

Consumption of Molecular Hydrogen Prevents the Stress-Induced Impairments in Hippocampus-Dependent Learning Tasks during Chronic Physical Restraint in Mice

Kazufumi Nagata¹, Naomi Nakashima-Kamimura¹, Toshio Mikami², Ikuroh Ohsawa^{1,3}
and Shigeo Ohta¹

1. ¹Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Graduate School of Medicine, Nippon Medical School, Kawasaki, Japan
2. ²Department of Health and Sports Science, Nippon Medical School, Kawasaki, Japan
3. ³Center of Molecular Hydrogen Medicine, Institute of Development and Aging Sciences, Nippon Medical School, Kawasaki, Japan

Correspondence: Professor S Ohta, Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Graduate School of Medicine, Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki 211-8533, Japan, Tel: +81 44 733 9267, Fax: +81 44 733 9268, E-mail: ohata@nms.ac.jp

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Abstract

We have reported that hydrogen (H₂) acts as an efficient antioxidant by gaseous rapid diffusion. When water saturated with hydrogen (hydrogen water) was placed into the stomach of a rat, hydrogen was detected at several μM level in blood. Because hydrogen gas is unsuitable for continuous consumption, we investigated using mice whether drinking hydrogen water *ad libitum*, instead of inhaling hydrogen gas, prevents cognitive impairment by reducing oxidative stress. Chronic physical restraint stress to mice enhanced levels of oxidative stress markers, malondialdehyde and 4-hydroxy-2-nonenal, in the brain, and impaired learning and memory, as judged by three different methods: passive avoidance learning, object recognition task, and the Morris water maze. Consumption of hydrogen water *ad libitum* throughout the whole period suppressed the increase in the oxidative stress markers and prevented cognitive impairment, as judged by all three methods, whereas hydrogen water did not improve cognitive ability when no stress was provided. Neural proliferation in the dentate gyrus of the hippocampus was suppressed by restraint stress, as observed by 5-bromo-2'-deoxyuridine incorporation and Ki-67 immunostaining, proliferation markers. The consumption of hydrogen water ameliorated the reduced proliferation although the mechanistic link between the hydrogen-dependent changes in neurogenesis and cognitive impairments remains unclear. Thus, continuous consumption of hydrogen water reduces oxidative stress in the brain, and prevents the stress-induced decline in learning and memory caused by chronic physical restraint. Hydrogen water may be applicable for preventive use in cognitive or other neuronal disorders.