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Age-related changes in the brain of obese Zucker rat: Morphological and immunochemical analysis.

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Metabolic syndrome (MetS) is defined as a combination of glucose intolerance, arterial hypertension, dyslipidemia and obesity with insulin resistance as the main cause of these imbalances. In general, obesity increases the risk of vascular diseases. Both cardiovascular and cerebrovascular disorders are often linked to impaired cognitive functions. A relationship between metabolic disease and mild cognitive impairment, and/or vascular dementia was hypothesized.

The obese Zucker rat (OZR), represents a model of obesity and type 2 diabetes exhibiting a moderate degree of arterial hypertension. OZRs are characterized by the simultaneous occurrence of hyperglycaemia, hyperinsulinaemia and hyperlipidaemia. This study has investigated brain microanatomy of OZRs compared with their non-obese cohort lean Zucker rats (LZRs) to assess possible relationships between MetS and brain damage.

Male OZRs and LZRs of 12, 16 and 20 weeks of age were used. Body weight, blood pressure and blood chemistry parameters were checked every two weeks and before killing. The brain was dissected out and processed for immunochemical and immunohistochemical analysis of nerve cells identified by neuronal specific nuclear protein (NeuN) and axons identified by neurofilament (NF) immunohistochemistry. Glial-fibrillary acid protein (GFAP) immunoreactive astrocytes were also investigated.

OZRs of different ages, were characterized by a high body weight, an increase of systolic pressure, glycemia, triglycerides and cholesterol levels in comparison with LZRs. An age-dependent increase of these parameters was observed in OZRs.

A decrease of brain/body weight ratio was found in OZRs. In frontal cortex and hippocampus, morphological and immunochemical analysis revealed a decrease of NeuN immunoreactive neurons not related to apoptosis in older OZRs group compared to age matched LZRs. In OZRs a decrease of NF immunoreaction and an increase of GFAP immunoreactive astrocytes was observed compared to LZRs

These findings suggest that OZRs, used for investigating mechanisms and pathophysiology of obesity and type 2 diabetes, may also represent a model for assessing the influence of MetS on brain.

Keywords

Metabolic Syndrome, Obese Zucker rat, brain, morphology, immunohistochemistry.