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Disquisition on psychometric behavior and the morphine-binding protein P23K in the rat hippocampus in a model of chronic stress.

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High circulating levels of glucocorticoids can adversely affect learning aptitude and reduce memory capacity in mammals. The precise mechanisms by which prolonged excess glucocorticoids such as under conditions of chronic stress impair memory, however, are not fully understood, but there is evidence that they involve cellular changes in the hippocampus. The present study investigated how chronic administration of the glucocorticoid corticosterone for 60 days affects the distribution of corticosterone target proteins in rat hippocampus using semi-quantitative two-dimensional sodium-dodecylsulfate polyacrylamide gel-electrophoresis (SDS-PAGE), Western blotting, MALDI-TOF mass spectrometry and bioinformatic network mapping with molecular pathway analysis. Using a holeboard memory test, the study also investigated if and how chronic corticosterone affects the morphine-binding protein P23K, a.k.a. phosphatidylethanolamine-binding protein (PEBP1), in the hippocampus in relation to hippocampus-sensitive memory performance, which is thought to play a prominent role in chronic cellular stress-related neurodegenerative diseases such as Alzheimer's disease. Results show that the chronic administration of corticosterone for 60 days suppressed P23K expression in the adult rat hippocampus which was associated with a significant memory impairment in the animals. These changes were paralleled by regulation of various putative corticosterone target proteins in the hippocampus that included cytoskelatal compounds, folding agents and metabolic components, reflecting an active proliferative and differentiative protein turnover in the tissue during the chronic corticosterone. Based on these results and previous data on the morphine-binding protein P23K, we derive the conclusion that P23K expression is part of a hitherto unknown regulative mechanism in adaptive management of chronic glucocorticoids in the hippocampus and acts as a physiological mediator of tissue responses to changes in supply and demand of cholinergic components during such forms of stress. As part of a feed-back/feed-forward cycle in neuroprotective response, P23K may be an as yet undescribed molecular switch in the hippocampus that influences memory and cognitive integrity of rats under chronically elevated corticosterone, respectively stress, possibly acting via the septo-hippocampal system, neurogenesis, and/or reactive oxygen species downstream of the glutamate/NMDA receptor excitotoxicity cascade.