Brain glycogen: The novel energy source of exercising brain

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During endurance exercise, the supply of energy to active organs, such as skeletal muscles and the brain, is the essential issue to continue exercise. Although muscle glycogen, the glucose storage molecule, is the essential energy source in exercising muscles, the energetics of the exercising brain is still largely unknown. Since brain glycogen is stored in astrocytes producing lactate as a neuronal energy source transported by monocarboxylate transporter (MCT) and decreases during prolonged exhaustive exercise, we have hypothesized that brain glycogen plays an important role in energetics in the exercising brain. To test this hypothesis, we employed a rat model of prolonged exhaustive exercise on a treadmill with high-power microwave irradiation (10 kW, 1.2 sec), which is a sacrificing method and the gold standard for detecting brain metabolites, including glycogen, in vivo. We found that prolonged exhaustive exercise increased blood lactate levels and induced hypoglycemia, depleted muscle glycogen, decreased but did not deplete brain glycogen levels, and increased neuronal MCT2 protein levels. At the end of exhaustive exercise (time to exhaustion, 84.4 ± 2.9 min), metabolomics revealed increases in brain lactate levels, but not in muscle, with sustained concentrations of glycolytic sources. Simultaneously, brain ATP levels were maintained, while muscle ATP levels were depleted. Finally, a blockade of brain glycogenolysis and MCT2 during exercise, by icv-injection with 1,4-Dideoxy-1,4-imino-d-arabinitol (DAB) and α-cyano-4-hydroxy-cinnamate (4-CIN), respectively, decreased ATP in the brain, resulting in lowered endurance capacity. Our findings demonstrate for the first time that lactate derived from brain glycogen is required to generate ATP in the brain during prolonged exhaustive exercise, providing a new understanding of energetics in the exercising brain. Brain ATP maintenance with residual glycogen is a possible defense mechanism for neuronal functions/lives during prolonged exhaustive exercise.