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Streszczenie w języku angielskim, rozprawy doktorskiej: „Corticosterone Regulation of Synaptic Plasticity: Mechanisms in Primary Cortical and Hippocampal Neurons".

**Summary**

Synaptic plasticity, a form of neuroplasticity, underlies the proper functioning of the brain. Because the brain's predominant chemical synapses reside on dendritic spines, synaptic plasticity can be studied by analyzing spine morphology and/or density. Even slight deviations from typical dendritic spine morphology can lead to dysfunction at the level of single cells and entire neuronal networks. Therefore, understanding how various biological factors influence dendritic spine morphology, and thus synaptic plasticity, is crucial.

One factor that affects dendritic spine morphology is chronically elevated corticosterone (CORT). Chronically elevated CORT results in a reduction in the number of spines on cortical and hippocampal neurons and in modifications of their structure. However, it remains unknown whether CORT is a direct driver of spine morphological changes and, if so, to what extent and which specific structural parameters are altered in cortical and hippocampal neurons by prolonged elevated CORT. Moreover, the signaling pathways through which CORT affects dendritic spine structure have not been fully elucidated. One protein whose activity is linked to spine reorganization and may be indirectly modulated by CORT is focal adhesion kinase (FAK). Despite indications suggesting potential involvement of FAK in CORT-induced morphological changes of dendritic spines in cortical and hippocampal neurons, definitive data confirming this hypothesis are still lacking.

In light of the above, the primary aim of this doctoral thesis was to test the hypothesis that prolonged elevation of CORT induces morphological changes in dendritic spines of cortical and hippocampal neurons, and then to characterize the observed changes. The second goal was to test the hypothesis that FAK is involved in CORT-induced morphological changes of dendritic spines in cortical and hippocampal neurons.

To achieve these aims, mouse primary cortical and hippocampal cultures were incubated with chronically elevated CORT; their dendritic spines were then visualized and imaged using

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confocal microscopy and analyzed with respect to selected structural parameters. Additionally, using pharmacological tools such as a FAK activator and inhibitor, as well as molecular biology methods such as the real-time polymerase chain reaction (RT-qPCR), we examined the role of FAK in CORT-induced changes in dendritic spine morphology.

In the first stage, we experimentally identified a CORT concentration that triggers a glucocorticoid-signaling response without affecting the viability of primary cells or the overall neuronal morphology.

In the next stage, we demonstrated that chronic elevation of CORT differentially influences dendritic spine morphology in primary hippocampal versus cortical neurons. For cortical neuron spines, we observed an increasing trend, while hippocampal neuron spines showed a decrease in their mean length. Additionally, in primary cells from both regions, we noted a reduction in spine head width. Furthermore, we showed that manipulating FAK activity can mimic or counteract the effects of CORT. In primary cortical neurons, applying an inhibitor of FAK phosphorylation caused changes in spine morphology similar to those seen with prolonged CORT exposure. These results were not observed in primary hippocampal cells. Conversely, activating FAK counteracted changes in spine length and head width in cortical cultures but not in hippocampal cultures, where FAK activation only reversed the CORT-induced decrease in average head width and had no effect on the decline in average spine length. We also observed time-dependent changes in the mRNA levels of the gene encoding FAK in cortical cells, but no such changes occurred in hippocampal cells. Finally, we found no effect of chronic CORT elevation on total and phosphorylated FAK protein levels in either cortical or hippocampal cells.

In summary, this doctoral dissertation provides new insights into how chronically elevated CORT shapes the morphology of dendritic spines in cortical and hippocampal primary neurons. It also indicates a potential role for FAK in spine morphological changes observed both under CORT-deprived conditions and in response to CORT.