Physiological Responses to Hypoxia in the Absence of Brain Glycogen

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Background and Hypothesis:
Glycogen is a highly branched polymer of glucose and is an important form of energy storage in mammals. The brain is able to form glycogen in astrocytes and neurons via glycogen synthase and branching enzyme. Once formed, brain glycogen functions as the only stored energy source for these cells. Various physiological roles for brain glycogen have been hypothesized, including memory consolidation and sleep regulation, as well as a protective role during various physiological stressors, such as hypoglycemia and hypoxia. For instance, rat brain glycogen levels were decreased 10 minutes after vaginal birth, but not after a C-section. This suggested that cerebral hypoxia experienced during vaginal birth induced the utilization of brain glycogen to minimize neurodegeneration during the hypoxic event. Symptoms of hypoxia can range from tachycardia, tachypnea, shortness of breath, and diaphoresis to confusion, loss of motor coordination and cognitive function, neurodegeneration, and brain death. The many causes of hypoxia include lungs diseases (COPD, pneumonia, pulmonary edema), CNS depressants (opiates), heart problems (CHF), anemia, and obstructive sleep apnea (OSA). We hypothesized that the lack of brain glycogen would cause a noticeable detrimental effect to the survival time and physiologic functions of mice exposed to acute hypoxia.

Experimental Design or Project Methods:
We subjected mice, with or without glycogen synthase disrupted in the brain, to carbon dioxide- or nitrogen-induced hypoxia and monitored effects on brain glycogen levels, behavior, and survival time.

Results:
We found that mice lacking brain glycogen exhibited the characteristic physiologic responses to hypoxia, but expired ~50% sooner than mice with brain glycogen.

Conclusion and Potential Impact:
These results provide evidence that brain glycogen is imperative in responding to hypoxic events. Further, these findings suggest that brain glycogen may protect patients with OSA against other comorbidities, especially neurodegeneration and cognitive impairment.