硫化水素の産生過剰が統合失調症に影響

Article

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Excess hydrogen sulfide and polysulfides production underlies a schizophrenia pathophysiology

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Abstract

Mice with the C3H background show greater behavioral propensity for schizophrenia, including lower prepulse inhibition (PPI), than C57BL/6 (B6) mice. To characterize as-yet-unknown pathophysiologies of schizophrenia, we undertook proteomics analysis of the brain in these strains, and detected elevated levels of Mpst, a hydrogen sulfide (H_2S)/polysulfide-producing enzyme, and greater sulfide deposition in C3H than B6 mice. *Mpst*-deficient mice exhibited improved PPI with reduced storage sulfide levels, while *Mpst*-transgenic (Tg) mice showed deteriorated PPI, suggesting that "sulfide stress" may be linked to PPI impairment. Analysis of human samples demonstrated that the H_2S/polysulfides production system is upregulated in schizophrenia. Mechanistically, the *Mpst*-Tg brain revealed dampened energy metabolism, while maternal immune activation model mice showed upregulation of genes for H_2S/polysulfides production along with typical antioxidative genes, partly via epigenetic modifications. These results suggest that inflammatory/oxidative insults in early brain development result in upregulated H_2S/polysulfides production as an antioxidative response, which in turn cause deficits in bioenergetic processes. Collectively, this study presents a novel aspect of the neurodevelopmental theory for schizophrenia, unraveling a role of excess H_2S/polysulfides production.

Keywords energy metabolism; epigenetics; hydrogen sulfide and polysulfides; prepulse inhibition; proteomics

Subject Categories Chromatin, Transcription & Genomics; Neuroscience

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