Early abnormalities in brain glucose and energy metabolism have been documented in sporadic Alzheimer's disease (sAD) pathology. Taking into account that preconditioning is one of the most powerful mechanisms of protection, this study was designed to investigate the effects of hypoxic preconditioning (HP) on cognition and brain glucose/energy metabolism in the intracerebroventricular (icv) streptozocin (STZ)-induced model of sAD. Rats were randomly divided into four groups:

1. Control (sham operation/vehicle administration);
2. STZ (bilateral icv injection of STZ at the dose of 3mg/Kg);
3. HP (exposure to brief periods of moderate hypoxia (10% O₂ for 2 hours) during 3 days, followed by sham operation and vehicle treatment);
4. HP + STZ (as group 3, but submitted to icvSTZ injection).

The severe deficits in learning and memory resulting from icvSTZ administration are antagonized by HP. Moreover, HP significantly attenuates icvSTZ-associated energy hypometabolism, which is characterized by decreased activities of aconitase and isocitrate dehydrogenase and increased activity of malate dehydrogenase (enzymes of tricarboxylic acid cycle) as well as decreased activities of hexokinase and glucose 6-phosphate dehydrogenase and increased activity of lactate dehydrogenase (glycolytic enzymes). HP also prevents impaired cortical and hippocampal mitochondria function observed in icvSTZ-treated rats. Collectively, these results demonstrate the effectiveness of HP to counteract the cognitive decline and brain glucose/energy metabolism abnormalities in a rat model of sAD.

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