Institute: Institute of Zoology and Biomedical Research

Topic: Neural basis of circadian changes in animal motivation.

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Background information:
The regulation of circadian rhythms in animals is a complex process that involves the integration of multiple neural and molecular pathways. One important aspect of this regulation is the modulation of motivation, which can vary depending on the time of day. Previous studies have shown that the lateral habenula (LHb) plays a key role in this process, with changes in LHb activity influencing the expression of motivated behaviours at different times of day. Recent research has also suggested that the serotonergic system may be involved in the regulation of circadian changes in animal motivation. Specifically, the serotonergic input to the LHb has been suggested to be involved in the modulation of motivated behaviours across the day/night cycle [1, 2]. However, the exact neural mechanisms underlying this regulation are still not well understood. Thus, the project aims to investigate the role of serotonergic input to the LHb in regulating circadian changes in motivated behaviours. This will involve a combination of neurophysiological, anatomical, and behavioural analyses, to better understand the neural circuits and molecular pathways involved in this process.

The main question and tasks:
Does serotonergic innervation of the lateral habenula participate in the circadian changes in the activity of the mammalian reward system. In particular: 1) what is the circadian profile of serotonin release in the lateral habenula?; 2) what is the anatomy of the pathway connecting the serotonergic system and elements of the reward system via the lateral habenula?; 3) how the manipulation of the elements of this circuit affects the behaviour of animals.

Information on the methods:
The studies will be performed on adult male rats. The following experimental techniques are planned to be used: 1) Fibre photometry: measurement of serotonin dynamics in the lateral habenula of anaesthetized and freely moving rats around the circadian cycle; 2) Neuroanatomy: neuronal tract-tracing with the use of anterograde, retrograde and transsynaptic viral vectors and classical chemical markers; 3) Behaviour: testing of animal behaviours during optogenetic and chemogenetic manipulation of studied neuronal pathway.

Special requirements from the student:
The student should have experience in the following research techniques: injections of viral vectors into the selected structures of the rodent brain; experience in fibre photometry measurements of neurotransmitter release; behavioural testing of laboratory animals (rats); preparation and microscopic analysis of the histological material of immunocytochemically stained nerve tissue. In addition, the student should have the following skills, training and qualities: training to perform procedures and experiments and to kill animals (in accordance with the applicable Act on the protection of animals used for scientific or educational purposes, of January 15, 2015); good command of the English language.

References:
[1] Pradel K, Drwięga G, Chrobok L, Błasiak T (2022) Racing and Pacing in the Reward System: A Multi-Clock Circadian Control Over Dopaminergic Signalling. Front Physiol.13:932378. doi: 10.3389/fphys.2022.932378.
[2] Zhang H, Li K, Chen HS, Gao SQ, Xia ZX, Zhang JT, Wang F, Chen JG (2018) Dorsal raphe projection inhibits the excitatory inputs on lateral habenula and alleviates depressive behaviors in rats. Brain Struct Funct. 223(5):2243-2258. doi: 10.1007/s00429-018-1623-3.