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Sub-Chronic Exposure to Dexamethasone Impairs Cognitive Function and Insulin in Prefrontal Cortex of Male Wistar Rats

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Abstract : Chronic stress or prolonged glucocorticoid administration impairs higher cognitive functions in rodents and humans. However, the mechanisms are not fully clear. Insulin and receptors are expressed in the brain and are involved in cognition. Insulin resistance accompanies Alzheimer's disease and associated cognitive decline. The goal of this study was to evaluate the effects of sub-chronic administration of a glucocorticoid, dexamethasone (DEX) on behavior and biochemical changes in prefrontal cortex (PFC). Male Wistar rats were administered DEX (2, 4 & 8 mg/kg, IP) or saline for seven consecutive days and behavior was assessed in the following paradigms: "Y" maze, elevated plus maze, Morris' water maze and novel object recognition (NOR) tests. Insulin, lactate dehydrogenase (LDH) and Superoxide Dismutase (SOD) activity were evaluated in homogenates of the prefrontal cortex. DEX-treated rats exhibited impaired prefrontal cortex function manifesting as reduced locomotion, impaired novel object exploration and impaired short- and long-term spatial memory compared to normal controls ($p < 0.05$). These effects were not consistently dose-dependent. These behavioral alterations were accompanied by a decrease in insulin concentration observed in PFC of 4 mg/kg DEX-treated rats compared to control (10μIU/mg vs. 50μIU/mg; $p < 0.05$) but not 2mg/kg. Furthermore, we report a modification of brain stress markers LDH and SOD ($p > 0.05$). These results indicate that prolonged activation of GCs disrupt prefrontal cortex function which may be related to insulin impairment. These effects may not be attributable to a non-specific elevation of oxidative stress in the brain. Future studies would evaluate mechanisms of GR-induced insulin loss.

Keywords : dexamethasone, insulin, memory, prefrontal cortex
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