Universität Basel

Research Project

Investigation of midbrain circuitry underlying motor and cognitive behaviors

Third-party funded project

Project title Investigation of midbrain circuitry underlying motor and cognitive behaviors
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Motion, cognition including decision making and conditioned learning as well as anxiety-related states are behavioral responses we produce in our everyday life. My team has dedicated time and effort into the circuit dissection of such functions with a special focus on the specific cell types and their related pathways involved in the generation of movement initiation and maintenance, fine motor skills precisely reaching and grasping, conditioned learning and anxiety. In this project we focus on two main lines:

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1- "Role of Zona Incerta subpopulations under anxiogenic and fearful states"

As the name implies, the Zona Incerta is a region shrouded with mystery. Interestingly, clinical studies have reported that deep brain stimulation (DBS) of the ZI alleviates symptoms of movement disorders such as Parkinson's disease and tremor disorders. Additionally, ZI DBS resulted in lower measures of anxiety and depression (Burrows et al., 2012). This suggests a link between the ZI and these emotional states. Despite this interesting clinical observation, the role of the ZI in anxiety has not been investigated. We hypothesized that **specific neuronal subpopulations in the ZI encode anxious states** and propose a multi-level approach that will address the following questions:

– What are the neuronal cell types expressed in the ZI?
– What is the input-output connectivity of each ZI neuronal cell population?
– How do ZI neurons respond to anxiogenic/fearful events?

This research proposal relies on the use of cutting edge technologies which are fully established and functional in our laboratory, including in situ fluorescent hybridization (FISH), anatomical mapping of specific cell types, *in vitro* patch clamp recordings, *in vivo* calcium imaging (Inscopix mini-endoscope) in freely behaving mice, motor-, fear-, and anxiety-related behavioral tasks and *in vitro* as well as *in vivo* optogenetic manipulations.

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2- "Input-specific synaptic plasticity underly reaching skills"

The Red Nucleus (RN) is required for limb control, specifically fine motor coordination. Our previous work reports unprecedented findings showing that Vglut2-expressing RN neurons undergo plastic changes to encode the optimization of fine movements (Rizzi et al., 2019). Here we propose a follow up study which will **identify the excitatory inputs involved in the synaptic plastic modifications underlying the acquisition of the reaching movement**. To do so we will address the following aims:

– What are the monosynaptic inputs onto Vglut2- positive RN cells?
– How does each input neuron type encode information during learning in the reaching task?
– Which of these selective synapses undergo plastic changes during learning in the reaching task?

To accomplish this project, we will perform complementary experiments including anatomical mapping of specific cell types, *in vivo* multi-unit recordings in awake behaving animals, *in vitro* patch clamp recordings, single pellet reaching task and optogenetic photo-identification.

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