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Molecular hydrogen reduces LPS-induced neuroinflammation and promotes recovery from sickness behaviour in mice

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Abstract

Molecular hydrogen has been shown to have neuroprotective effects in mouse models of acute neurodegeneration. The effect was suggested to be mediated by its free-radical scavenger properties. However, it has been shown recently that molecular hydrogen alters gene expression and protein phosphorylation. The aim of this study was to test whether chronic ad libitum consumption of molecular hydrogen-enriched electrochemically reduced water (H-ERW) improves the outcome of lipopolysaccharide (LPS)-induced neuroinflammation. Seven days after the initiation of H-ERW treatment, C57Bl/6 mice received a single injection of LPS (0.33 mg/kg i.p.) or an equivalent volume of vehicle. The LPS-induced sickness behaviour was assessed 2 h after the injection, and recovery was assessed by monitoring the spontaneous locomotor activity in the homecage for 72 h after the administration of LPS. The mice were killed in the acute or recovery phase, and the expression of pro- and antiinflammatory cytokines in the hippocampus was assessed by real-time PCR. We found that molecular hydrogen reduces the LPS-induced sickness behaviour and promotes recovery. These effects are associated with a shift towards anti-inflammatory gene expression profile at baseline (downregulation of TNF- α and upregulation of IL-10). In addition, molecular hydrogen increases the amplitude, but shortens the duration and promotes the extinction of neuroinflammation. Consistently, molecular hydrogen modulates the activation and gene expression in a similar fashion in immortalized murine microglia (BV-2 cell line), suggesting that the effects observed *in vivo* may involve the modulation of microglial activation. Taken together, our data point to the regulation of cytokine expression being an additional critical mechanism underlying the beneficial effects of molecular hydrogen.

Figures

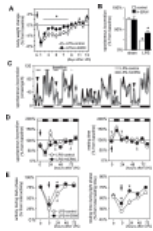


Figure 1. Effects of molecular hydrogen in...

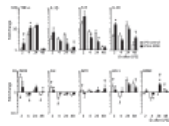


Figure 2. Analysis of LPS-induced changes in...

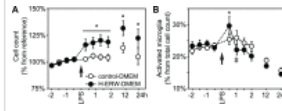


Figure 3. Longitudinal analysis of proliferation and...

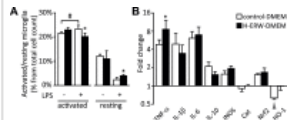


Figure 4. Analysis of activation and gene...

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