NENS Exchange Grant Report

In vivo Ca+2 imaging of CA1 pyramidal neurons in the ventral hippocampus during discrete behavioral states.

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Home Programme: Signal Processing in Neurons (SPIN) doctoral school

Home Lab: Prof. Francesco Ferraguti Laboratory, Department of Pharmacology, Innsbruck Medical University, Innsbruck (Austria)

Host Programme: Neuroscience Network Basel

Host Lab: Andreas Lüthi Laboratory, Friedrich Miescher Institute for Biomedical Research, Basel (Switzerland)

Overview:

The aim of my training stay was to acquire the technical skills required to perform in vivo Ca+2 imaging experiments in behaving mice and learn how to process and analyze the data. We decided to take this approach in order to characterize the effects of the lack of mGlu5 receptors on the activity of principal neurons of the CA1 region of the hippocampus during social behaviors and high anxiety states.

A large body of evidence has implicated an altered signalling or expression of the mGlu5 receptor in the pathology of several neuropsychiatric disorders, including autism, anxiety disorders and schizophrenia. Recent research suggests that systemic deviations in any direction of mGlu5 receptor function may lead to social dysfunction. So far however, it remains unclear how mGlu5 receptors contribute to the expression of social preference and anxiety and particularly which neural circuits underlying these behaviours are preferentially affected by activity of these receptors.

Preliminary data from our group suggests that the lack of mGlu5 receptors in the ventral hippocampus pyramidal neurons alters the expression of discrete social as well as anxiety-like behaviors. During my training stay with Prof. Lüthi, we aimed at characterizing how the lack of mGluR5 in the ventral CA1 region of the hippocampus (vCA1) modulate the excitability of these cells in relationship with changes in social behavior and anxiety.

As a first step in my training, I learned how to perform the surgical procedure required to perform this technique. Briefly, I stereotactically injected 8-10 week old mGluR5 Fl/Fl mice with a combination of AAV-CamKIIa-Cre or saline (control) into the vCA1 region together with AAV-CaMKII-GCaMP6f. Subsequently, a 0.6mm gradient index (GRIN) lens was implanted above the injection site and fixed to the skull. Four to six weeks after surgery, enabling mice to fully recover and allowing for optimal viral expression, mice were checked for GCaMP6f expression through the miniature microscope. Microscope base plates were glued with dental acrylic one week before the experiments start under light anesthesia.

Experimental mice were then tested in a battery of tests: the classical three chambered social task to evaluate social preference and novelty, an elevated plus maze to test for anxiety and a novel social fear conditioning paradigm developed by Dr.Fustiñana and Dr.Bitterman in the lab of Prof.Lüthi.

Calcium imaging raw movies were acquired during the behavioral tests through the miniature microscope at 20Fps. Once all imaging data was acquired for a given mouse, raw videos were concatenated, transformed, spatially down-sampled, motion corrected across frames and dFoF was extracted using custom-made Matlab scripts. Single cell regions of interest were extracted and filtered using both PCA/ICA and CNMFe methods, in order to extract calcium traces. These traces were then split back to original video lengths and Z scored. Using again custom Matlab scripts, we timely paired the behavioral scores in each test with the calcium traces.

Our preliminary results show that vCA1 pyramidal cells display complex activity patterns in high anxiogenic environments and during social interactions, and that mGlu5 receptors are crucial modulators of the activity in this area.

Thanks to my training I have been able to obtain important preliminary results for my PhD project and to learn this very complex and demanding technique. In the next few months I will establish this technique in my home lab and continue my experiments there.

My stay at the FMI in Basel has been very fruitful, both in terms of learning the technique and advancing in my PhD project. The FMI has a vibrant and excellent neuroscience community made of extraordinary scientists. It has been a pleasure to be surrounded by all these colleagues who willingly offered help, insights and excellent scientific input. It was truly delightful, and therefore I would like to thank the NENS Committee of Higher Education and Training for having given me this magnificent opportunity and provide me with the necessary funding to cover the high cost of living in Switzerland for the last few months.

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