

Three years ago we discovered that the posterior hypothalamic area (PHa), including the supramammillary nucleus and posterior hypothalamic nuclei, is able to generate local cholinergic theta field potentials independently of the hippocampal formation. Interestingly, electrophysiological mechanisms underlying the generation of this EEG phenomenon in the PHa and its physiological functions are still largely unknown.

Experiments performed over the last few years have revealed that human theta oscillations can be considered as a non-specific indicator of many pathological processes that can be observed in the central nervous system. For example, significant changes in theta band oscillations were observed in Alzheimer's disease (AD) patients. It was shown that cognitive decline is associated with increased synchronization in theta band in AD patients. Alterations in theta characteristics might serve as a diagnostic and prognostic biomarker in early AD in the future, and the study of this EEG phenomenon could yield important information concerning the etiology of AD. It was also demonstrated that there is a clear link between human theta oscillations and stress response of an organism. It is known that working memory-related theta activity is decreased under acute stress and that stress-related performance decreases in the high workload condition, which is related to theta rhythm decrease. On the other hand, there are also studies showing large-scale increase in theta-band synchrony in post-traumatic stress disorder (PTSD) patients. This increase is significantly correlated with a number of cognitive and behavioral outcomes, including measures of attention, depression and anxiety. Stressful environmental conditions elicit activation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in a number of metabolic, emotional and immunological changes. The last stage of these processes is the synthesis and secretion of glucocorticoids by the adrenal gland: corticosterone in rodents, cortisol in humans. The effects induced by glucocorticoids are critical for the ability of individuals to adapt metabolically and behaviorally to stressful events. It has been reported that sustained alterations in the HPA axis activity, which induce elevated glucocorticoid levels, may underlie the pathophysiology of such disorders as depression, precipitation of psychoses, increased vulnerability to addictive substances, and PTSD. A precise understanding of how acute and chronic stress interferes with neuronal networks engaged in the generation of theta-band oscillations is of great importance for the treatment of stress disorders and for the development of novel diagnostic methods and therapeutic interventions.

The research hypothesis states that the modulation of local corticosteroid receptors in the posterior hypothalamic area would positively affect posterior hypothalamic theta oscillations, which would be reflected in their electrophysiological properties that are responsible for emergence and control of this EEG phenomenon. We are convinced of the pioneering nature of the presented research proposal. In the present research, we propose a complex examination of the phenomenon of local theta rhythmicity in the PHa and its modulation by corticosterone. *In vivo* and *in vitro* extracellular recordings will be complemented with intracellular *in vitro* examinations. These experiments will shed light on possible ionic mechanisms involved in generation of posterior hypothalamic oscillatory activity. Such multi-level approach to the PHa theta rhythmicity will give a full functional characterization of this EEG phenomenon. Finally, the studies performed on freely moving animals would give the opportunity of evaluation of physiological functions of posterior hypothalamic theta rhythm in behaving animals and its relationship to the stress response of an animal.