CSC-RUB PhD Project Proposal

Title: Electrophysiological signatures of voluntary memory control

Sector of research: Cognitive neuroscience

Degree awarded: PhD in Neuroscience

Keywords: Memory control, emotional memories, intracranial EEG recordings, human single unit recordings, directed forgetting, think/no-think

Supervisor of PhD project: Prof. Dr. Nikolai Axmacher, Dept. of Neuropsychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum

Research focus of supervisor: How are experiences represented in the brain and transformed into memory traces? How do these experiences shape our personality? And how is memory compromised by trauma and Alzheimer's disease? In my group, we investigate the neural foundations of memory functions and dysfunctions using advanced cognitive neuroscience methods (fMRI at 3T and 7T, simultaneous EEG/fMRI, intracranial EEG, and human single unit recordings). Representations in neural networks are explored via distributed patterns of BOLD activity patterns and EEG oscillations and related to action potentials in single cells. We are particularly interested in the processing of specific contents by the brain, and study how stimulus specific representations can be decoded using algorithms from deep learning and artificial intelligence. We investigate a wide range of memory processes (working memory, long-term memory, memory consolidation during resting state and sleep, and autobiographical memory). Our vision is to track the brain mechanisms that support the transformation of sensory representations into memory traces and their modification during complex memory processes.

Publications:

- Liu J [...] Axmacher N*, Xue G*. Transformative neural representations support long-term episodic memory. **Sci Adv** (in press)
- Bierbrauer A [...] Axmacher N (2020) Unmasking selective path integration deficits in Alzheimer's disease risk carriers. **Sci Adv** 6(35):eaba1394.
- Kunz L [...] Axmacher N (2019) Hippocampal theta phases organize the reactivation of large-scale electrophysiological representations during goal-directed navigation. **Sci Adv** 5: eaav8192.
- Oehrn CR [...] Axmacher N. Direct Electrophysiological Evidence for Prefrontal Control of Hippocampal Processing during Voluntary Forgetting. **Curr Biol** 28(18):3016-3022.e4.
- Kunz L [...] Axmacher N (2015) Reduced Grid-cell-like Representations in Adults at Genetic Risk for Alzheimer's Disease. **Science** 350: 430-3.

H-index of the last 5 years: 38; number of publications in the last 5 years: 50

Summary of research plan

Background: While most memory studies focus on the formation and retrieval of relevant memories, the forgetting of unwanted experiences is equally relevant. Forgetting not only serves to avoid interference and to focus resources onto relevant information, but also to inhibit unwanted and emotionally distressing memories. Indeed, various studies demonstrated that unwanted information can be selectively inhibited during encoding and retrieval, and that this ability is critical for our mental health and wellbeing. Using intracranial EEG recordings in epilepsy patients, we recently showed that voluntary suppression of memory encoding relies on causal interactions between dorsolateral prefrontal cortex (DLPFC) and hippocampus (Oehrn et

al., *Curr Biol* 2018). Suppression of memory retrieval can be studied via the Think/No-Think paradigm, but the electrophysiological basis of this effects has never been investigated. In addition, it is not clear whether encoding and retrieval of negative emotional items can be suppressed as well, and whether this involves additional interactions with the amygdala.
Study objective: Our goal is a mechanistic understanding of the neural processes underlying inhibitory memory control for both neutral and negative material via direct electrophysiological recordings from the human brain. We aim to identify the neural mechanisms, in terms of stimulus-specific representations and frequency-specific oscillatory signatures within and between areas, during voluntary inhibition of memory encoding and retrieval.
Expected Results: We expect that memory control during both encoding and retrieval relies on inhibitory prefrontal-hippocampal interactions. However, we also expect differences in the timing of inhibitory influences during encoding and retrieval, e.g. with regard to the phase of hippocampal theta oscillations. We further hypothesize that inhibition of negative items relies on additional interactions with the amygdala. We expect that the results yield several high-impact publications.
Methods: We will study the inhibitory control of memory encoding and retrieval using intracranial EEG recordings in epilepsy patients. Two complementary paradigms will be conducted that target memory inhibition during encoding and retrieval (the item-method directed forgetting paradigm and the think/no-think paradigm, respectively). We will further scrutinize interactions with the amygdala during inhibition of emotionally negative material. This research will build on our long-standing expertise on intracranial EEG recordings (>15 years). Recordings will be conducted at several clinical sites throughout Germany and Europe with whom collaborations have been successfully established.

Candidate Requirements: We are seeking for candidates with a background in psychology, cognitive neuroscience, biomedicine or a related discipline, experience with the acquisition and analysis of EEG data, and strong statistical and programming skills. Good English language skills are required.

Motivation for CSC application: The successful applicant will receive rigorous and in-depth training of the complex methodological skills that are required for conducting highly advanced analyses of intracranial EEG data. This includes the acquisition of intracranial EEG data (in collaboration with our clinical partners) and data analyses using state-of-the-art methods (including time-frequency analyses and machine learning methods). All Ph.D. students of the Department of Neuropsychology have regular weekly meetings with the lab PI (Nikolai Axmacher), which ensures detailed supervision and feedback on all steps of this challenging project. In addition, students are co-supervised by an experienced postdoctoral researcher and interact closely with all other lab members. They will actively communicate with national and international collaborators, allowing them to become integrated into a scientific network at leading research institutions. The Department of Neuropsychology has an outstanding publication track record in leading international journals including *Science*, *Nature Neuroscience*, *Science Advances* etc. Because of the highly advanced methodology and the timely topic of the project, we expect the results to be published in high-impact journals as well. This will put the Ph.D. student in an optimal position for a subsequent postdoctoral fellowship at an internationally leading institution and a successful scientific career. All Ph.D. students present their results regularly at international conferences and receive training on their presentation skills. Students will be encouraged for short-term visits at collaborating labs, allowing them to further deepen their expertise. Ph.D. students will be integrated into the Ruhr University Research School and benefit from the opportunities of interdisciplinary exchange.