Institute of Physiology and Pathophysiology

Chair of Physiology

Address
Universitätsstraße 17
91054 Erlangen
Phone: +49 9131 8522295
Fax: +49 9131 8522497
www.physiologie1.fau.de

Director
Prof. Dr. med. Christian Alzheimer

Contact
Prof. Dr. med. Christian Alzheimer
Phone: +49 9131 8522400
Fax: +49 9131 8522497
Christian.Alzheimer@fau.de

Research focus
- Neurophysiologic substrates of higher brain functions
- Transduction, integration, plasticity in primary nociceptive neurons
- Trigeminal nociception and headache generation
- Properties of peripheral human C-fibers
- Functional imaging of brain activity by fMRI

Structure of the Institute

Professorships: 3
Personnel: 48
- Scientists: 22 (thereof funded externally: 7)
- Graduate students: 7

Special structural features
The Institute houses experimental set-ups of the Departments of Anesthesiology, Medicine 1 and 4, and a Junior Group of the IZKF, each with close methodical and thematic ties to the research groups of the Institute.
The Institute of Cellular and Molecular Physiology comprises the Chair of Physiology (Systems Physiology) and the Professoship of Cardiovascular Physiology. The chair of physiologyand the professor of cardiovascular physiology serve as director and deputy director of the Institute, respectively.

Research

The overarching research objective at our Institute is to understand the bioelectrical and neurochemical processes that constitute the basic language of the nervous systems and enable communication between nerve cells.
What factors elicit an electric impulse in a neuron, if, for instance, pain or temperature stimuli influence the body?
What mechanisms mediate signal transmission between nerve cells and how is information processed in neuronal networks?
Answers to questions like these will also help to elucidate the underpinnings of cognition and emotion and of disorders thereof. We explore such issues with a broad spectrum of methods, ranging from modern electrophysiological, optical, cell and molecular biological techniques to microneurography and fMRI in healthy volunteers and patients.

Neurophysiologic substrates of higher brain functions

PI: Prof. Dr. C. Alzheimer, Dr. F. Zheng, PD Dr. Dr. T. Huth
Our research focuses on the electric behavior of neurons and neuronal networks under normal and pathological conditions. Using high-resolution neurophysiological and optical techniques, we investigate functions and regulation of ion channels and synapses. Our aim is to understand fundamental neural processes that are essential for cognitive functions as well as for affective behavior and whose dysfunctions might give rise to neuropsychiatric disorders. In particular, we are studying the following topics:
1) Role of activin, a member of the Transforming Growth Factor-β family, as a "master molecule" tuning glutamatergic and GABAergic neurotransmission, and its impact on cognition, emotions, and neuroprotection
2) Interaction between BACE1, a crucial enzyme in the amyloid cascade of Alzheimer's disease, and properties and expression of Na^+ and K^+ channels
3) Neuropsychiatric disease models and mechanisms of drug action (in collaboration with the Department of Psychiatry and Psychotherapy)

Transduction, integration, plasticity in primary nociceptive neurons

PI: Prof. Dr. S. Sauer, Prof. Dr. P.W. Reeh
The research focuses on primary nociceptive neurons, their electrophysiological and neurochemical responses to noxious and pruritogenic stimuli and chemical mediators. Isolated preparations and cultured dorsal root ganglion cells as well as transfected cell lines are used to study action potential discharge, ionic currents, calcium transients, and release of the neuropeptides substance P and calcitonin gene-related peptide. Aim is to elucidate nociceptive transduction and integration of stimuli as well as possible pharmacological interventions. Specific topics are sensitization by tissue acidosis, inflammatory mediators, metabolites, toxins and gasotransmitters as well as their intracellular signal transduction. Transgenic mouse strains lacking different metabotropic and ionotropic receptors or thermally activated ion channels (i.a. TRPV1, TRPA1) are studied. Voltage-controlled ion channels (NaV, Kv7.2, HCN, CaV3.2) came in focus because only few subtypes decide on excitability, i.e. on generation, frequency, and propagation of action potentials to the central nervous system. Neuroimmunology is a rapidly growing field that, for example, studies the interaction of substance P with the immune system that may essentially contribute to chronic inflammatory, including autoimmune diseases.

Trigeminal nociception and headache generation

PI: Prof. Dr. K. Messlinger
Our group is working on nociceptive mechanisms in the cranial dura mater, the trigeminal ganglion, and the spinal trigeminal nucleus as the neurobiological basis for the generation of headaches. Extracellular recordings from single afferent fibers in the isolated rodent dura mater are performed to study the sensitivity and response of meningeal afferents and the role for receptors and ion channels that are probably involved in the generation of headaches in humans. In a similar preparation, we examine by which mechanisms the neuropeptide CGRP is released from the cranial dura mater as an indicator for trigeminovascular activation. Using immunohistochemical and molecular biological methods, we aim at detecting the intracellular signal pathways that are induced by these substances. To study the central processes of headache generation, we examine the response properties of neurons in the spinal trigeminal nucleus, record the peripheral and central blood flow, and assess the effects of potential headache therapeutics.

Properties of peripheral human C-fibers

PI: PD Dr. B. Namer
Morphological and electrical properties of peripheral unmyelinated neurons (C-fibers) are studied directly in healthy subjects, patients with painful and painless neuropathies or chronic pruritus. Especially patients with defined mutations of ion channels that change the excitability of peripheral C-fibers are of interest, which change pain and itch sensations. Neurons and mechanisms signaling pain and itch sensations are examined. The methods to examine C-fibers in awake humans include non-invasive assessment of axon reflexes and psychophysical studies as well as microneurography. Our aim is to build a bridge from patients and their symptoms of chronic itch and pain to mechanistic research on cells and ion channels.

Functional imaging of brain activity by fMRI

PI: Prof. Dr. C. Forster

Functional magnetic resonance imaging (fMRI) is a well-established method to image the activity of the human brain during the processing of various stimuli and tasks. The method is used to identify brain regions involved in the central processing of pain and itch. By variation of the experimental paradigms, the function of various brain regions and their contribution in the perception of the corresponding stimulus should be determined. Common projects with the Department of Medicine 1 analyze the central changes induced by chronic itch in patients suffering from cholestatic pruritus.

Teaching

In addition to its contribution to the preclinical curricula of students of Medicine, Dentistry, and Molecular Medicine, the Institute gives lectures, seminars, and practical courses in physiology for students of the Faculties of Engineering and of Sciences, in particular courses for the degree programs Medical Technology and Pharmacy. The Institute supervises Bachelor and Master theses as well MD and PhD theses.

Selected publications

Babes A, Ciotu CI, Hoffmann T, Kichko TI, Selescu T, Neacsu C, Sauer SK, Reeh PW, Fischer MJM. Photosensitization of TRPA1 and TRPV1 by 7-dehydrocholesterol: implications for the Smith-Lemli-Opitz syndrome. Pain 2017, 158: 2475-2486

Denner AC, Vogler, B, Messlinger K, De Col R. Role of transient receptor potential ankyrin 1 (TRPA1) receptors in rodent models of meningeal nociception - experiments in vitro. Eur J Pain 2017, 21: 843-854

Hartmann S, Zheng F, Kyncl M, Karch S, Voelkl K, Zott B, D'Avanzo C, Lomoio S, Tesco G, Kim DY, Alzheimer C, Huth T. β-Secretase BACE1 promotes surface expression and function of Kv3.4 at hippocampal mossy fiber synapses. J Neurosci 2018, 38: 3480-3494

Karch S, Broichhagen J, Schneider J, Böning D, Hartmann S, Schmid B, Tripal P, Palmisano R, Alzheimer C, Johnsson K, Huth T. A new fluorogenic small molecule labeling tool for surface diffusion analysis and advanced fluorescence imaging of β-site amyloid precursor protein (APP)-cleaving enzyme 1 based on silicone rhodamine: SiR-BACE1. J Med Chem 2018, Jul 10. doi: 10.1021/acs.jmedchem.8b00387

Hoffmann T, Sharon O, Wittmann J, Carr RW, Vyshnevska A, De Col R, Nassar MA, Reeh PW, Weidner C. NaV1.7 and pain: contribution of peripheral nerves. Pain 2018, 159: 496-506

Obreja O, Rukwied R, Nagler L, Schmidt M, Schmelz M, Namer B. Nerve growth factor locally sensitizes nociceptors in human skin. Pain. 2018 Mar;159(3):416-426

International cooperations

Prof. S. Werner, Institute of Molecular Health Sciences, ETH Zürich: Switzerland

Prof. S. Todorovic, U of Colorado School of Medicine, Aurora, CO: USA

Prof. A. Babes, University of Bukarest, Bukarest: Romania

Dr. M. Dux, Institute of Physiology, University of Szeged: Hungary

Prof. E. Jorum, Department for Neurophysiology, Rikshospitalet, University of Oslo, Oslo: Norway