Therapeutic galactose effect on metabolic dysfunction and cognition in sporadic rat model of Alzheimer's disease

Ana Knezovic[1], Jelena Osmanovic Barilar[1], Ana Babic[1], Robert Bagaric[2], Vladimir Farkas[2], Peter Riederer[3,4], Melita Salkovic-Petrisic[1]

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

[2]Department of Experimental Physics, Rudjer Boskovic Institute, Zagreb, Croatia

[3]Center of Mental Health, Department of Psychiatry, Psychosomatics and Psychotherapy, University Hospital, Würzburg, Germany

[4]Department and Research Unit of Psychiatry, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark

Background

Metabolic dysfunction in the brain is considered to be one of the main pathophysiological hallmarks of sporadic Alzheimer's disease (sAD). Galactose may serve as an alternative source of energy which could be of a therapeutic value for the cerebral glucose hypometabolism in sAD. Our previous research has shown that oral galactose might prevent cognitive deficit in a rat model of sAD. This study aims to explore whether chronic oral galactose treatment could have therapeutic effects on metabolic and cognitive deficit manifested already at the time of initiation of galactose treatment in intracerebroventricular streptozotocin (STZ-icv) - treated rats.

Methods

Adult male Wistar rats were injected bilaterally icv on 1st and 3rd day with STZ (2x1.5 mg/kg) or vehicle (controls, CTR). Daily oral (200 mg/kg) galactose treatment was initiated one month after the STZ-icv administration and lasted for 2 months after which rats were sacrificed. Before sacrifice cognitive performance was tested by Morris Water Maze (MWM) and Passive Avoidance (PA) tests, and glucose uptake by PET scan. Insulin, glucagon-like peptide 1 (GLP-1), glucose and galactose levels were measured in plasma and cerebrospinal fluid (CSF). Data were analysed by Kruskal-Wallis and Mann-Whitney U-test ($p<0.05$).

Results

Two-month oral galactose treatment improved learning and memory functions (increment of time spent in the target quadrant /+40% vs STZ/ and prolonged post-shock latency time /+349% vs STZ/ in PA) previously altered by STZ-icv administration in rats (-86% vs CTR/PA and -56% vs CTR/MWM). In galactose-treated compared to galactose-untreated STZ-icv rats, memory improvement was accompanied by improvement in cerebral glucose hypometabolism (+14%) and increment in active GLP-1 levels (+70%). With the exception of a mild decrease in glucose plasma concentration of galactose treated STZ-icv animals (~-27%), no changes were found in insulin, galactose and glucose levels.

Conclusions

Presented data provide first evidence on beneficial effects of chronic oral galactose treatment on already developed learning and memory deficit and cerebral glucose hypometabolism in STZ-icv rat model of sAD which might partly result from galactose-mediated increment in the activity of GLP-1 known to have neuroprotective role in the brain.

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