CSC-RUB PhD Project Proposal

Title: Investigation of the role of the connectome of spatial memory encoding in the rodent brain using DREADDs, gene expression analysis, and functional magnetic resonance imaging

Sector of research: Systems and cellular neuroscience, synaptic plasticity, neuromodulation

Degree awarded: PhD in Neuroscience

Keywords: memory mechanisms, spatial memory, cortical plasticity, transgenics, chemogenetics, *in vivo* electrophysiology, fluorescence in situ hybridization,f unctional magnetic resonance imaging, rodent

Supervisor of PhD project: Prof. Dr. Denise Manahan-Vaughan, Medical Faculty, Dept. Neurophysiology, Ruhr University Bochum

Research focus of supervisor:

In my department we study the mechanisms underlying information storage and memory in the brain. In particular we want to understand how synaptic and cortical plasticity enables long-term information storage and memory retention. To do this we use a highly multidisciplinary neuroscientific approach including, for example, in vitro electrophysiology (patch clamp, multielectrode array, field potential recordings) and in vivo electrophysiology (single-unit, local field potential and brain oscillation recordings), optogenetics, chemogenetics, fluorescence in situ hybridization, immunohistochemistry, behavioral neurobiology, advanced signal analysis, wide-field calcium imaging and functional magnetic resonance imaging (fMRI) in rodents. PhD candidates typically start their project by focussing on developing strong expertise in one of these methods, but depending on the talent of the individual the methodological portfolio of the project is expanded. We investigate a wide range of processes involved in memory formation including the neurotransmitter basis, impact of neuromodulation, role of sensory input and affective state.

Publications:

Kemp A, Manahan-Vaughan D (2012) Passive spatial perception facilitates the expression of persistent hippocampal long-term depression. Cerebral Cortex. 22: 1614-1621.

Hauser M, Colitti-Klausnitzer J, Bellebaum C, Manahan-Vaughan D (2020) Event-related potentials evoked by passive visuospatial perception in rats and humans reveal common denominators in information processing. Brain Structure & Function. 41:1153-1166.

Hoang TH, Böge J, Manahan-Vaughan D (2021) Hippocampal subfield-specific Homer1a expression is triggered by learning-facilitated long-term potentiation and long-term depression at medial perforant path synapses. Hippocampus. In Press. doi: 10.1002/hipo.23333

Strauch C, Angenstein F, Manahan-Vaughan D (2021) Olfactory information encoding engages subcortical and cortical brain regions that enable sensory information processing and valence encoding. Cerebral Cortex In Press. doi: 10.1093/cercor/bhab226

Strauch C, Manahan-Vaughan D (2020) Orchestration of hippocampal information encoding by the piriform cortex. Cerebral Cortex. 30: 135-147.

H-index of the last 5 years: 34; **number of publications in the last 5 years**: >50

Summary of research plan

Background: The hippocampus is a key structure for the creation of associative and spatial memories in the brain. This process is supported by hippocampal synaptic plasticity and gene encoding at the level of immediate early genes in hippocampal neurons (Kemp and Manahan-Vaughan, 2008; Hoang et al., 2021). Less is known about how other brain structures are involved in the creation of spatial memory. In fact, **the connectome of this process is currently unclear**.

My lab has established novel methodology that permits the identification of brain. Structures involved in olfactory information processing using functional magnetic resonance imaging (fMRI) (Strauch et al., 2021). This approach offers unique opportunities to examine how extrahippocampal brain structures contribute to spatial memory processing. Another fascinating approach using DREADD technology (Alexander et al., 2009: DOI: 10.1016/j.neuron.2009.06.014), offers the possibility to chemogenetically 'label' memory engrams that are created during spatial experience. These can be subsequently re-activated using a so-called designer drug (CNO) so that memory circuitry can be scrutinized in detail.

Study objective: The objective of the PhD project is to examine the connectome of spatial memory encoding in the rodent brain. The goals of the project are **1**. To conduct behavioral learning experiments in transgenic mice that insert a human muscarinic receptor into brain cells that engage in the learning event. **2**. Using CNO, this circuitry will be subsequently re-activated during fMRI in mice **3**. We will then verify the participation of key structures in this process using fluorescence in situ hybridisation (FISH) to identify neuronal cell bodies that express immediate early genes as a result of the spatial learning event (Hoang et al., 2021).

Expected Results: We are confident that the three main goals of the project will be achieved and will result in a number of high-ranking publications.

Methods: We will trigger hippocampal synaptic plasticity in transgenic mice *in vivo* by means of electrophysiological stimulation. We shall use DREADD technology to label all neurons that participated in this event. Subsequently, we shall use CNO to re-activate these neurons during fMRI recordings. Fluorescence *in situ* hybridisation will be used to identify immediate early gene expression in neurons of significantly activated areas.

Candidate Requirements: Candidates should have studied neuroscience, neurobiology, or a related discipline**.** Experience with the acquisition and analysis of fMRI, in vivo electrophysiology and/or FISH data, and strong statistical and programming skills would be highly advantageous. Experience in working with live rodents and an understanding of rodent neuroanatomy would be helpful. Good English language skills are required.

Motivation for CSC application: The successful applicant will receive stringent and in-depth training in the complex methodological skills that are required for conducting fMRI recordings in rodents. He/She will be trained in the analysis of 7T fMRI data and experimentation and analysis skills for FISH). This includes training in the handling and habituation of rodents for 7-Tesla fMRI, acquisition and analysis of 7T fMRI data. The PhD candidate will also be trained in the implementation of FISH methodology and instructed in the accurate identification and counting of positively stained neuronal cell bodies. By this means the PhD candidate will conduct neuroimaging on both cellular and systems levels with the goal of understanding how sensory information processing leads to long-term memories in the brain. The Department of Neurophysiology is a vibrant environment that hosts scientists from all over the world and from a variety of scientific disciplines. PhD candidates will be supported by a highly skilled team of technicians and senior scientists, who ensure that an effective support system is always in place. The PhD project will be closely supervised by Prof. Manahan-Vaughan, who is internationally recognised in the field of synaptic plasticity and memory research. State of the art infrastructure and expertise is available for all elements of the project. PhD candidates are integrated into the internationally renowned graduate programme of the International Graduate School of Neuroscience that provides state-of-the art training in neuroscientific and professional skills.