Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : Neuroscience Paris Seine
Research Unit Director : Hervé Chneiweiss
Research Team Director : Régis Lambert and Nathalie Leresche
Team name : Neural Networks and Physiopathological Rhythms

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2. Internship project title:

Unraveling the role of the anterior pretectum in shaping sensory perception.

3. Internship Description :

Conscious perception of the information flowing from the outside world relies on the coordination in space and time of the spiking activity of neurons located in many cortical areas. Such coordination is achieved by cortico-cortical connections and the interactions between cortex and different thalamic nuclei.

Thalamic nuclei are divided into two types, namely first-order and high-order nuclei. While first-order thalamic nuclei constitute the entry point of the information flowing from the outside world to the cerebral cortex, the roles of high-order thalamic nuclei remain to be established. Indeed high-order thalamic nuclei, which constitute most of the thalamus, do not receive substantial direct sensory inputs. Therefore, it has been suggested that they mostly relay signals from one cortical region to another.

If we take the somatosensory thalamus as a system model, two distinct high-order nuclei are involved: the Posterior group (PO) and the Mediodorsal nucleus (MD). PO receives its major inputs from the somatosensory and motor cortices and projects back to these structures. It was therefore proposed that it conveys sensory information that is contingent on motor instructions. The relevance of MD in cognition is rooted in its dense connections with frontal cortical regions involved in multimodal sensory integration and decision-making.

PO and MD nuclei are under the control of GABAergic afferents that arise in a set of nuclei outside the thalamus, namely the zona incerta (ZI) and the anterior pretectum (APT). Although much is known about the anatomical and physiological substrates of ZI and APT connectivity, the specific contributions of

these structures to the sensory processing operated by PO and MD neurons and their consequences on tactile perception are completely unknown.

In this context, we started a project that aims at understanding the role of APT-PO connectivity in shaping sensory perception. We choose to focus on this pathway because, despite the fact that APT to PO terminals are the largest and most complex inhibitory terminals of the brain described so far, APT is among the least studied regions of the brain; its name does not even appear in the index of most textbooks.

Using patch-clamp recording in brain slices, we found that APT neurons display intrinsic properties that allow them to discharge at extremely high-frequency (approaching the theoretical maximal firing rate of 1000 Hz). Moreover, we found that tissue-specific genetic modification of the intrinsic properties of APT neurons using a viral vector dramatically change the threshold for tactile perception under some conditions.

These preliminary results raise some specific questions such as:

1) What are the firing patterns evoked in APT neurons during tactile stimulations?

2) What are the roles of APT neurons in shaping the patterns of activity in PO neurons during tactile stimulations? Do they shape the spatial and temporal components of the spiking activity? Do they limit the time of action of excitatory events? Are they involved in modulating the intrinsic electrophysiological properties?

During his internship, the student will address these questions by combining state of the art multi-site single-unit recordings in APT and thalamus of anesthetized and awake mice. The spiking activity will be studied in relation with the motion of the whiskers. Indeed, while human and non-human primates use their fingers to gather information about their nearby environment, rodents explore their immediate environment using their whiskers. Because of the clear organization of the whisker pad and the fact that the neuronal pathways that transmit information from the whiskers to the sensory cortex are pretty well understood, this sensory system is an attractive model for the study of APT-PO interactions.

The specifics role of APT neurons in modulating the patterns of activity in PO neurons will be investigated through an optogenetic approach. Activating and inhibiting opsins will be expressed in APT neurons using both transgenic animals (AI32 x PV-Cre mice) and viral vectors (AAV-retro CAG-Cre x AAV DIO-ChR2-mCherry viruses or AAV-retro CAG-Cre x AAV8 DIO-ArchT-GFP viruses).

This internship can be considered as a prelude to a Ph.D. research project during which, the impact of the recruitment of the APT-PO pathway on behavior will also be investigated. Furthermore, depending on the available time, a similar study will be performed to unravel the role of the APT-MD pathway in sensory perception.

Selected publication:

Halassa MM, Kastner S (2017) Thalamic functions in distributed cognitive control. Nat Neurosci 20:1669–1679 Available at: http://dx.doi.org/10.1038/s41593-017-0020-1.