

Behaviours facilitating gain of food, reproductive mate and other natural rewards as well as avoiding predators or pain and discomfort are one of necessities for survival of specimen and species. Reward induces pleasurable feelings and leads to association of the reward with environmental stimuli or conditions that had been present at the time of reward acquisition. Similarly, occurrence of aversive stimulus (or punishment) causes avoidance along with reduction of associated behaviours. The perspective of reward acquisition or aversive event avoidance essentially drives decision making and learning.

One of the key structures of the so-called reward system is ventral tegmental area (VTA). This structure, located in ventral midbrain, consist mainly of neurons synthetizing dopamine. Occurrence of unexpected reward, reward related cue or novelty results in phasic increase of dopamine neurons activity as well as increase of amount of secreted dopamine. Phasic changes in dopamine neurons activity allows to compare delivered reward with expected reward, resulting in updating reward expectations and learning. Likewise, occurrence of aversive stimuli or punishment inhibits or attenuates dopamine neurons activity resulting in decrease of dopamine secreted.

Recent studies had distinguished population of dopaminergic cells within VTA that are, contradictory to what was previously assumed, excited by appearance of aversive stimuli. Highlighting their disparity, those cells also appear to be localized in specific region of VTA. Notion of two different populations of dopamine neurons within VTA, responding to the aversive stimuli with either pause or elevated activity can be questioned based on our results from recordings of VTA dopamine neurons' responses to the aversive stimulus. Obtained results indicate existence of VTA neurons that can be both excited and inhibited by aversive stimulus occurrence depending on animal's brain state.

In order to further investigate this matter, we are planning to record responses of VTA dopaminergic neurons to the aversive stimulus in urethane anaesthetized rats. Urethane is an anaesthetic widely used in electrophysiological studies. It creates a long lasting, steady anaesthesia characterized by spontaneous brain state alternations similar to those observed during natural sleep and therefore is proposed as its model. Not only VTA dopaminergic neurons will be recorded but GABA (gamma-aminobutyric acid) synthetizing cells as well. GABAergic neurons within VTA are thought to locally control dopaminergic neurons activity. However, our preliminary results suggest that dopaminergic neurons' responses to the aversive stimulus are not controlled on local level. Therefore, one of the major inhibitory inputs to the VTA will be investigated - recordings of rostral-midline tegmental nucleus (RMTg) neurons' responses will allow to establish role of this structure in modulating VTA dopaminergic neurons in encoding the aversive stimulus response. During study we are planning to use method that allows to visualize, precisely localize and biochemically characterize recorded neurons. Based on these results, map of dopaminergic and GABAergic neurons' responses to the aversive stimulus will be created.

Implementation of this study will allow to characterize VTA dopaminergic and GABAergic neurons' responses to the aversive stimuli across alternating brain states under urethane anaesthesia and complement current knowledge about the role of RMTg in reward system. Physiological and biochemical characterization of neurons responding to the aversive stimulus in brain state dependent manner will entail better understanding of mechanisms engaged in encoding of responses to the aversive stimuli as well as mechanisms modulating dopaminergic neurons of the reward system. Better understanding of how reward-punishment system works and is modulated can contribute to explanation of mechanisms' dysfunctions laying at the root of some nervous system disorders such as addiction, anxiety, PTSD or some of depression symptoms (anhedonia or lack of motivation).