

EFFECT OF ACUTE GALACTOSE ADMINISTRATION ON OXIDATIVE STRESS AND METABOLISM IN BRAIN STEM OF RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE

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Chronic oral galactose treatment prevents cognitive deficit in rat model of sporadic Alzheimer's disease (sAD) induced by intracerebroventricular streptozotocin (STZ-icv) administration. On the contrary, chronic parenteral galactose treatment induces pathological changes associated with aging and it is used as an accelerated aging animal model. The aim of the study was to determine the effect of acute peroral or intraperitoneal galactose in order to elucidate mechanisms responsible for detrimental and beneficial effects. During the development of sAD neuropathological changes occur in brain stem before the ones in supratentorial brain regions. Moreover, brain stem represents an important integrative center of metabolic and immune homeostasis. For this reason, we decided to focus on the brain stem changes, particularly those in the dorsal motor nucleus of the vagus nerve (DMNX). Plasma and cerebrospinal fluid (CSF) glucose and galactose concentration was evaluated after acute galactose administration. Enzyme-linked immunosorbent assay was used to determine changes in total and active fraction of glucagon-like peptide 1 (GLP-1) and insulin in plasma and CSF of galactose-treated animals. Oxidative stress was evaluated by measurement of catalase activity, reduced glutathion and lipid peroxidation. Metabolic effects in the whole brain stem were assessed by investigation of key metabolic pathway protein phosphorylation changes by western blot. Immunofluorescence was used to determine changes in insulin signaling, autophagy, metabolism, glucose transport and GLP-1 receptor expression in DMNX. Results suggest acute galactose administration modulates oxidative stress and metabolism in brain stem, as well as GLP-1 and insulin secretion. Our research indicates that the effect of galactose is dependant on the route of administration (oral or intraperitoneal) and previous animal treatment (control or STZ-icv treated animas), but further research is needed in order to fully understand the observed differences.

Key words: galactose, brain stem, Alzheimer's disease, metabolism, oxidative stress