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# Effects of Molecular Hydrogen Assessed by an Animal Model and a Randomized Clinical Study on Mild Cognitive Impairment

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## Abstract

**Background:** Oxidative stress is one of the causative factors in the pathogenesis of neurodegenerative diseases including mild cognitive impairment (MCI) and dementia. We previously reported that molecular hydrogen (H<sub>2</sub>) acts as a therapeutic and preventive antioxidant.

**Objective:** We assess the effects of drinking H<sub>2</sub>-water (water infused with H<sub>2</sub>) on oxidative stress model mice and subjects with MCI.

**Methods:** Transgenic mice expressing a dominant-negative form of aldehyde dehydrogenase 2 were used as a dementia model. The mice with enhanced oxidative stress were allowed to drink H<sub>2</sub>-water. For a randomized double-blind placebo-controlled clinical study, 73 subjects with MCI drank ~300 mL of H<sub>2</sub>-water (H<sub>2</sub>-group) or placebo water (control group) per day, and the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) scores were determined after 1 year.

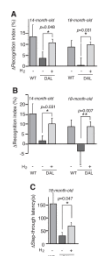
**Results:** In mice, drinking H<sub>2</sub>-water decreased oxidative stress markers and suppressed the decline of memory impairment and neurodegeneration. Moreover, the mean lifespan in the H<sub>2</sub>-water group was longer than that of the control group. In MCI subjects, although there was no significant difference between the H<sub>2</sub>- and control groups in ADAS-cog score after 1 year, carriers of the apolipoprotein E4 (APOE4) genotype in the H<sub>2</sub>-group were improved significantly on total ADAS-cog score and word recall task score (one of the sub-scores in the ADAS-cog score).

**Conclusion:** H<sub>2</sub>-water may have a potential for suppressing dementia in an oxidative stress model and in the APOE4 carriers with MCI.

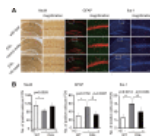
**Keywords:** ADAS-cog score; ApoE4; aldehyde dehydrogenase 2; hydrogen; hydrogen water; mild cognitive impairment; oxidative stress; randomized clinical study.

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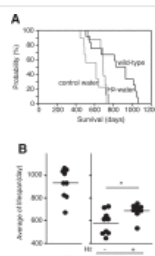
## Figures



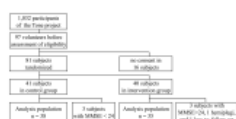
**Fig. (1) Hydrogen water prevented cognitive decline....**



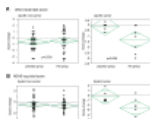
**Fig. (2) Hydrogen water suppressed neurodegeneration. (...**



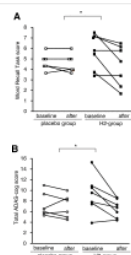
**Fig. (3) Extension of the average lifespan...**



**Fig. (4) Profile of the recruitment, randomization,...**



**Fig. (5) Distribution of changes of sub-...**



**Fig. (6) Changes in a sub-score and...**

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