

OBESITY-RELATED TO TYPE-2 DIABETES AND BRAIN CHOLINERGIC DYSFUNCTION: EVIDENCE FROM OBESE ZUCKER RATS

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Obesity is associated with glucose intolerance, type 2 diabetes, and dyslipidemia. Type-1 and type-2 diabetes are related with reduced performance on cognitive function likely depending by changes of the cholinergic system. The obese Zucker rats(OZR), with leptin receptors mutation, represent a model of obesity related to type-2 diabetes. This study has investigated cholinergic system of OZR compared with non-obese cohort lean Zucker rats(LZR) to assess possible relationships between obesity and brain disorder.

Male OZR and LZRs of 12, 16 and 20 weeks of age were used. Behavioural tests were performed to identify cognitive changes. Body weight, blood pressure and blood parameters were checked. The brain was processed for immunochemical and immunohistochemical analysis of neuronal specific nuclear protein(Neu-N) and axonal neurofilament(NF). Vesicular acetylcholine transporter (VAcHT), nicotinic(nAChR α 7) and muscarinic(mAChR) receptors subtypes were also evaluated.

OZR of different ages, showed body weight, systolic pressure, glycemia, insulin, triglycerides and cholesterol levels higher in comparison with LZRs. Behavioural tests revealed in older OZR anxiety and changes in emotional learning tasks.

In frontal cortex and hippocampus, morphological and immunochemical analysis revealed a decrease of Neu-N and NF immunoreaction in older OZR compared to LZRs. In older OZR, a decrease of VAcHT and nAChR α 7 immunoreaction was observed. Different modulation was detected for the muscarinic receptors subtypes.

These results may represent the first step to characterize neurological and cholinergic changes potentially occurring in brain of obese rats. This preclinical evidence may be useful to clarify the pathophysiology of brain damage reported in obese individuals.