

**Objectives:** The general objective of the project is to elucidate processes taking place in brain in response to chronic treatment with the hormone and to understand the relationship between the lifestyle and the response to corticosterone. The specific aim of the project is to unravel hippocampal transcriptomic responses to cycles of high levels of corticosterone mimicking daily stress alternating with normal levels during periods of sleep and to link detected changes in transcription with various physiological processes. Subsequent immunostaining of brain slices will enable us to identify cellular localization of gene expression (neurons, astrocytes) and will also provide data for other brain regions. First, we want to investigate changes in transcription during the period of sleep following 12 hours of corticosterone administration in drinking water. Second, we plan to investigate changes in transcription in response to chronic administration of corticosterone mimicking chronic daily stress. Finally, we plan to investigate the relationship between response to the stress hormone and voluntary exercise. We assume that changes in transcription will depend on duration of increased level of corticosterone because it activates negative feedback loop inhibiting the transcriptional activity of glucocorticoid receptors and at the same time it alters expression of other transcription factors. Therefore, we should expect that prolonged treatment with corticosterone will be associated with gradually diminishing transcriptional activity of glucocorticoid receptors and increased secondary effects induced by other transcription factors. However, it is not easy to predict the final effect because high levels of corticosterone induced by stressful experiences are usually interrupted by periods of sleep and because of additional epigenetic modifications that are induced by the hormone. **Methods:** Experiments will be performed on outbred Swiss-Webster male mice. We will use microarrays to detect transcriptomic responses in mouse hippocampus. Corticosterone will be delivered via drinking water at a dose of 75 µg/ml following previously validated method. Animals will be sacrificed at different latencies depending on the experiment. We will record the food intake (every day) and body weight (once a week at the time when animals receive clean cages) to monitor the response to the corticosterone. These measurements are sensitive indicators of stress response and do not constitute a source of additional stress, which could confound the results. Other indicators of the stress / corticosterone response will be recorded post mortem. These indicators include measurement of the blood corticosterone level and recording the weight of adrenal glands, thymus and spleen. Selected genes derived from microarray data will be validated with PCR. Precise cellular and anatomical localization of expression of selected molecules will be determined in brain slices labeled with antibodies. The analysis of slices will allow us to extend the data to other brain regions. **Impact of the project:** Release of the corticosterone is a key mechanism involved in stress response. Furthermore, an inappropriate stress response or lack of stress adaptation contributes to the mechanism of various diseases. Therefore, understanding the biological processes triggered by the corticosterone is crucial for the treatment and prevention of stress-induced diseases.