

Department of Psychiatry and Psychotherapy

Chair of Psychiatry and Psychotherapy

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Research focus

- Depression
- Dementias
- Addictive behavior
- Clinical neurochemistry and neurochemical dementia diagnosis
- Neurophotronics
- Health Services Research
- Sensors
- Molecular psychiatry

Structure of the Chair

Professorships: 3

Personnel: 225

- Doctors (of Medicine): 36
- Scientists: 25 (thereof funded externally: 11)
- Graduate students: 84

Clinical focus areas

- Depression
- Memory disorders
- Dementia
- Schizophrenia
- Addiction
- Anxiety disorders

Research

Our research is based on a broad spectrum of methods, ranging from basic clinical research to clinical research and care research.

Depressions

Sphingolipids are essential components of the nerve cell membrane and regulate the flow of signals between neurons. We were able to show that alcohol exerts a paradoxical antidepressant effect on the influence of an important sphingolipid-metabolizing enzyme. In addition, we also described altered alternative splicing of this enzyme in patients with depressive disorders

which makes it also a target for improved pharmacotherapy.

Funding: DFG, BMBF, and IZKF

Results from a multicenter randomized controlled study of the efficacy of a bouldering psychotherapeutic group intervention in people with depression showed an improvement in depressive symptoms as compared to a home-based supervised exercise program.

Funding: DFG

Dementia

A study showed that the A β peptide A β 1-40 is also reduced in the inflammatory central nervous system diseases Multiple Sclerosis (MS) and bacterial meningitis, but not in Alzheimer's disease. Thus, the use of the ratio A β 1-42 / A β 1-40 allows a sharper diagnostic separation between these diseases (AD). The finding also speaks against the view of AD as a potentially infect-triggered immunopathology.

In another study, the population of peripheral helper T helper (Th) was studied in various stages of AD with a significant increase in the interleukin-17-secreting Th17 cells in the stage of mild cognitive impairment, indicating that not only the innate, but also the adaptive immune system could be involved in the pathogenesis of AD.

The DeTaMAKS study is the first controlled, randomized study of the effectiveness of the non-drug MAKS-therapy[®] in day care in combination with a short-term telephone intercom. The results for the six months intervention period showed a significant effect of the MAKS-therapy[®], stabilizing cognitive as well as everyday practice abilities of people with cognitive impairments at least at the initial level while they lessened in the control group.

The national graduate school „Optimization strategies for dementia“ (OptiDem), granted by the Karl and Veronica Carstens foundation, was successfully completed with eleven graduate students.

Addiction disorders

International multicenter studies identified new genetic mechanisms involved in the development of alcohol addiction. In the animal model, it was possible to characterize the physiological mechanisms in the brain via which spontaneous genetic changes lead to a reduced function of the reward system.

Funding: DFG, IZKF

We asked which role the protein EFhd2 plays in the control of alcohol addiction-associated behavior. We found that EFhd2 knock out mice

drink more alcohol than controls and spontaneously escalate their consumption. This coincided with a sensation-seeking and low anxiety phenotype.

Funding: IZKF

We were able to provide evidence that intrauterine androgen exposure poses the risk of substance abuse, externalizing behaviors in childhood, suicides, and adult physical disorders. In addition, it can also shorten life expectancy. We also found smaller 2D:4D levels for alcohol dependence and binge drinking in clinical and non-clinical cohorts. This biomarker suggests that testosterone exposure before birth increases the subsequent risk of alcohol-related disorders.

In a series of studies, we have proven the validity and reliability of the new criteria for internet gambling disease and the pathological use of social networks.

Clinical neurochemistry and neurochemical dementia diagnostics

The ISO 15189-accredited laboratory participated in two large-scale, EU-funded projects dealing with neurochemical dementia diagnostics (BiomarkAPD and IMI-EMIF) and coordinated two work packages. Both projects led to improvement of the understanding of the role of CSF biomarkers in the diagnostics of neurodegeneration disorders, like AD, including approaches to validate Neurofilament Light (NfL) as a blood-based biomarker.

Erlangen Score interpretation algorithm, developed in the Laboratory for Clinical Neurochemistry, was further validated and meanwhile entered routine application, also in some other European centers.

The laboratory coordinated the first international inter-center proficiency testing scheme for CSF biomarkers biobanking.

Neurophotronics

The group developed a new method for the optical measurement of nerve cell network connectivity and published its first results in 2017. This project was funded by the Else-Kröner-Fresenius Foundation and is now exploring the mode of action in the second section of antidepressants.

An ongoing project funded by the DFG investigated the properties of antipsychotic drugs that are relevant for efficacy at the synapse.

In addition, various chemotherapeutic agents have been tested for their safety in the function of nerve cells in collaboration with the neurosurgical clinic.

Health Services Research

In cooperation with the interdisciplinary pain center, an instrument for the operationalization of successful treatment which is based on Patient Reported Outcomes (PROs) was developed in order to evaluate routines of the care. A validation with long-term data of chronic pain patients was performed and showed in an international publication that the instrument differentiates satisfactorily between long-term successfully treated patients and low-responders. In health services research, there are few long-term studies that extend beyond a period of five years. It is therefore a special feature that the course of stroke patients up to 7.5 years after discharge from inpatient neurological rehabilitation was investigated and published in a cohort study in cooperation with the specialist hospital Herzogenaurach, division of neurorehabilitation.

Sensors

We investigated the influence of macronutrients on olfactory, cognitive, metabolic, and psychophysiological parameters in three human studies. In the first placebo-controlled study, nutrient solutions (protein, carbohydrate or fat, 600 kcal) or placebo were slowly administered intravenously. With regard to hunger and food craving, cognition and olfaction, the nutrient solutions did not differ. The second study investigated the effects of an isocaloric and isovolumic nutrient solution (600 kcal) as a function of different oral administration (normal intake versus slow interval intake). The third study is a placebo-controlled study in which various nutrient solutions (protein, carbohydrate or fat, 600 kcal) or placebo were administered orally at a normal rate of intake.

The newly developed odor test for food-associated odors could be further validated. The comparison of the test with the already validated identification test of the Sniffin 'Sticks test showed that both tests do not differ in terms of identification rate and intensity.

Molecular psychiatry

As part of the research network GeNeRARE (German Network for RASopathy Research), the causes of cognitive impairment that occur in the rare RASopathy Noonan Syndrome (NS) were investigated in an animal model. We showed that, despite the hyperactivity of the neuronal RAS signaling pathway, gene expression following neuronal stimulation in the mutants was severely blunted, which could explain the cognitive deficits.

Funding: BMBF

In collaboration with Prof. Dr. T. Walter (University of Tübingen) and using functional MRI, we dissected regional and temporal dynamics of glutamatergic transmission upon single administration of antidepressant ketamine in healthy volunteers.

Funding: DFG

Using live-cell imaging in neurons we studied physiological role of amyloid beta in regulation of synaptic vesicle cycling. This peptide is associated with AD and our data indicate that dysregulation of presynaptic homeostasis might contribute to early synaptic dysfunction observed in AD long before measurable cell loss and plaque formation.

Funding: DFG

Our further publications deal with establishment of synaptic specificity and mechanism underlying regulation of neurotransmission by anxiolytic drug riluzole and upon manipulation of neuronal extracellular matrix.

Funding: DFG:

Teaching

The Department of Psychiatry and Psychotherapy participates with compulsory and elective subjects in the curricular teaching of Medicine and Logopedics. Particularly noteworthy here is the interdisciplinary teaching within the framework of the cross-sectional subjects EKM, Q9 (clinical pharmacology / pharmacotherapy) and Q10 (prevention and health promotion) and in the context of the compulsory elective subject of sexual medicine.

The Department has further expanded the simulation program of patients. Students can practice acting in difficult situations with agitated, affective, rejecting and uncooperative patients. In addition, Objective Structured Clinical Examinations (OSCE) stations were developed to validate communication and investigation skills. Bachelor's and Master's theses as well as MD and PhD theses are supervised.

Selected publications

Altmüller F, Pothula S, Annamneedi A, Nakhaei-Rad S, Montenegro-Venegas C, Pina-Fernández E, Marini C, Santos M, Schanze D, Montag D, Ahmadian MR, Stork O, Zenker M, Fejtova A. Aberrant neuronal activity-induced signaling and gene expression in a mouse model of RASopathy. *PLoS Genet.* 2017 Mar 27;13(3):e1006684

Bachlechner S, Denzer-Lippmann MY, Wielopolski J, Fischer M, Buettner A, Doerfler A, Schöfl C, Münch G, Kornhuber J, Thürauf N. The Effects of Different Isocaloric Oral Nutrient Solutions on Psychophysical, Metabolic, Cognitive, and Olfactory Function in Young Male Subjects. *Front Psychol.* 2017 Nov 23;8:1988

Lenz B et al. Prenatal and adult androgen activities in alcohol dependence. *Acta Psychiatr Scand.* 2017 Jul;136(1):96-107

Straubmeier M, Behrndt E-M, Seidl H, Özbe D, Luttenberger K, Graessel E. Non-pharmacological treatment in people with cognitive impairment. *Dtsch Arztebl Int.* 2017 Dec 1;114(48):815-821

Mielenz D et al. EFhd2/ Swiprosin-1 is a common genetic determinant for sensation seeking/ low anxiety and alcohol addiction. *Mol Psychiatry.* 2018 May;23(5):1303-1319

Stelzer EM, Book S, Graessel E, Hofner B, Kornhuber J, Luttenberger K. Bouldering psychotherapy reduces depressive symptoms even when general physical activity is controlled for: a randomized controlled trial. *Heliyon.* 2018 Mar 23;4(3):e00580

International cooperations

Prof. G. Schumann, Institute of Psychiatry Psychology and Neurology, King's College London, London: UK

Prof. M. Filip, Institute of Pharmacology, Polish Academy of Sciences, Krakow: Poland

Dr. Z. Hassan, Centre for Drug Research, Universiti Sains Malaysia, Penang: Malaysia

Prof. H. Zetterberg, Sahlgrenska Academy, Mölndal: Sweden