Institute: Institute of Zoology and Biomedical Research

Topic: The influence of dopamine released in the motor cortex on the acquisition of precise motor skills.

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Background information:
The motor cortex gives rise to major descending circuits that control voluntary movement and are critically involved in learning motor skills, e.g. reaching, grasping and manipulating objects. The mechanisms by which motor learning occurs are still not fully understood. This is partly due to the complexity of the circuits of the motor cortex, containing a wide variety of types of pyramidal neurons [1]. One possible process by which learning and motor updating is achieved is error-based learning. The best-known error signal in the mammalian brain is the dopamine (DA) encoded reward prediction error [2]. This suggests that DA-dependent modulation of neural assemblies in the motor cortex may be required to refine precise movements. However, a causal relationship between DA release and neuronal activity in the motor cortex has not yet been described.

The main question and tasks:
How spatiotemporal differences in DA levels relate to ongoing neuronal activity in the motor cortex and influence behaviour in awake mice performing motor task. In particular: 1) to measure DA release in the motor cortex and calcium dynamics in genetically defined types of cortical neurons; 2) to determine the functional role of DA-sensitive cells in motor cortex by performing chemogenetic and optogenetic manipulations during ongoing behavior.

Information on the methods/description of work:
The studies will be performed on adult male mice congenic with C57BL/6N strain, harbouring a Cre recombinase expressed under the control of the Drd1a (D1 receptor) or Drd2 (D2 receptor) gene promoters. The following experimental techniques are planned to be used: 1) *In vivo*, fibre photometry: imaging of DA release and intracellular calcium concentration in defined populations of motor cortex pyramidal neurons in head-restrained animals performing motor tasks; 2) Behavioural: mice will learn to maneuver the joystick up to a certain threshold to receive a water reward while activity of the studied population of cortical neurons will be chemogenetically or optogenetically manipulated.

Additional information:
The student should have experience in the following research techniques: injections of viral vectors into the selected structures of the rodent brain; fibre photometry imaging of neuronal activity in an *in vivo* preparation of head restrained mice; behavioural testing of laboratory animals (mice). 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:
Economo Michael, Viswanathan Sarada, Tasic Bosiljka, Bas Erhan, Winnubst Johan, Menon Vilas, Graybuck Lucas, Thuc Nghi Nguyen, Smith Kimberly, Yao Zizhen, Wang Lihua, Gerfen Charles, Chandrashekar Jayaram, Zeng Hongkui, Looger Loren, Svoboda Karel (2018) Distinct descending motor cortex pathways and their roles in movement. Nature 563(7792):79-84.
Schultz Wolfram, Dayan Peter, Montague Read (1997) A neural substrate of prediction and reward. Science 275(5306):1593–1599.