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Metformin Eased Cognitive Impairment Induced by Chronic L-methionine Administration: Potential Role of Oxidative Stress.

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Abstract: Chronic administration of L-methionine leads to memory impairment, which is attributed to increase in the level of oxidative stress in the brain. On the other hand, metformin is a commonly used antidiabetic drug with strong antioxidant properties. In the current study, we tested if chronic metformin administration prevents memory impairment induced by administration of L-methionine. In addition, a number of molecules related to the action of metformin on cognitive functions were examined. Both metformin and L-methionine were administered to animals by oral gavage. Testing of spatial learning and memory was carried out using radial arm water maze (RAWM). Additionally, hippocampal levels or activities of catalase, thiobarbituric acid reactive substances (TBARs), glutathione peroxidase (GPx), glutathione (GSH), oxidized glutathione (GSSG) and GSH/GSSG ratio were determined. Results showed that chronic L-methionine administration resulted in both short- and long- term memory impairment, whereas metformin treatment prevented such effect. Additionally, L-methionine treatment induced significant elevation in GSSG and TBARs, along with reduction in GSH/GSSG ratio and activities of catalase, and GPx. These effects were shown to be restored by metformin treatment. In conclusion, L-methionine induced memory impairment, and treatment with metformin prevented this impairment probably by normalizing oxidative stress in the hippocampus.