The effect of oral galactose on glucose homeostasis and memory in a transgenic mice model of familial Alzheimer's disease

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AIMS: Decreased glucose metabolism and energy in the brain accompanies sporadic Alzheimer's disease (sAD). Our recent research revealed that oral galactose, an alternative source of energy, successfully prevented the development/normalized early-developed cognitive deficits in a non-transgenic sAD rat model. We aimed to explore whether oral galactose has therapeutic effects on cognitive deficits in transgenic mice model of familial AD.

METHODS: 80 male transgenic Tg2576 (WT/TG) and wild-type (WT/WT) mice aged 5 and 10 months underwent 2-month drink of oral galactose solution (+GAL) or tap water. Morris Water Maze (MWM), intraperitoneal glucose tolerance test, and fluorodeoxyglucose Positron-Emission-Tomography (PET) scanning were performed before sacrifice.

RESULTS: MWM showed no deficits in 7-month but significant ($p=0.029$) cognitive decline in 12-month aged WT/TG mice compared to their respective WT/WT controls (-75%/probe trial) associated with markedly decreased movement pattern which worsened by galactose treatment in WT/WT and WT/TG groups. PET scans demonstrated increased (+19.65%) and decreased (-17.70%) glucose uptake/metabolism in the whole brain of 7- and 12-month aged WT/TG mice, which were normalized by galactose (decreased -13.90%/7-month and increased +32.09%/12-month aged WT/TG+GAL mice) respectively. Compared to WT/WT, WT/TG group showed impaired glucose tolerance only at 12-months (glucose level increased +16 to +72%) further worsened by galactose treatment (additional +21 to +51% increment, $p<0.05$). Galactose treatment had no effects in 12-month aged WT/WT group but lowered glucose levels in 7-month old group (-32 to -45%).

CONCLUSION: Oral galactose worsens peripheral but improves central glucose homeostasis without affecting memory in cognitively impaired transgenic AD mice.

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