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Administration of molecular hydrogen during pregnancy improves behavioral abnormalities of offspring in a maternal immune activation model

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Abstract

The aim of the present study was to investigate long-term outcomes of the offspring in a lipopolysaccharide (LPS)-induced maternal immune activation (MIA) model and the effect of maternal molecular hydrogen (H_2) administration. We have previously demonstrated in the MIA mouse model that maternal administration of H_2 attenuates oxidative damage and neuroinflammation, including induced pro-inflammatory cytokines and microglial activation, in the fetal brain. Short-term memory, sociability and social novelty, and sensorimotor gating were evaluated using the Y-maze, three-chamber, and prepulse inhibition (PPI) tests, respectively, at postnatal 3 or 4 weeks. The number of neurons and oligodendrocytes was also analyzed at postnatal 5 weeks by immunohistochemical analysis. Offspring of the LPS-exposed dams showed deficits in short-term memory and social interaction, following neuronal and oligodendrocytic loss in the amygdala and cortex. Maternal H_2 administration markedly attenuated these LPS-induced abnormalities. Moreover, we evaluated the effect of H_2 on LPS-induced astrocytic activation, both in vivo and in vitro. The number of activated astrocytes with hypertrophic morphology was increased in LPS-exposed offspring, but decreased in the offspring of H_2-administered dams. In primary cultured astrocytes, LPS-induced pro-inflammatory cytokines were attenuated by H_2 administration. Overall, these findings indicate that maternal H_2 administration exerts neuroprotective effects and ameliorates MIA-induced neurodevelopmental deficits of offspring later in life.

Figures

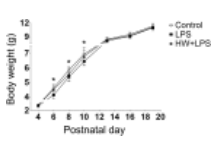

Figure 1 Offspring growth as evidenced by...

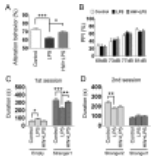

Figure 2 Effects of LPS and H...

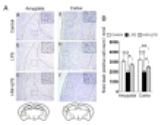

Figure 3 Effect of H_2 on...

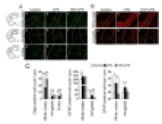

Figure 4 Effect of H_2 on...

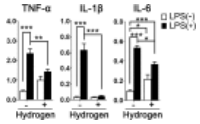

Figure 5 Effect of H_2 on...

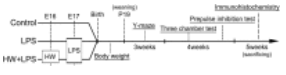

Figure 6 Schematic timeline of the *in*...

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