MECHANISM OF HYDROGEN SULFIDE AGAINST PROGRESSION OF SEVERE ALZHEIMER'S DISEASE

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Background. Like the other neurodegenerative conditions (Giuliani et al., 2017), Alzheimer's disease (AD) is a progressive neurodegenerative and incurable disease and is also the most common form of dementia. It has been previously reported that brain hydrogen sulfide (H2S) synthesis is severely decreased in Alzheimer's disease (AD) patients, and plasma H2S levels are negatively correlated with the severity of AD (Liu et al., 2008). Recently we found that sodium hydrosulfide and a spa-water (with a high sulfydrometric degree) significantly protect against brain alterations and consequent impairment in learning and memory in a rat model of mild Alzheimer's disease (AD), and in a triple-transgenic (3xTg-AD) mouse model that most closely mimics human AD (Giuliani et al., 2013).

Aim. To study whether a donor of hydrogen sulfide induces neuroprotection and slows down progression of severe Alzheimer's disease (AD).

Methods. We used 3xTg-AD mice [harbor human transgenes APP (Swe), PS1(M146V) and tau (P301L)], aged (at the start of the study) of 9 and 12 months. In this experimental model of severe AD we evaluated the potential beneficial effect of a treatment (for 3 months) with the H2S donor sodium hydrosulfide. We investigated the neuroprotective effects of the H2S donor through analysis of cognitive tests (Morris water-maze test) and biomolecular analysis.

Results. Treatments with sodium hydrosulfide showed a light protection against impairment in learning and memory in a 3xTg-AD mouse.

Biochemical and biomolecular investigations revealed other important aspects of the neuroprotective profile of sodium hydrosulfide. Indeed, the excitotoxicity-triggered was counteracted by treatment with the H2S donor, as indicated by the reduced phosphorylation levels of proteins that play a key role in the central events in AD pathophysiology, namely amyloid precursor protein (APP), isoforms phosphorylated of Tau and Aβ1-42 in hippocampus and cerebral cortex of 3xTg-AD mice in both age periods examined .

The inflammatory response was attenuated in the hippocampus and cortex at 9 and 15 months, as reduction of p38 activity [a member of the mitogen-activated protein kinase (MAPK) family directly involved in cellular responses of pro-inflammatory phenomena], shows.

Conclusions. In 3xTg-AD mice (6 and 12 months old at the beginning of the study) treated with a donor of H2S for three months we obtained neuroprotective activity. The results on neuroprotection obtained with this severe models of AD are promising and should encourage further preclinical and clinical studies.

References.

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