Olfactory Recognition in Glycogen Synthase Knockout Mice

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Abstract

Glucose stored in the brain as the branched polysaccharide glycogen has been reported to play a role in associative learning. The effect of brain glycogen levels on sensory learning in *mus musculus* is rarely studied and, as a model species for human studies, has implications for learning in people, especially those experiencing low glucose availability to the brain. Wild-type mice and mice without brain glycogen were allowed to investigate the scent of a fruit juice for 5 minutes after a habituation period. Twenty-four hours later, the mice were allowed to investigate the scent of the same juice or a novel juice. The amount of time the mouse spent "exploring" the scent was measured on both days, and the times were compared between genotypes with the hypothesis that wild type mice would spend less time than knockout mice on a familiar scent 24 hours later. However, analysis of this data shows similar results between the two genotypes, implying that brain glycogen may not have a significant impact on sensory learning. When compiled with other behavioral studies with brain glycogen variables, this study improves understanding of the importance of mammalian brain glycogen levels for behavioral learning.

Background

Increasing comprehension of the effects brain glycogen levels have on various types of learning can narrow the focus of further academic research as well as treatment development for diabetics. Neurochemical research on glycogen turnover during memory formation has shown that healthy rates of glycogenolysis are required for strongly-reinforced learning (Gibbs). Furthermore, research has indicated that brain glycogen is important for motor and cognitive memory (Duran), which was studied in this experiment. In contrast, the mouse model lacking brain glycogen which is used in the studies presented here is not impaired in associative learning tests. The overall goal of this work is to collect data from mice with and without brain glycogen as they encounter a novel sensory experience and observe their recall of the memory 24 hours later. The primary objective was to then analyze this data and draw conclusions about the extent to which brain glycogen impacts sensory learning within this context.

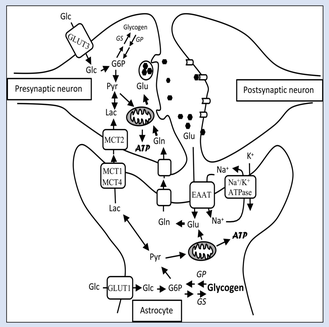

Figure 1. Brain glycogen pathways

Results & Discussion

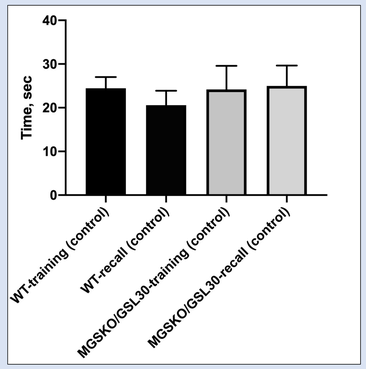

Figure 5. Control training and recall by genotype. Sample size is 18-21.

Hypothesis: For control studies, both WT and MGSKO/GSL30 (HOG) mice would spend equal amounts of time on training and recall due to novel scents both days. For experimental studies WT mice are expected to spend less time on recall than training. If brain glycogen is important for olfactory learning, MGSKO/GSL30 mice will spend more time on training day than WT mice.

Control data shows that MGSKO/GSL30 and WT type mice spent similar times exploring during both training and recall (*Figure 5*). In experimental time spent on recall was decreased to similar levels in both genotypes (*Figure 6*). Differences between training and recall are due to mouse familiarity with scent (sensory memory) rather than to familiarity with the experiment conditions.

This data *does not* support that hypothesis as the (training – recall) difference between genotypes was shown to be statistically insignificant.

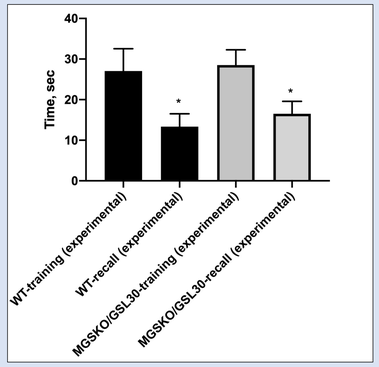

*Figure 6. Experimental data by genotype. Sample size is 16. *p < 0.05 compared to training in same genotype.*

Conclusions

The data collected during this experiment suggests that the presence of glycogen synthase (and therefore the capacity for glycogenolysis as well as the presence of glycogen itself) in mammalian brains does not significantly impact olfactory recognition.

If olfactory recognition is to be considered as representative for other senses as well, then this research is also evidence against the significance of glycogen in broader sensory learning. However, this will require further experimentation to confirm.

Methods and Materials

Mouse model: *Mus musculus* species mouse lines were generated that store abnormal amounts of glycogen in variable areas of the body. MGSKO/GSL30 mice have the gene (GYS1) for glycogen synthase knocked out while also overexpressing GYS1 in muscle. This results in undetectable levels of glycogen in the brain (*Figure 2*) but elevated glycogen levels in muscle. Wild-type (WT) mice did not.

Olfactory recognition: Three cages in a bin had cardboard inserts in between them to prevent mouse-mouse interaction. Each cage contained bedding and an empty cup taped inside. A copper-lined mat was taped underneath the empty cup to measure proximity of mice to scent cup . Quiet conditions without the introduction of the novel scent for 0.5 hours in 8.0-10.0 lux light adjusted the mice to their new environment (*Figure 3)*. After 0.5 hours of this habituation, pre-prepared "scent cups" similar to *Figure 4* were placed into the empty cups. Fruit juice (200 µl) was pipetted onto a 1x1" square of paper towel within a cup with a pre-drilled lid. Mice were videotaped while being allowed to interact with the novel scent in the cup for 5 minutes, after which mice were returned to their home cages. Twenty-four hours later, the experiment was repeated. This time, for recall, control mice interacted with a different fruit juice. Experimental mice interacted with the same scent during training and recall. For both training and recall, the amount of time that a mouse's nose was within 1 cm of the scent cup was recorded. (Jacobs).

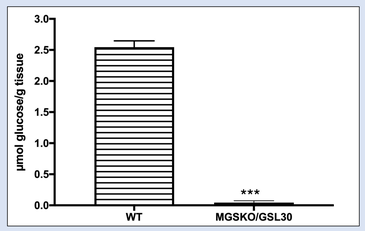

Figure 2.

Glycogen levels in wildtype vs MGSKO/GSL30 mice.

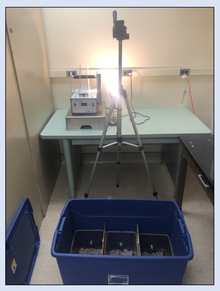

Figure 3. Experimental setup with camera.

Figure 4. Scent cup.

References

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