<sup>1</sup>Department of Psychiatry, Psychosomatics, and Psychotherapy, Center of Mental Health, University Hospital Würzburg, Würzburg, Germany | <sup>2</sup>Department of Psychology, University of Würzburg, Würzburg, Germany | <sup>3</sup>Institute for Translational Psychiatry, University of Münster, Münster, Germany | <sup>4</sup>Department of Psychiatry and Psychotherapy, Medical Center – University of Freiburg, Freiburg, Germany | <sup>5</sup>Center for Basics in NeuroModulation, University of Freiburg, Freiburg, Germany | <sup>6</sup>Department of Psychology, Humboldt-Universität zu Berlin, Berlin, Germany | <sup>7</sup>Institute for Systems Neuroscience, University Medical Center Hamburg Eppendorf, Hamburg, Germany | <sup>8</sup>Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, University Hospital Frankfurt – Goethe University, Frankfurt am Main, Germany | <sup>9</sup>Kbo Inn Salzach Hospital Clinical Center for Psychiatry, Wasserburg am Inn, Germany | <sup>10</sup>Department of Psychiatry, LMU Munich, Munich, Germany

Impaired differentiation of threat and safety cues and excessive fear generalization are considered vulnerability factors for anxiety disorders. They supposedly interact with adverse experiences in disorder development, but because longitudinal studies are scarce, their precise interplay remains unclear. Here, we examined how individual differences in experimental fear conditioning and generalization measures modulate adjustments in negative affect during the COVID-19 pandemic. Between 2013 and 2020, participants (N=441) were characterized regarding anxiety and depression and underwent two fear acquisition blocks in which one of two female faces (conditioned stimulus, CS+), but not the other (CS-), was associated with a loud scream (unconditioned stimulus, US), and a subsequent generalization block in which both CSs and four morphs between them (generalization stimuli, GS1-GS4) were presented. After the onset of the pandemic in 2020, participants again reported anxiety and depression symptomatology. Participants showed increased levels of negative affect after pandemic outbreak, which were partly modulated by measures of general threat responsiveness and differentiation of threat and safety cues. Effects were larger on depression than on anxiety scores, and mostly related to subjective arousal ratings. Measures of fear generalization did not predict changes in either depression or anxiety scores. These findings complement research suggesting that the shape of generalization gradients might be less relevant to the psychopathology of anxiety and depression than overall measures of threat responsiveness and CS differentiation. As effects were small, they should be replicated to further characterize how individual differences in threat processing interact with adverse experiences in the development of psychopathology

Keywords: *fear generalization, negative affect, longitudinal*

## 5. Multiple pathways to widespread fears: Disentangling idiosyncratic fear generalization mechanisms using computational modeling

Kenny Yu<sup>1</sup>, Francis Tuerlinckx<sup>1</sup>, Wolf Vanpaemel<sup>1</sup>, & Jonas Zaman<sup>2,3</sup>

<sup>1</sup>*Quantitative Psychology and Individual Differences, Faculty of Psychology and Educational Sciences, KU Leuven* | <sup>2</sup>*School of Social Sciences, University of Hasselt* | <sup>3</sup>*Centre for Learning and Experimental Psychopathology, Faculty of Psychology and Educational Sciences, KU Leuven*

Human generalization research aims to understand the mechanisms and processes underlying the transfer of prior experiences to new contexts. To capture differences in a generalization process, descriptive statistics are predominantly used to parameterize generalization gradients extracted from aggregated group or individual data. Unfortunately, such an approach fails to disentangle various mechanisms underlying generalization behavior, leaving both inter- and intra-individual variation unaccounted for. In the current work, we combine a multi-assessment approach with a computational model to mechanistically scrutinize between learning, perceptual and generalization mechanisms at the individual level. This multi-assessment enabled us to identify and differentiate the different components of generalization behavior among participants. Our analysis revealed meaningful variations in how different mechanisms contribute to generalization behavior. Our work highlights how the adoption of the computational modeling framework can 1) help to shift the theoretical attention away from forecasting group-level generalization behavior and toward understanding how such phenomena emerge at the individual level; 2) disentangle mechanisms of generalization behavior and serve as a potential tool for differential diagnosis in generalization-related psychiatric disorders. In sum, the current research suggests the need for revising the theoretical and analytic foundations in the field to account for the distinctive characteristics of human generalization behavior.

*Keywords: human fear generalization, cognitive modeling, individual differences*

# Abstracts – Symposium 4

## Conceptual Advances in Human Fear Conditioning

23<sup>rd</sup> May, 11:00 - 12:30

### 1. Threat conditioning and episodic memory: towards an integrated account of emotional associative learning

Olivier de Vries<sup>1</sup>, Sascha Duken<sup>2</sup>, Raoul Grasman<sup>1</sup>, Merel Kindt<sup>1</sup>, Vanessa van Ast<sup>1</sup>

<sup>1</sup>University of Amsterdam, Amsterdam, The Netherlands | <sup>2</sup>University of Utrecht, Utrecht, the Netherlands

We are constantly in the process of actively predicting the future on the basis of previous experience. Using a variety of strategies ranging from simple incremental learning to complex recombination of information encoded at different points in time, aversive outcomes can be anticipated and avoided. The associative structures underlying these abilities are typically studied in one of two ways: Whereas threat conditioning experiments typically measure physiological responses to predictors of motivationally relevant outcomes, episodic memory experiments measure whether certain cues bring their associated content to mind. Although often considered to rely on distinct processes, these measures may very well interact in important ways that will remain elusive when studied in isolation. Based on recent data from experiments that combine ideas from threat conditioning and episodic memory research, I will present new insights into the ways by which newly learned threats may touch on existing neutral memories, affecting them in terms of both content and physiological expression. Ultimately, investigating the dynamic mechanisms of associative learning that govern an individual's predictions of the future may help to better understand the etiology and treatment of anxiety disorders.

Keywords: *episodic memory, fear conditioning*

### 2. Beyond analogue fear conditioning paradigms: The complex interplay between dissociation and other conditioned responses to trauma scripts in individuals with posttraumatic stress disorder

Sarah K. Danböck<sup>1</sup>, Michael Liedlgruber<sup>1</sup>, Laila K. Franke<sup>1</sup>, Stephan F. Miedl<sup>1</sup>, Sabrina Hettegger<sup>1</sup>, Rainer-Christian Weber<sup>2</sup>, & Frank H. Wilhelm<sup>1</sup>

<sup>1</sup>Division of Clinical Psychology and Psychopathology, Department of Psychology, Paris Lodron University Salzburg, Salzburg, Austria | <sup>2</sup>Center of Psychotraumatology, BG Klinik Bad Reichenhall, Bad Reichenhall, Germany

Exposure to traumatic incidents is a prototypical fear-conditioning paradigm evoking fear and autonomic arousal. After a traumatic fear-conditioning episode, individuals might re-experience peritraumatic responses when exposed to trauma reminders, which constitutes one of the hallmark symptoms of posttraumatic stress disorder (PTSD). Importantly, many individuals with PTSD do not only acquire fear- and arousal responses, but also other responses like dissociation and immobility. Yet, to date, the interplay between those responses is unclear. Defense-cascade-models suggest a critical role of dissociation and link it to immobility, an autonomic shut-down, and emotional numbing. To evaluate the evidence for these claims, we conducted a pre-registered script-driven imagery study in 71 individuals with PTSD. Participants were exposed to highly standardized, detail-enriched trauma- and neutral-scripts, and resting-periods. Stabilometry, eyetracking, physiology, and self-report data were collected. Our results did not link dissociative responding to immobility or staring. However, dissociative responding was linked to higher nonspecific skin-conductance-fluctuations, higher high-frequency heart rate variability, and displayed an inverted U-shaped relationship with heart rate responses to trauma-scripts. Further, dissociative responding was linked to higher self-reported negative-affect responses to trauma-scripts. Our findings paint a complex picture of conditioned responses in patients with PTSD and suggest an inverted U-shaped relationship between dissociation and overall autonomic arousal

likely resulting from sympathetic and parasympathetic co-activation. However, on an experiential level, our data did not confirm dissociation-induced numbing, questioning theoretical notions. These findings may help expand experimental fear conditioning approaches to better adapt them to clinical presentations of conditioned fear and related symptoms.

Keywords: *PTSD, dissociation, biomarker*

### **3. How adverse childhood experiences get under the skin: A systematic review, integration and methodological discussion on threat and reward learning mechanisms**

Julia Ruge<sup>1</sup>, Mana R. Ehlers<sup>1</sup>, Alexandros Kastriogiannis<sup>1</sup>, Maren Klingelhöfer-Jens<sup>1</sup>, Alina Koppold<sup>1</sup>, & Tina B. Lonsdorf<sup>1,2</sup>

<sup>1</sup>University Medical Center Hamburg-Eppendorf, Institute for Systems Neuroscience, Hamburg, Germany |

<sup>2</sup>University of Bielefeld, Bielefeld, Germany

Exposure to adverse childhood experiences (ACEs) is a major risk factor for the development of behavioural, somatic and psychopathological conditions. Learning is the central mechanism through which environmental inputs shape emotional and cognitive processes as well as behaviour. In this review, we lay out a systematic and methodological overview and integration of the impact of ACEs on threat and reward learning processes in experimental paradigms based on systematic literature (following PRISMA guidelines) which resulted in a total of 66 studies (threat: N=36, reward: N=29). In addition, we discuss heterogeneity in operationalization and assessment of ACE exposure across these studies. Across the threat and reward learning fields, we observed a converging pattern of blunted learning in individuals exposed to ACEs independent of sample characteristics, ACE subtypes and outcome measures. Specifically, blunted threat learning was reflected in reduced discrimination between threat and safety cues, primarily driven by blunted responding to threat cues, while attenuated reward learning manifested in reduced accuracy and learning rate. Importantly, this pattern emerged despite substantial heterogeneity in ACE assessment and operationalization. We conclude that blunted threat and reward learning may represent two mechanistic routes by which ACEs may become biologically embedded and ultimately increase the risk for psychopathology. In closing, we discuss potentially fruitful future directions for the research field, including methodological and assessment considerations.

Keywords: *fear conditioning, reward learning, aversive childhood experiences*

### **4. Trait anxiety is associated with increased reliance on context during Pavlovian learning**

Ondrej Zika<sup>1,2</sup>, Katja Wiech<sup>3</sup>, Andrea Reinecke<sup>4,5</sup>, Michael Browning<sup>4,5</sup>, & Nicolas Schuck<sup>1,2,6</sup>

<sup>1</sup>Max Planck Research Group NeuroCode, Max Planck Institute for Human Development, Berlin, Germany |

<sup>2</sup>Max Planck UCL Center for Computational Psychiatry and Aging Research, Berlin, Germany, and London, UK |

<sup>3</sup>Wellcome Center for Integrative Neuroimaging (WIN), Nuffield Department of Clinical Neurosciences,

University of Oxford, Oxford, UK | <sup>4</sup>Department of Psychiatry, University of Oxford, Oxford, UK | <sup>5</sup>Oxford Health

NHS Trust, Warneford Hospital, Oxford, UK | <sup>6</sup>Institute of Psychology, Universität Hamburg, Hamburg, Germany

Updating beliefs in changing environments can be achieved either by gradually adapting expectations or by identifying a hidden structure composed of separate contexts (i.e., states), and inferring which fits one's observations best. Previous studies have found that a state inference mechanism might be associated with relapse phenomena, such as return of fear, that commonly represent a major obstacle in clinical treatment of anxiety disorders. Here, we tested whether variability in trait anxiety among healthy individuals is associated with a tendency towards inferring a hidden structure of an aversive environment, as opposed to learning gradually from observations. In a Pavlovian probabilistic aversive learning paradigm, participants had to follow changes in cue-associated shock contingencies by providing probability ratings on each trial. In three sessions, the contingencies switched between high and a low levels of shock probability (60/40%, 75/25% or 90/10%). High trait anxiety was associated with steeper learning and after reversal and less learning from oddball events. To elucidate the computational mechanisms behind these behavioural patterns, we compared a "1-state" model, which reflects gradual updating, with a novel state-

inference model (“n-state”). High trait anxiety was associated with improved fit of the state inference model compared to the gradual model in the session with largest shock contingency changes. This finding provides evidence that trait anxiety is associated with a tendency to infer hidden causes, and, in consequence, to rely more on contextual information. This association may contribute to relapse phenomena observed among high trait anxious individuals.

Keywords: *anxiety, extinction, computational modelling*

## **5. Occasional reinforced extinction as a method for relapse prevention: A critical review and future directions**

María J. Quintero<sup>1,2</sup>, Francisco J. López<sup>1,2</sup>, Miguel A. Vadillo<sup>3</sup>, & Joaquín Morís<sup>1,2</sup>

<sup>1</sup>*Departamento de Psicología Básica, Universidad de Málaga, Spain* | <sup>2</sup>*Instituto de Investigación Biomédica de Málaga–IBIMA, Spain* | <sup>3</sup>*Departamento de Psicología Básica, Facultad de Psicología, Universidad Autónoma de Madrid, Spain*

It is widely known that fear extinction is more vulnerable than the original fear memory, as relapse phenomena have systematically shown in the literature with different species and procedures. One strategy potentially useful to mitigate relapse is the occasional reinforced extinction treatment. In contrast to a standard procedure, this strategy consists of the inclusion of a gradual and sparse number of CS-US pairings within the standard extinction treatment, which may potentiate the effects of the latter. Although it might be a potentially useful technique, the current evidence assessing its effectiveness does not appear to be consistent. Here, we provide a comprehensive review of the available literature, highlighting differences in the relapse phenomena being studied, variables of interest and specific effects obtained. The observed methodological variability makes it difficult to draw a robust conclusion of the effectiveness of an occasional reinforced intervention to reduce different forms of relapse as the strategy has not consistently proved a general advantage over standard extinction.

Keywords: *conditioning, extinction, relapse, occasional reinforced extinction*

# Abstracts – Symposium 5

## Behavioural Avoidance in Fear Conditioning

24<sup>th</sup> May, 09:00 - 10:30

### 1. Half the shock, half the avoidance?

Pauline Dibbets, Kristof Vandael, & Linda Vancleef

*Maastricht University, Faculty of Psychology and Neuroscience, Dept. Clinical Psychological Science*

The expectation of an upcoming fearful event motivates goal-directed avoidance. Lowering the aversiveness of this event should coincide with less avoidance. The aim of the present study is to examine this premise. In a fear conditioning paradigm participants learned that pictures of one category (e.g., sunny CSs+) were always followed by an aversive electrical shock (US), while pictures of another “safe” category were not (e.g., rainy CSs-). Next, in the avoidance phase, participants could prevent the shock by pressing the spacebar during picture presentations (goal-directed US avoidance). Before commencing to the test phase, for half of the participants the shock level was reduced by 50% (USlow); for the remaining half the US intensity was not adjusted (UShigh). In the test phase previously presented pictures were given (CSs+, CSs-), novel pictures of the same categories (GCSs+ and GCSs-) and ambiguous stimuli (e.g., rainbow; AmbCSs). Based on the premise that fear motivates avoidance, reduction of US intensity should lower avoidance. The results will be presented at the EMHFC conference.

Keywords: *US devaluation, avoidance categorical learning*

### 2. Exploring strategies to prevent return of pain-related avoidance behaviour after successful extinction with response prevention

Ann Meulders

*Maastricht University, Maastricht, The Netherlands | KU Leuven, Leuven, Belgium*

Avoidance behavior is adaptive in the acute pain stage, but when it persists beyond healing time, it may become disabling. Previous research has focused on passive fear correlates (arousal and verbal reports) largely ignoring active behavioral avoidance. However, there is no one-to-one relationship between fear and avoidance, and they affect each other. For example, avoidance behavior during exposure may hamper corrective learning because the non-occurrence of the feared event is misattributed to the avoidance response. Therefore, exposure protocols usually imply *response prevention with extinction (RPE)*, i.e, avoidance is prohibited. This technique however may shift the problem because the unavailability of the avoidance response may constitute a context-switch (from therapy context to the patient’s daily life) impeding the transfer of corrective learning and leading to return of avoidance or *renewal* (return of fear due to context-switch). I will present new data testing two potential interventions to prevent relapse: (1) increasing positive affect (using an experimental affect induction) which is thought to strengthen inhibitory learning, and (2), increasing approach/reward motivation towards the previously feared and avoided movement (operationalized by lottery tickets increasing the chance of winning a valued price) to compete with avoidance behavior. In addition, we also tested the effect of cognitive load on extinction retrieval. Extinction and inhibiting the retrieval of the first-learned excitatory memory after RPE are resource-demanding processes that may be impaired by low availability of cognitive resources, leading to more return of pain-related avoidance and fear. Results and clinical implications will be discussed.

Keywords: *avoidance, positive affect, reward motivation*

### 3. Avoiding movement or space? Disentangling the roles of movement-related vs. spatial cues in learned movement avoidance

Xaver Fuchs<sup>1,2</sup> & Tobias Heed<sup>1,2</sup>

<sup>1</sup>*Cognitive Psychology, Department of Psychology, University of Salzburg, Salzburg, Austria* | <sup>2</sup>*Centre for Cognitive Neuroscience, University of Salzburg, Salzburg, Austria*

Avoidance of pain-associated movement is an important factor in chronic pain. Studies have presented pain during movements to investigate learning of such associations. However, participants might also learn contingencies with other simultaneously available visual spatial cues, e.g., when a cursor represents the participant's movement, and the pain stimulus is triggered when the cursor is at a specific location. Here, we separated movement from spatial cues. Thirty-eight healthy participants grasped the handle of a robotic manipulandum and performed center-out diagonal movements from a start to a target position. In the acquisition phase, pain was elicited when the movement crossed a specific, invisible and unannounced location in space. Participants could avoid pain stimuli by curving the movement around this location. In two generalization phases, participants performed a new movement that went through the same location, and the same movement in a new location (achieved by repositioning the participant's chair). We compared the frequency of curved trajectories in these generalization phases as indicators of location- and movement-related learning. Participants performed more curved movements when this helped avoid the pain-eliciting location than when it did not, suggesting that participants had associated pain with a specific location. Yet, participants who avoided in one generalization context also avoided in the other, indicating that the movement per se was also associated with pain. Previous research has often overlooked the role of spatial cues in the employed experimental paradigms, calling for more clearly defined experimentation and, potentially, re-interpretation of previous findings.

Keywords: *pain, movement, avoidance*

### 4. The neurocomputational link between bradycardia and approach-avoidance decision-making under threat

Felix H. Klaassen<sup>1</sup>, Linda de Voogd<sup>1,3</sup>, Anneloes M. Hulsman<sup>1,2</sup>, Jill X. O'Reilly<sup>4</sup>, Floris Klumpers<sup>1,2</sup>, Bernd Figner<sup>1,2</sup>, & Karin Roelofs<sup>1,2</sup>

<sup>1</sup>*Radboud University, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands* | <sup>2</sup>*Radboud University, Behavioural Science Institute (BSI), Nijmegen, The Netherlands* | <sup>3</sup>*Leiden University, Leiden, The Netherlands* | <sup>4</sup>*University of Oxford, Department of Experimental Psychology, Oxford, United Kingdom*

In approach-avoidance conflict situations we weigh the potential reward and punishment outcomes of our decision. This is particularly relevant under acute threat when a defensive freezing state is triggered, characterized by heart rate deceleration (bradycardia) and bodily immobility. This bradycardia state has been suggested to facilitate decision-making under threat (e.g., by enhancing sensory processing and action preparation). However, it remains unclear how it affects the computations underlying value-based approach-avoidance decisions and associated neural pathways. We hypothesized three routes through which the computations underlying approach-avoidance decisions may be altered during the bradycardia state. Namely, by affecting the processing of punishment outcomes (aversive value; AV), the comparison of rewards and punishments (value comparison; VC), and the invigoration of subsequent action (action invigoration; AI). To test this, we recruited 58 participants to make passive and active approach-avoidance decisions associated with varying reward and punishment prospects (1-5 euros/shocks). Simultaneously, we measured heart rate (to assess bradycardia) and brain activity (using fMRI). Replicating previous work, we observed increased approach vs avoid choices for higher money vs shock amounts, respectively. Next, approach-avoidance arbitration recruited the amygdala, ventral striatum, and the vmPFC. Additionally, trial-by-trial bradycardia was associated with a stronger effect of shocks on avoidance, supporting an interaction between freezing and aversive value (AV). Model-based fMRI analysis revealed that this effect was associated with decreased activation in the amygdala. Together, we delineate a neural circuit involved in approach-avoidance arbitration



under threat with specific involvement of the amygdala in integrating aversive value and psychophysiological state during avoidance.

Keywords: *approach-avoidance decision-making, freezing, computational modelling*

## 5. Mechanisms underlying costly fearful avoidance in patients with affective disorders

Anneloes Hulsman<sup>1,2</sup>, Felix Klaassen<sup>1,2</sup>, Nadine Cremer<sup>1,2</sup>, Linda de Voogd<sup>1,2,3</sup>, Joppe Klein Breteler<sup>1,4</sup>, Nessa Ikani<sup>1,4,5</sup>, Gert-Jan Hendriks<sup>1,4</sup>, Karin Roelofs<sup>1,2\*</sup>, & Floris Klumpers<sup>1,2\*</sup>

<sup>1</sup>*Behavioural Science Institute, Radboud University Nijmegen, Nijmegen, the Netherlands* | <sup>2</sup>*Donders Institute, Radboud University, Nijmegen, the Netherlands* | <sup>3</sup>*Leiden University, Leiden, the Netherlands* | <sup>4</sup>*Overwaal, Center of Expertise for Anxiety, Obsessive-Compulsive, and Posttraumatic Stress Disorders, Pro Persona, Institute for Integrated Mental Health Care, Nijmegen, the Netherlands* | <sup>5</sup>*Tilburg University, Tilburg, the Netherlands*

\* *Shared last authorship*

Excessive avoidance is a key symptom of anxiety and depression and might be a better predictor of poor disease outcome than subjective fear levels. In excessive avoidance, potential rewards are often sacrificed to avoid potential negative outcomes. Although costly avoidance is highly prevalent in affective disorders, little is known about the underlying mechanisms. We developed a Fearful Avoidance Task (FAT) in which subjects decide to approach or avoid combinations of potential rewards and threats. With this task we previously found that avoidance depends on a trade-off between potential rewards and threats in healthy participants. Moreover, well-known risk factors for affective disorders, female sex and trait anxiety, were associated with increased avoidance depending on reward and threat. In ongoing studies, we examine the impact of clinical symptoms on avoidance in affective disorder patients (current N=31, DSM-diagnosis anxiety and/or depression) using the FAT. Initial findings suggest that like healthy controls, patients weigh both reward and threat in approach-avoidance decisions. However, patients avoid significantly more than controls (12-21% more avoidance), especially in conditions where reward and threat are low (suggesting generalization) and where reward is low and threat is high (15-29% more avoidance). Our parallel MRI study (current N=8 patients, N=10 high-risk for affective disorders, N=19 controls) confirmed similar behavioural patterns and identified alterations in active but particularly passive avoidance. These findings support recent literature by confirming both aberrant reward and threat processing in avoidance tendencies central to affective psychopathology and set the stage for investigations of the psychobiological underpinnings. We expect to present more extensive results at the meeting.

Keywords: *avoidance, transdiagnostic patient study, reward*

# Abstracts – Symposium 6

Neuroscientific Advances & Data Sharing Initiatives

24<sup>th</sup> May, 11:00 - 12:30

## 1. Investigating the effects of threat and safety cues on the perception and neural processing of unpleasant tactile stimuli

Valentina Jelinčić, Ilse Van Diest, Mari Sone, Diana Torta, & Andreas von Leupoldt

*Research group Health Psychology, KU Leuven, Leuven, Belgium*

In both acute and chronic illnesses, somatic symptoms such as pain are often exacerbated by fear and anxious responding, which can lead to avoidance of physical activity and reduced quality of life. Neural mechanisms underlying this increase in perception are still poorly understood. The current study investigated the effects of differential fear conditioning (FC) on the perception and neural processing of mildly aversive electrocutaneous stimuli (ES). Fifty-one healthy participants received paired ES (ISI=500ms) of a moderate intensity while viewing neutral female faces serving as threat and safety cues (CS+/CS-). The unconditioned stimulus (US) was a shrill scream which followed the CS+ face with 100% contingency. To assess attentional orienting to ES, we recorded event-related potentials using electroencephalography, and measured peak N1 and P2 responses to the first ES, as well as the peak N1 response to the 2nd over the 1st ES (neural gating ratio). Participants reported their perceived intensity and unpleasantness of discrete ES pairs during the FC protocol, as well as their US expectancy and fear of the CSs. Participants rated the ES as lightly intense and unpleasant, and reported significantly higher US expectancy and fear when presented with the CS+. We found significantly increased N1 during the threat cues, but no effects on perceived intensity/unpleasantness, P2 or neural gating. The present protocol successfully conditioned fear of the CS+, and increased early attentional orienting to aversive tactile stimuli. The null effects on perception may be explained by low intensities of ES or high intensity of the US.

Keywords: *somatosensation, attention, event-related potentials*

## 2. The effects of age and trait anxiety on Pavlovian threat acquisition and extinction: An ERP study comparing adolescents and adults

Gil Shner-Livne, Ido Shitrit, Nadav Barak, & Tomer Shechner

*School of Psychological Sciences and the Integrated Brain and Behavior Research Center, University of Haifa, Israel*

Understanding the link between the neural basis of threat learning and anxiety disorders is critical, especially from a developmental perspective. Nevertheless, developmental research on threat acquisition and extinction is limited, and no study has examined the late positive potential (LPP) during threat learning in youth. The LPP is an event-related potential component that reflects a response to emotionally significant stimuli and may serve as a critical biomarker for learning. We compared 65 adults and 63 adolescents during threat learning while measuring LPP, self-reported fear, threat expectancy, and skin conductance response (SCR). Participants completed a threat acquisition task including three blocks of 10 CS+ and 10 CS- presentations, with a 60% reinforcement rate. Following 24 hours, they completed six blocks of threat extinction task. Results showed that adolescents and adults exhibited similar differential threat acquisition and extinction. Those with higher self-reported anxiety had increased fear towards the CS+ during acquisition ( $p=.005$ ) and a slower decrease in fear during extinction ( $p=.020$ ). While differential fear and SCR decreased during extinction, LPP remained higher towards the CS+ compared to the CS- during extinction ( $p=.000$ ). Developmental differences emerged primarily in LPP, with adolescents exhibiting a larger LPP than adults during both acquisition and extinction ( $ps<.000$ ). Anxiety symptoms were positively associated with greater differential LPP during middle and late stages of extinction in adolescents but not adults ( $p=.002$ ). These findings suggest that LPP plays a crucial

role in sustained attention to threat cues that are less sensitive to extinction, especially among adolescents with higher anxiety symptoms.

Keywords: *development, threat learning, late positive potential (LPP)*

### 3. The neurokinin 3 receptor system and fear modulation in both mice and humans

Eric Velasco<sup>1,2,3</sup>, Jaime Fabregat<sup>2,3,4</sup>, Miquel Angel Fullana<sup>5,6</sup>, Rafael Torrubia<sup>7,8,9,10</sup>, & Raul Andero<sup>11</sup>

<sup>1</sup>Institut de Neurociències | <sup>2</sup>Universitat Autònoma de Barcelona | <sup>3</sup>Cerdanyola del Vallès, Barcelona, Spain | <sup>4</sup>Departament de Psicobiologia i de Metodologia de les Ciències de la Salut | <sup>5</sup>Centro de Investigación Biomédica En Red en Salud Mental CIBERSAM | <sup>6</sup>Instituto de Salud Carlos III, Madrid, Spain | <sup>7</sup>Unitat de Neurociència Traslacional | <sup>8</sup>Parc Taulí Hospital Universitari | <sup>9</sup>Institut d'Investigació i Innovació Parc Taulí I3PT | <sup>10</sup>Institut de Neurociències, Universitat Autònoma de Barcelona | <sup>11</sup>ICREA, Barcelona, Spain.

The tachykinin 3 neuropeptide system, composed of Neurokinin B (encoded by TAC3) and Neurokinin 3 receptor (encoded by TAC3R) is highly expressed in limbic structures of mice and humans (Andero et al., 2014, Allen Brain atlas). Studies in rodents show that this system regulates fear memory consolidation and the stress responses to isolation (Andero et al., 2014, Zelikowsky et al., 2019). In mice, NK3R antagonism shortly after fear acquisition has a sex dependent effect decreasing fear expression in males and enhancing it in females. An effect that was traced to central amygdala Tac2 neurons (Florido et al., 2021). In a cohort of elderly humans with mild cognitive impairment, the single nucleotide polymorphism (SNP) rs2765 in the TAC3R is associated with differences in performance in a wordlist learning verbal task and right hippocampus volume (Silva et al., 2013). Here we showed that the AA genotype in the SNP rs2765 of TAC3R is related to impaired CS discrimination during fear expression in the whole sample as measured by FPS (compared to G carriers). Analyses by sex showed that this effect was driven by AA males who have impaired CS discrimination throughout the whole fear expression as measured by FPS and SCR. A mild effect for the AA genotype was observed in females as they had impaired discrimination in the first block of fear expression but were able to discriminate at later phases. Together, these results suggest that AA genotype is associated with deficits in fear processing that are specially pronounced in males.

### 4. FEAR BASE – a curated, dynamically growing database and living analyses of publicly available fear conditioning data

Mana R. Ehlers<sup>1</sup> & Tina B. Lonsdorf<sup>1,2</sup>

<sup>1</sup>University Hospital Hamburg-Eppendorf, Hamburg, Germany | <sup>2</sup>University of Bielefeld, Bielefeld, Germany

Data sharing holds promise for advancing and accelerating science by facilitating and fostering collaboration, reproducibility and optimal use of sparse resources. However, advantages of open data can only be used if data are comprehensible to third parties and are ideally prepared and streamlined in a way to allow immediate reuse. We provide a status-quo report for the field of fear conditioning research and highlight that there is room for improvement with respect to *FAIR-ness* (findable, accessible, interoperable, re-usable). Here, we would like to introduce the FEAR BASE – an inventory of open data in the field of fear conditioning that will culminate in a living and dynamically growing, sustainable database with live analysis features. In a first step towards this goal, we created a curated collection of publicly available datasets using the fear conditioning paradigm totalling 103 studies and 8839 participants illustrating the potential and richness of the freely available data corpus. In cooperation with an infrastructure partner, we are working on transferring the curated data collection to a homogenized database, which will facilitate the dynamic growth of the FEAR BASE as new research comes out by creating a dedicated web-interface according to the needs of the research community. We hope that the input from the research community and the future formation of a consortium will further incentivize data sharing within the project and will hence foster collaboration, cumulative knowledge generation and large scale mega-, meta- and psychometric analyses.

Keywords: *open data, cooperative database, collaborative research*

## 5. Unraveling fear learning ENIGMAs by sharing data

Miquel A. Fullana<sup>1</sup>, Janna Marie Bas-Hoogendam<sup>2,3,4</sup>, Nynke A. Groenewold<sup>2,3,4</sup>, Dan J. Stein<sup>5</sup>, & Nic J. A. van der Wee<sup>3</sup>

<sup>1</sup>Hospital Clínic/IDIBAPS (Barcelona) [FUNDING: Instituto de Salud Carlos III (ISCIII), PI19/00272, co-funded by the European Union] | <sup>2</sup>Department of Developmental and Educational Psychology, Leiden University, Institute of Psychology, Leiden, The Netherlands | <sup>3</sup>Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands | <sup>4</sup>Leiden Institute for Brain and Cognition, Leiden, The Netherlands | <sup>5</sup>Department of Psychiatry & Mental Health, Neuroscience Institute, University of Cape Town, South Africa

It is likely that to accurately answer many research questions in behavioral sciences, we need “to go big”, i.e., increase our sample sizes. Fear learning is not an exception, especially if such questions concern individual differences. Sharing individual-level data via research consortiums is an excellent option to achieve this. Here, I will introduce the ENIGMA consortium, which brings together brain-imaging researchers to understand brain structure and function, and the recently established ENIGMA fear conditioning subgroup within the ENIGMA-Anxiety working group. Moreover, I will invite those of you who are not yet members of ENIGMA-Anxiety Fear Conditioning to join it. I will also highlight some advantages and challenges of sharing data (e.g., ethical and methodological issues). Finally, I will also talk about how the data collected through ENIGMA-Anxiety Fear Conditioning may help answer some critical questions in the field.

Keywords: *fear conditioning, neuroimaging, ENIGMA*

# Abstracts – Poster Session 1

Stress, Neuroscience, Clinical Populations, & Interventions

22<sup>nd</sup> May, 20:30 - 22:30

## 1. The influence of stress on context-dependent reinstatement

Christian J. Merz & Oliver D. Wolf

*Ruhr University Bochum, Bochum, Germany*

Timing-dependent effects of stress hormones on extinction memories have been described before. In particular, high cortisol concentrations before retrieval reduced extinction memory retrieval. In the current study, this effect will be applied to the combination of context-dependent reinstatement and renewal. In total, 128 participants (64 women) underwent habituation, fear acquisition (both context A) and extinction training (context B) on the first experimental day. Only during fear acquisition training, the CS+ was paired with an electrical stimulation (US), the CS- was not paired. On the second experimental day, after exposure to acute stress or a control condition, unsignalled presentations of the US (reinstatement) were applied in context A or B. Subsequently, retrieval of conditioned responding was tested in context A and B in a within-subjects design. Results showed successful fear and extinction learning with increasing and decreasing skin conductance responses (SCRs) towards CS+ vs. CS-. Exposure to stress increased blood pressure and cortisol concentrations compared to the control condition. During retrieval, stress modulated conditioned SCRs in context B only, if reinstatement occurred in context A. Thus, stress context-dependently shaped extinction memory retrieval. Furthermore, a generalized reinstatement effect occurred with increasing conditioned responses from the end of extinction training to the beginning of retrieval (independent of CS type). Exposure to stress reduced this generalized reinstatement in women, but rather increased it in men. This sex-dependent stress effect might indicate a different susceptibility for men and women for the integration of unsignalled danger signals in the face of acute stress.

Keywords: *context-dependency, reinstatement, stress hormones*

## 2. The impact of pre-extinction stress vs. exercise on contextual retrieval and generalization

Lianne N. Wolsink, Katharina Beck, Christian J. Merz, Oliver T. Wolf, & Valerie L. Jentsch

*Department of Cognitive Psychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum, Bochum, Germany*

Stress hormones timing-dependently modulate the strength and context-dependency of extinction memories. Exposure to stress or cortisol before extinction leads to a strong and less context-dependent extinction memory (STaR model; Meir Drexler et al., 2019). However, common stress protocols have disadvantages, such as increases in negative affect. Therefore, we need a more positively appraised stress-hormone associated intervention to promote extinction memory retrievability and to mitigate fear relapse. Physical exercise is a potential candidate: it also increases cortisol, it improves emotional memory consolidation, and it is typically associated with positive affect. Here we compare the effects of physical exercise (treadmill running) and psychosocial stress (Trier Social Stress Test (TSST)) before extinction training on contextual retrieval and generalization 24h later. Healthy participants underwent fear acquisition on day 1, the exercise, stress, or control intervention followed by extinction on day 2, and a retrieval and reinstatement test on day 3. During the interventions, HPA axis (salivary cortisol) and SNS (alpha-amylase and heart rate) activity were assessed. Skin conductance responses (SCRs) and pupil dilation served as outcome measures during the fear conditioning paradigm. We predicted that pre-extinction stress and exercise both facilitate extinction memory consolidation context-independently. Preliminary results (N = 63, planned N = 120) showed that the stress and exercise intervention both significantly increased heart rate as compared to the control group. Fear and extinction learning, as measured by SCRs,

were both successful and did not differ between groups. Both interventions seemed to reduce fear renewal, but these effects did not reach significance yet.

Keywords: *fear extinction, stress, exercise*

### **3. Non-genomic and genomic cortisol effects on the return of fear after contextual extinction generalization**

Jaël K. Caviola, Katharina Beck, Lianne N. Wolsink, Valerie L. Jentsch, Oliver T. Wolf, & Christian J. Merz

*Department of Cognitive Psychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum, Germany*

Return of fear (ROF) after successful fear extinction poses a major challenge to the long-term effectivity of its clinical counterpart, exposure therapy. Alongside process-related factors, like renewal due to context changes, subject variables play a role in the probability of ROF: Previous work has shown timing-dependent effects of stress hormones on memory, and specifically, an impairment of extinction memory retrieval. Beyond these non-genomic effects, not much is known about the genomic effects of cortisol, although its mechanisms of action are highly relevant for the understanding of relapse in patients with anxiety and stress-related disorders. The current study aims to investigate non-genomic and genomic cortisol effects on ROF after extinction training in multiple contexts. To this end, 120 healthy participants (60 female) will undergo a well-established fear conditioning paradigm during which a contingency between an unconditioned stimulus (UCS) and two conditioned stimuli (CS+) will be acquired in a specific background context. A third stimulus will not be reinforced (CS-). The succeeding extinction training will take place in one (non-generalized, CS+N) or four (generalized, CS+G) other contexts for the two CS+, respectively. The following day, participants will be randomly assigned to one of three groups (placebo control, non-genomic cortisol, genomic cortisol) before the start of a retrieval and reinstatement test phase. This phase will include presentations of all three CS in the acquisition, extinction and one novel context. Expectancy ratings, affect and skin conductance responses serve as indicators of ROF. Preliminary results of data acquired so far will be presented and discussed.

Keywords: *genomic and non-genomic cortisol; return of fear; extinction generalization*

### **4. Involvement of neocortical areas in context-dependent fear extinction**

Fatemeh Yavari, Michael Nitsche, & Yunabo Ma

*Department of Psychology and Neurosciences, Leibniz Research Center for Working Environment and Human Factors, Dortmund, Germany*

Abstract available from the authors upon request

### **5. Polygenic prediction of fear conditioning learning mediated by brain connectivity in the human extinction network**

Javier Eduardo Schneider Peñate<sup>1</sup>, Carlos Alexandre Gomes<sup>1,2</sup>, Erhan Genc<sup>3</sup>, Katharina Forkmann<sup>2</sup>, Ulrike Bingel<sup>2</sup>, Harald Engler<sup>2</sup>, Sigrid Elsenbruch<sup>1</sup>, Christian J. Merz<sup>1</sup>, Oliver T. Wolf<sup>1</sup>, Harald Quick<sup>2</sup>, Onur Güntürkün<sup>1</sup>, Tamas Spisak<sup>2</sup>, Dagmar Timmann-Braun<sup>2</sup>, Nikolai Axmacher<sup>1</sup>, & Robert Kumsta<sup>1,4</sup>

<sup>1</sup>Ruhr University Bochum, Germany | <sup>2</sup>University Duisburg-Essen, Germany | <sup>3</sup>IfADO Dortmund, Germany | <sup>4</sup>University of Luxemburg, Luxemburg

Abstract available from the authors upon request

## 6. Neural correlates of avoidance learning and threat extinction

Zohar Klein<sup>1</sup>, Gil Shner Livne<sup>1</sup>, Nitsan Rosenfeld<sup>1</sup>, Romie Livni<sup>1</sup>, Marta Andreatta<sup>2</sup>, Bram Vervliet<sup>3</sup>, & Tomer Shechner<sup>1</sup>

<sup>1</sup>*School of Psychological Sciences and the Integrated Brain and Behavior Research Center, University of Haifa, Israel* | <sup>2</sup>*Department of Clinical Psychology, Erasmus University Rotterdam, Netherlands* | <sup>3</sup>*Faculty of Psychology and Educational Sciences, KU Leuven, Leuven, Belgium*

While threat avoidance is essential for survival, excessive and persistent avoidance in the absence of real danger can become maladaptive. It is difficult to extinguish avoidance because avoidant behavior prevents individuals from confronting excessive threat beliefs, thereby perpetuating fear and avoidance. This study aims to examine the behavioral, cognitive, and neural correlates of avoidance learning and how individual differences in Intolerance of Uncertainty (IU) and Trait Anxiety (TA) are associated with these processes. The paradigm comprises of four phases. During threat acquisition, one stimulus (CS+) is repeatedly paired with an aversive sound (US), while another (CS-) serves as a safety cue. During avoidance learning, participants can avoid the US by pressing a button, which prevents the upcoming US in 80% of trials. Participants will then be randomized into either a Pavlovian or operant extinction learning condition. In the Pavlovian extinction condition, the avoidance button will be removed. In the operant extinction condition, participants can choose to avoid the US and receive a low reward or not to avoid it and receive a high reward. Finally, the avoidance button will reappear to examine return of avoidance after extinction. Throughout all phases, avoidance responses, self-reported fear and relief, and two EEG components – Late Positive Potentials (LPP), measuring emotional valence, and Feedback-related Negativity (FRN), measuring prediction-error – will be measured. We hypothesize that individuals with high IU and TA will exhibit greater avoidance responses and higher fear ratings. Furthermore, the potential roles of LPP, FRN, and relief ratings in avoidance learning will be explored.

Keywords: *avoidance, extinction, ERP*

## 7. Neural correlates of fear learning processes in EEG

Kim M. Sobania, Hannes Per Carsten, Kai Härpfer, Franziska M. Kausche, & Anja Riesel

*University of Hamburg, Hamburg, Germany*

Fear conditioning processes, including adequate fear acquisition, generalization, and extinction are important requirements to protect an individual from threatening situations and ensure appropriate behavior. To date, research examining event-related potentials (ERPs) underlying fear conditioning is limited. In the current study (DFG - RI 2853/2-1), we investigate behavioral data (US-expectancy ratings) and ERPs (N1, LPP) in healthy participants (n = 38). A differential fear generalization paradigm consisting of four phases (habituation, acquisition, generalization, and extinction) was performed using geometrical forms in which one color was paired with an aversive electrical stimulation (CS+) and another was not (CS-). Three additional colors in between the CS+ and CS- served as generalization stimuli. Behavioral data indicate a successful fear acquisition which was generalized to the stimulus most similar in color to the CS+. Although a reduction in US-expectancy for the CS+ was visible during extinction, it remained significantly higher compared to the CS-. Significantly larger LPPs during fear acquisition for the CS+ compared to the CS-, a gradual downgrading during generalization with the largest LPP for the CS+, and no differences during extinction suggest successful fear acquisition, generalization, and extinction on a neural level. For the N1 no significant modulation was found. The present results suggest that both, behavioral and neural data, reflect fear learning. However, the behavioral and neural results are partially differential and do not correlate. This indicates the representation of different aspects in fear conditioning: Whereas behavioral data represent the cognitive aspect, neural data may reflect more unconscious attentional processes.

Keywords: *neural correlates, fear learning processes, EEG*

## 8. Neural response to trauma-film and pain stimulation and their association with the formation of audiovisual and pain intrusions

Stephan F. Miedl<sup>1</sup>, Laila K. Franke<sup>1</sup>, Sarah K. Danböck<sup>1</sup>, Michael Martini<sup>1</sup>, Martin Kronbichler<sup>2,3</sup>, Herta Flor<sup>4,5</sup> & Frank H. Wilhelm<sup>1</sup>

<sup>1</sup>Division of Clinical Psychology and Psychopathology, Department of Psychology, Paris Lodron University Salzburg, Salzburg, Austria | <sup>2</sup>Centre for Cognitive Neuroscience, University of Salzburg, Salzburg, Austria | <sup>3</sup>Neuroscience Institute, Christian-Doppler-Klinik, Paracelsus Medical University Salzburg, Salzburg, Austria | <sup>4</sup>Institute of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Germany | <sup>5</sup>Department of Psychology, School of Social Sciences, University of Mannheim, Germany

Posttraumatic stress disorder and medically unexplained pain co-occur with striking frequency, a condition that is particularly debilitating and associated with unfavourable prognosis for patients. While the experience of pain is common during a potentially traumatic event, the processing of pain during trauma and its relation to audio-visual and pain intrusions, conceptualized as conditioned responses, is poorly understood. The main goal of this paper is to close this gap by investigating the neural activity during painful analogue trauma and its link to intrusions. Sixty-five healthy women were examined using functional magnetic resonance imaging. An analogue trauma was induced by an adaptation of the trauma film paradigm extended by painful electrical stimulation in a 2 film (traumatic, neutral) x 2 pain (pain, no pain) design, followed by 7-day ambulatory intrusion assessment. Anterior insula and dorsal anterior cingulate cortex were both active during traumatic films and pain. Reduced anterior insula, as well as reduced ventromedial prefrontal cortex (VMPFC) activity in aversive (traumatic film and/or pain) vs. neutral no pain contrasts predicted greater probability of pain intrusions. Lower VMPFC activity also predicted higher pain and audio-visual intrusion frequency. Results indicate that the anterior insula may play a role for both trauma- and pain-processing. Reduced anterior insula reactivity as well as weak regulatory VMPFC activity during aversive tasks might be crucial mechanisms of pain intrusion formation.

Keywords: *trauma, pain, intrusion*

## 9. The role of cortico-spinal networks in defensive responses to threat

Elena Andres<sup>1</sup>, Evelyne Fraats<sup>1</sup>, Britt Stoffels<sup>1</sup>, José Marques<sup>1</sup>, Linda de Voogd<sup>2</sup>, & Karin Roelofs<sup>1,3</sup>

<sup>1</sup>Donders Institute for Brain, Cognition and Behaviour, Centre for Cognitive Neuroimaging, Radboud University Nijmegen, Nijmegen, The Netherlands | <sup>2</sup>Leiden University, Leiden, The Netherlands | <sup>3</sup>Behavioural Science Institute (BSI), Radboud University Nijmegen, Nijmegen, The Netherlands

Upon detection of an external threat, sensory information needs to be processed for an appropriate assessment and reaction. Freezing, a state characterized by arousal and increased muscle tone as well as inhibition of the motor response after threat encounter, allows for this processing and action planning. During freezing, the body and brain must have well-coordinated information relay and integration, which is facilitated by the spinal cord. Previous findings (Vahdat et al., 2017) have shown distinct cortico-spinal connectivity patterns at rest, however, there is a gap in knowledge regarding cortico-spinal connectivity during threat anticipation. In a new study we aim at investigating the role of cortico-spinal networks in defensive responses to threat. Measuring brain and spinal cord activity simultaneously using fMRI, we first will try to replicate Vahdat et al., showing connectivity between dorsal and ventral regions of the spinal cord (dsSpC/vSpC) with the sensory and motor brain areas, respectively. Second, a threat of shock paradigm will be implemented to study whether dsSpC-sensory and vSpC-motor connectivity change during threat anticipatory freezing compared to rest. Lastly, participants will subsequently undergo a threat conditioning and extinction paradigm. We will address the questions whether individual physiological responses, such as heart rate changes and skin conductance responses, during anticipatory freezing at conditioning are related to extinction learning success and changes in cortico-spinal connectivity. Overall, our study aims to provide a better understanding of the interplay between the brain and spinal cord during threat processing and response.



Keywords: *cortico-spinal connectivity, threat anticipation, freezing*

## **10. Startle responses and event-related potentials during threat anticipation in patients with anxiety spectrum disorders**

Hannes Per Carsten, Franziska Kausche, Kai Härpfer, & Anja Riesel

*University of Hamburg, Hamburg, Germany*

Defensive responding and attentional processes during threat anticipation are candidate mechanisms underlying anxiety. Consistent with a transdiagnostic perspective, we sought to examine psychophysiological correlates of transdiagnostic symptom dimensions alongside comparisons of diagnostic categories across the anxiety spectrum. Four groups (total  $N = 160$ , patients with obsessive-compulsive disorder, social anxiety disorder, specific phobia, and healthy controls) completed the NPU-threat test in which the temporal predictability of shocks was manipulated. We measured the startle reflex via electromyography and startle probe locked event-related potentials N1 and P3 via EEG, capturing automatic attentional engagement (N1) and attentional allocation (P3). Additionally, transdiagnostic symptom dimensions (i.e., trait worry, intolerance of uncertainty, and anxious arousal) were measured via questionnaires. Generally, participants showed increased startle and N1 in shock anticipation relative to no shock. The P3 to startle probes was suppressed in shock anticipation, irrespective of the predictability of shocks. Regarding associations with anxiety, no significant effects of the diagnostic groups emerged. However, irrespective of the diagnostic groups, trait worry was associated with increased N1 in unpredictable threat anticipation. Intolerance of uncertainty was associated with suppressed P3 in unpredictable threat anticipation. These results suggest that trait worry increases early attentional responding (N1), beyond the diagnostic category. The P3 suppression associated with intolerance of uncertainty suggests increased attentional allocation to threatening contexts in patients who perceive unpredictability and the associated feeling of uncertainty as aversive. As these transdiagnostic symptom dimensions were associated with attentional processes, these results underscore the importance of a transdiagnostic perspective on attentional mechanisms in anxiety.

Keywords: *individual differences, anxiety disorders, NPU-threat test*

## **11. Dissociable acquisition of conditioned fear responses by the motor and autonomic systems**

Sonia Betti, Marco Badioli, Sara Garofalo, Giuseppe di Pellegrino, & Francesca Starita

*Center for Studies and Research in Cognitive Neuroscience, Department of Psychology "Renzo Canestrari", University of Bologna, Bologna, Italy*

Environmental stimuli may acquire threat-related properties through pairing with an aversive event, and exert a powerful influence on behaviour. Nevertheless, the extent to which the human cortical motor system learns to prepare to aversive events remains largely unexplored. Here, in two experiments, we investigated whether and how changes in corticospinal excitability mark the acquisition of threat learning. A Pavlovian threat learning procedure was adopted so that two different neutral stimuli (coloured dots) acquired threat-related value by predicting a lateralized aversive shock, either to the left (left conditioned stimulus, CS+L) or right (CS+R) arm (Exp.1) or hand (Exp.2). Another stimulus (CS-) never predicted shock. Electrodermal activity (SCR) was collected to characterize changes in autonomic response between CSs. Critically, changes in corticospinal excitability were assessed by acquisition of motor-evoked potentials (MEP) recorded from the right hand (FDI muscle) and arm (ECR muscle), and elicited by transcranial magnetic stimulation (TMS) applied to the left primary motor cortex. We found increased SCR for CS+R and CS+L compared with CS-, which did not distinguish the laterality of impending shock. In contrast, a lateralized inhibitory effect emerged for corticospinal excitability. Indeed, we found a reduction in the FDI MEP amplitude for CS+R, compared with CS+L and CS-. Our results show the motor system's involvement in threat learning and highlight the existence of multiple, dissociable learning systems mediating Pavlovian conditioned responses, namely a non-lateralized autonomic system and a lateralized motor one.

Keywords: *fear conditioning, corticospinal excitability, motor-evoked potentials*

## **12. Effects of adjuvant glucose on the extinction of fear - results of two placebo-controlled studies**

Alexander Hauck, Tanja Michael, & Diana S. Ferreira de Sá

*Saarland University, Saarbrücken, Germany*

Numerous studies have shown that glucose has a beneficial effect on memory function and increases declarative memory performance. Glenn and colleagues (2014) examined the effect of glucose on hippocampus-dependent fear learning and demonstrated that glucose could enhance contextual fear learning. This is a first indication that fear learning processes can be influenced by glucose. In order to derive potential therapeutic interventions for the treatment of anxiety disorders, further research is needed regarding the effects on the extinction of fear. In two experimental studies with healthy participants, we investigated the effects of glucose on fear extinction and its consolidation. Participants completed a differential fear conditioning paradigm consisting of acquisition, extinction, fear recovery, and a retention test. Behavioral (expectancy ratings) and psychophysiological parameters (skin conductance, startle reflex) were collected. Participants were pseudorandomized and double-blinded to one of two conditions: They received either a drink containing glucose or a drink containing saccharine (placebo) before extinction (study 1) or after extinction (study 2). Preliminary analysis revealed that participants in the glucose group showed lower startle responses than participants in the placebo group during extinction (Study 1) and in the retention test (Study 2). These results suggest a faster (Study 1) and more stable extinction learning (Study 2) in healthy participants. Beneficial effects of glucose on extinction of fear may provide initial evidence for adjuvant use of glucose in the treatment of anxiety disorders and other anxiety-related disorders. Further research is needed to better understand the mechanisms of glucose effects on fear memory processes.

Keywords: *extinction learning, glucose, psychophysiology*

## **13. Overnight fasting facilitates safety learning by changing the neurophysiological response to reward (relief) prediction errors**

Silvia Papalini<sup>1,2</sup>, Tom Beckers<sup>2,5</sup>, Lukas Van Oudenhove<sup>2,3,4</sup>, & Bram Vervliet<sup>1</sup>

<sup>1</sup>Laboratory of Biological Psychology, Faculty of Psychology and Educational Sciences, KU Leuven, Belgium | <sup>2</sup>Leuven Brain Institute, KU Leuven, Belgium | <sup>3</sup>Laboratory for Brain-Gut Axis Studies, Translational Research Center for Gastrointestinal Disorders, Department of Chronic Diseases and Metabolism, KU Leuven, Belgium | <sup>4</sup>Cognitive & Affective Neuroscience Lab, Department of Psychological & Brain Sciences, Dartmouth College, Hanover, NH, USA | <sup>5</sup>Centre for the Psychology of Learning and Experimental Psychopathology, Faculty of Psychology & Educational Sciences, KU Leuven, Belgium

Relief is a putative index of (reward) prediction error processing during threat omissions that governs safety learning. Results from our previous behavioral study showed that hunger, compared to a fed state, decreases unnecessary/ineffective avoidance behaviors in healthy humans and that this effect was mediated by lower subjective relief during omissions of threat. Similarly, hungry participants later reported a steeper decrease in relief than fed participants during threat omissions in fear extinction. Here, we examine the neural mechanisms underpinning these effects. The same intervention diet was applied in a functional Magnetic Resonance Imaging setting. Fifty healthy females (N=25, Fasting Group, N=25 Re-feeding Group) performed a short version of the validated Avoidance Relief Task designed to evoke and measure prediction errors upon active as well as passive threat omission. We found that fasting increased effective (but not ineffective/unnecessary) avoidance and induced a steeper decrease in relief ratings during fear extinction. The latter result was accompanied by lower activations in the Ventromedial prefrontal cortex and Nuclei accumbens during threat omissions signaled by a safety (vs threat) stimulus. Nuclei accumbens activations during threat omissions were modulated by relief only after re-feeding. Fasting speeds up fear extinction learning via a reduction in the neurophysiological response to prediction error. This replication paves the way for the assessment of fasting in anxious

individuals. Conclusive evidence that fasting is effective in reducing excessive avoidance is still understanding.

Keywords: *relief, fasting, safety-learning*

#### **14. Nicotine reduces discrimination between threat and safety by reduction of hippocampal activations**

Madeleine Mueller<sup>1</sup>, Tahmine Fadai<sup>1,2</sup>, Jonas Rauh<sup>1,3</sup>, & Jan Haaker<sup>1</sup>

<sup>1</sup>University Medical Center Hamburg-Eppendorf (Germany), Department of Systems Neuroscience | <sup>2</sup>University Medical Center Hamburg-Eppendorf (Germany), Department of Child-and Adolescent Psychiatry and Psychotherapy | <sup>3</sup>University Medical Center Hamburg-Eppendorf (Germany), Department of Psychiatry and Psychotherapy, Psychiatry Neuroimaging Branch

Nicotine intake by cigarettes is linked to the maintenance and development of anxiety disorders and impairs adaptive discrimination of threat and safety in humans. Yet, it is unclear if nicotine itself exerts a causal pharmacological effect on the affective and neural mechanisms that underlie aversive learning. Here, we conducted this fMRI study to investigate the effect of acute nicotine on Fear Acquisition (ACQ) and a 24h subsequent Extinction training (EXT) with a Return of Fear (RoF) manipulation in healthy non-smokers (n=88). Participants were pseudo-randomly and double-blinded assigned to one of three experimental groups: 1. nicotine administration before Fear Acquisition, 2. nicotine administration before Extinction training or 3. placebo control group. Our results show that nicotine administration before both ACQ and EXT lead to decreased discrimination between threat and safety in self-reported fear. This effect is mirrored by decreased differential hippocampal activation during ACQ in the group that received nicotine, when compared to placebo controls. Our results provide mechanistic evidence for impaired discrimination between threat and safety by the acute intake of nicotine in non-smoking individuals. Nicotine intake directly impairs neural substrate of adaptive aversive learning and might therefore constitute a profound risk factor for the development of pathological anxiety.

Keywords: *fMRI, nicotine, stimulus discrimination*

#### **15. From the lab to the clinic: translating promoted fear extinction by non-invasive vagus nerve stimulation to exposure-based treatment in phobic individuals**

Christoph Szeska<sup>1</sup>, Kai Klepzig<sup>2</sup>, Alfons O. Hamm<sup>2</sup>, & Mathias Weymar<sup>1</sup>

<sup>1</sup>Department of Biological Psychology and Affective Science, University of Potsdam, Potsdam, Germany | <sup>2</sup>Department of Physiological and Clinical Psychology/Psychotherapy, University of Greifswald, Greifswald, Germany

Fear extinction is considered a prime mechanism underlying exposure-based treatments of anxiety disorders. Thus, identification of novel strategies to promote fear extinction has been of great importance to the field to enhance therapeutic success. Recent laboratory research in animals and humans demonstrated, that fear extinction may be promoted by vagus nerve stimulation, increasing transmission in neural circuitry underlying fear extinction. Yet, a translation of this stimulation technique to clinical practice is lacking. Hence, we tested whether non-invasive vagal stimulation may promote the reduction of excessive fear during exposure to real-life threat cues (spiders) in phobic individuals. In this two-day sham-controlled and double-blinded study, 32 spider-phobic women either received transcutaneous auricular vagus nerve stimulation (taVNS) or a placebo sham stimulation during exposure *in vitro* (viewing spider pictures). Afterwards, participants underwent exposure *in vivo* towards a real tarantula, which was repeated twenty-four hours later to test for potential long-term effects of taVNS. During exposure sessions, fear was measured on multiple levels of expression (verbal report, heart rate, corrugator muscle activity, behavioral avoidance). During exposure *in vitro*, participants receiving taVNS showed reduced heart rate acceleration and corrugator muscle activity. Such fear reducing effects by taVNS were transferred to exposure to a living spider: Participants, who had received taVNS, showed stronger reduction of avoidance behavior towards a real tarantula compared to sham-stimulated participants. Our study suggests that vagal stimulation may be useful to enhance the efficacy of

exposure treatment by promoting the reduction of excessive physiological and behavioral defensive responding.

Keywords: *fear extinction, exposure therapy, non-invasive vagus nerve stimulation*

## **16. Low-frequency rTMS of the prefrontal cortex disrupts threat memory consolidation in humans**

Simone Battaglia<sup>1,2</sup>, Claudio Nazzi<sup>1</sup>, Miquel A. Fullana<sup>3,4</sup>, Giuseppe di Pellegrino<sup>1</sup>, & Sara Borgomaneri<sup>1,2,3,4,5</sup>

<sup>1</sup>Center for Studies and Research in Cognitive Neuroscience, Department of Psychology, University of Bologna, Bologna, Italy | <sup>2</sup>Department of Psychology, University of Torino, Torino, Italy | <sup>3</sup>Adult Psychiatry and Psychology Department, Institute of Neurosciences, Hospital Clinic, Barcelona, Spain | <sup>4</sup>Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), CIBERSAM, Barcelona, Spain | <sup>5</sup>IRCCS Fondazione Santa Lucia, Rome, Italy

Background: It is still unclear how the human brain consolidates aversive (e.g., traumatic) memories and whether this process can be disrupted. Hypothesis: We hypothesized that targeting the dorsolateral prefrontal cortex (dlPFC) within the memory stabilization time window (i.e., 6 hours after learning) by repetitive transcranial magnetic stimulation (rTMS) would effectively disrupt the expression of threat memory, thus disclosing the crucial involvement of this brain region in threat memory consolidation. Methods: In four separate experiments, involving 72 healthy participants, we combined a differential threat-conditioning paradigm over two days with rTMS targeting different brain regions at different time points. Results: In the critical condition, rTMS was delivered over dlPFC after threat learning, and resulted in reduction of defensive reactions (as shown by their skin conductance responses) to threat, immediately after, 1 h, and 24 h after brain stimulation. In stark contrast, no decrease was observed when participants received either control rTMS (i.e., active control site and sham stimulations), or rTMS over dlPFC delivered outside the memory stabilization period, thus showing both anatomical and temporal specificity of our intervention. Conclusion: We provide causal evidence that selectively targeting the dlPFC within the early consolidation period prevents the persistence and return of conditioned responses to threat. Furthermore, memory disruption lasted longer than the stimulation period of the rTMS, which suggests that we influenced dlPFC neural activity and hampered the underlying, time-dependent consolidation process of lasting memories. These results provide new insights for future clinical applications aimed at interfering with the consolidation of aversive, threat-related memories.

Keywords: *threat conditioning, transcranial magnetic stimulation, memory consolidation*

## **17. Devaluation of threat memory or associated neutral cues through bilateral eye movement**

Steven Klein, Alexander Hauck, Tanja Michael, & Diana S. Ferreira de Sá

*Division of Clinical Psychology and Psychotherapy, Department of Psychology, Saarland University, Saarbrücken, Germany*

One of the core components of Eye Movement Desensitization and Reprocessing (EMDR), is bilateral alternating stimulation (BAS). Despite previous attempts to better understand its effects on emotional devaluation of the aversive memory, important aspects remain unexplained. Previous studies have examined the effects of BAS only during the retrieval of an unconditioned stimulus (US). However, neutral stimuli (CS) are often responsible for the recurrence and maintenance of the aversive memory. To compare the effectiveness of BAS, we conducted an online study in which subjects recalled 1) the fear-inducing event itself (US-retrieval) versus 2) associated neutral stimuli (CS-retrieval) versus 3) no stimuli. Retrieval was followed by the BAS. In addition to ratings of US expectancy, subjects rated mental images in terms of vividness, emotional intensity, and difficulty of recall following the BAS intervention and at the end of the experiment. Preliminary analyses show that mental imagery was harder to recall and perceived as less vivid/unpleasant following BAS, regardless of the type of stimuli being recalled. Comparable results emerged for self-reported anxiety. There were no significant group differences in terms of US

expectancy after the intervention. The same was found for the final mental ratings. The results suggest that BAS proved to be effective in both experimental groups following the intervention. This indicates a potential role of BAS as an adjuvant to exposure therapy not only in relation to the fear-inducing stimuli. Although the BAS intervention appears to have an immediate effect, final ratings of mental imagery showed no differences between groups.

Keywords: *bilateral alternating stimulation, dual task, fear recall*

## **18. The effects of verbal instructions on fear extinction and extinction retrieval in patients with anxiety disorders and healthy controls**

Annalisa Lipp<sup>1</sup>, Marcella L. Woud<sup>2</sup>, & Armin Zlomuzica<sup>1</sup>

<sup>1</sup>*Department of Behavioral and Clinical Neuroscience, Mental Health Research and Treatment Center, Ruhr University Bochum, Bochum, Germany* | <sup>2</sup>*Mental Health Research and Treatment Center, Ruhr-University Bochum, Germany*

There is a considerable number of patients (19% to 62%) that experience a relapse of fear after completing therapy (Craske & Mystkowski, 2006). Patients with anxiety disorders (AD; Lissek et al., 2005) and highly anxious individuals show accelerated fear conditioning and diminished fear extinction (Duits et al., 2015). Thus, there is a need for improving extinction learning in AD patients. Instructions given prior to extinction training, stating that the unconditioned stimulus (UCS) will not be presented anymore, have been shown to improve extinction learning (e.g. Javanbakht et al., 2021). Furthermore, it has been shown that relapse of fear can be reduced by repeating the instructions before extinction retrieval (Javanbakht et al., 2021; Scheveneels et al., 2019). However, giving instructions before retrieval is not applicable to therapy since the therapist is not present during the time after therapy. Therefore, the aim of the present study is to examine whether explicit instructions at various time points affect extinction and the retrieval of extinction memory in both AD patients and healthy individuals. In a 3-day fear conditioning paradigm, we provide explicit instructions that the UCS won't be presented anymore before and/or after extinction. We will examine whether these instructions affect extinction learning on the second day and extinction retrieval and reinstatement on the third day. Furthermore, we will compare the fear acquisition and extinction learning rates of AD patients and healthy controls. Skin conductance responses, CS valence and UCS expectancy ratings will serve as conditioning measures. Preliminary results will be presented and discussed.

Keywords: *instructions, fear extinction, anxiety disorders*

## **19. Efficacy and treatment stability of imaginal exposure and imagery rescription: a randomized control trial**

Jarosław M. Michałowski, Julia Bączek, & Stanisław Karkosz

*SWPS University Laboratory of Affective Neuroscience, Poznan, Poland*

Imaginal exposure (IE) is a cognitive-behavioral therapy (CBT) technique that has been proven effective in treating various mental problems. Another imagery technique that is increasingly used for the treatment of mental disorders in recent years is imagery rescripting (ImRs). Previous research shows that ImRs can also contribute to symptom reduction. However, we lack conclusive evidences regarding the differences in the effectiveness and stability of treatment effects gained with ImRs when compared to IE. In our randomized controlled trial (RCT) we investigated the efficacy and treatment stability of ImRs and IE in reducing mental problems in young adults with high fear of failure. In a period of two weeks participants took part in 4-sessions of imagery rescription (N=49) or imaginal exposure (N=51). During treatment participants were presented with an autobiographical scene of being criticised (treatment scene) in a prolonged or rescripted version (IE or ImRs, respectively). Several psychological variables and skin conductance level (SCL, assessed during listening of various criticism scenes) were measured pre- and posttreatment as well as at 3-months and 6-months follow ups. For all participants, reductions were obtained for the SCL and for all psychological measures of psychopathology at post-treatment. The effects were largely maintained at follow-ups. We did not observe group differences in the subjective assessments at

any time point. However, there were several group differences for the SCL data. SCL decreased when the treatment scene was reactivated (i.e. when the criticism announcement was listened) at the beginning of the posttreatment session (vs pretreatment). This effect that was more pronounced in the IE (vs ImRs) group. Several results from the follow-up sessions indicate higher SCL reduction in the ImRs than the IE groups. This was true when the treatment scene was reactivated (i.e. when the criticism announcement was listened) at the 6-months follow-up in an unfamiliar room (renewal procedure) or after the criticism was presented (reinstatement procedure). The more pronounced SCL reduction in the ImRs (vs IE) group was also observed when the participants listened to the scenes of future criticism in the follow-ups.

## **20. The long shadows of early experiences: Evaluating the link between childhood maltreatment and psychopathology using a fear conditioning and generalization paradigm**

Maren Klingelhöfer-Jens<sup>1</sup>, Katharina Hutterer<sup>2</sup>, Miriam Schiele<sup>3,5,6</sup>, Elisabeth J. Leehr<sup>4</sup>, Dirk Schumann<sup>1</sup>, Karoline Rosenkrantz<sup>1</sup>, Joscha Böhnlein<sup>4</sup>, Jonathan Repple<sup>4,8</sup>, Jürgen Deckert<sup>3</sup>, Katharina Domschke<sup>3,5,6</sup>, Udo Dannlowski<sup>4</sup>, Ulrike Lueken<sup>3,7</sup>, Andreas Reif<sup>8</sup>, Marcel Romanos<sup>9</sup>, Peter Zwanzger<sup>10</sup>, Paul Pauli<sup>2</sup>, Matthias Gamer<sup>2</sup>, & Tina B. Lonsdorf<sup>1,11</sup>

<sup>1</sup>Institute of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany | <sup>2</sup>Department of Psychology, Center of Mental Health, Julius Maximilians University of Würzburg, Würzburg, Germany | <sup>3</sup>Department of Psychiatry, University Hospital Würzburg, Würzburg, Germany | <sup>4</sup>Institute for Translational Psychiatry, University of Münster, Münster, Germany | <sup>5</sup>Department of Psychiatry and Psychotherapy, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany | <sup>6</sup>Center for Basics in NeuroModulation, University of Freiburg, Freiburg, Germany | <sup>7</sup>Department of Psychology, Humboldt-Universität zu Berlin, Berlin, Germany | <sup>8</sup>Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, University Hospital Frankfurt – Goethe University, Frankfurt am Main, Germany | <sup>9</sup>Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Center of Mental Health, University Hospital of Würzburg, Würzburg, Germany | <sup>10</sup>Kbo Inn Salzach Hospital Clinical Center for Psychiatry, Wasserburg am Inn, Germany, Department of Psychiatry, LMU Munich, Munich, Germany | <sup>11</sup>University of Bielefeld, Bielefeld, Germany

Adverse childhood experiences (ACEs) are strong risk factors for somatic and psychopathological conditions. Environmental input – such as exposure to ACEs – shapes cognitive and emotional processes through learning mechanisms, making fear conditioning a prime paradigm in this context. Different theories have been proposed on how this link might be established, resulting in substantial heterogeneity in ACE operationalization and highlighting the necessity to evaluate prevailing theories. N=1402 healthy participants underwent a fear conditioning paradigm including a fear acquisition and generalization phase, while acquiring skin conductance responses (SCRs) and ratings (arousal, valence and contingency). We operationalized ACE exposure as assessed by the childhood trauma questionnaire (CTQ) using (1) dichotomization based on published cut-offs, (2) the specificity model, (3) the cumulative risk model, and (4) the dimensional model. In general, individuals exposed to ACEs showed blunted physiological reactivity in SCRs during fear acquisition and generalization, and reduced discrimination between CS+ and CS-, mainly driven by blunted CS+ responding. However, there were no group differences in ratings. The different operationalizations employed suggest that dichotomization into exposed and unexposed individuals fits the data best. Notably, in the literature, a remarkably different pattern of increased responding to the safety signal has been described in patients suffering from anxiety and stress-related disorders. Given that exposure to ACEs is an important risk factor for psychopathology, exposed individuals may represent a distinct patient subgroup that has not been previously identified. Further research is needed to refine theories connecting ACEs to psychopathology, which could inform novel prevention or intervention approaches.

Keywords: *childhood maltreatment, fear conditioning, generalization*

## **21. Establishing a potent reward for counterconditioning**

Anna Z. L. Wester<sup>1,2</sup>, Tom Beckers<sup>1,3</sup>, Ben J. Harrison<sup>4</sup>, Kim L. Felmingham<sup>5</sup>, & Bram Vervliet<sup>1</sup>

Aversive-to-appetitive counterconditioning has been regarded as a promising potential mechanism to treat anxiety disorders. However, effect sizes of counterconditioning studies have been mostly modest. One of the most profound differences between such studies is the different type of reward that is used. That is, counterconditioning stimuli include but are not limited to pictures, movies, money, tones, and food items. No research so far has directly compared the effectiveness of these stimuli directly. We assess the learning rate and counterconditioning effectiveness using a reward learning paradigm and a standard counterconditioning experiment. Moreover, we assess whether personal reward preference can predict the learning rates and counterconditioning effectiveness, measured as a decrease in US expectancy and a change in CS valence related to that reward. With this research, we assess which rewards yield the highest learning rates and are overall outperforming other rewards in a counterconditioning task. For clinical purposes, we examine whether we can predict the effectiveness of a reward by assessing the personal reward preferences. With this knowledge, we can try to optimize our counterconditioning paradigms and therapeutic interventions in the future.

Keywords: *counterconditioning*

## **22. Impaired action-safety learning and excessive relief during avoidance in patients with anxiety disorders**

Rianne De Kleine, Moniek Hutschemaekers, Gert-Jan Hendriks, Mirjam Kampman, Silvia Papalini, Agnes Van Minnen, & Bram Vervliet

*KU Leuven, Leuven, Belgium*

Anxiety-related disorders are characterized by high levels of avoidance, but experimental research into avoidance learning in patients is scarce. To fill this gap, we compared healthy controls (HC,  $n = 47$ ) with patients with obsessive-compulsive disorder (OCD,  $n = 33$ ), panic disorder with agoraphobia (PDA,  $n = 40$ ), and post-traumatic stress disorder (PTSD,  $n = 66$ ) in a computer-based avoidance learning task, in order to examine (1) differences in rates of avoidance responses, (2) differences in action-safety learning during avoidance, and (3) differences in subjective relief following successful avoidance. The task comprised aversive negative pictures (unconditional stimulus, US) that followed pictures of two colored lamps (conditional stimuli, CS+), but not a third colored lamp (safety stimulus, CS-), and could be avoided by pressing a button during one CS+ (CS+ avoidable) but not the other (CS+ unavoidable). Participants rated their US-expectancy and level of relief on a trial-by-trial basis. Compared to the HC group, patient groups displayed higher levels of avoidance to the safety stimulus, and higher levels of US-expectancy and relief following the safety and avoidable danger stimulus. We propose that patients with anxiety disorders have low confidence in the safety consequences of avoidance actions, which induces increased relief during US omissions that reinforce the avoidance action.

# Abstracts – Poster Session 2

Approach/Avoidance, Pain, Uncertainty, & Generalization

23<sup>rd</sup> May, 20:30 - 22:30

## 1. Subjective relief as a proxy for predictor error dynamics in avoidance learning

Bram Vervliet & Antonio Gonzalez-Rodriguez

*KU Leuven, Leuven, Belgium*

Prediction errors are the motor of learning. In the case of avoidance learning, successful omissions of the expected aversive event trigger a reward prediction error that guides learning to associate the safe outcome to the foregoing action. This is the theory, but there has been little direct focus on assessing the temporal dynamics of prediction error processing over the course of avoidance learning. Our lab has shown over the past years that ratings of subjective relief follows the hypothesized pattern of the prediction error, which makes it a putative behavioral marker of prediction error processing (in the context of threat omissions). In the current experiment, we further investigated the relation between subjective relief and prediction error, by using an avoidant decision-making task with changing probabilities so that trial-by-trial learning and updating is required to guide adaptive behavior. Eighty participants made 'left' or 'right' decisions on each trial to avoid an upcoming aversive electrical stimulation. After each successful omission, they rated how relieved they felt. We use a computational modeling approach to simulate, on an individual basis, the omission prediction errors on each trial, and we will correlate these with the relief ratings on a trial-by-trial level. Next, we will use a t-test to see, on the group level, whether these individual correlation coefficients are significantly larger than zero. The results will determine whether subjective relief ratings can indeed be used as a proxy to prediction error processing in the context of threat omissions. This would promote the use of relief ratings in the MRI scanner to examine neural prediction error processing. Moreover, given that prediction errors are also the mechanism of change in exposure-based treatments for anxiety, assessing subjective relief during the course of therapy could provide information about the success of the exposure exercises and predict overall treatment outcome.

## 2. Psychophysiological responses in active vs. passive approach-avoidance conflict decision task

Menghuan Chen & Andre Pittig

*University of Würzburg, Würzburg, Germany*

Abstract available from the authors upon request

## 3. Navigating the approach-avoidance matrix: exploring individual differences in a novel virtual reality foraging task

Alexandros Kastrinogiannis<sup>1</sup> & Tina B. Lonsdorf<sup>1,2</sup>

<sup>1</sup>University Medical Center Hamburg-Eppendorf | <sup>2</sup>University of Bielefeld, Biological Psychology and Cognitive Neuroscience, Bielefeld, Germany

A key characteristic of adaptive fear is avoiding genuinely threatening situations or stimuli. However, excessive avoidance of hazardous stimuli or circumstances can have negative long-term consequences on preventing the acquisition of safety information, leading to the maintenance of anxiety. Recent research has concentrated on investigating approach-avoidance (AA) conflicts in foraging tasks under predation threat, with a focus on decision-making strategies. However, the influence of inter-individual variations on AA tactics within a threatening context remains unclear. We present an approach-avoidance paradigm in a virtual foraging task that is based on a matrix-



designed environment that facilitates the tracking and visualisation of AA behaviour as a function of spatial movement. Participants have to gather an adequate number of food tokens in three simulated environments (forest, water, desert) over 24 trials to attain virtual survival. An AA conflict is induced by proportionally linking the potential reward to the probability of encountering an aversive (electrical) stimulus. To achieve this goal, each individual is required to perform a specific AA behaviour in terms of time spent in each context and spatial movement along the field. We present data demonstrating the validity of our task and highlighting the utility of using reward and punishment in a gamified design within virtual reality to elicit AA behavior as a novel method for investigating this phenomenon in a continuous manner. Additionally, we demonstrate findings towards our goal of identifying subgroups based on behavioral task performance and physiological activity (skin conductance level).

Keywords: *approach-avoidance, virtual reality, individual differences*

#### **4. The impact of experimentally controlled degrees of safety behaviour on protection from fear extinction**

Andre Pittig<sup>1</sup> & Alex H. K. Wong<sup>2</sup>

<sup>1</sup>*Translational Psychotherapy, University of Göttingen, Germany* | <sup>2</sup>*Department of Psychology, Education and Child Studies, Erasmus University Rotterdam, Netherlands*

Abstract available from the authors upon request

#### **5. Confronting fear after trauma? The impact of avoidance on intrusive memories in a trauma-film fear conditioning paradigm**

Arlinda Gashi, Stephan F. Miedl, Anna Kirchner, Lukas Forstmeier, Michael Liedlgruber, & Frank H. Wilhelm

*Division of Clinical Psychology and Psychopathology, Department of Psychology, Paris Lodron University Salzburg, Salzburg, Austria*

The development and persistence of posttraumatic stress disorder (PTSD) are strongly associated with intrusive memories, which are thought to be conditioned responses to trauma-related cues. Avoidance behavior, a hallmark symptom of PTSD, may interfere with extinction learning (an effect known as Protection-from-Extinction) and contribute to the development and maintenance of the disorder. This study used a fear conditioning task with trauma-films as UCS to investigate the development of intrusive memories in relation to fear conditioning and avoidance. The research questions focused on whether avoidance behaviour leads to reduced extinction and increased fear response to trauma cues, and whether it predicts more frequent and distressing intrusive memories. A total of 183 subjects were tested using neutral images as conditioned stimuli (CS) and aversive film clips as unconditioned stimuli (US). After the fear acquisition, an extinction phase followed, in which participants were randomly assigned to an avoidance (N = 87) and an extinction group (N = 96). After the experiment, a memory-triggering task was performed. Statistical analyses are in progress and results will be presented at the conference. The anticipated findings that avoidance behavior predicts reduced extinction, increased fear response, and more frequent and distressing intrusive memories could have important research and clinical implications. Specifically, the results may inform the development of interventions targeting extinction learning and reduction of avoidance behavior, leading to more effective treatments for individuals with PTSD symptoms.

Keywords: *avoidance, extinction, posttraumatic stress disorder*

## 6. No joy - why bother? Higher anhedonia relates to reduced pleasure from and motivation for threat avoidance

Lu Leng<sup>1,3</sup>, Tom Beckers<sup>1,3</sup>, & Bram Vervliet<sup>2,3</sup>

<sup>1</sup>Center for the Psychology of Learning and Experimental Psychopathology, KU Leuven, Belgium | <sup>2</sup>Laboratory of Biological Psychology, KU Leuven, Belgium | <sup>3</sup>Leuven Brain Institute, KU Leuven, Belgium

Anhedonia impairs various components of the pleasure cycle, including wanting, liking, and the learning of pleasure-related associations. While successfully controlling threats might be inherently pleasurable, it remains unclear whether anhedonia affects this form of pleasure as well. To investigate the role of anhedonia during active avoidance learning process, we conducted an online study ( $N = 200$ ) with aversive pictures as threats and a lab study ( $N = 40$ ) with electric shocks as threats using a similar paradigm. Participants first learned cue-threat associations for different cues (threat vs. safety cues). In a subsequent avoidance learning phase, these cues signaled either avoidable, unavoidable, or no threat; participants could perform avoidance responses to prevent the upcoming threats during those cue presentations. Subjective relief pleasantness was measured after each threat omission. We found that higher trait anticipatory and consummatory anhedonia were both associated with lower relief pleasantness. Higher trait anticipatory anhedonia was also associated with fewer avoidance attempts. Since reduced threat-controlling behavior is reminiscent of a learned-helplessness state, the current results contribute to a better understanding of the connections between anhedonia and learned helplessness that have mostly been studied separately in the context of mood disturbance.

Key words: *avoidance, relief, anhedonia*

## 7. How does the interplay between conjunctive and elemental context representation guide avoidance behaviour?

Francesco Tortora, Matthias Gamer, & Marta Andreatta

*University of Würzburg, Würzburg, Germany*

Modulating one's behavior according to the environmental information is crucial for survival. The absence of behavioral flexibility underlies the development and maintenance of different psychopathologies, such as anxiety disorders. Animal research supports the importance of the interplay between an elemental and a conjunctive context representation (dual-process theory) in guiding behavior. Notwithstanding the research efforts in this field, it remains unclear how these representations interact to regulate human behavior. To address this issue, healthy participants will be subjected to a virtual reality cue-in-context conditioning paradigm divided into three stages. During the first phase (context encoding), participants will be invited to actively explore two virtual offices (CXT A, CXT B) one minutes each. The contexts will be completely different from each other except for two stimuli (two lamps: one yellow and one blue). During the second phase (threat conditioning), participants will visit the offices alternately multiple times and in CXT A one lamp (e.g., the yellow one) will be associated with an unconditioned stimulus (US) while the blue one will not. In CXT B contingencies will be reversed. Then, in the behavioral test (third phase), participants will actively explore CXT A and CXT B plus a new context (CXT C) which contains the same lamps. We hypothesize to detect the dual contribution of conjunctive and elemental representations during learning construction both physiologically and behaviorally. Notably, we expect an opposite behavioral dissociation in the third phase that would result in an inverse pattern of threat cue avoidance driven by contextual information.

Keywords: *cue-in-context conditioning, virtual reality, avoidance behaviour*

## 8. Temporal dynamics of costly avoidance in anxiety disorders

Juliane M. Boschet-Lange<sup>1</sup> & Andre Pittig<sup>2</sup>

<sup>1</sup>University of Würzburg, Würzburg, Germany | <sup>2</sup>University of Göttingen, Göttingen, Germany

Anxiety disorders are characterized by excessive avoidance despite severe costs and impairments. Recent findings suggest that such elevated costly avoidance in clinical anxiety may be linked to altered decision-making under approach-avoidance conflict. However, evidence on what specific decision processes are altered in which way is still scarce. We thus examine whether individuals with anxiety disorders show specific deficits in approach-avoidance decision processes when avoiding an aversive unconditioned stimulus (US) conflicts with gaining monetary rewards. To this end, participants with social anxiety disorder, agoraphobia and/or panic disorder as well as matched healthy controls completed an approach-avoidance paradigm. In each of 294 trials, participants chose repeatedly between a fixed safe/low reward option and a threat/high reward option with varying threat (probability of US delivery: 0%, 10%, 30%, 45%, 60%, 75%, or 100%) and reward information (reward magnitude: 30, 36, 42, 50, 63, 83, or 188 Cents). Computer mouse movements recorded during decision-making will be analysed using time-continuous multiple regressions to uncover the temporal dynamics of the decision process (i.e., how strongly threat and reward information impact the momentary decision preference at each timepoint). We hypothesize that in individuals with anxiety disorders (a) the temporal impact of reward information during the decision process will be attenuated and (b) the temporal impact of threat information will be amplified compared to healthy controls. Results that are expected to provide novel insights into approach-avoidance decision processes in anxiety disorders will be presented at the conference.

Keywords: *anxiety disorders, approach avoidance, decision making*

## **9. No elevated persistence of extensively trained avoidance in participants with anxiety disorders in an outcome devaluation study**

Valentina M. Glück<sup>1</sup>, Juliane M. Boschet<sup>1</sup>, Roxana Pittig<sup>2</sup>, & Andre Pittig<sup>1</sup>

<sup>1</sup>University of Würzburg, Würzburg, Germany | <sup>2</sup>University of Göttingen, Göttingen, Germany

*Background:* A habitual avoidance component may enforce the persistence of maladaptive avoidance behavior in anxiety disorders. Whether habitual avoidance is acquired more readily in anxiety disorders is unclear. *Methods:* Individuals with current social anxiety disorder, panic disorder and/or agoraphobia (n = 62) and matched healthy individuals (n = 62) completed a devaluation paradigm with extensive avoidance training, followed by the devaluation of the aversive outcome. In the subsequent test phase, habitual response tendencies were inferred from compatibility effects. Neutral control trials were added to assess general approach learning in the absence of previous extensive avoidance training during the test phase. *Results:* The compatibility effects indicating habitual control did not differ between patients with anxiety disorders and healthy controls. Patients showed lower overall approach accuracy, but this effect was unrelated to the compatibility effects. *Conclusions:* In this study, anxiety disorders were characterized by reduced approach but not more substantial habitual avoidance. These results do not indicate a direct, substantial association between anxiety disorders and the acquisition of pervasive habitual avoidance in this devaluation paradigm.

Keywords: *anxiety disorders, avoidance, habits*

## **10. The degree of safety behaviors to a safety stimulus predicts development of threat beliefs**

Alex H. K. Wong<sup>1</sup>, Eva A. M. van Dis<sup>2</sup>, Andre Pittig<sup>3</sup>, Muriel A. Hagenaars<sup>2</sup>, & Iris M. Engelhard<sup>2</sup>

<sup>1</sup>Erasmus University Rotterdam, Rotterdam, The Netherlands | <sup>2</sup>Utrecht University, Utrecht, The Netherlands | <sup>3</sup>University of Göttingen, Göttingen, Germany

Safety behaviors are behavioral responses that aim to prevent or minimize an imminent threat when confronting a feared stimulus. Despite its adaptive purpose, preliminary evidence suggests that unnecessary safety behaviors to a safety stimulus induce threat beliefs to this stimulus. Using a dimensional measure of avoidance, this study tested whether the degree of safety behaviors to a safety stimulus predicts the subsequent level of threat expectancies to it. To this end, participants first acquired safety behaviors to a threat-related stimulus (A). Safety behaviors then became available only for one safety stimulus (C), but not to another safety stimulus (B). When safety

behaviors became unavailable for all stimuli, participants exhibited greater threat expectancies to C compared to B, albeit with a small effect size. Importantly, the degree of safety behaviors not only predicted the increase in threat expectancies to a safety stimulus in the same phase, but also predicted an increase in threat expectancies when safety behaviors were no longer available. The current findings suggest that safety behaviors to safety stimuli are linked to a development of threat beliefs.

Keywords: *avoidance, threat belief, risk factor*

## **11. Optimizing extinction with approach behavior**

Naomi Carpentier<sup>1</sup>, Sara Scheveneels<sup>1,2</sup>, & Dirk Hermans<sup>1</sup>

<sup>1</sup>*KU Leuven, Leuven, Belgium* | <sup>2</sup>*Open University of the Netherlands, Heerlen, The Netherlands*

An inherent aspect of exposure therapy is encouraging approach behavior towards the feared stimulus. However, in extinction protocols, the laboratory model for exposure, these instrumental aspects are usually not included. Therefore, in this study, we included approach behavior in an extinction procedure. Our aim is to receive insight into operant mechanisms at work in fear extinction, and into the added value of putting additional focus on approach behavior during exposure treatment. The study spanned three days. On day one, participants (N=72) underwent an aversive conditioning task, where three images (CSs) were reinforced by electrical stimuli (US). On the following extinction day, all three stimuli lacked reinforcement. For one image (CSa), participants received a cue to zoom in with a joystick during its presentation. A second image stayed static (CSb). The third image served as a yoked stimulus (CSc) to the CSa. It zoomed in without intervention, allowing us to disentangle effects related to the visual input of approach and those related to the action itself. The third session consisted of an extinction retention test phase, a reinstatement test phase and an approach-avoidance test (AAT). Verbal and physiological responses to the stimuli will be compared, expecting extinction learning and retention to be facilitated for stimulus a, and reinstatement to be impeded. Finally, we will compare the reaction times for responding to the stimuli during the AAT, expecting the facilitation of approach action tendencies towards CSa versus the other stimuli. Analysis is currently ongoing, but results will be presented at the meeting.

Keywords: *approach, extinction, exposure*

## **12. Effects of reinforcement rate on fear acquisition training, extinction and renewal**

Mana R. Ehlers<sup>1</sup> & Tina B. Lonsdorf<sup>1,2</sup>

<sup>1</sup>*University Hospital Hamburg-Eppendorf, Hamburg, Germany* | <sup>2</sup>*University of Bielefeld, Bielefeld, Germany*

In a classical fear conditioning paradigm, an initially neutral conditioning stimulus, the CS+, is repetitively paired with an aversive unconditioned stimulus, the US. A common assumption in the field is that a strong experimental situation, that is a pairing of the CS+ with the US in 100% of all trials during acquisition training leads to faster extinction. This effect is in part based on operant conditioning literature that suggests that partially reinforced behaviour is more resistant to extinction. However, little research has been performed in humans to systematically investigate this hypothesis. In the current study, 90 participants completed a cued fear conditioning paradigm including fear acquisition training on day 1 followed by a delayed extinction period and renewal 24 hours later. Skin conductance responses (SCRs), fear potentiated startle and trial-by-trial fear ratings were collected at both measurement time points. Participants were randomly assigned to three experimental groups with reinforcement rates of 50, 75 and 100 % during fear acquisition training. Preliminary analyses suggest that the effects may depend on the outcome measure. While the analysis of SCRs revealed a differential effect of reinforcement rate on renewal despite no differences during fear acquisition, for fear ratings a reinforcement rate dependent effect on fear acquisition but not on subsequent phases became evident. The preliminary pattern of results may suggest that physiological and subjective measures of fear conditioning are susceptible to the effects of partial reinforcement in different ways.

Keywords: *reinforcement rate, partial reinforcement, extinction effect*

### **13. Uncertainties about the role of Intolerance of Uncertainty in fear extinction**

Marcelo Malbec<sup>1</sup>, Marta Andreatta<sup>1,2</sup>, & Matthias J. Wieser<sup>1</sup>

<sup>1</sup>*Department of Psychology, Educational Sciences, and Child Studies, Erasmus University Rotterdam, Rotterdam, The Netherlands* | <sup>2</sup>*Department of Psychology, University of Würzburg, Würzburg, Germany*

Intolerance of uncertainty (IU) reflects the degree to which uncertain situations are perceived as threatening and is closely related to anxiety. Previous research has suggested that high levels of IU may be related to impaired fear extinction. In this study we investigated the role of IU on the defensive responses present in the fear extinction process, through the multi-modal assessment of a well-powered sample. We tested 181 undergraduate students by means of brain responses (steady-state visually evoked potentials; ssVEPs), skin conductance responses (SCR), and ratings (expectancy, arousal, and valence). Stimuli consisted of two female faces (CSs), one of them was associated with a loud aversive sound (90 dB) only in the acquisition phase (75% reinforcement rate). No significant ssVEPs differences were observed during habituation, but a larger response for CS+ vs. CS- was seen during acquisition and extinction. Ratings similarly distinguished between safe and threat stimuli. SCR responses were divided into early and late phases to explore its temporality, showing larger amplitude for CS+ during acquisition, and early extinction but not late extinction. We included IU (IUS-12) as a covariate (ANCOVA) in the previous models and correlated IU with difference scores of the aforementioned variables, but both analyses failed to reveal any significant associations with IU. Our results conflict some of previous findings in this field. To gain more clarity about how IU influences how humans recover from a sense of threat to feel safe again, more large-scale replications seem necessary.

Keywords: *intolerance of uncertainty, EEG, fear extinction*

### **14. Uncovering individual freezing-like behavior in relation to threat proximity in the context of threat and uncertainty**

Alina Koppold<sup>1</sup> & Tina B. Lonsdorf<sup>1,2</sup>

<sup>1</sup>*University Medical Center Hamburg Eppendorf, Department of Systems Neuroscience, Hamburg, Germany* |

<sup>2</sup>*University of Bielefeld, Biological Psychology and Cognitive Neuroscience, Bielefeld, Germany*

When facing threat, defensive circuits are activated to ensure survival. In the context of survival, blunted physiological responding is associated with action preparation, but little is known about humans responding to threat imminence. Here we present a paradigm which is intended to capture defensive psychophysiological responding and action preparation under varying levels of threat imminence, uncertainty and safety. In a multimethodological approach, we combine the human postural sway, a proxy for freezing-like behavior in humans, and fear potentiated startle (EMG) and behavioral task performance as outcome measures. First results (n = 200) revealed a generally reduced freezing-like behavior on the stabilometric-force platform in the experimental conditions of threat imminence and uncertainty as compared to safety. Strikingly, we observed decreased EMG responding during preparation for action under threat as compared to responses in the inter-trial interval. On a behavioral level, high threat conditions resulted in faster reaction tendencies at the expense of accuracy as compared to low threat. The findings extrapolate from animal models on the defensive mechanism of shifting from freezing to action under threat, unveiling a crucial valence-specific response pattern and provide empirical evidence for the contribution of defensive reactions such as postural freezing and startle inhibition in action preparation.

Keywords: *defensive responding, freezing, psychophysiology*

### **15. In and out of control: the impact of having and losing control over threat on the acquisition and extinction of conditioned fear**

Michalina Dudziak<sup>1</sup>, Bram Vervliet<sup>2,3</sup>, & Tom Beckers<sup>1</sup>

<sup>1</sup>Center for the Psychology of Learning and Experimental Psychopathology, Faculty of Psychology and Educational Sciences, KU Leuven, Belgium | <sup>2</sup>Leuven Brain Institute, KU Leuven, Belgium | <sup>3</sup>Laboratory for Biological Psychology, Faculty of Psychology and Educational Sciences, KU Leuven, Belgium

Threat controllability is an actual or perceived ability to control an aversive event. Recently it has been shown that threat controllability influences aversive learning processes. Particularly, it has decreased fear expression during fear extinction. An open question is how the experience of a loss of control would affect fear learning and extinction. The current study investigated whether threat controllability reduces fear expression and enhances fear extinction learning in healthy humans and whether a loss of control conversely has a detrimental effect on fear expression and extinction. Participants ( $N = 90$ ) were equally assigned to either a full-control (FC) group, a yoked lack-of-control (LA) group, or a partially-yoked loss-of-control (LO) group. Participants underwent a fear conditioning procedure consisting of acquisition and extinction phases. In the acquisition phase, participants were repeatedly presented with two geometrical shapes, one of which was consistently paired with an aversive electrical stimulus (US). Depending on group allocation, participants could either terminate the US with a button press (FC group) or could not control its duration (LA group). Participants in the LO group were first allowed to terminate the US, and then they lost control over the US duration. In the extinction phase, both CSs were repeatedly presented without the US. Participants provided US-expectancy ratings, CS-fear ratings, and their skin conductance responses. We expect that fear extinction will occur more readily in the FC group and less readily in the LO group than in the LA group across dependent variables. The results will be presented at the meeting.

Keywords: *threat controllability, fear conditioning, extinction*

## **16. Mechanisms of appetitive and aversive pain-related learning in health and chronic back pain**

Kira Schmidt, Frederik Schlitt, Jaspreed Kaur, Lea Busch, Jialin Li, & Ulrike Bingel

*Department of Neurology, Center for Translational Neuro- and Behavioural Sciences, University Medicine Essen, Essen, Germany*

Abstract available from the authors upon request

## **17. Pre-traumatic risk factors for the development of classically conditioned pain intrusions: A fear-and pain-conditioning trauma-analogue study**

Sabrina E. Hettegger, Sarah K. Danböck, Laila K. Franke, Stephan F. Miedl, Michael Liedlgruber, & Frank H. Wilhelm

*Division of Clinical Psychology and Psychopathology, Department of Psychology, Paris Lodron University Salzburg, Salzburg, Austria*

Classical conditioning has been suggested as a mechanism for developing pain intrusions after traumatic incidents in post-traumatic stress disorder (PTSD). Still, it is unclear why some individuals are more prone to developing pain intrusions after traumatic events than others. To address this gap, this study aims to examine pre-traumatic risk factors for the development of conditioned pain intrusions. Sixty-seven women completed questionnaires assessing trait anxiety, rumination, previous traumatic and pain experiences, as well as symptoms of somatoform disorder, PTSD, and depression. Participants then underwent a differential classical conditioning paradigm in which painful electro-cutaneous stimulation and aversive film clips served as unconditioned stimuli (US). Conditioned stimuli (CS) were neutral pictures displaying neutral objects from the films. On the next day, participants were re-exposed to the CSs in a memory-triggering-task (MTT), during which conditioned pain responses were assessed via self-report. Furthermore, subjects reported spontaneously occurring pain intrusions via e-diary over the following seven days. We particularly expect (subclinical) symptoms of somatoform disorder and PTSD as well as pain before conditioning and rumination to be positively associated with pain intrusions in the MTT and during daily life. Analyses are in progress and results will be presented at the conference. This study is expected to provide novel insights into pre-traumatic risk factors for the development of conditioned pain

intrusions and therefore might have implications for prevention and treatment of pain syndromes in PTSD.

Keywords: *pain intrusions, risk factors, PTSD*

## **18. Observational fear learning of interoceptive threat**

Ena Alcan, Christoph Benke, & Christiane Pané-Farré

*Department of Clinical Psychology, Experimental Psychopathology, and Psychotherapy, Philipps-University Marburg, Germany*

Observational learning has been identified as one of the pathways through which clinically significant fears can be acquired. Here we investigated whether fear in response to interoceptive threats or threats coming from inside the body can be acquired by observing the aversive experiences of others in an experimental setting. Our study included forty, healthy participants who underwent an observational fear conditioning paradigm consisting of two phases. During the first, observational learning phase, participants watched a video of a demonstrator experiencing aversive respiratory symptoms (US), such as difficulty breathing, paired with one of the conditioned stimuli (CS+, e.g., blue square), but not with the other conditioned stimuli (CS-, e.g., yellow circle). In the second, direct expression phase, participants were presented with the same visual stimuli as the demonstrator they had previously observed, however, in the absence of direct experience with the aversive event (no US). As expected, participants successfully discriminated between conditioned stimuli, showing greater skin conductance responses towards CS+ as compared to the CS- at the beginning of the direct expression phase, as well as larger startle potentiation to the CS+ as compared to the ITI. Participants also demonstrated greater subjective fear responses towards CS+ compared to CS- in both experimental phases. Our results provide experimental evidence that fear of interoceptive threats can be learned by observing others, thereby implicating the role of observational learning in the etiology of fear of bodily symptoms associated with panic and somatic symptom disorders.

Keywords: *observational learning, fear conditioning, interoceptive threat*

## **19. Individual differences in generalizing fear extinction learning across the spectrum of trait anxiety**

Edgar Nazareus<sup>1,2</sup>, Eva-Lotta Brakemeier<sup>2</sup>, & Jan Richter<sup>1</sup>

*<sup>1</sup>University of Hildesheim, Department of Experimental Psychopathology | <sup>2</sup>University of Greifswald, Department of Clinical Psychology and Psychotherapy*

This study investigates the process of fear extinction generalization across the spectrum of trait anxiety and in clinical patients. Three groups of 25 healthy subjects each with low, moderate, and high levels of trait anxiety, and 25 anxiety patients participated in two newly developed paradigms. One paradigm was designed for the investigation of extinction generalization across a range of cues, including a fear-conditioned and extinguished cue, a fear-conditioned but not extinguished cue, a non-conditioned safety cue, and several generalization cues. The other paradigm focuses on context-related extinction generalization, or the recall of extinction learning in several generalization contexts. Both protocols involve instructed fear acquisition and a 24-hour consolidation phase before extinction training and subsequent generalization tests immediately following extinction and 24 hours later. Outcomes included skin conductance responses, fear-potentiated startle, and heart rate. Additionally, unconditioned stimulus (US) expectancy ratings and skin conductance responses (SCR) during US omission (omSCR) were used to evaluate prediction error processes. As of this submission, we have successfully recruited a cohort of 94% of the intended subjects. Processing of different levels of data (i.e. physiological measures) is still ongoing, but initial analysis indicates that the paradigms we established are capable of effectively measuring the extent of extinction generalization across different cues and contexts, possibly providing valuable insights into individual differences of fear extinction processes. We look forward to presenting our results at the EMHFC, specifically focusing on whether or not subjects with a

higher anxiety load express less pronounced cue- and context-related fear extinction generalization capacities.

Keywords: *fear conditioning, extinction learning, extinction learning generalization*

## 20. Perceptual similarities increase the generalisation of fear

Leonie Rumpf, Lukas Neugebauer, Madeleine Müller, & Jan Haaker

*Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf*

Fear is an important emotion for learning and memory as it is essential for recognising danger. However, fear can become maladaptive if it is generalized to perceptually similar stimuli. Therefore, in this behavioural pilot study, we tested not only the strength, but also the specificity of fear memory using a two-day fear conditioning paradigm. Participants (N=15) completed an acquisition training on day one and were tested 24h later for retrieval and generalisation trials. Outcome measures were subjective ratings of fear, arousal and the expectancy of receiving an US. For stimulus material, we used Gabor Patches that can be rotated 180 degrees around the CS+. Thereby, the CRs are expected to follow a generalisation gradient. Additionally, to test the likelihood of the stimuli to be perceived as being different, we tested the perceptual differences (i.e. perceptual space) of the stimuli orientation by means of Maximum Likelihood Difference Scaling (MLDS). Subjective ratings showed that participants significantly learned to discriminate between the CS+ and CS- after the acquisition training. This discrimination was no longer significant after the retrieval. Regarding the specificity, still, we found evidence for a generalisation gradient, indicated by higher subjective ratings to stimuli that were more similar to the CS+. Likewise, the results of the MLDS showed that GS, which are orientation-wise more similar to the CS+, also have a position more closely to the CS+ in a perceptual space. Taken together, our results show that generalisation gradients are linked to learned associations along with perceptual processes.

Keywords: *fear conditioning, generalization, perceptual space*

## 21. Does variability make a difference? Return of fear after extinction learning with perceptually similar generalization stimuli

Paula Engelke<sup>1</sup>, Alex H. K. Wong<sup>2</sup>, & Andre Pittig<sup>3</sup>

<sup>1</sup>University of Würzburg, Department of Psychology (Biological Psychology, Clinical Psychology, and Psychotherapy), Würzburg, Germany | <sup>2</sup>Erasmus University of Rotterdam, Department of Psychology, Educational Sciences, and Child Studies, Rotterdam, Netherlands | <sup>3</sup>University of Göttingen, Institute of Psychology, Translational Psychotherapy, Göttingen, Germany

Although cognitive-behavioral therapy (CBT) is highly effective for treating anxiety disorders, some patients experience a return of fear. Extinction learning procedures serve as a laboratory model for mechanisms underlying exposure exercises, a crucial element of CBT. However, studies show limited generalization of extinction learning if a similar generalization stimulus (GS) is used. As real-life exposure is usually conducted with generalization stimuli, limited extinction generalization to other stimuli suggests a risk mechanism for return of fear in patients. This study examined whether using multiple, perceptually similar GSs would enhance GS-extinction generalization. A healthy sample (N = 120) underwent a two-day fear conditioning paradigm. During extinction training, participants repeatedly experienced A) a single GS, B) multiple GSs, or C) the CS+. US expectancy ratings and skin conductance responses to a novel GS and the CS+ were measured immediately, 24 hours later, and after a reinstatement manipulation. Results indicate fear acquisition and extinction learning at US expectancy level. Furthermore, averaged across groups, immediate return of US expectancy was evident for the new stimulus and the CS+, while spontaneous recovery on Day 2 occurred only for the CS+. Contrary to our hypotheses, groups did not differ in test phases, suggesting comparable generalization of extinction learning independent of which stimuli were used for extinction training. The results point to questions about the possible influence of (missing) awareness of differences between CS+ and GSs for extinction learning and its generalization.

Keywords: *extinction, generalization, return of fear*



## 22. Dynamics of fear-generalization processes and their predictive value for the development of anxiety-related psychopathology in adolescents

Jessica Reinhart<sup>1</sup>, Julia Reinhard<sup>1</sup>, Katharina Hutterer<sup>2</sup>, Andre Pittig<sup>3</sup>, Angelika Erhardt-Lehmann<sup>2,4</sup>, Marcel Romanos<sup>1</sup>, & Jürgen Deckert<sup>2</sup>

<sup>1</sup>Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Würzburg, Würzburg, Germany | <sup>2</sup>Department of Psychiatry, Psychosomatics and Psychotherapy, Center of Mental Health, University Hospital Würzburg, Würzburg, Germany | <sup>3</sup>Translational Psychotherapy, University of Göttingen, Göttingen, Germany | <sup>4</sup>Max Planck Institute of Psychiatry, Munich, Germany

Enhanced fear generalization is assumed to be associated with anxiety disorders. Yet, the extent to which fear generalization acts as a risk factor for initial development of anxiety disorders remains unclear, highlighting the need for longitudinal studies tracking fear generalization and anxiety symptoms. Furthermore, the transition from childhood to adolescents represents a crucial period for the development of anxiety disorders, yet we still lack a comprehensive understanding of the developmental trajectory of fear generalization during this period. Our longitudinal study involves the reassessment of initially healthy volunteers in Würzburg (DFG SFB-TRR 58: Project Z02, FP2-FP3). All participants undergo a fear generalization paradigm (modified version of the “screaming lady paradigm”) which was already performed at previous time points. It consists of two fear acquisition blocks in which one of two female faces (CS+) is associated with a loud noise (US), while the other face is never followed by the US (CS-). In the generalization phase CS+, CS- as well as four generalization stimuli (GS1-4, gradual morphs from CS+ to CS-) are. SCR, heart rate and subjective ratings (arousal, valence, US expectancy) are measured as indicators of conditioned fear. Additionally, questionnaires are used to assess anxiety symptoms. Overall, the study aims to assess the stability of fear generalisation processes alongside the developmental period from youth (starting at age 8) to early adulthood and its predictive value for anxiety symptomatology. We will present and discuss analytical procedures to estimate this predictive value.

Keywords: *fear generalization, childhood, longitudinal*

## 23. Increased generalized threat expectations in threatening contexts

Asimina Aslanidou<sup>1</sup>, Marta Andreatta<sup>1,2</sup>, & Matthias J. Wieser<sup>1</sup>

<sup>1</sup>Department of Psychology, Education and Child Studies, Erasmus University Rotterdam, Rotterdam, The Netherlands | <sup>2</sup>Department of Biological Psychology, Clinical Psychology, and Psychotherapy, University of Würzburg, Germany

Defensive responses have been shown to generalize according to contextual information. Given the enhancing effect of stress on fear generalization, in this study we investigated whether people would generalize their defensive responses to a wider range of visual stimuli in a threatening compared to a safe context. To this aim, 48 participants underwent a differential threat conditioning protocol with a generalization test. Two female faces appeared on a computer screen in two different contexts. These contexts consisted of two different arrays of geometrical shapes (triangles or circles) in the screen corners on gray backgrounds presented for two minutes. One of the faces (CS+) in the threat context (CTX+) was followed by a female scream (US) 80% of the time, while the other face (CS-) and both faces presented in the other context (CTX-) were never reinforced. In the generalization test, participants saw four more morphs (GS), along with the CS+ and CS-, that varied in similarity with the CS+ in steps of 20%. All faces were presented in both contexts. Successful acquisition of the conditioned defensive responses to the cues was registered for all measures except for the steady-state visual evoked potentials. US-expectancy, skin conductance responses and visuocortical responding were heightened in CTX+ while the affective ratings were not sensitive to the contextual information. During test, generalized responses were evident for all measures. Despite increased overall US-expectancy ratings in CTX+, participants exhibited cue overgeneralization in both contexts, which suggests that threatening contextual information did not influence the degree of generalization.

Keywords: *fear generalization, cue-in-context conditioning, psychophysiology*