Research Article

Pharmacology

Pharmacology 2019;103:50–60
DOI: 10.1159/000494113

Received: July 27, 2018
Accepted after revision: September 26, 2018
Published online: November 16, 2018

Mechanisms of Hydrogen Sulfide against the Progression of Severe Alzheimer's Disease in Transgenic Mice at Different Ages

Eleonora Vandini[a] Alessandra Ottani[a] Davide Zaffe[b] Anita Calevro[a] Fabrizio Canalini[a] Gian Maria Cavallini[c] Rosario Rossi[d] Salvatore Guarini[a] Daniela Giuliani[a]

[a]Department of Biomedical, Metabolic and Neural Sciences, Section of Pharmacology and Molecular Medicine, University of Modena and Reggio Emilia, Modena, Italy; [b]Department of Biomedical, Metabolic and Neural Sciences, Section of Anatomy, University of Modena and Reggio Emilia, Modena, Italy; [c]Department of Ophthalmology, University of Modena and Reggio Emilia, Modena, Italy; [d]Department of Cardiology, University of Modena and Reggio Emilia, Modena, Italy

Keywords

Hydrogen sulfide · Severe Alzheimer's disease · Learning · Memory · 3x-Tg-Alzheimer's disease · Neuroprotection

Abstract

Backgroud: Alzheimer disease is an age-related severe neurodegenerative pathology. The level of the third endogenous gas, hydrogen sulfide (H_2S), is decreased in the brain of Alzheimer's disease (AD) patients compared with the brain of the age-matched normal individuals; also, plasma H_2S levels are negatively correlated with the severity of AD. Recently, we have demonstrated that systemic H_2S injections are neuroprotective in an early phase of preclinical AD. ***Objectives:*** This study focuses on the possible neuroprotection of a chronic treatment with an H_2S donor and sulfurous water (rich of H_2S) in a severe transgenic 3×Tg-AD mice model. ***Method:*** 3×Tg-AD mice at 2 different ages (6 and 12 months) were daily treated intraperitoneally with an H_2S donor and sulfurous water (rich of H_2S) for 3 months consecutively. We investigated the cognitive ability, brain morphological alterations, amyloid/tau cascade, excitotoxic, inflammatory and apoptotic responses. ***Results:*** Three months of treatments with H_2S significantly protected against impairment in learning and memory in a severe 3×Tg-AD mice model, at both ages studied, and reduced the size of Amyloid β plaques with preservation of the morphological picture. This neuroprotection appeared mainly in the cortex and hippocampus, associated with reduction in activity of c-jun N-terminal kinases, extracellular signal-regulated kinases and p38, which have an established role not only in the phosphorylation of tau protein but also in the inflammatory and excitotoxic response. ***Conclusion:*** Our findings indicate that appropriate treatments with various sources of H_2S, might represent an innovative approach to counteract early and severe AD progression in humans.

KARGER

E-Mail karger@karger.com
www.karger.com/pha

Daniela Giuliani
Department of Biomedical, Metabolic and Neural Sciences
Section of Pharmacology and Molecular Medicine
University of Modena and Reggio Emilia, via G. Campi 287, IT–41125 Modena (Italy)
E-Mail daniela.giuliani@unimore.it