



## **GK Summer School**

# **9 YEARS OF EMOTIONS: from the molecular basis to the emotional experience**

**October, 8<sup>th</sup> – 10<sup>th</sup>, 2015**

**Thursday, October 8<sup>th</sup> 2015**

**9.15 am** *Arrival and Coffee*

**9.45 am** **Official Start of the Meeting**

**Prof. Paul Pauli**

**10.15 am** **Lecture**

**Dr. Markus Ising**

*“Stress & Depression – Role of  
Genetic Risk and Resilience  
Factors”*

Valentina Haspert  
Esin Candemir

**11.45 am** *Coffee Break*

**12.00 am** **Poster Session (all posters)**

**1.00 pm** *Lunch*

**2.30 pm** **Alumni Symposium**

**Dr. Stefanie Biehl**

**Dr. Adrian Meule**

**Thorsten Erle**

*„The variety of psychological  
motion”*

Sina Kollert  
Štěpán Bahník

**4.00 pm** *Coffee Break*

**4.15 pm** **Master Class of Alumnis**

**5.15 pm** *Leisure Time*

**6.00 pm** *City tour through Marktbreit*

**7.30 pm** *Dinner and Jazz Concert*

## Friday, October 9<sup>th</sup>, 2015

**8.00 am** *Breakfast*

<b>9.30 am</b>	<b>Lecture</b>	<p><b>Jun Suk Kim</b> <i>"Philosophy as Therapy – Spinoza's theory of emotion"</i></p> <p><b>Dr. Ingrid Vendrell Ferran</b> <i>"Phenomenology of the Emotions"</i></p>	Jun Suk Kim
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**11.15 am** *Coffee Break*

<b>11.30 am</b>	<b>Alumni Symposium</b>	<p><b>Dr. Marta Andreatta</b> <b>Antonia Post</b> <b>Dr. Sarah Nietzer</b> <i>„From Unpleasant to Pleasant Emotions of Mice, Men, and Machines“</i></p>	<p>Ramona Baur Sandy Popp Dominik Kiser</p>
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**1.00 pm** *Lunch*

**2.30 pm** **Master Class of Alumnis**

**3.30 pm** *Coffee break*

<b>3.45 pm</b>	<b>Lecture</b>	<p><b>Prof. Andreas Keil</b> <i>"Face processing in social anxiety: Inter-individual differences in cortical networks within and beyond the classical visual hierarchy."</i></p>	<p>Bastian Söhnchen Hannah Genheimer</p>
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**5.15 pm** *Leisure Time*

**6.00 pm** *Walk to Obernbreit (bus ride in case of bad weather)*

**7.00 pm** *Wine tasting and dinner at Family Löther in Obernbreit*

## Saturday, October 10<sup>th</sup>, 2015

**8.00 am** *Breakfast*

**9.30 am** **Symposium  
Alumnis** **Anna Kastner**  
**Dr. Monika Fricke**  
**Dr. Johannes Schick** Uri Ramirez Pasos  
**Dr. Lingdan Wu**  
*„Clinical Neuroscience: Its Application and  
Theoretical Implications“*

**11.30  
am** *Coffee Break*

**11.45  
am** **Master Class of Alumnis**

**12.45  
am** *Lunch*

**2.00 pm** **Special Guest** **Prof. Rainer Thome**  
*"Digital disruption"* Christoph Schartner

**3.00 pm** *Coffee break*

**3.15 pm** *Finissage*

<b>Number</b>	<b>Member</b>	<b>Title of Poster</b>
1	Lea Ahrens	Examining Fear Generalization with steady-state Visually Evoked Potentials (ssVEPs)
2	Štěpán Bahník	If it's difficult to pronounce, it might not be risky: Fluency, risk perception, and random sampling of stimuli
3	Ramona Baur	Emotion processing and emotion regulation in adult ADHD – preliminary data
4	Loïc Botrel	Trainings and predictors for performance in a brain-computer interface controlled by sensorimotor rhythms
5	Victoria Cabello	Animal model for Coffin-Lowry syndrome: function of Rsk2 in Adult Neurogenesis and Behavior
6	Esin Candemir	Interaction of NOS1AP with the NOS I PDZ domain and its effects on dendritic morphology
7	Mathias Eidel	Psychophysiological correlates of coping and quality of life in patients with chronic diseases
8	Elena Flohr	On the Influence of Smells on Heart Rate and Different Measures of Social Interaction
9	Hannah Genheimer	Extinction and Return of Fear: Does Vagus Nerve Stimulation reduce Anxiety?
10	Hina Ghafoor	Emotional Intelligence (EI) as a Predictor of Quality of Life (QoL) in Chronic Heart Failure: A Cross-cultural study
11	Daniel Gromer	psymisc: An R package for facilitating data analysis of factorial experiments
12	Valentina Haspert	Regulation of pain with cognitive strategies: Acceptance vs. Reappraisal vs. Suppression
13	Dorothea Neueder	Overgeneralization of context conditioned fear in human CB1-polymorphism
14	Uri Ramirez Pasos	Analysis of Single Unit, LFP, and EEG Activity in the Human Subthalamic Nucleus during Presentation of Emotional Visual and Acoustic Stimuli
15	Christoph Schartner	Allelic variations in Corticotropin-Releasing Hormone Receptor 1 changes receptor activity by alternative splicing
16	Bastian Söhnchen	Follow the eyes – Influence of Emotional Expression on Visuospatial Attention

## Abstracts Talks

**Markus Ising. *Stress & Depression – Role of Genetic Risk and Resilience Factors.***  
*PG Molecular Psychology, Max Planck Institute of Psychiatry, Munich - Germany.*

Adverse experiences and chronic stress are well-known risk factors for development of major depression and other mental disorders, and acute stress may trigger the onset of new disease episodes. Many symptoms of acute depression resemble signs of chronic stress, and elevated stress hormone levels as well as an impaired stress response regulation are laboratory findings frequently observable in these patients. Variants in genes of the stress response regulation contribute to the vulnerability for depression in traumatized subjects suggesting an important role of genetic and epigenetic factors. Most consistent findings have been observed for FKBP5 expressing a chaperone protein to the glucocorticoid receptor, and thus, an important regulatory element of the stress response. Reporting data from the Munich Antidepressant Response Signature (MARS) project, we will show that change in FKBP5 gene expression is associated with antidepressant treatment outcome. However, this effect is modulated by the respective genotype. Findings from participants of a longitudinal epidemiological study suggest that subjects remitted from depression still show signs of an impaired stress response regulation. However, the modulating effects of FKBP5 have changed in remitted depression, which seems to be associated with certain epigenetic changes that may act as resilience factor in these subjects. We conclude from these findings that genes involved in stress response regulation, specifically FKBP5, play an important role in vulnerability, acute and long-term outcome of major depression. Targeting these genes within new treatment approaches might be a promising avenue for the development of future antidepressant drugs.

**Ingrid Vendrell Ferran.** *Phenomenology of the Emotions.* Institute of Philosophy, University of Magdeburg, Germany.

I will begin my talk with an overview of the different phenomenological approaches to the emotions developed during the last hundred years. After presenting this overview I will focus in one of these phenomenological contributions: the claims on the emotions developed by a group of philosophers called “the early phenomenologists”. I shall elaborate the main claims about the emotions defended by this group, articulating them through the following five topics: 1) the stratification of emotional life; 2) the qualitative aspect of emotional experience; 3) the foundation of the emotions in cognitive acts; 4) the intentionality of feeling and the emotions; and 5) their moral dimension.

**Andreas Keil, *Face processing in social anxiety: Inter-individual differences in cortical networks within and beyond the classical visual hierarchy*, University of Florida, USA.**

A plethora of studies suggest that the motivational or biological relevance of external stimuli facilitate sensory processing. This phenomenon is readily demonstrated when observers high in social anxiety view pictures of faces expressing strong affect. In this presentation, we discuss conceptual issues regarding the characterization of perception and attention such as the bottom-up and top-down dichotomy, with respect to real-world stimuli such as faces. We then turn to experimental explorations of behavioral and neurophysiological dynamics as healthy observers and individuals diagnosed with disorders in the social anxiety spectrum view emotion faces. Capitalizing on neuroimaging techniques with fine-grained temporal resolution we find that activity in lower-tier visual cortex reflects the motivational relevance of face stimuli. Connectivity analyses and advanced signal processing demonstrate that subgroups of patients defined by their primary symptoms can be readily classified based on their electrocortical response. Findings will be discussed in a theoretical framework that views emotions as action dispositions, implemented in widespread cortical and sub-cortical networks.

**Rainer Thome, *Digital disruption***, Department of Business Integration, University of Würzburg, Germany.

## Abstracts Alumni Symposia

### Symposium 1 – “The Variety of Psychological Motion”

**Stefanie Biehl**, *The perception of biological motion in healthy ageing*, Department of Clinical Psychology and Psychotherapy, University of Tübingen, Germany.

Previous studies report an impaired perception of biological motion in old age. However, in healthy older adults this impairment is often restricted to biological motion presented either in noise or in otherwise unfamiliar ways (e.g. inverted). Our study therefore aimed to investigate the neural correlates of biological motion processing as a potentially more sensitive measure. We collected fMRI data of 20 older (mean age 68 years) and 20 younger (mean age 23 years) participants viewing simple circular motion as well as biological motion stimuli. Preliminary data analyses point to the absence of broad changes in motion processing with increasing age, while some slighter changes might still exist.

**Thorsten Erle**, *The Grounded Nature of Psychological Perspective-taking*, Department of Social Psychology, University of Würzburg, Germany.

Although visuo-spatial and psychological perspective-taking are linguistically strongly related (e.g., “put yourself in my place”), connections between them have rarely been investigated. Furthermore, while research on the psychological kind is primarily concerned with outcomes and less with its underlying mechanisms, for visuo-spatial perspective-taking the opposite is true.

Visuo-spatial perspectives are assumed by mentally rotating one’s body schema until it matches that of a target person, that is, by literally putting oneself into another’s place. I hypothesized that this mechanism is also involved in psychological perspective-taking.

Three series of experiments indeed suggest that the two kinds of perspective-taking correlate on a dispositional level, and that experimental manipulations of either kind affect the respective other. Thus, psychological perspectives are grounded in visuo-spatial ones.

**Adrian Meule**, *Chocolate Craving*, Department of Psychology, University of Salzburg, Austria.

Chocolate’s sensory characteristics, macronutrient composition, and psychoactive ingredients make it a hedonically ideal substance. Accordingly, it is the most often craved food in Western societies and the food for which people most often report having problems controlling its consumption. Yet, there are also gender and cultural differences in the frequency of chocolate cravings. In this talk, correlates of trait and

state chocolate craving will be presented. These include, for example, associations between chocolate craving, salivary flow, and ad libitum chocolate consumption in the laboratory and the differentiation between current chocolate craving and hunger. Furthermore, the effects of chocolate deprivation and chocolate thought suppression on chocolate craving and related measures as a function of trait chocolate craving will be presented.

## **Symposium 2 – “From Unpleasant to Pleasant Emotions of Mice, Men, and Machines”**

**Marta Andreatta**, *The two sides of the same coin*, Department of Biological Psychology, Clinical Psychology, Psychotherapy, University of Würzburg, Germany.

Pain is an unpleasant experience, which every organism does not wish to repeat. For this reason, when encountering a pain-associated stimulus, both animals and humans show fear responses like amygdala activation or avoidance. Strikingly, the termination of pain, which is the relief, entails pleasant properties and both animals and humans show reward-like responses like striatal activation or approach. Here, I investigated the role of relief in human learning. In 4 studies, participants underwent a relief conditioning during which a geometrical shape (the conditioned stimulus, CS) followed an aversive unconditioned stimulus (US). Before and after learning, participants rated CS valence (positive vs. negative) and arousal (intensity). As learning indices, startle response (Study 1 and Study 3) and brain activity (Study 2 and Study 4) were collected. Specifically, in Study 1 and Study 2 I investigated whether the relief might work as appetitive US and consequently elicits appetitive conditioned responses. Accordingly, the relief-associated stimulus as compared to a control neutral stimulus induced startle attenuation and elicited striatal activation, which parallel reward-like responses. Contrarily, participants reported the relief-CS as more negative and arousing than the control. In Study 3, I compared the appetitiveness of the relief with a reward. To this purpose, half of the participants underwent a relief conditioning, while the other half underwent an appetitive conditioning during which the CS signaled the delivery of a reward (i.e., chocolate or salty prezel). Interestingly, I found comparable startle attenuation to the relief- and the reward-associated stimuli indicating similar appetitive responses. On the verbal level, the relief-CS was again rated significantly more negative and arousing than the reward-CS. In Study 4, I investigated whether the relief is a pain-specific response or rather a response, which follows aversive events in general. To this purpose, a desperate female scream was presented as aversive US. As expected, the relief-CS elicited greater striatal activation (paralleling the results with the painful US, Study 2) as compared to the control. In conclusion, the relief is an appetitive response, which elicits similar responses as a reward on the implicit level and importantly it seems to follow aversive events in general and not being pain specific.

**Sarah Nietzer**, *Emotions in Tissue Engineering*. Department of Tissue Engineering and Regenerative Medicine, University Hospital of Wuerzburg, Germany.

Tissue Engineering is a field of research rather distant from that of psychology or emotions. However, I'd like to present our 3D tumor models which we develop at the department of Tissue Engineering and regenerative Medicine. We are developing a

test system suitable for testing substances against lung cancer in an artificial human tissue. Moreover, an in-silico model is being designed to predict the treatment efficacy of drugs. This programmed model can also be used to find new options for treatment. In addition, I shall also include some descriptive studies of the emotions you face every day when working with bioreactors or preparing tissues.

**Antonia Post, *Behavioral consequences of prenatal environmental enrichment in CD1 mice: relevance for the etiology of psychiatric disorders.* Clinic for Psychiatry, Psychosomatic and Psychotherapy, University of Frankfurt, Germany.**

Retrospective studies in humans as well as experimental studies in rodents have shown prenatal stress to be a risk factor for psychiatric disorders or behavioral changes, in later life. Possible mediators include changes in the hypothalamus-pituitary-adrenal axis and the serotonergic system. While these adverse prenatal effects are well studied, little is known about positive life conditions during pregnancy and whether they affect resilience towards stress in the offspring's later life.

Pregnant CD1 mouse dams were either housed under standard laboratory conditions (pnCTRL) or housed in a more positive environment with more space and toys (pnEE). After birth, pups were randomized into three groups: standard laboratory conditions (CTRL), postnatal stress in the form of maternal separation (MS) followed by standard laboratory conditions and positive environment with toys (EE). Starting at the age of 8 weeks, mice were tested in a battery of behavioral tests as well as for changes in gene expression and corticosterone levels.

Prenatal treatment (pnEE vs pnCTRL) yielded strong effects in the ANOVAs for most behavioral tests, arguing that this sensitive time is not only influenced by stressors, but also by positive factors. For example, pnEE mice were significantly more active in the Open Field test, were less immobile in the Forced Swim test, but also spent more time in the dark area of the Light Dark Box test and entered the lit areas later than pnCTRL mice. In a nutshell, they were showing a mild hyperactivity, reduced depression-like behavior, while anxiety-like behavior was elevated. Moreover, quantitative Real-Time PCR revealed a hypoexpression of the serotonin receptor 1A in the frontal cortex, amygdala and the raphe nuclei of the pnEE group compared to the pnCTRL group, arguing for an involvement of the serotonergic system.

Not only the prenatal treatment itself, but also its interaction with the postnatal treatment produced interesting results: during Cued Fear Conditioning, pnEE mice that underwent MS showed a tendency to freeze more than all the other groups when presented with the tone, thus showing an elevated fear response.

This is in accordance with the mismatch hypothesis of psychiatric disease, which states that mismatches between psychosocial environments in early and later life could be used to explain the occurrence of psychiatric disease .

During the course of the experiments, mice were repeatedly tested for Sucrose Preference (SP) and for corticosterone levels in feces to determine the development of anhedonic-like behavior and stress. SP revealed a stable reduced sucrose preference for the pnCTRL group that was housed under EE conditions but not for any of the other groups. Corticosterone levels in fecal samples were significantly lower basally for the male pnEE group, but skyrocketed after the beginning of the behavioral tests, whereas the corticosterone levels for the male pnCTRL group were stable throughout behavioral testing.

Concluding, prenatal environment seems to be important not only in regard to stress, but also to more positive aspects, as it influences adult behavior and also neurobiological systems that are important in the etiology of psychiatric disease.

### **Symposium 3 - „Clinical Neuroscience: Its Application and Theoretical Implications”**

**Monika Fricke**, *From basic research to clinical development. Boehringer Ingelheim Center, Vienna, Austria.*

**Anna K. Kastner**, *Contextual Anxiety, Cue-specific Fear and their Influence on Faces. Department of Biological Psychology, Clinical Psychology, Psychotherapy, University of Würzburg, Germany.*

Anxiety is an affective state characterized by a sustained, long-lasting defensive response, induced by unpredictable, diffuse threat. In comparison, fear is a phasic response to predictable threat. Context conditioning, in which the context serves as the best predictor of a threat due to the absence of any conditioned cues, is seen as an operationalization of sustained anxiety.

A differential context conditioning paradigm was used to examine sustained attention processes in a threat context compared to a safety context for the first time. In three studies, the attention mechanisms during the processing of contextual anxiety were examined by measuring heart rate responses and steady-state-visually evoked potentials (ssVEPs). An additional focus was set on the processing of social cues (i.e. faces) and the influence of contextual information on these cues. In a last step, the correlates of sustained anxiety were compared to evoked responses by phasic fear, which was realized in a previously established paradigm combining predictable and unpredictable threat. All three studies endorsed anxiety as a long-lasting defensive response. Due to the unpredictability of the aversive events, the individuals reacted with hypervigilance in the anxiety context, reflected in a facilitated processing of sensory information and an orienting response. This hypervigilance had an impact on the processing of novel cues, which appeared in the anxiety context. Considering the compared stimuli categories, the stimuli perceived in a state of anxiety received increased attentional resources, irrespective of the emotional arousal conveyed by the facial expression. Both predictable and unpredictable threat elicited sensory amplification of the contexts, while the response in the unpredictable context showed longer-lasting sensory facilitation of the threat context.

**Johannes F.M. Schick**. *Life - Body - Technique: Towards an Eco-Techno-Anthropology. University of Cologne, Germany.*

My talk is presenting a research project that I am currently developing. It ultimately aims at an interdisciplinary Eco-Techno-Anthropology, i.e. a model of the complex interrelations of human beings, technical and non-technical objects and the environment, based on interdisciplinary research. Human beings are in the unique

position to not only structure, but to also create entirely new environments with technological objects. Their relation with the environment – be it natural or technological – is essentially affective. Human beings share this affectivity with other living beings. The capacity to invent allows human beings to distance themselves from their environment. However, the environment strikes back, also in its technological form: It affects the constitution of human beings as they affect the environment. This reciprocity becomes apparent in our daily routines (e.g. by using tools, smartphones) and on the scientific level (e.g. the discussion on neuroenhancement). Ultimately, the abolishment of the borders between material objects and living organisms aims for the enhancement of human life itself. The fundamental anthropological question of the definition of human beings and life is thus enhanced by a new quality: how can a interdisciplinary anthropology aimed at the comprehensive description of human behaviour be developed starting with the material entanglement of human beings in their environment?

## **Abstracts Actual Members**

### **Ahrens, L., Wieser, M. J., Reif, A., Pauli, P. *Examining Fear Generalization with steady-state Visually Evoked Potentials (ssVEPs)***

Many studies suggest that anomalies in fear generalization play a crucial role in the etiology of anxiety disorders. Still, little is known about their underlying mechanisms. Hence, the present study examines the contribution of visual neuron activity to fear generalization. 67 subjects were conditioned to two different faces (conditioned stimulus [CS]; CS+: reinforced; CS-: non-reinforced) flickering at a frequency of 12 Hz, which were paired with a fearful face and a shrill scream (unconditioned stimulus [US]). To investigate fear generalization, morphs of the two faces (GS: generalization stimuli) were presented which varied in their similarity to the original faces. The conditioned response was measured via steady-state visually evoked potentials (ssVEPs) as well as valence, arousal and US expectancy ratings. Analyses revealed generalization gradients in all three subjective ratings with highest fear responses to the CS+ and a progressive decline of these reactions to intermediate GS as a function of their similarity to CS-. In the ssVEP signal, we observed a trend with highest amplitude for the CS+ and lowest for the generalization stimulus closest to the CS+ (GS1). While the former findings might reflect an increased readiness to react to actual threat, the latter might point to inhibitory interactions of adjacent neurons in the visual cortex to maximize the contrast among stimuli with and without affective value. Further research is needed to elucidate the role of neural activity in the visual cortex during fear generalization.

### **Bahník, S., Vranka, M. *If it's difficult to pronounce, it might not be risky: Fluency, risk perception, and random sampling of stimuli***

Previous research has shown that people perceive food additives and amusement-park rides with harder pronounceable (i.e. disfluent) names as more risky. The present study explored a possibility that the association between processing fluency and riskiness might be in the opposite direction for some categories of stimuli. While we initially found some support for the hypothesis, further studies showed that the effect of processing fluency is largely dependent on the stimuli used. We showed this dependency even for the original effect. While we were able to replicate it using original items, the effect disappeared for new randomly sampled items.

**Baur, R., Pauli, P., Nehfischer, M., Jost, M. S., Schorb, M., Müller, M., Wagner, K., Romanos, M., Lesch, K.-P., Mühlberger, A., Conzelmann, A. *Emotion processing and emotion regulation in adult ADHD – preliminary data***

More and more findings point to ADHD patients having problems in emotion processing and emotion regulation. Still, emotional reactivity especially in adult ADHD patients is still under investigated.

The aim of our study was to assess emotional reactions of adult ADHD patients and healthy controls induced by social interaction in a virtual ball-tossing game and a penalty kicking paradigm in virtual reality. We expected that ADHD patients, in comparison to healthy controls, to show weaker emotional reactions to pleasant events, stronger emotional reactions to unpleasant events, and worse emotion regulation capabilities.

We applied cyber ball and a virtual penalty kicking paradigm to 22 adult ADHD patients and 23 healthy controls. Participants were instructed to respond naturally vs. explicitly show vs. hide their emotional reactions to the respective game. We assessed emotional reactions on an explicit (valence and arousal ratings, PANAS scores) and an implicit level (facial muscle activity, skin conductance).

Compared to controls, patients reported slightly stronger negative and lower positive affect in response to unpleasant respectively pleasant events, and showed lower M. zygomaticus activations and lower skin conductance responses to pleasant events. Regulating emotions in some experimental conditions evoked increased M. corrugator and decreased M. zygomaticus activations in patients vs. controls. Interestingly, we found lower baseline skin conductance levels in patients vs. controls.

Patients responded stronger to unpleasant and weaker to pleasant events than healthy controls both explicitly and implicitly and showed weaker peripheral physiological arousal at baseline.

Unexpectedly, regulation of emotions did not lead to differences in emotional experience in patients vs. controls. The higher corrugator activations might be interpreted as higher effort that patients spent on the regulation task.

**Botrel, L. Blankertz, B., Kübler, A. *Trainings and predictors for performance in a brain-computer interface controlled by sensorimotor rhythms***

Psychological predictors such as ability to concentrate and visuomotor coordination abilities have been shown to predict performance in a sensorimotor-rhythms based brain-computer interface (SMR BCI). Following a pre-post design, we randomly affected 39 healthy participants to an intervention training: relaxation intervention(RL), visuomotor coordination(VM) or book reading(BR) during 4 sessions of 23 minutes on consecutive days(1-4). The performance in SMR BCI was first measured beforehand on day 1 and after all training sessions on day 5. Results indicated an increase in performance between pre and post conditions but no effect

of intervention. Psychological variables correlated with post BCI performance: self-efficacy(+), self-regulation(-), post state-mindfulness scale(+) and visuomotor coordination precision(+).

Although no effect on performance followed repeated training, the predictor visuomotor coordination precision ("Critical mean duration") from previous studies was replicated, also, the new predictors found in this study display a possible relationship between BCI performance and perception and regulation of self.

**Cabello, V., Groma, M., Schmitt, A.G., Fischer, M. *Animal model for Coffin-Lowry syndrome: function of Rsk2 in Adult Neurogenesis and Behavior***

Loss-of-function mutations in the RPS6KA3 gene, which encodes Ribosomal s6 kinase 2 (Rsk2), cause Coffin-Lowry syndrome (CLS), an X-linked mental retardation syndrome. Rsk2 knockout (KO) mice have been created as an animal model to study human CLS and present spatial learning and fear conditioning deficits. The Rsk2 protein has been shown to be relevant for the birth of new neurons in the developing brain. Hippocampal adult neurogenesis (AN), generation of new neurons in the adult hippocampus, influences learning and memory processing. Our main goal is to investigate how Rsk2 deficiency affects hippocampal AN, anxiety- and depression-like behaviour, locomotor activity and impulsivity in this mouse model.

For the AN study, quantitative immunohistochemistry with antibodies detecting DCX, MCM2 and BrdU followed by stereological analysis using the StereoInvestigator software was performed. Using these three different AN markers we could not detect significant differences in stem cell proliferation, immature neurons and 28 days survived cells in the dentate gyrus of the two Rsk2 genotypes.

Applying different behavioural tests we found similar performances of Rsk2 KO and wildtype mice in Open Field Test and Elevated Plus Maze. But, in Light/Dark Box and Porsolt Swim Test, Rsk2 KO mice showed increased locomotor activity. Following these results, we decided to explore more in detail the behaviour of these mice by using the IntelliCage (NewBehaviour), device designed for long term investigations of mouse behaviour in a social context. Test of sucrose preference to reveal anhedonia-like behaviour, were performed in the IntelliCage. The results showed a significant preference for sucrose of Rsk2 KO. HPLC results shown and increase Dopamine metabolite in Rsk2-KO compared with Rsk2-WT, which could explain the hyperactivity behavior. Results of IntelliCage and Porsolt Test seem to indicate a hedonic behaviour and possible resistance for depression in Rsk2-KO compared with Rsk2-WT mice.

**Candemir, E., Kollert, L., Freudenberg, F., Reif, A. *Interaction of NOS1AP with the NOS I PDZ domain and its effects on dendritic morphology***

Schizophrenia is a severe mental disorder that is characterized by a variety of symptoms including hallucinations, delusions and disorganized thoughts. Neuronal nitric oxide synthase (NOS-I) and its adaptor protein (NOS1AP) have repeatedly and consistently been associated with schizophrenia. NOS1AP competes with PSD95 for

interaction with the NOS I PDZ domain and disruption of the NOS-I/PSD-95 interaction is required for coupling of N-methyl-D-aspartate receptor (NMDAR) mediated Ca<sup>2+</sup> influx and NOS I enzymatic activity. The disruption of NMDAR/ NOS-I/PSD-95 complex has been shown to result in altered neuronal development and morphology, especially at the cortical and the limbic areas.

In this study, we aimed to explore the involvement of the NOS1AP/ NOS I PDZ interaction in dendritic development. We have disrupted the interaction of PSD95 with NOS-I by rAAV-based overexpression of different NOS1AP isoforms and observed the consequences on dendrite/spine development in fluorescently labelled primary neuron cultures from mice hippocampus and cortex. Even though the overexpression of NOS1AP isoforms caused a mild effect on dendritic development, it resulted in highly disturbed dendritic spine development. In neurons overexpressing different NOS1AP isoforms (especially the ones having the PTB domain), we have observed excessive growth of filopodia and decreased number of mature spines, which is an important neuropathological feature observed in the post-mortem brains from schizophrenia patients. Our findings clearly state the involvement of NOS1AP domains in the regulation of spine development and also point out that this regulation might require additional proteins interacting with NOS1AP.

As future direction, disruption of NOS1AP/ NOS I PDZ interaction will be investigated in the selected areas of mice brain in order to understand whether it results in behavioral phenotypes related to schizophrenia and its comorbidities.

### **Eidel, M. Kleih, S., Kübler, A. *Psychophysiological correlates of coping and quality of life in patients with chronic diseases***

Chronic Obstructive Pulmonary Disease (COPD) is known to have a substantial impact on quality of life (QoL). Models of coping suggest that patients with chronic diseases reporting low QoL should show facilitated access to disease-related words. In a recent EEG study, a reduced N400 amplitude within an unpredictable disease-related context was shown to correlate with this facilitated lexical access in patients with ALS. This method may now be applied to COPD and other diseases.

### **Flohr, E.L.R., Andreatta, M., Gromer, D., Mühlberger, A., Pauli, P. *On the Influence of Smells on Heart Rate and Different Measures of Social Interaction***

The sense of smell is the oldest sense in the development of the human race. Apart from the influence of human pheromones, an impact of purely olfactory cues on social interaction has been shown. Namely, pleasant odors are known to alter prosocial behavior and perceived attractiveness. Additionally, unpleasant odors are associated with negative personality traits.

A virtual reality paradigm has been established in order to measure the influence of odors of different valence on social interaction in a realistic environment. Three virtual office rooms and three virtual agents were used in a blocked design. Two rooms and one agent were used in the “context” block, in which a pleasant and an unpleasant odor were associated with one of the rooms. In the “social” block, one

room and two agents were used to associate the pleasant vs. unpleasant odor with the agents.

In a first experiment (n = 31), explicit ratings of sympathy and active withdrawal behavior from the agents in the rooms were assessed. In a second study (n = 29), we examined the amount of money participants offered to agents in a pleasant vs. unpleasant olfactory context. In both experiments, heart rate and skin conductance level were recorded.

Agents in an unpleasant olfactory context were rated as less likable than agents in a pleasant olfactory context. This effect was larger in the social than in the contextual block. Additionally, pairing with unpleasant odors led to a decrease in the difference between emotional facial expressions. Participants spent more time withdrawing from agents in an unpleasant olfactory context, whereas no difference was found for the actual distance. Besides, agents in an unpleasant olfactory context were offered less money. No effects were found on skin conductance level. For heart rate changes, it was shown that unpleasant odors led to a smaller increase while participants approached the agents in the rooms.

Taken together, we were able to draw a detailed picture on the influence of hedonic odors on different measures of social interaction. Explicit variables were partly reflected on the implicit level.

### **Genheimer, H., Andreatta, M., Asan, E., Pauli, P. *Extinction and Return of Fear: Does Vagus Nerve Stimulation reduce Anxiety?***

The investigation and facilitation of fear extinction is essential to decrease reinstatement in anxiety patients. An animal study demonstrated facilitation of fear extinction through vagus nerve stimulation. Here, we aimed to transfer these findings to humans.

Seventy-five healthy participants underwent contextual fear conditioning. During acquisition (Day1), participants perceived electric shocks (unconditioned stimuli, US) unpredictably when guided through one virtual office (anxiety context, CXT+) but never through another (safety context, CXT-). During extinction (Day2), no US was delivered. One group of participants received t-VNS, one sham and one no stimulation at all. On Day3, participants perceived three US for reinstatement, which was followed by a test phase.

After acquisition, participants showed startle potentiation to CXT+ compared to CXT-, which disappeared after extinction. Lower valence, higher arousal and anxiety ratings in CXT+ after Day1 and Day2 indicated successful conditioning but weak extinction. On psychophysiological level, all groups showed fear reinstatement to both contexts.

Fear extinction combined with t-VNS was expected to increase neuronal plasticity in brain areas involved in extinction learning and reduction of reinstatement. In line, we found slight attenuation of startle response in the t-VNS group. However, the results demand further research on the impact and clinical consequences of t-VNS.

**Ghafoor, H., Schulz, S.M., Pauli, P. *Emotional Intelligence (EI) as a Predictor of Quality of Life (QoL) in Chronic Heart Failure: A Cross-cultural study***

Chronic Heart Failure (CHF) is found highly comorbid with anxiety and poor Quality of life (QoL). Emotional Intelligence (EI) helps to buffer distress caused by anxiety & CHF by regulating emotions, thus improves QoL. However, emotional regulation preferences are highly influenced by both culture and emotional intelligence. On the other hand, Polyvagal theory posits that parasympathetically mediated vagal tone supports emotional expression and regulation through its neural connection with peripheral structures. The planned research will be comprised of two studies. In Study 1, a cross-cultural questionnaire based assessment is planned to assess 200 CHF patients in Germany and Pakistan. We expect a positive correlation between EI and QoL. In study II, an experimental randomized controlled design will examine immediate effects of EI based coping strategies (ER) vs Vagal stimulation in CHF patients. Our findings will help to identify cultural variations in development and maintenance of CHF-related distress. It may help to increase our understanding on how to improve quality of life using psychological and biopsychological interventions, such as Emotional regulation and vagus nerve stimulation (culture independent) resulting in increased heart rate variability. It may also enhance culture competence to remove health disparities within and between countries.

**Gromer, D., *psymisc: An R package for facilitating data analysis of factorial experiments***

psymisc is an R package that provides a set of convenient functions for recurring tasks in data analysis of factorial experiments.

Results of statistical analyses are typically reported according to the guidelines of the American Psychological Association, which describe how the results of, for example, a t-test should be presented in a manuscript. Hence the researcher has to extract the information from outputs generated by statistical software, which is both time-consuming and prone to mistakes. The schoRsch package for R introduced functions that directly format the results of statistical analyses according to the aforementioned guidelines. The psymisc package extends this approach by providing not only the possibility to format results, but also to export to different output formats (e.g. Word docx, LaTeX).

Furthermore, the package includes functions for obtaining summary statistics (mean, standard deviation, etc.) of factorial experiments using a simple formula interface, either in a tabular format or as plots. These functions facilitate the workflow compared to base R methods.

Additional features include an interface for variable recoding, calculation of Cohen's d effect size from different input parameters, outlier detection and removal, and highlighting of significant differences between groups directly upon plot production.

**Haspert, V., Reicherts, P., Pauli, P., Wieser, M.J. *Regulation of pain with cognitive strategies: Acceptance vs. Reappraisal vs. Suppression***

The effectiveness of the regulation strategies such as Acceptance, Reappraisal and Suppression in decreasing negative emotions as well as subjective and physiological pain experiences have been shown in previous studies. Results so far suggest that Reappraisal and Acceptance are more effective than Suppression. However, only few studies in the field of pain regulation are available that compared two of these strategies and even no study exists that compared all three strategies. The main goal of the outlined project is to compare these three strategies with each other and in addition to provide a control condition. Previous studies indicated that suppression might lead to increased pain perception when the pain stimulus is long. In our project, the pain stimuli are going to be either longer heat pain stimuli or brief electric shocks in order to compare the strategies in the context of different pain types and lengths. The pain stimulus will be adjusted for each participant on the basis of the individual pain threshold. Participants will be instructed about the use of each regulation strategy and the control condition and practice each condition before the actual experiment. A cue will be presented during each trial on the screen indicating the respective strategy, followed by the pain stimulus. After each trial, pain intensity and unpleasantness ratings will be gathered. Additionally, physiological correlates of pain (regulation) such as heart rate (ECG), skin conductance response (SCR) and somatosensory evoked potentials (SEP) will be conducted. Our goal is to examine whether there are strategy differences in the effectiveness of regulating pain perception that depend on the stimulus length.

**Kim, J. S., *Philosophy as Therapy – Spinoza’s theory of emotion***

Today, Spinoza is regarded as one of the most influential philosophers who are deeply concerned with the problem of emotions. Unlike most modern philosophers who analyze merely theoretical what emotion is, he conceived the idea that philosophy should be a kind of therapy. According to him, human freedom can be achieved if we can control our emotions. In my short talk I will present some fundamental thoughts of his theory of emotion and try to show how we can change our own emotions.

**Neueder, D., Andreatta, M., Blum, R., Deckert, J., Pauli, P. *Overgeneralization of context conditioned fear in human CB1-polymorphism***

Sustained anxiety and overgeneralization of fear are a crucial in the etiology and maintenance of many anxiety disorders. Recently, the influence of the cannabinoid receptor 1 gene (CNR1) on impaired extinction of conditioned fear has been demonstrated.

To investigate the impact of CNR1 variants on generalization processes participants were genotyped for the functional CNR1 rs2180619 polymorphism and underwent a contextual fear conditioning and generalization paradigm in virtual reality (VR).

During acquisition, one virtual office room (anxiety context, CXT+) was paired with an unpredictable electric stimulus (unconditioned stimulus, US), whereas another virtual office room was never paired with the US (safety context, CXT-). During generalization, three additional generalization contexts were presented, creating a continuum of similarity between the anxiety and the safety context. To assess fear responses, we recorded fear potentiated startle, skin conductance response and subjective ratings.

Preliminary results in ratings demonstrated successful acquisition of contextual fear indicated by more negative valence, higher arousal and anxiety and higher US-CTX+ contingency ratings for the anxiety versus the safety context in G-allele carriers, but only marginally differentiations in A/A homozygotes in these variables.

After generalization, response gradients in ratings displayed the grade of similarity of the generalization contexts between the anxiety and the safety context independently from genotype.

Thus, the paradigm seems appropriate to investigate generalization of contextual anxiety further.

### **Ramirez Pasos, U., Volkman, J. *Analysis of Single Unit, LFP, and EEG Activity in the Human Subthalamic Nucleus during Presentation of Emotional Visual and Acoustic Stimuli***

The human subthalamic nucleus (STN) has been in recent years divided into three functional zones involved in limbic, associative, and motor processing in the anterior, mid, and posterior regions respectively (Lambert et al, 2012) and is therefore considered to be part of the limbic system. The limbic territory receives prefrontal-subthalamic inputs in primates via the hyperdirect pathway (Haynes, 2013), specifically from the ventromedial prefrontal cortex (vmPFC), orbitofrontal cortex (OFC), and dorsal anterior cingulate cortex (dACC). In order to probe whether the STN codes emotional stimuli differentially according to sensory modality, we will analyze single unit, LFP, and EEG data from intraoperative microelectrode recordings and implanted PC+S (Medtronic) recordings extracted from Parkinsonian patients during trials involving emotional picture and digital sound presentation. Due to limbic connectivity via the hyperdirect pathway, we expect STN activity to be modulated by stimuli rated as highly arousing, with negative valence stimuli triggering a lower activation due to amygdalar dysfunction in Parkinsons disease.

### **Schartner, C., Weber, H., Kollert, S., Wischmeyer, E., Kent, L., Domschke, K., Deckert, J., Reif, A. *Allelic variations in Corticotropin-Releasing Hormone Receptor 1 changes receptor activity by alternative splicing***

The corticotropin releasing hormone receptor 1 (CRHR1) is a major regulator of the hypothalamic-pituitary-adrenal (HPA) axis and thus a crucial regulator of the stress

response. The CRHR1 gene encodes a G-coupled receptor with highest affinity for CRF in the pituitary gland and directs the release of ACTH, which again controls the release of cortisol from the adrenal gland. Variations of CRHR1 gene are associated with several psychiatric disorders including mood and anxiety disorders. In a previous study, we found the minor allele of CRHR1's SNP rs17689918 to be associated with panic disorder accompanied by increased ASI and ACQ sum scores for risk allele carriers. In a sample of human post mortem brain tissue, risk allele carriers showed reduced mRNA expression of CRHR1 in amygdalae and forebrains, but not in midbrains. Here, we characterized the role of rs17689918 in regulation of CRHR1 expression and its contribution to panic disorder.

In silico analyses of rs17689918 and its proxy SNPs were conducted to investigate possible changes in binding sequences for transcription factors, splice enhancer/silencer or binding sites for other regulatory elements. Expression analyses of transcript variations were performed with quantitative real-time PCR (qPCR). Further characterization of transcripts variants were assessed by in vitro transcription of relevant transcript variants in oocytes of *Xenopus laevis* followed by electrophysiological characterization.

Functional prediction revealed 89 perfect proxy SNPs of rs17689918 mainly located in CRHR1 intron regions or intergenic regions towards neighboring genes C17orf69, IMP5 and MAPT. Intronic SNPs were further analyzed for changes in neuron-specific splicing enhancer or silencer sites and 21 were found to change predicted binding sites for either enhancer or silencer. Further 29 SNPs alter recognition sequences for neuron-relevant transcription factor binding sites. Expression analyses of CRHR1 transcript variants revealed an increased expression of transcript variant 1c and 5 in risk allele carriers in forebrain of a post-mortem brain tissue sample, whereas transcript variant 1b was significantly decreased in risk allele carriers. Electrophysiological recordings were performed to investigate possible changes in receptor activities of transcript variant 5/MGC57346-CRHR1 readthrough compared to transcript variant 1b and 1c.

Our analyses reveal a shift of proportions of transcript variants in dependence on allelic variation of CRHR1 SNP rs17689918 in forebrain. Risk allele carriers show a higher proportion of transcript isoform 5 - a readthrough from upstream pseudogene MGC57346 - compared to non-risk allele carriers. However, whether this effect is solely caused by rs17689918 or a combination of several functional relevant proxy SNPs remains unsolved. The changes in functionality for isoform 5 might have direct consequences for CRHR1 functionality and by this for the HPA-axis in risk allele carriers. Taken together, we found a functional variation in the CRHR1 gene which has direct consequences on receptor activity and by this might cause changes in stress response and eventually contribute to the pathophysiology of Panic Disorder.

**Söhnchen, B., Kastner, A.K., Flohr, E.L.R., Wieser, M.J., Pauli, P. *Follow the eyes – Influence of Emotional Expression on Visuospatial Attention***

Perceived gaze direction has been shown to introduce shifts in visuospatial attention. The present study investigated reaction times (RTs) and event-related potentials (ERPs) during those gaze-cued shifts. In addition context conditioning was used to induce a threatening context. During a learning phase participants learned to associate one ambient light color with the possible occurrence of an unpleasant burst of white noise. In the testing phase participants had to conduct a simple target detection task, where target probes were presented on the left or right side of a screen. Prior to the target presentation, a cue stimulus was displayed at central fixation. The cue consisted of various faces, gazing to the left or to the right. Additionally, the facial expression varied and was either neutral, angry, or fearful. Behavioral results show the expected congruency effect for fearful faces, independent of the context. In other words participants were faster when gaze direction and target location were congruent. The opposite effect was observed for angry expressions. Here participants were faster in the incongruent trials, but only in the threatening context. Electrophysiological results show that the N2pc component, an ERP associated with spatial shifts in attention, was significantly modulated by emotional expression and gaze-target congruency. For neutral faces N2pc difference scores were higher in congruent, than in incongruent trials. This was the other way around for trials with angry faces. To conclude, emotional expression influences shifts in visuospatial attention. However, the effect differs between expressions and is in some cases context dependent.

**This is the end, beautiful friend  
This is the end, my only friend, the end  
Of our elaborate plans, the end  
Of everything that stands, the end  
No safety or surprise, the end [...]**

**(The Doors)**