Position: PhD positions
Subject: To study neural circuits of pain

The Collaborative Research Centre SFB 1158 ‘From nociception to chronic pain: Structure-function properties of neural pathways and their reorganisation’ is newly established in Heidelberg, Germany. Nineteen multidisciplinary projects spanning diverse top-class clinical and basic research institutions make this a remarkably vibrant and comprehensive collaborative centre.

Research in this consortium promises to deliver a structural and functional understanding of circuits and networks underlying sensory and affective components of pain and their modulation by circumstances which induce structural reorganization and functional plasticity, including disease states, negative emotions and stress. A mechanistic analysis of chronic neuropathic pain of peripheral and central origin in rodent models and in human patients will be a strong focus.

How to apply: The recruiting graduate school is The Harmut Hoffmann-Berling International Graduate School (HBIGS). Please apply to open PhD positions marked SFB 1158 on the HBIGS website: www hbigs.uni heidelberg.de

Salary: Fully-funded doctoral positions as per German regulations (TVL-13, 65%)
Contract length: PhD positions typically run for 3 years with the option of extending by 1 year.
Website of the Collaborative Research Centre: http://www.sfb1158.de/index.php/en/career-eng

Cortical signature of nociception and pain

Job ID: SFB1158_Baumgaertner
Project leader: PD Dr. med. Ulf Baumgärtner
Application Deadline: 15 August 2015
Start of PhD project: at the earliest
Source of Funding: SFB 1158

Project Description:
In the framework of Individual Project B05 of the collaborative research grant „Sonderforschungsbereichs SFB 1158 („Schmerz-SFB“; Heidelberg/Mannheim)“ we plan to map the cortical representation for nociceptive and non-nociceptive (tactile) stimuli in comparison applied to the hand and foot using functional magnetic resonance imaging (fMRI). Apart from the well-known so called homunculus, a cortical map of the body for touch and motor function within the primary somatosensory and motor cortices (SI, MI) the presence of additional maps of the body within both the second somatosensory (SII) and operculo-insular cortices (OIC) was published recently, among others, by this research group.
The specificity of these maps is still under debate and needs clarification. On the one hand, the brain areas that are activated by painful and non-painful control stimuli are to be mapped and summarized in a larger group (approx. n=50) of healthy volunteers. The coordinates of these areas serve as basis for investigations of cortical oscillatory activity in the same volunteers by means of electro- and magneto-encephalography (EEG, MEG) performed by colleagues working within the same project. On the other hand, the effect of a strong but brief pain stimulus on the cortical organisation of the body map and quantification of regional shifts will be investigated as measure of cortical reorganisation and/or plasticity. From the results, we expect to gain further insights into the cortical processing of nociception and pain, and into mechanisms of pain chronification.

Location: The fMRI-measurements will be done in Mannheim at the University Clinic (“Universitätsklinikum”); temporal flexibility is necessary to adapt to the available fMRI scanning times.

References:


Methods that will be used:
fMRI (functional magnetic resonance imaging), application of nociceptive and non-nociceptive stimuli, capsaicin application (skin), psychophysical testing of nociception/pain and somatosensation in healthy volunteers

Collaboration Partners:
PD Dr. Andre Rupp, MEG-unit (Section of Biomagnetism) of the Dpt. of Neurology, Prof. Dr. Andreas Draguhn, Dpt. of Physiology, Heidelberg University

Profile of candidate’s qualification:
Prerequisites (obligatory): study of medicine, dental medicine, psychology or biology (or alike), either finished or in progress (towards the end); fluent German and/or English language
Desirable: experience in fMRI data acquisition and analysis (e.g., spm or FSL), knowledge in matlab code, programming skills in general or specifically for Presentation® (Stimulus presentation software)

Keywords:
Human nociception, cortical representation, neuroimaging, reorganisation, brain networks

Structural and functional analyses of peripheral nerves in diabetic neuropathy in transgenic mice.

Job ID: SFB1158_KunerR_Gangadharan
Project leader: Prof. Dr. Rohini Kuner (Supervisor: Dr. Vijayan Gangadharan)
Application Deadline: 15th August, 2015
Start of PhD project: at the earliest
Source of Funding: SFB 1158

Project Description:
Diabetic polyneuropathy (DPN) comprises a wide spectrum of paradoxical symptoms related to functional changes of neural circuits associated with diabetes such as tingling, burning pain, heat hypersensitivity, loss of pain perception and numbness. This project is aimed to identify structural and functional changes in peripheral sensory fibers using various transgenic mouse lines and non-invasive multi-photon imaging of distinct classes of sensory nerves in mouse models of diabetic neuropathic pain.

References:

Methods that will be used:
Multi-photon in-vivo imaging in transgenic mice, confocal microscopy, image analyses, behavioural analyses of sensory function in mice and immunohistochemistry.

Collaboration Partners:
Prof. Thomas Kuner, Dr. Paul Heppenstall, Dr. Stephan Lechner, Prof. Peter Nawroth
Profile of candidate’s qualification:

We look for a highly enthusiastic, scientifically motivated student who can work independently as well as in team and holds masters degree in biology, neuroscience or biochemistry. The student should be interested in working with mice.

Keywords:

Multi-photon imaging, diabetes, pain, transgenic mice

Structural and functional interactions between nociceptive and non-nociceptive systems within the spinal trigeminal nucleus

Job ID: SFB1158_Carr

Project leader: PD Dr. Richard Carr

Application Deadline: 15 August 2015

Start of PhD project: 15 January 2015

Source of Funding: SFB 1158

Project Description:

Sensory signal processing in the trigeminal system displays clear signs of cross-modal integration. The perception of trigeminal activity can be modulated by the simultaneous activation of other sensory modalities including touch, smell, hearing, or vision. An extreme example is the triggering of migraine or other forms of headache by innocuous cross-modal sensory stimulation. The anatomical basis of this cross-modal integration is not well understood. In the case of interactions within the trigeminal system itself, sites of signal integration could exist at several levels of processing. Peripheral innocuous fibres, such as cool fibres or touch fibres, may affect signalling in nociceptive afferents via interneurons or via neuropeptides and their receptors. At higher centres, synaptic convergence may constitute a pathway for signal integration at the level of trigeminal projection neurons in the brainstem. Trigeminal signal integration with non-trigeminal systems, like the olfactory system, has also been documented in the periphery, in thalamic nuclei and in various cortical areas. In this project, the neuroanatomical and physiological processes whereby non-trigeminal sensory systems can impact on nociceptive signalling will be explored.

References:


**Methods that will be used:**

- Extracellular nerve terminal and brainstem recordings
- Intra-axonal calcium and sodium imaging
- Confocal and deconvolution microscopy
- 3D reconstruction with optional *in silico* simulations of firing behaviour in NEURON
- Behavioural experiments

**Collaboration Partners:**

Prof. Stephan Frings, COS, Heidelberg

**Profile of candidate’s qualification:**

A bachelor’s degree in the natural sciences (biology, physics or chemistry), mathematics (pure or applied), informatics or engineering is required and an interest in physiology and biophysics are essential for this project. Requisite training for each of the techniques will be provided during the candidature.

**Keywords:**

Trigeminal nociception, headache, Olfactory signalling

**Epigenetic control of structural and functional plasticity in spinal circuits**

**Job ID:** Bading0115

**Project leader:** Dr. Daniela Mauceri, Prof. Dr. Hilmar Bading

**Application Deadline:** 15 August 2015

**Start of PhD project:** As soon as position is filled (autumn 2015)

**Source of Funding:** DFG, SFB1158
Project Description:

Neurons have a highly specialized morphology, key to their functioning, which can undergo remodeling. Structural changes take place in response to physiological as well as to pathological stimulation. One of the pathological states in which maladaptive morphological rearrangements can be observed is chronic pain. The molecular players and genes regulating the structural changes underlying the critical transition between acute pain and chronic pathological pain have not been thoroughly investigated. Recently, it has been demonstrated that the shift from normal nociception towards hypersensitivity and hyperalgesia typical of chronic pain requires changes in gene expression in neurons of the dorsal horn of the spinal cord. Nuclear calcium is one of the most prominent regulators of gene transcription in hippocampal and spinal cord neurons. It modulates gene expression by directly acting on transcription factors or by regulating epigenetic processes. Interestingly, genes regulated by nuclear calcium signaling are emerging as key regulators of neuronal morphology. However, if and how epigenetic gene regulatory events control structural remodeling of spinal cord circuits and central sensitization remains to be investigated.

We hypothesize that, in the dorsal horn of the spinal cord, epigenetic processes modulate nociception-induced gene transcription and contribute to circuitry remodeling and central sensitization.

The PhD project will investigate epigenetic-regulated transcription and neuronal architecture remodeling in pathological pain states. The project includes *in vivo* experiments in which neurons of the spinal cord dorsal horn of adult mice are being manipulated using genetic tools and analyzed functionally and morphologically. Additional experiments will be done with dissociated cultured mouse spinal cord neurons. The project relies on an integrative approach that combines molecular, genetic, and biochemical methods with *in vitro* and *in vivo* imaging techniques and behavioral assays in mice.

References:


Methods that will be used:
Adeno-associated viruses and their delivery in vivo, morphometric analyses, mouse models of acute, chronic inflammatory and neuropathic pain, primary dissociated neuronal culture; behavioural testing, confocal and multiphoton imaging, short hairpin RNA (shRNA) gene silencing techniques; RNASeq analysis and standard molecular and cell biology methods.

Collaboration Partners:
Rohini Kuner (Institute of Pharmacology), Thomas Kuner (Institute for Anatomy and Cell Biology)

Profile of candidate’s qualification:
The candidate should be highly motivated, with an attitude towards independent work and must hold good interpersonal and communication skills. Applicants should have a strong background in molecular, cell biology and/or neuroscience. Candidates with prior experience with animal handling, the spinal cord system, stereotactic surgery, behavioural analyses and/or molecular biology will have priority. Fluency in English and the ability to work in an international environment is mandatory.

Keywords:
Neuronal morphology, epigenetics, pathological pain, neurons, spinal cord

Characteristics and consequences of subcellular calcium signaling in spinal neurons and glia in chronic inflammatory and neuropathic pain

Job ID: Bading_Sprengel0115

Project leader: Prof. Hilmar Bading, Dr. Rolf Sprengel

Application Deadline: 15 August 2015

Start of PhD project: 01 October 2015

Source of Funding: DFG, SFB1158

Project Description:
Activity-induced changes in intracellular calcium levels play an invaluable role in processes that control persistent adaptations within the central nervous system. Indeed, calcium signaling in spinal cord neurons, astrocytes, and microglia is strongly implicated in maladaptive pain plasticity. While it is well accepted that the spatiotemporal characteristics of a given calcium rise determine cellular responses, surprisingly little is known about the features of synaptic activity-triggered calcium signals in distinct subcellular compartments within spinal neuroglial networks, whether and how they are altered in chronic pain, and how they contribute to the cellular plasticity underlying pain
hypersensitivity. We hypothesize that calcium represents a key trigger for the long-lasting functional changes in cellular excitability and activity that underlie persistent pain sensitivity, and that altered cellular responsiveness following an acute painful insult may contribute to pain chronicity in a feed-forward manner via concomitant changes in sensory afferent activity-evoked calcium transients. We further propose that nuclear calcium signaling in spinal neurons and glia triggers functional and morphological plastic changes in these cells that are propagated throughout the entire spinal neuroglial network to ultimately result in the generation and maintenance of a persistent pain phenotype.

The PhD project aims to address these hypotheses first through a comprehensive analysis of the cellular (excitatory neurons, astrocytes, at least three classes of inhibitory neurons) and subcellular (cytoplasmic, nuclear, synaptic spines, fine astrocytic processes) calcium activation circuitry of spinal neurons and glia in naïve and persistent pain states. A second set of experiments employing nuclear calcium signaling inhibitors in defined cell types of the spinal cord dorsal horn (excitatory neurons, astrocytes, microglia, at least three classes of inhibitory neurons) should clarify the role of this signaling pathway for triggering the morphological changes involved in central sensitization and ultimately resulting in chronic pain hypersensitivity.

References:


Methods that will be used:

Live calcium imaging of acute spinal cord slices using subcellularly-targeted genetically encoded calcium indicators, suction electrode stimulation of spinal dorsal root afferents, viral-mediated gene transfer in vivo, mouse models of inflammatory and neuropathic pain, genetically encoded inhibitors of nuclear calcium signalling, behavioural testing, morphometric analyses, confocal and multiphoton imaging, and standard molecular and cell biology methods.
Collaboration Partners:
Rohini Kuner (Institute of Pharmacology), Daniela Mauceri (Department of Neurobiology)

Profile of candidate’s qualification:
We are looking for a highly motivated and self-driven PhD student with strong analytical and mathematical competencies. Applicants should have a Master’s degree in biological or physical sciences and a sound background in cellular physiology. The ideal PhD candidate has had experience performing live fluorescence imaging and/or electrophysiology and has strong skills in image analysis and MatLab/IgorPro/ImageJ. Experience with acute slice preparation, animal handling, stereotactic surgery, and/or behavioural analyses will be advantageous.

Keywords:
Calcium signalling, chronic pain, neurons, glia, spinal cord