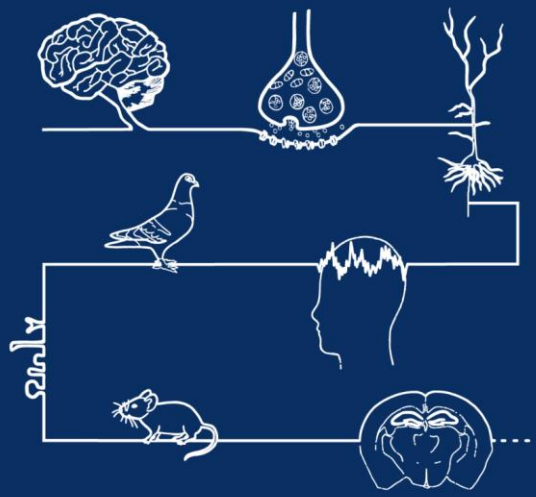
UNIVERSITÄT OSNABRÜCK

9th Westerberger Herbsttagung
on the
Perspectives of Molecular Neurobiology

"Psychological and biological aspects of explicit and implicit memory"

Thursday, September 27, 2018

Bohnenkamp-Haus,
Botanical Garden of the University of Osnabrück



Onur Güntürkün
(Bochum)

Manfred Hallschmid
(Tübingen)

Ron de Kloet
(Leiden, Netherlands)

Johanna Kißler
(Bielefeld)

Hannelore Ehrenreich
(Göttingen)

André Fischer
(Göttingen)

Tobias Navarro Schröder
(Trondheim, Norway)

Oliver Ambrée
(Osnabrück)

Martin I. Antov
(Osnabrück)

Marina Rierola
(Osnabrück)

Organizing Committee:
Lidia Bakota, Roland Brandt, Thomas Gruber, Roman Osinsky, Ursula Stockhorst, Chadi Touma

For further information, visit: http://www.neurobiologie.uni-osnabrueck.de/ *Contact: brandt@biologie.uni-osnabrueck.de*

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Introduction

The '*Westerberger Herbsttagung on the Perspectives of Molecular Neurobiology*' takes place already the ninth time since the founding of the Department of Neurobiology at the University of Osnabrück and has become a local tradition. Aim of the symposium series is to bring together an international group of neuroscientists for one day on the Westerberg Science Campus for intense discussions on a special topic. Booklets of the past meetings are available on the homepage of the Department (www. neurobiologie.uni-osnabrueck.de).

This time, the '*Westerberger Herbsttagung*' is organized together with members of the Department of Behavioural Biology and the Institute of Psychology and aims to foster a transdisciplinary discussion between biologists and psychologists on "Psychological and biological aspects of explicit and implicit memory". The conference is supported by the University of Osnabrück as part of a strategy process to promote interdisciplinary research projects.

Following up on the tradition of the previous Westerberg symposia, we were again able to convince high profile speakers from different research institutions in Germany and abroad to come together in Osnabrück and share their latest results and conceptional views in six keynote lectures. The three sessions on "Mechanisms of Memory", "Stress and Memory" and "From Bench to Bedside" comprise also four shorter so-called 'progress talks', where PhD students and postdocs give insights into their ongoing projects fresh from the lab bench. The symposium is complemented by a poster session, where young scientists display some of their current research projects to explain and discuss them with our guests.

The organizers from the Institute of Psychology (T. Gruber, R. Osinsky, U. Stockhorst) and the Departments of Behavioral Biology (C. Touma) and Neurobiology (L. Bakota and myself) are looking forward to an exciting meeting. We are all convinced that an interdisciplinary collaboration of biologists and psychologists promises novel insights and promotes the development of new approaches, especially in the transfer of results from basic psychological and biological research for a better understanding and treatment of psychiatric and neurological diseases.

I would like to thank everybody who made this meeting possible, especially the members of the organizational committee, who assembled the scientific program. In addition, I would like to thank Henning Borgstädde, Bettina Flenker, Beate Grimmelsmann, Dr. Wilfried Hamann, Vanessa Herkenhoff, and the doctoral students of our Department for their invaluable help in booking hotels, choosing the buffet, organizing the poster session, preparing coffee, editing the booklet, and creating the poster. I would also like to take the opportunity to thank our sponsors Diagonal GmbH&Co. KG, Carl Roth GmbH&Co. KG, Ewald Innovationstechnik GmbH, Macherey-Nagel GmbH&Co. KG, Serva Electrophortesis GmbH for their continuous support.

Of course, a special thank goes to all speakers for coming to Osnabrück and for contributing to an exciting meeting on "Psychological and biological aspects of explicit and implicit memory".

Roland Brandt

(Director of the Department of Neurobiology,
School of Biology/Chemistry, University of Osnabrück)

Program

9:00 Opening and Welcome address: R. Brandt (University of Osnabrück)

Session I: Mechanisms of memory (Chair: U. Stockhorst and T. Gruber)

9:15 Keynote lecture 1: O. Güntürkün (Bochum): „*The avian extinction network*"

9:45 Keynote lecture 2: J. Kißler (Bielefeld): "*Effects of medial temporal lobe resections on the visual processing of negative stimuli*"

10:15 Progress talk 1: T. Navarro Schröder (Trondheim, Norway): "*Electrophysiological markers of grid cell population activity across species*"

10:30 Progress talk 2: M. Rierola (Neurobiology, Osnabrück): "*Tau in neuronal signalization*"

10:45 Coffee Break

Session II: Stress and memory (Chair: C. Touma and R. Osinsky)

11:15 Keynote lecture 3: R. de Kloet (Leiden, The Netherlands): "*Significance of stress hormones for bio-psychological research*"

11:45 Keynote lecture 4: M. Hallschmid (Tübingen): „*Metabolic contributions to memory function*"

12:15 Progress talk 3: M. Antov (Experimental Psychology II and Biological Psychology, Osnabrück): „*Fear circuitry and beyond: Plasticity and the human visual cortex in fear conditioning*"

12:30 Progress talk 4: O. Ambrée (Behavioural Biology, Osnabrück): *"Immune mediated consequences of psychosocial stress and stress reactivity on emotional behavior"*

12:45 Lunch buffet, Coffee and Poster session

Session III: From bench to bedside (Chair: L. Bakota and R. Brandt)

15:00 Keynote lecture 5: A. Fischer (Göttingen): "*Epigenetic mechanisms of memory function in health and disease*"

15:30 Keynote lecture 6: H. Ehrenreich (Göttingen): "*Erythropoietin for treating cognitive dysfunction in neuropsychiatric disease: From man to mouse and back*"

16:00 Concluding Remarks, Closing, End of Meeting, Coffee

16:15 Panel Discussion on Research Perspectives (Speakers of key lectures and organizers)

Organizing Committee: Lidia Bakota, Roland Brandt, Thomas Gruber, Roman Osinsky, Ursula Stockhorst, Chadi Touma

List of Posters

Poster #01	**Does microtubule-associated protein tau affect Long Term Potentiation in the hippocampus?**	Nânci Monteiro Abreu
Poster #02	**Structural and functional alterations of the hippocampus and cognitive decline in SAPAP4-deficient mice**	Mariya Hrynchak
Poster #03	**Amyloid-beta effect on dendritic spines of hippocampal neurons: what happens if tau is not present?**	Marina Rierola
Poster #04	**Alterations of long-term potentiation in the hippocampus of mice selected for extremes in stress reactivity**	Julian Rottschäfer
Poster #05	**Late-onset cognitive impairments after early-life stress are shaped by inherited differences in stress reactivity**	Silja McIlwrick
Poster #06	**Mitochondria & Mood: can mitochondrial dysfunction and oxidative stress bridge emotional and metabolic disturbances?**	Virginie Rappeneau
Poster #07	**Social phobia, skin temperature and social recognition in men and mice**	Jan Seidel
Poster #08	**Low 17β-estradiol status is associated with stronger fear recall and impaired extinction recall: Evidence from prefrontal oscillations**	Philipp Bierwirth
Poster #09	**Embodied emotion: Role of sex hormones and first-wave stress in emotions components**	Dali Gamsakhurdashvili
Poster #10	**Emotional modulation of picture-, face- and word- evoked ERPs following right temporal lobe resection – an ongoing EEG study**	Malena Mielke
Poster #11	**Effects of right temporal lobe resection on visual emotion processing: An ongoing fMRI study**	Lea Marie Stieghorst
Poster #12	**Cortical oscillations during successful retention in human working memory**	Sebastian Graetz
Poster #13	**Library for Universal Virtual Realty Experiments: luVRe**	Benjamin Schöne
Poster #14	**Dual Realities, One Process: Mnemonic Mechanisms Underlying Virtual Reality**	Joanna Kisker

Poster #15	**Debunking the monkey: Sustained inattentional blindness in virtual reality and under conventional laboratory conditions**	Benjamin Schöne
Poster #16	**Electrophysiological correlates of gist perception: A steady state visually evoked potentials study**	Elise L. Radtke
Poster #17	**Reinforcement learning signals and the integrated value of immediate and future action outcomes**	Lena Rommerskirchen, Leon Lange

Keynote Lectures

Keynote Lecture #01

The Avian Extinction Network

Onur Güntürkün

Biopsychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, 44780 Bochum, Germany

Most studies on the neural basis of extinction learning stem from fear conditioning experiments in rodents. This thorough, but also narrow view on the mechanisms of extinction creates the possible illusion that (1) we pretty much know the entire extinction network in the brain, and (2) understood most of its mechanisms. I'm convinced that this is wrong. To have a deeper understanding on the variant and the invariant mechanisms of extinction, we also have to study this phenomenon in a radically different model organism. To this end, we study in my lab the neural fundaments of extinction of appetitive conditioning in pigeons in complex designs that permit to analyze the neural events governing acquisition, extinction and renewal along the full time frame. In my talk, I aim to present results on key events and interactions between areas at the cellular and at the overall systems level. These data show that extinction learning alters the functional properties of a large number of different brain areas.

Effects of medial temporal lobe resections on the visual processing of negative stimuli

Johanna Kißler

Department of Psychology and Center of Excellence "Cognitive Interaction Technology" CITEC, University of Bielefeld, Postfach 100 131, 33501 Bielefeld, Germany

Medial temporal lobe regions, in particular the amygdala, are thought vital for enhanced attention allocation to and subsequent memory of emotional stimuli. However, much of the extant evidence in humans is correlational rather than causal. My presentation will firstly introduce standard findings and models on the role of the medial temporal lobes (MTL) in emotion and memory and the surrounding controversies and then focus on an ongoing project in our group. This project combines a lesion model with electrophysiology and hemodynamic neuroimaging to address the causal role of these structures in emotion and memory processing. In particular, we test the impact of unilateral MTL resections on functional magnetic neuroimaging and electrophysiological (EPN: Early Posterior Negativity; LPP: Late Positive Potential) responses to negative and neutral pictures, faces, and words as well as their subsequent recognition and emotional appraisal.

FMRI data from so far 15 patients with right medial temporal lobe resections comprising amygdala and hippocampus reveal widespread reduced visual cortex activation in patients compared to age and gender-matched healthy controls, regardless of emotional content of the stimuli. Reductions are particularly pronounced for pictorial stimuli. Emotion-specific reduction is also observed, particularly ipsilesionally for fearful faces. However, EEG event-related potential data obtained from the same participants reveal the presence of typical EPN and LPP emotion modulations, although these appear more variable and descriptively smaller than in controls. Strikingly, in patients the LPP response is dramatically reduced compared to controls, regardless of its modulation by emotional stimulus content. The data pattern suggests both MTL-dependent and independent generator for emotional ERP enhancements.

Finally, behavioral assessment including additional data from 11 patients with left medial temporal lobe resection unsurprisingly reveals overall reduced recognition performance in the patient groups. Following right-sided resection emotional memory enhancement is reduced for pictures and faces, whereas it is intact for pictures, but not for faces and words following left-hemispheric resection. Regarding emotional appraisal, unlike controls, both patient groups showed undifferentiated valence ratings for fearful compared with neutral faces, whereas arousal ratings did not differ between groups.

These findings contribute to a more detailed mechanistic picture and provide direct causal evidence on the role of amygdala and hippocampus in emotion and memory, revealing some emotion- and stimulus-specific, but also several domain general effects.

Keynote Lecture #03

Significance of Stress Hormones for Bio-psychological Research

Ron de Kloet,

Dep. of Endocrinology, Leiden University Medical Center, Leiden, The Netherlands

One of the challenges in stress research is to identify the mechanism underlying individual differences in stress-adaptation and coping. Another equally important quest is to understand how the switch occurs from protective to harmful actions of stress hormones, if coping with stress fails. Also, the issue of early life programming of stress- and fear circuitry is a hot topic. To make progress, it is pertinent to examine information processing all the way from the perception of the stressor until the organization of behavioural and physiological adaptations. The latter responses are coordinated by the sympathetic nervous system and the hypothalamus-pituitary-adrenal (HPA) axis with its glucocorticoid endproducts cortisol and corticosterone. These stress hormones exert feedback action precisely on the circuits that have initially triggered the stress response, while causing a profound modulation of cognitive processes linked to e.g. fearful, reward, motivational and resilient behaviour. In this contribution I will discuss:

1. How cortisol measurements contribute to understanding the stress response system. This concerns the analysis of ultradian rhythmicity important for the responsivity of the stress response system as well as the dynamics of stress-induced HPA-axis activation.
2. How the localization and properties of cortisol receptor types in brain may help to understand the different phases in information processing. This starts with the significance of mineralocorticoid receptors (MRs) for attention/vigilance, appraisal processes, selection of coping style, learning and retrieval of information to defend the 'self'. Subsequently, with rising cortisol levels glucocorticoid receptors (GRs) become activated causing a shift in energy allocation from salient towards executive circuitry engaged in 'rationalization, contextualization and recovery' from the stressor. Then, in a longer time frame, GR-mediated actions promote 'memory storage' of the experience, while priming brain circuitry for future threats.
3. How early life experience tunes the stress response system for later life; how the brain changes during transition from acute to chronic stress experience; and how pharmacological interventions of MR and GR functions are capable to reset information processing and the stress response system are important research questions also. To examine such questions translational studies are invaluable, not only from a mechanistic point of view, but also for testing preventive and curative strategies in the treatment of stress-related disorders.

Selected reading

de Kloet ER, Joëls M, Holsboer F. Stress and the brain: from adaptation to disease. *Nat Rev Neurosci*. 2005 Jun;6(6):463-75.
Joëls M, Karst H, Sarabdjitsingh RA The stressed brain of humans and rodents. *Acta Physiol (Oxf).* 2018 Jun;223(2):e13066. doi: 10.1111/apha.13066.
de Kloet ER, Meijer OC, de Nicola AF, de Rijk RH, Joëls M. Importance of the brain corticosteroid receptor balance in metaplasticity, cognitive performance and neuro-inflammation. *Front Neuroendocrinol*. 2018 Apr;49:124-145.

Metabolic contributions to memory function

Manfred Hallschmid, PhD

Department of Medical Psychology and Behavioral Neurobiology, University of Tuebingen, Germany;
German Center for Diabetes Research (DZD), Tuebingen, Germany;
Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tuebingen (IDM), Tuebingen, Germany

Central nervous control of energy turnover and metabolism relies on the input of endocrine messengers from the periphery, including the pancreatic hormone insulin. The hypothalamic hormone oxytocin, a regulator of parturition and lactation, is known for its effects on psychosocial function. Recent studies indicate that insulin improves higher cognitive processes and, in particular, memory function, and that oxytocin contributes to the control of food intake and metabolism. In a series of experiments using the intranasal route of administration, which bypasses the blood-brain barrier and delivers neuropeptides to the brain compartment in the relative absence of peripheral uptake, we have investigated the effects of insulin and oxytocin on metabolic as well as cognitive parameters. We demonstrate that intranasal insulin not only decreases food intake in healthy humans by acting on brain structures with relevance for eating behavior, but also improves declarative memory. Oxytocin administered via the nose curbs calorie intake and moreover enhances glucose homeostasis by increasing beta-cell responsivity and glucose tolerance.
These and related results demonstrate that endocrine signals involved in metabolic control and, respectively, higher cognitive function influence domains that extend beyond their “traditional” targets, thereby linking metabolic control and higher brain function. Further metabolic signals with such “dual” roles include the peptide hormone ghrelin from the gastrointestinal tract, the adipokine leptin and the incretin glucagon-like peptide 1. Research into the cognitive effects of these metabolic messengers appears of particular relevance when considering epidemiological findings that suggest a link between cognitive dysfunctions and metabolic impairments like obesity and diabetes. Against this background, beneficial acute and long-term effects of metabolic factors obtained in preclinical experiments might also bode well for potential clinical applications.

Keynote Lecture #05

Epigenetic mechanisms of memory function in health and disease

Andre Fischer

Dep. for Systems Medicine and Epigenetics, German Center for Neurodegenerative Disease (DZNE), Göttingen
University Medical Center (UMG), Göttingen, Von Siebold Str. 3A, 37075 Göttingen
Germany

The pathogenesis of multifactorial brain diseases is driven by complex interactions of genetic and environmental risk factors. Such genome-environment interactions are regulated by epigenetic processes. In this presentation we will discuss published and unpublished data showing that changes in epigenetic gene-expression underlie the pathogenesis of neuropsychiatric diseases such as schizophrenia and neurodegenerative diseases such as Alzheimer's disease.

Erythropoietin for treating cognitive dysfunction in neuropsychiatric disease: From man to mouse and back

Hannelore Ehrenreich

Clinical Neuroscience, Max Planck Institute of Experimental Medicine, and DFG Research Center for Molecular Physiology of the Brain (CMPB), Göttingen, GERMANY

Executive functions, learning and attention are imperative facets of cognitive performance, affected in many neuropsychiatric disorders. In clinical studies on patient groups as different as chronic schizophrenia, chronic progressive multiple sclerosis, treatment-resistant major depression and bipolar disease, we have consistently found that recombinant human erythropoietin (EPO) lastingly improves higher cognitive functions, ranging from learning and memory to attention and speed of processing. In schizophrenia, we even measured a reduction of gray matter loss in EPO treated patients. We repeated this unexpected finding later in individuals with affective disorders. Interestingly, normal genetic variation in the EPO and EPO receptor (EPOR) genes co-determines the level of cognitive performance.

Employing mice for obtaining insight into the mechanisms of action of EPO, we showed that EPO treatment of young mice as well as EPOR overexpression in pyramidal neurons of hippocampus and cortex leads to a remarkable enduring improvement of different facets of higher cognition, together with enhanced hippocampal long-term potentiation, an electrophysiological correlate of learning and memory.

At the cellular level, we observed that a 3-week EPO treatment leads to an increase in the absolute number of pyramidal neurons and oligodendrocytes in the hippocampus by ~20%. Surprisingly, numbers of mature cells increased in the absence of cell proliferation and without decrease in apoptosis. In fact, EPO caused pre-existing precursors to differentiate into mature neurons and oligodendrocytes, unmasking this growth factor as mediator of a novel mechanism of postnatal neurogenesis and on-demand delivery of new neural cells. We have generated and start now to employ cell-type specific EPO and EPO receptor deletion mutant mice in order to delineate the cellular underpinnings of endogenous and exogenous EPO effects on cognition. Taken together, EPO acts as a potent modulator of neuroplasticity and should be exploited in novel treatment strategies for human brain diseases.

Progress Talks

Electrophysiological markers of grid cell population activity across species

Tobias Navarro Schröder

Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway

Grid cells in the rodent and human entorhinal cortex are a critical component of the brain's spatial coding system. In virtual-reality (VR) navigation tasks in humans, the fMRI BOLD signal in the entorhinal cortex exhibits hexadirectional modulations that may reflect population activity of grid cells. However, it remains unknown whether and how grid cell population activity specifically gives rise to this hexadirectional hemodynamic fMRI signal. Here we address this issue in two steps. First, we employed a VR navigation experiment using magnetoencephalography (MEG) in human participants and found hexadirectional signal modulations in the high-gamma band, source-localised to the medial temporal lobe. Next, we conducted analyses to test the relationship between grid cell activity and local field potential (LFP) recordings in freely moving rats. We found hexadirectional modulations in the same frequency band as in the human MEG navigation experiment. The orientation of this hexadirectional LFP modulation was aligned to the orientation of the hexagonally symmetric firing patterns of grid cells. Together, these findings describe new ways to measure grid cell population activity and their non-invasive source localisation using MEG. Crucially, we link grid cell activity to measures of population activity in rats and humans, thereby elucidating the physiological basis of non-invasive grid cell population measures previously revealed with fMRI. Since grid cell function is affected early in Alzheimer's disease, understanding how to measure their activity with non-invasive methods is of high clinical relevance.

Progress Talk #02

Tau in neuronal signalization

Marina Rierola, Roland Brandt, Lidia Bakota

Department of Neurobiology, University of Osnabrück, Germany

Tau is a microtubule-associated protein known to play a determining role in several neurodegenerative diseases, called tauopathies. Several attempts were made in the past years to introduce drugs or immunization methods by which the tau protein levels can be lowered or diminished. These clinical trials are ongoing without a clear understanding how the lack of tau would influence neuronal structure and function.
Here we addressed this question by using a highly accessible ex vivo model based on hippocampal slice cultures, where neurons maintain their organotypic organization. We focused on analyzing possible alterations in neuronal signalization in the absence of the tau protein using tau knockout mice (tau KO) and their controls (C57BL/6). In order to achieve that we were addressing structural aspects of dendritic spines, which represent the major excitatory postsynaptic compartments. Furthermore, we tested if structural changes have consequences on the function of neurons by analyzing electrophysiological properties.
For structural analysis, cultured hippocampal tissue was exposed to a viral vector expressing a fluorescent protein. Dendritic segments from pyramidal neurons of CA1 subfield of the hippocampus were imaged under a confocal laser scanning microscope and the micrographs were analyzed via 3D blind deconvolution and an algorithm-based program was used to determine spine parameters. Electrophysiological recordings were performed on acute hippocampal tissue slices using a microelectrode array system.
Our results show that CA1 neurons from tau KO hippocampal slices present a decreased fraction of mushroom spines compared to neurons from control mice, which results in a shift towards the fraction of immature spines. Interestingly, when human tau was introduced in tau KO hippocampal slices, we observed a recovery in the fraction of mushroom spines. We could not recapitulate this observation after treating the tissue culture with Epothilone D (EpoD), a microtubule stabilizing agent. In accordance to structural data, electrophysiological recordings showed that long-term potentiation (LTP) is also compromised in tau KO animals and it can be recovered by the presence of EpoD in an acute treatment; however, such event showed to be independent from structural changes in cultured slices.
Therefore, data suggests that the lack of tau is compromising spine morphing and negatively influences long-term memory formation with the latter being rescued by microtubule stabilization.

Fear circuitry and beyond: Plasticity and the human visual cortex in fear conditioning

Antov, Martin I.[1], Plog, Elena[1], Bierwirth, Philipp[1], Keil, Andreas[2], & Stockhorst, Ursula[1]

1 University of Osnabrück, Institute of Psychology, Experimental Psychology II and Biological Psychology
2 Department of Psychology and Center for the Study of Emotion & Attention University of Florida, Gainesville, FL, USA

Classical fear conditioning – including acquisition and extinction – is a model for studying implicit emotional memory formation, maintenance and recall in health and disease. We use fear conditioning in healthy human volunteers to study (1) stress effects on memory, (2) the influence of sex hormones, and (3) the contribution of sensory cortical mechanisms to associative memory. Reviewing our findings, we argue that also in fear conditioning (1) stress effects on memory strongly depend on the timing of stress relative to encoding and (2) interact with the hormones status of women, specifically with estradiol. Looking at the brain (3), we will make a case for studying implicit emotional memory in an extended neuronal network, beyond the amygdala, hippocampus, and prefrontal cortex. Specifically, we emphasize the importance of associative neuroplasticity in the sensory cortex.
In our recent experiment, we track trial-by-trial changes in mass-cortical activity using steady-state visually evoked potentials and show a tuning to the threat-relevant CS+ in the visual cortex. We also find that this tuning diminishes with extinction training. Furthermore, higher order visual areas show sustained changes in visual tuning 24 h after extinction. Thus, associative learning dynamically biases sensory tuning to relevant feature dimensions and some of this bias may be long-lived and resistant to extinction. Finally, we will show preliminary evidence, that stress immediately before fear acquisition may enhance the tuning to a CS+ in the visual cortex.

Progress Talk #04

Immune mediated consequences of psychosocial stress and stress reactivity on emotional behavior

Oliver Ambrée

Department of Behavioral Biology, University of Osnabrück

Dysregulation of the immune response has frequently been described in chronic stress and in stress-associated mental illness such as major depressive disorder (MDD). In rodents, enhanced circulating cytokine levels as well as altered innate immune cell numbers have been found after stress exposure. However, it is yet unclear whether specific differences in the innate immune system are associated with stress susceptibility or resilience or with individual differences in stress reactivity.
In a first experiment, we characterized peripheral and brain-invading myeloid cells by flow cytometry in stress-susceptible and resilient animals after chronic social defeat, a model of depression-like behavior and stress vulnerability. In a second experiment, we assessed myeloid cells in mouse lines that have been selectively bred for extremes in stress reactivity. These mouse lines have been shown to model endophenotypes of the psychotic and melancholic (high stress reactivity, HR) and atypical (low stress reactivity, LR) subtypes of depression, respectively.
Socially defeated mice showed reduced percentages of $CD11c^{+}$ dendritic cells (DCs) in the spleen when compared to non-defeated controls. Exclusively in susceptible mice DCs showed up-regulated expression of MHC class II and co-stimulatory CD80 molecules, pointing toward an enhanced maturation phenotype of these cells. Susceptible, but not resilient animals exhibited an increase in peripheral inflammatory $Ly6C^{hi}$ monocytes and higher numbers of spleen-derived $CD11b^{+}$ cells that produced the pro-inflammatory cytokine tumor necrosis factor (TNF) upon LPS stimulation. In the brain, cellular infiltrates of peripheral $CD45^{hi}$ $CD11b^{+}$ myeloid cells of susceptible mice contained higher percentages of $CCR2^{+}$ $Ly6C^{hi}$ monocytes representing an inflammatory phenotype. Mice of the HR and LR lines showed specific differences in similar innate immune cell subsets compared to intermediate stress reactivity (IR) control mice. HR mice presented reduced numbers of splenic DCs, however with equivalent numbers of DCs producing the T cell differentiation cytokine interleukin (IL)-12. In contrast, LR mice showed increased numbers of TNF-producing $CD11b^{+}$ cells similar to stress susceptible mice after social defeat.
Thus, we defined specific stress-related immune signatures involving conventional DCs, inflammatory $Ly6C^{hi}$ monocytes, and TNF-producing $CD11b^{+}$ myeloid cells in susceptible and resilient mice. Distinct alterations in high and low stress reactive mice might indicate altered stress vulnerability in these genetically predisposed mouse lines. Future studies will reveal how these mouse lines react to chronic stress with regard to the immune response and effects on behavior. Together, our findings suggest an impact of the innate immune system in vulnerability to stress-related disorders such as major depression. Moreover, changes in the immune system might be distinct for subtypes of major depression, which might contribute to novel personalized therapeutic approaches.

Poster Abstracts

Poster #01

Does microtubule-associated protein tau affect Long Term Potentiation in the hippocampus?

Nânci Monteiro Abreu, Abdala Ussif, Gunnar Jeserich, Roland Brandt and Lidia Bakota

Department of Neurobiology, University of Osnabrück

Alzheimer's disease is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills, and eventually the ability to carry out the simplest tasks. One of the key molecules that have been linked to the disease is the microtubule-associated protein tau since it is a principal component of the neurofibrillary tangles, which are present in neurons of the diseased brain. Given that tau plays an important role in dementia's pathogenesis and therapy, it is important to understand the physiological function of tau in the central nervous system. However, it is unknown how a protein that is primarily located in axons is involved in a disease that is believed to have a synaptic origin. To investigate a possible synaptic function of tau, we resorted to electrophysiological recordings as it allows the study of the functional connectivity-map of neuronal circuits in relation to their normal physiological function and pathological alterations.

Here we used planar titanium nitride microelectrode array (MEA) with electrodes that are 30 µm in diameter and 200 µm apart to obtain spatially distinct recordings from the *stratum radiatum* and *stratum pyramidale* of acute mouse hippocampal slices. Recordings involved input-output (IO) test, paired pulse facilitation (PPF) and theta-burst induced LTP. Input/output (I/O) tests were performed by delivering a series of increasing stimulus intensities ranging from 250 mV to 3000 mV at a time interval of 1 min. Paired pulse facilitation tests were done by delivering a pair of stimuli of the same intensity but variable interstimulus intervals ranging from 20 ms to 200 ms. LTP was induced by one train of theta burst (5 bursts of 4 pulses at 100Hz with 200 ms interval). To gain information if the presence or absence of tau protein is potentially influencing the signals elicited from the two strata slices from 3-months-old and 1-year-old B6 and TauKO male mice were analyzed.

We observed significant differences between the two genotypes, mainly in the *stratum pyramidale*, which was more pronounced in the 3-months-old group with regards to all electrophysiological tests. At this younger age group, TauKO mice showed higher responses in the *stratum pyramidale* than B6 when 1V and 1,5V were applied in the I/O test. Notably, genotype-related differences regarding the LTP were present only in the *stratum pyramidale*. Interestingly, in young animals, B6 mice were showing significantly higher potentiation as well as maintenance of the LTP signal after theta-burst stimulation, whereas in old animals the complete opposite was noticed.

The data indicate that tau has a complex effect on synapse function, which is dependent on the developmental stage of the animals.

Poster #02

Structural and functional alterations of the hippocampus and cognitive decline in SAPAP4-deficient mice

Mariya Hrynchak[1], Roland Brandt[1], Lidia Bakota[1], Claudia Schob[2], Fabio Morellini[3], Ora Ohana[4], Stefan Kindler[2]

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4Institute for Molecular and Cellular Cognition, Centre for Molecular Neurobiology Hamburg, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany

Within the PSD of excitatory brain synapses, the four members of the SAPAP family, SAPAP1-4, promote the assembly of postsynaptic signalling complexes. Mutations in human genes encoding SAPAPs (*DLGAP*1-4) have been associated with different neuropsychiatric conditions and intellectual disability. Limited information on SAPAP4 has motivated us to explore its role for the functional integrity of synapses, neuron morphology as well as the respective hippocampal neuronal circuits underlying cognitive performance by generating and characterizing SAPAP4 deficient mice.

Absence of wild-type mRNA and protein was confirmed in *Dlgap4*$^{geo/geo}$ mice via Northern and Western blot analysis, respectively. Dendritic spines and neuronal morphology of CA1 hippocampal neurons were analysed by cross-breeding *Dlgap4*$^{geo/geo}$ mice with thy1-GFP line M animals, which exhibit sparse enhanced green fluorescent protein (EGFP) labelling of hippocampal pyramidal neurons. cLSM images of dendritic segments or entire neurons were evaluated by respective software. Analysis of potential functional alterations in synaptic transmission was performed by extracellular field potential recordings from CA1 pyramidal neurons in acute hippocampal slices. Spatial memory formation was probed using Morris water maze. Thus, we observed a significant decrease in dendritic complexity of CA1 neurons, which is mainly due to the alterations occurring at the apical arbor. However, the spine density in *Dlgap4*$^{geo/geo}$ mice remained unchanged compared to *Dlgap4*$^{+}$/$^{+}$ controls (3-4 months old). Considering different type of dendritic spines, a slight but significant decrease in the fraction of stubby spines in *Dlgap4*$^{geo/geo}$ animals was observed. A closer look at the dendritic spine ultrastructure revealed a 70% increase in average PSD size in *Dlgap4*$^{geo/geo}$ animals. Despite this increase, long-term potentiation (LTP) - induced by repetitive theta-burst stimulation of the Schaffer collaterals - stayed intact, while long-term depression (LTD), induced by low-frequency stimulation, was impaired in knockout mice. At the cognitive level, mice lacking SAPAP4 protein exhibited severe cognitive deficits, as it is evident from Morris water maze test.

Taken together, our data suggest that SAPAP4 controls the development, morphology and functionality of hippocampal synapses and neurons, governs neuronal network functions and cognitive performance. These findings indicate that SAPAP4 plays a driver role in PSD assembly and remodelling and implicates *Dlgap*4 as a neurodevelopmental disorder candidate gene in humans.

Poster #03

Amyloid-beta effect on dendritic spines of hippocampal neurons: what happens if tau is not present?

Marina Rierola, Roland Brandt, Lidia Bakota

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One of the main hallmarks of Alzheimer's disease (AD) is the presence of increased concentration of amyloid-β (Aβ) species. Aβ species are formed when the amyloid precursor protein (APP) is cleaved by secretases at different positions within the protein. According to the amyloid cascade hypothesis, Aβ peptides induce changes of tau, a microtubule-associated protein, by which they trigger a neurodegenerative triad in AD consisting of: i) decreased dendritic spine density and changes in spine morphology, ii) dendritic simplification, and iii) region-specific neuronal loss. Several studies have attempted to reduce tau and, consequently, reduce the toxic outcome in AD. Therefore, we aim to investigate the effects of the absence of tau on Aβ induced changes on dendritic spine parameters.

In order to address this question, we used an ex vivo model of hippocampal slice cultures from heterozygous APPSDL animals bred on a tau knockout (KO) background, their littermates (tau KO controls) and C57BL/6 animals (tau controls). For structural analysis, cultured hippocampal tissue was exposed to a viral vector expressing a fluorescent protein. 3D confocal images were taken from dendritic segments of CA1 hippocampal pyramidal neurons and the deconvolved micrographs were further analyzed by algorithm-based method.

Our results show that neurons on a tau KO background present lower fraction of mushroom spines compared to neurons from C57BL/6 animals, suggesting that the lack of tau is compromising the maintenance of permanent spines. Considering the presence of an increased amount of Aβ on a tau KO background, we observed a shift from thin to stubby spines, an event related to an increase in the synaptic surface. Interestingly, when human tau was introduced in tau KO hippocampal slices, we observed a recovery in the fraction of mushroom spines, independent of the presence or absence of increased Aβ levels. However, we could not recapitulate this observation after treating tau KO APPSDL tissue culture with Epothilone D, a microtubule stabilizing agent, suggesting that tau interaction with microtubules is not the only mechanism through which tau affects spine morphology when the amount of Aβ species is increased.

Poster #04

Alterations of long-term potentiation in the hippocampus of mice selected for extremes in stress reactivity

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Susceptibility to stressors and stress-coping style play an important role in the development of affective disorders, including major depression. Moreover, these disorders are frequently coupled with cognitive dysfunctions. Therefore, in this study, we investigated whether genetic differences in stress reactivity affect electrophysiological properties of hippocampal circuits related to memory formation. We employed a microelectrode array (MEA) system with 60 electrodes, allowing the recording of extracellular potentials in multiple positions simultaneously.

To this end, a mouse model was used that was generated by selectively breeding mice of the CD-1 mouse strain for differences in hypothalamic-pituitary-adrenal (HPA) axis reactivity to a psychological stressor. Three breeding lines were established based on corticosterone secretion upon stress exposure: high reactivity (HR), intermediate reactivity (IR) and low reactivity (LR) mice.

The behaviour of adult male HR, IR and LR mice was assessed regarding their hippocampus-dependent memory (Y-maze test) and stress-coping behaviour (forced swim test). Following these tests, electrophysiological analyses were conducted on acute dorsal hippocampal slices, focusing on CA1 neurons. Electrophysiological responses were recorded from the *stratum pyramidale* and the *stratum radiatum*, respectively. The mouse lines were tested for differences regarding input-output curves, paired pulse facilitation and long-term potentiation (LTP) over 1h induced by a theta oscillation.

The results of the forced swim test showed clear differences in stress-coping behaviour between the mouse lines. As previously reported, HR mice showed much more active struggling behaviour and less floating behaviour, while LR mice adopted a more passive coping style. Furthermore, the Y-maze test revealed a deficit in the spatial memory performance of HR mice in comparison to the other two lines. These cognitive differences were also reflected in the assessed LTP in the hippocampus of the animals. Namely, HR mice showed significantly lower long-term potentiation in comparison to the other two lines.

Taken together, our results show that mice with high reactivity to psychological stressors have also specific deficits in neuronal functions related to cognition, i.e. showing similarities to patients suffering from affective disorders.

Poster #05

Late-onset cognitive impairments after early-life stress are shaped by inherited differences in stress reactivity

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Early-life stress (ELS) has been associated with lasting cognitive impairments and with an increased risk for affective disorders. A dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis, the body's main stress response system, is critically involved in mediating these long-term consequences of adverse early-life experience. It remains unclear to what extent an inherited predisposition for HPA axis sensitivity or resilience influences the relationship between ELS and cognitive impairments, and which neuroendocrine and molecular mechanisms may be involved.

To investigate this, we exposed animals of the stress reactivity mouse model, consisting of three independent lines selectively bred for high (HR), intermediate (IR), or low (LR) HPA axis reactivity to a stressor, to ELS and assessed their cognitive performance, neuroendocrine function and hippocampal gene expression in early and in late adulthood.

Our results show that HR animals that were exposed to ELS exhibited an HPA axis hyper-reactivity in early and late adulthood, associated with cognitive impairments in hippocampus-dependent tasks, as well as molecular changes in transcript levels involved in the regulation of HPA axis activity (*Crh*) and in neurotrophic action (*Bdnf*). In contrast, LR animals showed intact cognitive function across adulthood, with no change in stress reactivity. Intriguingly, LR animals that were exposed to ELS even showed significant signs of enhanced cognitive performance in late adulthood, which may be related to late-onset changes observed in the expression of *Crh* and *Crhr1* in the dorsal hippocampus of these animals.

Collectively, our findings demonstrate that the lasting consequences of ELS at the level of cognition differ as a function of inherited predispositions and suggest that an innate tendency for low stress reactivity may be protective against late-onset cognitive impairments after ELS.

McIlwrick S, Pohl T, Chen A and Touma C (2017): Late-onset cognitive impairments after early-life stress are shaped by inherited differences in stress reactivity. *Frontiers in Cellular Neuroscience* 11:9. doi: 10.3389/fncel.2017.00009.

Poster #06

Mitochondria & Mood: can mitochondrial dysfunction and oxidative stress bridge emotional and metabolic disturbances?

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Disturbances in energy metabolism involving mitochondrial dysfunction and oxidative stress are often observed in patients and animal models of major depressive disorders (MDDs). Yet, the cellular and molecular mechanisms by which alterations in mitochondria connect psychological and physiological symptoms of MDDs are incompletely understood.
As individual variability in stress responsiveness greatly weighs on vulnerability and resilience to develop MDDs, a mouse model established by selective breeding for high (HR), intermediate (IR) or low (LR) stress reactivity was used to determine whether emotional and metabolic phenotypes are associated with changes in mitochondrial function in tissues with high metabolic demands.
Male mice of the three stress reactivity lines were tested for anxiety- and depression-like behaviours in the sucrose preference (SPT), open field (OFT), forced swim (FST) and dark/light box tests. Body weight, food intake and body fat composition were monitored. Oxygen consumption of isolated mitochondria from the liver and the hippocampus was measured using a Seahorse XFe96 Analyser as a proxy for mitochondrial functional capacity. In addition, profiles of mitochondria-focused gene expression were analysed in the hippocampus using real-time quantitative PCR (qRT-PCR). Furthermore, the qRT-PCR was used to estimate the mitochondrial DNA (mtDNA) copy number and the extent of accumulated mtDNA damages in the hippocampus.
We found that, compared to IR and LR mice, HR mice showed hyperactive locomotion and coping behaviour in the OFT and FST respectively. HR mice also presented significantly lower body weight but higher relative food intake. When compared to IR mice, LR mice showed increased anxiety-related behaviour and a trend for lower body fat accumulation. Anhedonia-like behaviour in the SPT was not statistically different between the lines. No major changes in mitochondrial biogenesis and functional capacity were observed between the lines. For instance, the oxygen consumption rate of isolated hippocampal and hepatic mitochondria was not significantly different among the three lines. Only slight changes in mRNA expression of some markers of oxidative stress and apoptosis were observed in the hippocampus of LR mice, yet they were not associated with changes in the lesion frequency at the mtDNA.
Overall, our results suggest that individual differences in stress reactivity barely influence mitochondrial function under non-stressful conditions in mice. Further work should investigate whether mitochondria play an important role in the mechanisms by which chronic stress regulate cellular energy metabolism, and ultimately vulnerability/resilience to the development of MDDs.

Poster #07

Social phobia, skin temperature and social recognition in men and mice

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Impairments in social skills are central to mental disease, making the development of tools for their assessment in mouse models essential. Here we present the SocioBox, a new behavioral paradigm to measure social recognition. Using this paradigm, we show that male wildtype mice of different strains can readily identify an unfamiliar mouse among 5 newly acquainted animals. In addition to a simple quantification of social interaction time of mice based on predefined spatial zones (zone-based method), we developed a set of unbiased, data-driven analysis tools based on heat map representations and characterized by greater sensitivity. Using this novel tool, we provided first proof-of-principle that the SocioBox allows diagnosis of social recognition deficits.

By serendipity, we detected that 4 weeks after exposure to the SocioBox, mice showed abnormal behavior in the Y maze sociability task, best described as avoidance of social contacts or social phobia. In several independent follow-up experiments, we reproduced this effect. Intriguingly, sociophobic behavior was not present in mice that underwent the SocioBox without stimulus mice (empty boxes instead of mice as control condition). We thus conclude that the inescapable confrontation with other mice in the SocioBox set-up rather than the narrow box itself induced sociophobic behavior. Most importantly, we unexpectedly discovered the first animal model of sociophobia.

Since this condition is of highest relevance in humans, where it is crucial to distinguish it phenotypically and biologically from autism spectrum disorders, we further pursue this model (in parallel to our established autism models). Using sensitive infrared thermography (IRT) as novel non-invasive stress readout, we will be able to measure subtlest changes in body temperature. We hypothesize that (1) induction of sociophobia in the SocioBox is associated with increased stress levels (perhaps as drivers of the disorder) and (2) that there is a negative relationship between body temperature as stress marker and social recognition performance. In testing these hypotheses, we plan to translate point (2) to humans, using IRT as measurement of stress in a facial recognition task. Ultimately, our work aims to establish IRT not only in translational animal research exploring social behavior and social deficits, but also to adopt it as a non-invasive tool for diagnostic and therapeutic assessment of neuropsychiatric diseases, such as social phobia, autism spectrum disorder, and schizophrenia.

Poster #08

Low 17β-estradiol status is associated with stronger fear recall and impaired extinction recall: Evidence from prefrontal oscillations

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Fear recall and extinction recall are important features of implicit memory in Pavlovian fear conditioning, indicating persistence of the fear memory trace (fear recall) vs. expression of an alternative memory trace after extinction (extinction recall) allowing to experience an environment as more safe again. Neurophysiological animal studies suggest an important role of prefrontal neuronal oscillations. A first study in humans revealed that theta oscillations in the dorsal anterior cingulate cortex (dACC) accompanied fear recall whereas gamma oscillations in the ventromedial prefrontal cortex (vmPFC) were associated with extinction recall [1]. Behavioral and imaging data showed that the female sex hormone 17β-estradiol (E2) improves extinction recall. However, there is no study examining the modifying role of E2-status for these prefrontal oscillations. To compare natural conditions of E2-status, we examined 20 free-cycling women during mid-cycle (high E2, low progesterone [P4]), 20 women using oral contraceptives (low E2, low P4) and 20 men (low E2, low P4). To differentiate between fear recall and extinction recall, we used differential conditioning consisting of four pictures of male faces as the conditioned stimuli (CS), and a 95-dB white-noise burst as the unconditioned stimulus (US). During fear acquisition, two CS were paired with the US (CS+), whereas the other two were not (CS-) (factor contingency). During subsequent extinction learning, only one CS+/CS- pair was presented without US (factor extinction: extinguished vs. not-extinguished). Fear recall and extinction recall were assessed 24h after fear acquisition. Electroencephalogram (64-channel EEG) was recorded. Standardized low resolution electrotomography (sLORETA) served to examine the source localization of theta and gamma oscillations. Furthermore, CS-related skin conductance responses (SCRs) and subjective ratings were assessed. SCR indicated successful fear acquisition and immediate extinction on Day 1. During fear and extinction recall on Day 2, we found stronger and more persistent fear memories in men and OC women compared to MC women, evident in stronger differential SCRs and enhanced differential dACC theta power to not-extinguished but also to extinguished CS. However, MC women did not show this enhanced differential theta power in the dACC. Gamma power in the vmPFC was not modulated by fear vs. extinction recall, but additional gamma-analyses are pending. Our results emphasize the importance of E2 as a modulator of fear and extinction recall. Furthermore, theta oscillations were not only associated with fear recall but also with a failure of extinction recall, seen in low-E2 groups only.

[1] Mueller E. et al. (2014), J Neurosci., 34, 7059-7066.

Poster #09

Embodied emotion: Role of sex hormones and first-wave stress in emotions components

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Examining embodied emotions so far mainly uses the manipulation of somatosensory and motor body-to-brain feedback. We here conceptualize embodiment via hormone-to-brain feedback of sex and stress hormones. Both types of steroid hormones act on brain areas involved in emotion and cognition, i. e. amygdala, hippocampus, and prefrontal cortex. The female menstrual cycle constitutes a useful quasi-experimental model to examine phase-specific variations of the female sex-hormones estradiol (E2) and progesterone (P4). Endogenous E2 and P4 are suppressed under hormonal contraceptives (HC). E2 and P4 have particular and, in some sense, opposing roles in cognitive and emotional processing: e.g., high E2-status was associated with positive mood and improved memory for positive content; high P4-levels were accompanied by a specific memory-advantage for material of negative valence especially after stress, and impaired detection of facially-expressed basic emotions. But data are partly inconsistent and limited. Research mainly addresses emotional declarative memory, thereby neglecting cognitive and affective empathy, mimic emotion expression and physiological reactivity. To uncover interactions between sex- and stress-hormones, we use a first-wave stressor (cold pressor test, CPT) administered immediately after encoding of declarative material of positive, negative and neutral content.
In a 3 x 2 x n mixed design, hormone status serves as our quasi-experimental variation with 3 groups: free-cycling women in the midcycle periovulatory phase (MC: E2 high, P4 low), mid-luteal phase (LU: P4 high, E2 moderate), and women taking HCs (endogenous E2, P4 low). Per hormone-status group, subjects are randomized to either a CPT stressor which quickly triggers a first-wave stress response, or to the warm water control. Within-subject variation covers valence of the stimulus material (positive, negative and neutral). Subjects participate in a 2-day experiment. Day 1 covers assessment of cognitive empathy (recognition of basic emotions in faces), memory encoding (material from the IAPS battery [International Affective Picture System]), CPT-stressor (vs. control), and post-stress basic-emotions recognition. On Day 2, we measure 24-h delayed surprise recall of declarative memory (IAPS pictures), cognitive and affective empathy, physiological reactivity and facial-muscle activity while exposed to further IAPS pictures (positive, negative, neutral valence). On both days, E2 and P4 levels and cortisol are assessed in saliva. CPT-stressor validation covers blood pressure, pulse, subjective pain, subjective arousal and anxiety.
We present first data on emotional memory and empathy from the ongoing study (36 subjects: 18 stressed/18 non-stressed; 18 free-cycling/18 OC-women).
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Poster #10

Emotional modulation of picture-, face- and word- evoked ERPs following right temporal lobe resection – an ongoing EEG study

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Emotional modulation of the early posterior negativity (EPN) and late positive potential (LPP) in event related potentials reflect the ability of the human brain to respond rapidly to emotionally salient visual stimuli. This emotional modulation is commonly explained by amygdala-driven feedback in visual processing. The present study investigates the impact of absence of right medial temporal lobe structures including amygdala and hippocampus on emotional modulation of EPN and LPP elicited by negative pictures, faces and words. In our preliminary study, so far 15 right Temporal Lobectomy (rTLE) patients (age M=37.00, SD=11.97; 9 females) and 15 healthy controls (age M=34.20, SD=7.96; 9 females) passively viewed randomized blocks of negative and neutral scenes and words as well as of fearful and neutral faces while their EEG was recorded. In controls, emotion effects on EPN and LPP were significant for faces and pictures, and absent for words. On EPN, in controls as well as patients, emotional modulations were found for pictures and faces, but not for words. On LPP, patients showed smaller ERPs than controls. For controls, the emotion effect was largest for pictures, followed by faces and not significant for words. For patients, the same pattern applies in an early LPP, whereas the late LPP was flat regardless of stimulus type.
Overall, absence of right medial temporal lobe structures reduces, but does not abolish emotional modulation of EPN and LPP, tentatively suggesting that these structures contribute to but are not exclusively responsible for emotional modulation of EPN and LPP. Furthermore, rTLE may affect later processing stages, reflected by the LPP, more than early processing stages.

Poster #11

Effects of right temporal lobe resection on visual emotion processing: An ongoing fMRI study

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Emotionally arousing stimuli trigger higher BOLD signal than neutral stimuli in brain areas involved in visual processing. One explanation for this effect is the modulation of visual pathways by feedback originating in the amygdala. To test this hypothesis, we examined visual emotion processing of different stimuli in epilepsy patients (currently n = 16, data collection is ongoing) with right unilateral temporal lobe resection comprising amygdala and hippocampus and healthy participants matched for age and gender. In a passive viewing fMRI paradigm, we compared the BOLD response for negative and neutral scenes, faces, and words. In healthy participants, negative scenes induced enhanced activation in the bilateral ventral visual pathways, while this effect was reduced in patients. For faces, emotional activation in healthy participants comprised typical face processing areas such as the bilateral lateral occipital cortex, fusiform gyrus and superior temporal sulcus. In patients, increased activation was restricted to the left fusiform gyrus. For negative words, healthy participants showed differential activations in the posterior cingulate cortex, whereas patients showed no emotion effect. Our results suggest that right medial temporal lobe structures are important, but not sole generators of visual processing enhancement for emotional stimuli, as ipsilesional responses to negative stimuli were reduced after right amygdala resection, but relatively preserved in the contralesional hemisphere.

Poster #12

Cortical oscillations during successful retention in human working memory

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Working memory (WM) processes are accompanied by oscillatory brain activity in several frequency ranges, i.e. theta, alpha, and gamma band, as well as their interaction)(e.g. phase-amplitude coupling; PAC). The present EEG study aimed to examine WM-related oscillatory activity during successful/unsuccessful retention of information in WM.
23 participants had to decide if line drawings of two objects, separated by a retention interval, were identical. We compared amplitude fluctuations during retention in the theta (~ 5.5 Hz), lower alpha (~ 9.2 Hz), upper alpha (~ 11.5 Hz) and gamma (~ 50 Hz) range and analyzed PAC between low-frequency phase and high-frequency gamma amplitudes in source space.
Lower alpha activity at left occipital sites was revealed to be task critical, i.e. a lower suppression for successfully as opposed to unsuccessfully matched items. In source space, successful WM retention was linked to an increase in parietal theta-gamma PAC, which might reflect central executive influences on memory formation. Furthermore, lower alpha-gamma PAC was stronger for successfully encoded items in left temporal areas, possibly indicating the reinstantiation of memory representations. Interestingly, the upper alpha-gamma PAC modulation was located within the same left-temporal cortical area but with an opposite effect direction.
Our results underline that the interplay between frequency-specific activity patterns allows to draw a more complete picture of WM functioning as compared to analyzing oscillatory power alone. Successful WM retention of item features might depend on object representations shaped by information integration via theta-gamma PAC in parietal areas and retained by alpha-gamma PAC in temporal areas.

Poster #13

Library for Universal Virtual Realty Experiments: luVRe

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VR-based paradigms could substantially increase the ecological validity of various psychological research topics as VR allows for submerging into real-life experiences under controlled laboratory conditions. LuVRe is a video database designed to provide a standardized set of virtual reality (VR) clips. Our goal is to provide a growing set of clips enabling researchers to study emotional and cognitive processes under realistic conditions while maintaining experimental control. LuVRe comprises 280 3D-360° videos and pictures covering a large variety of emotionally-evocative themes. Each video was recorded with a resolution of 4k at 60 fps and has a length of 30 seconds. Watching these videos with a head mounted display (HMD), such as the HTC Vive, Occulus Rift, or with a mobile phone, e.g. Samsung Gear VR, results in an immersive experience. Users can turn their head 360° in a stereoscopic scene.
The present study systematically investigates differences in emotional experiences between immersive VR experiences (3D-360°) and conventional laboratory experiments (2D). We investigated subjective as well as objective reactions, i.e. electropsychophysiological correlates of the motivational systems and heart rate, towards video clips from the database depicting real-life scenes.

As a result, experiences in virtual reality differ from laboratory conditions with respect to heart rate and frontal alpha asymmetries (FAA), but not subjective ratings, indicating a higher emotional saliency of virtual reality. Interestingly, FFAs as an index of avoidance or approach motivation, differ not only in their intensity but also regarding their general direction. Realistic VR conditions, as well as laboratory conditions, might thus elicit effects which as specific to their domain. We argue that VR allows for a better approximation of real life regarding and thereby bridges the gap between laboratory and real-life conditions.

Poster #14

Dual Realities, One Process: Mnemonic Mechanisms Underlying Virtual Reality

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Recently, it has been claimed that real-life, autobiographical events are processed differently compared to conventional laboratory events. Virtual reality might bridge the gap between real life and laboratory experiences and increase the ecological validity of psychological research. There is broad consensus that self-referential processing is essential for the formation of autobiographical memory. However, it is unclear whether autobiographical experiences can be created with commonly used paradigms, or if self-referentiality is unique to (virtual) reality. We thus set up an experiment in which participants explored a virtual Viking Village either in virtual reality or as a conventional first-person experience on a screen. As hypothesized, virtual reality experiences are vividly retrieved via recollection-based mnemonic processes, which are typical for autobiographical memory. In comparison, conventional screen experiences rather leave a feeling of familiarity. The encoding mechanism in virtual reality might closely resemble real-life mnemonic processing, making VR an ideal tool to study real-life cognition under controlled laboratory conditions.

Poster #15

Debunking the monkey: Sustained inattentional blindness in virtual reality and under conventional laboratory conditions

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Virtual reality (VR) might increase the ecological validity of psychological studies as it allows submerging into real-life experiences under controlled laboratory conditions. We intended to provide empirical evidence for this claim using the famous invisible gorilla paradigm (Simons & Chabris, 1999). In this experiment, the presentation of a gorilla often goes unnoticed, if the observer is engaged in a demanding visual task. This finding is surprising since in real life one would not expect to miss a gorilla, even in a busy scene.

To resolve this apparent puzzle, we confronted one group of participants - as in the original study - with a conventional 2D-video of two teams passing basketballs. The task of the participants was to count how many times one team passed the ball. Additionally, at some point, a person in a gorilla suit roams the scene. To a second group of participants, we presented the same stimulus material as a 3D360°-VR-video. Replicating the original findings, in the 2D-condition, only ~30% of the participants noticed the gorilla. However, in the realistic VR-condition, the detection rate was increased to ~70%. This finding might be explained by the fact that under natural conditions the attentional resources are not exhausted, resulting from a more efficient use of the visual system and increasing the availability of computational resources to detect task-irrelevant events.

We argue that VR mimics the perceptual characteristics of the real world and provides a useful tool for psychological studies, which demand for a close link to real-world scenarios.

Poster #16

Electrophysiological correlates of gist perception: A steady state visually evoked potentials study

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Gist perception refers to perceiving the substance or general meaning of a scene. To investigate neuronal mechanisms underlying gist perception, we used the steady state visually evoked potential (SSVEP) method. The SSVEP is an evoked oscillatory cortical response at the same frequency as a visual stimulus flickered at this frequency. For the present purpose, two neighboring stimuli were flickered at different frequencies f1 and f2, for example a drawing of a sun on the left side of the screen flickering 8.6 times per second (f1 = 8.6 Hz) and the drawing of a parasol on the right side of the screen flickering 12 times per second (f2 = 12 Hz). SSVEPs enabled us to separate the responses to the two distinct stimuli by extracting oscillatory brain responses at f1 and f2. Additionally, it allowed to investigate intermodulation frequencies (IF), that is, the brain's response at a linear combination of f1 and f2 (here at f1+f2 = 20.6 Hz). We assume that the IF indicated the processing of shared aspects of the input, that is, gist perception (here: a beach scene).
We recorded high-density EEG of 19 participants. Drawings of two objects were flickered at f1 and f2. To control for simple resonance phenomena of early visual processing, this setup was preceded by flickering squares at the positions of the subsequently superimposed object drawings. We compared the SSVEPs at f1, f2, and the IF to congruent (e.g., sun & parasol) versus incongruent (e.g., lemon & candle) stimulus pairs. Results revealed clear and separable neuronal oscillations at f1 and f2. Additionally, bilateral frontal and right parietal-occipital electrodes showed increased amplitudes at the IF in congruent as compared to incongruent pairs - indicating the activation of a gist network. Further analyses revealed in more detail how f1 and f2 interacted. The study demonstrates that SSVEPs are an excellent method to unravel mechanisms underlying the processing within multi-stimulus displays.

Poster #17

Reinforcement learning signals and the integrated value of immediate and future action outcomes

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According to recent theoretical work the anterior midcingulate cortex (aMCC) plays a crucial role in hierarchical reinforcement learning of action outcomes (Holroyd & Yeung, 2012). In particular, it has been assumed that the aMCC receives teaching signals from the ventral striatum and uses this information to learn the value of action and decision alternatives in a given setting. This process is probably mirrored by the so-called feedback-related-negativity (FRN) in the scalp-recorded electroencephalogram.
In prior studies we found that the FRN reflects a fine-grained integration of different outcome values linked to a single decision rather than a binary distinction of generally positive or generally negative consequences (Osinsky et al., 2017; Osinsky et al., 2017). In the present study we further investigated the integration of multiple, temporally differentiated consequences of a singular outcome event. For this purpose, we manipulated short, medium and long term consequences linked to a single decision independently from each other. N = 101 healthy students performed a choice task in which different consequences were probabilistically linked to different decision options. During this task we recorded EEG. For examining the temporal stability of individual FRN indices 35 students took part in a retesting four months later. First findings will be presented, indicating that FRN amplitude mainly reflects the additively integrated and, to a lesser degree, also the interactively integrated value of action outcomes. This is generally in line with the idea that the aMCC is involved in learning complex action-outcome values.

Pressemeldung
Nr. 177 / 2018
25. September 2018:

Einblick in die Gedächtnisforschung - Universität Osnabrück lädt zur 9. Westerberger Herbsttagung

Die „Westerberger Herbsttagung“ ist inzwischen gute Tradition: Bereits zum neunten Mal veranstaltet die Abteilung Neurobiologie der Universität Osnabrück, diesmal zusammen mit der Abteilung Verhaltensbiologie und dem Institut für Psychologie, am Donnerstag, 27. September, ein wissenschaftliches Symposium zur Gedächtnisforschung im Helikonien-Saal des Bohnenkamp-Hauses im Botanischen Garten. Zu den um 9 Uhr beginnenden Vorträgen sind Interessierte herzlich eingeladen.

Unter dem Titel »Psychological and Biological Aspects of Explicit and Implicit Memory« werden während der Herbsttagung neue Resultate der Gedächtnisforschung in Form von Vorträgen und Postern präsentiert. Dabei liegt der Fokus dieses Jahr auf der Förderung einer disziplinübergreifenden Zusammenarbeit zwischen Biologen und Psychologen. Die Veranstaltung findet im Rahmen der Forschungs-Profillinie „Kognition: Mensch-Technik-Interaktion” statt, die von der Universität im Rahmen des Strategieprozesses besonders unterstützt wird.

Im Vordergrund der Tagung steht das Ziel, das breite Spektrum und die neuen Möglichkeiten durch die aktuellen Entwicklungen in der neurowissenschaftlichen Forschung zu präsentieren, wie sie auch bei der Behandlung von Störungen des Nervensystems wichtig sind. »Dabei verspricht eine disziplinübergreifende Zusammenarbeit von Biologen und Psychologen spannende Einsichten und fördert die Entwicklung neuer Ansätze, insbesondere auch in der Übertragung von Ergebnissen aus der psychologischen und biologischen Grundlagenforschung zur Aufklärung und Behandlung psychiatrischer und neurologischer Erkrankungen“ so die Tagungsleiter Dr. Lidia Bakota, Prof. Dr. Roland Brandt und Prof. Dr. Chadi Touma aus dem Institut für Biologie, sowie Prof. Dr. Thomas Gruber, Prof. Dr. Roman Osinsky und Prof. Dr. Ursula Stockhorst vom Institut für Psychologie der Universität Osnabrück in ihrer Einladung.

Als externe Sprecher referieren Prof. Dr. Ron de Kloet (Leiden, Niederlande), Prof. Dr. Hannelore Ehrenreich (Göttingen), Prof. Dr. André Fischer (Göttingen), Prof. Dr. Manfred Hallschmid (Tübingen), Prof. Dr. Onur Güntürkün (Bochum), Prof. Dr. Johanna Kißler (Bielefeld) und Dr. Navarro Schröder (Trondheim, Norwegen). Hinzu kommen Vorträge aus den Osnabrücker Arbeitsgruppen sowie Posterpräsentationen.

Neben der Förderung durch die Universität wird die Tagung durch verschiedene Firmen unterstützt.

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Introduction by Prof. Dr. R. Brandt (University of Osnabrück) in the Bohnenkamp-House, Botanical Garden of the University of Osnabrück

Lectures and Progress Talks

Keynote lecture 1:
Prof. Dr. O. Güntürkün
(University of Bochum)

Keynote lecture 2:
Prof. Dr. J. Kißler
(University of Bielefeld)

Progress talk 1:
Dr. T. Navarro Schröder (Norwegian University of Science and Technology, Trondheim, Norway)

Progress talk 2:
M. Rierola (University of Osnabrück

Lectures and Progress Talks

Keynote lecture 3:
Prof. Dr. R. de Kloet (Leiden University Medical Center, The Netherlands)

Keynote lecture 4:
Prof. Dr. M. Hallschmid (University of Tübingen)

Progress talk 3:
Dr. M. Antov (University of Osnabrück)

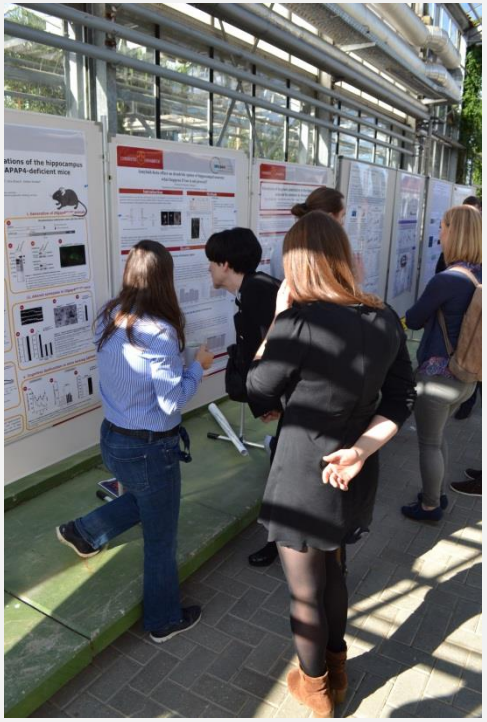
Progress talk 4:
Dr. O. Ambrée (University of Osnabrück)

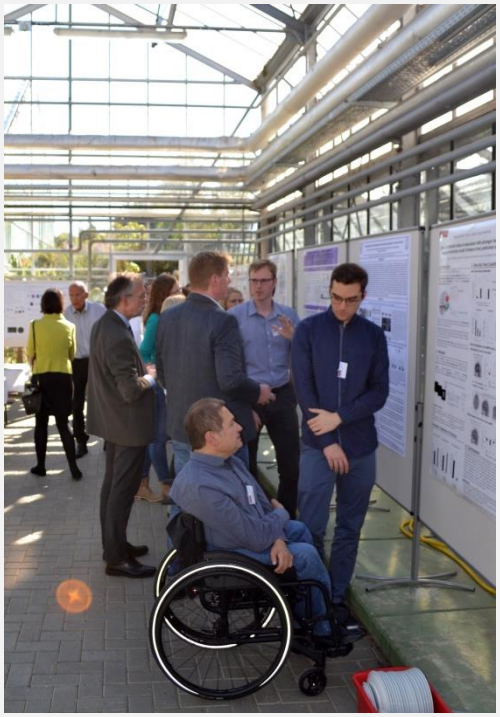
Lectures and Progress Talks

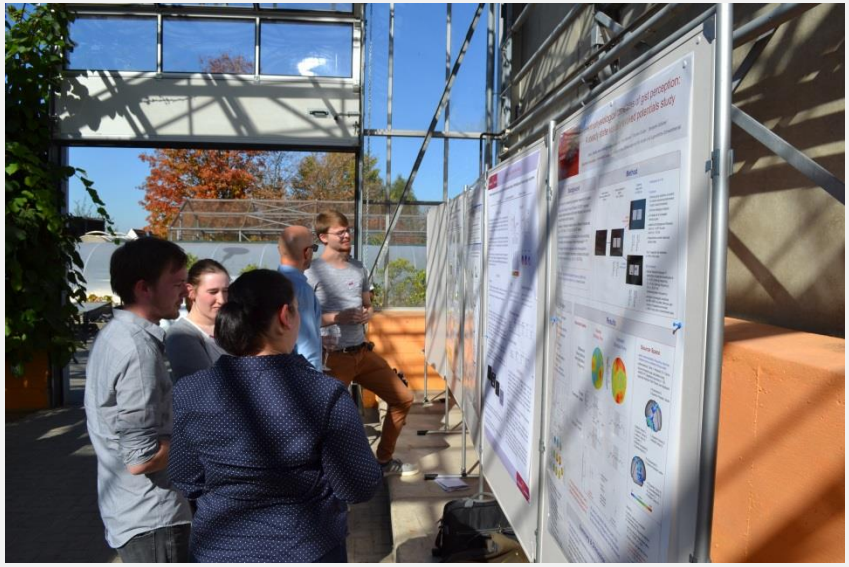
Keynote lecture 5:
Prof. Dr. A. Fischer (Deutsches Zentrum für Neurodegenerative Erkrankungen, Göttingen)

Keynote lecture 6:
Prof. Dr. H. Ehrenreich (Max-Planck-Institut für Experimentelle Medizin, Göttingen)

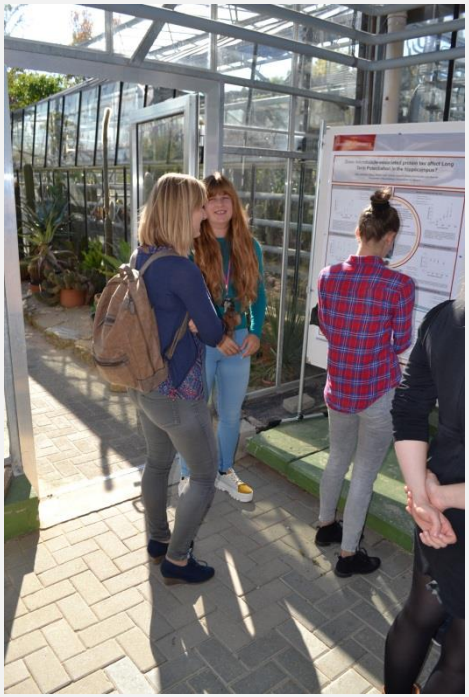
Poster Presentation and Discussion

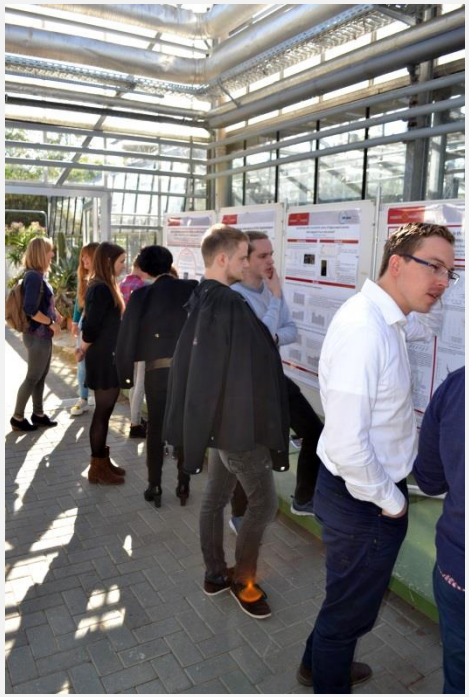


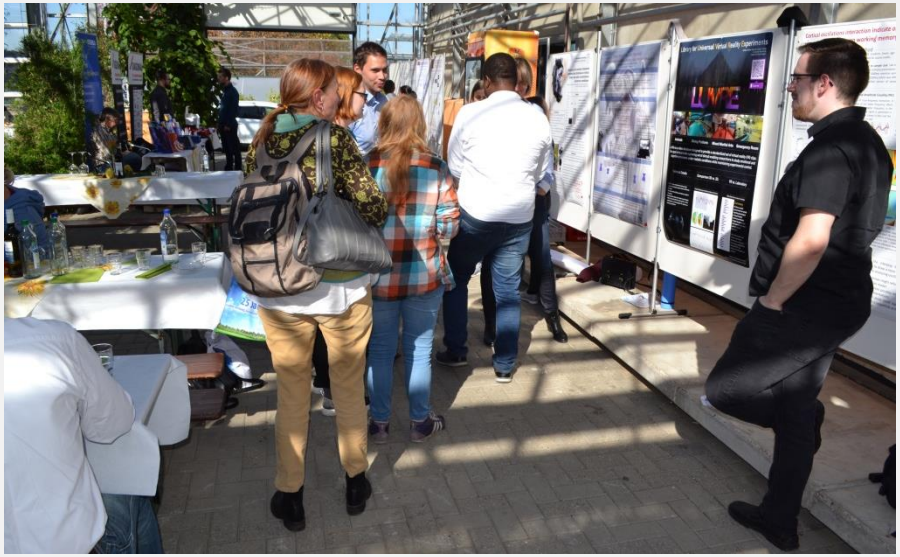


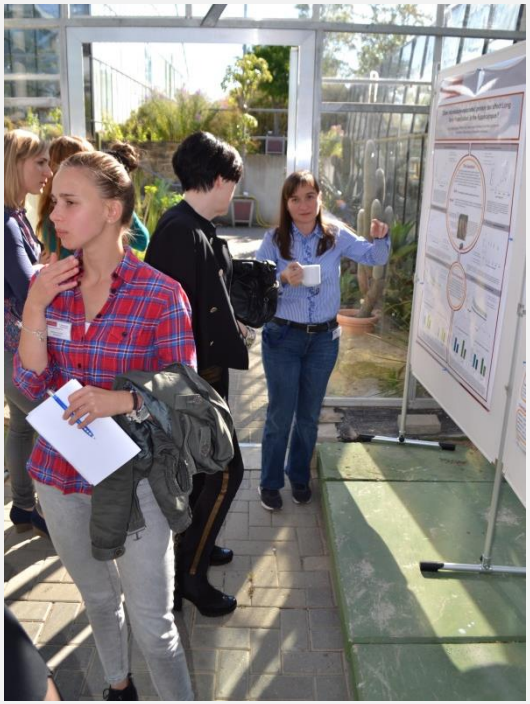


Poster Presentation and Discussion









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