Dissecting the biochemical background of galactose-induced transient hippocampal reductive shift

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J. Homolak[I,II], A. Babić Perhoč[I,II], A. Knezović[I,II], J. Osmanović Barilar[I,II], M. Šalković Petrišić[I,II]

[I]Department of Pharmacology, University of Zagreb School of Medicine, Zagreb, Croatia, [II]Croatian Institute for Brain Research, University of Zagreb School of Medicine, Zagreb, Croatia

We have previously shown that oral galactose treatment prevents and rescues cognitive decline in the streptozotocin-induced rat model of sporadic Alzheimer's disease. In contrast, chronic parenteral galactose administration causes oxidative stress in rodents and is therefore used as a model of accelerated aging. Interestingly, our results from the acute oral galactose treatment experiments suggest galactose can both increase oxidative stress and potentiate protective mechanisms, but the nature of this phenomena and its tissue specificity remain unknown.

Male Wistar rats were treated with D-galactose (200mg/kg) by orogastric gavage and sacrificed 30, 60, or 120 minutes after the treatment. Our novel method was used for spatial reductive analysis. 1,2,3-Trihydroxybenzene autooxidation, carbonato-cobaltate (III) complex formation, redox couple ORP, TBARS assay, and DTNB thiol quantification were used to determine redox parameters. Galactokinase and c-fos were measured by western blot. Total and reduced NADP were estimated colorimetrically. Hippocampal and plasma samples were analyzed. The principal component analysis was used for multivariate exploration.

Acute oral galactose treatment induces a robust activation of the hippocampal NADP system accompanied by a time-dependent increase in reduction potential. Oxidative stress parameters suggest the observed effect might be a consequence of hypercompensatory response to oxidative noxis. Galactose treatment increased hippocampal galactokinase, but decreased c-fos expression.

Acute oral galactose induces transient hippocampal reductive shift at least partially by fueling the nicotinamide adenine dinucleotide phosphate system. The obtained results suggest hormetic stimulation of antioxidant defense system as one potential mechanism responsible for its neuroprotective properties.