STUDY ON PROTECTIVE ACTION OF HYDROGEN SULFIDE IN RAT AND MOUSE MODELS OF ALZHEIMER'S DISEASE

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Background

Alzheimer's disease (AD) is a chronic disorder characterized by progressive neurodegeneration associated with cognitive decline and several behavioral deficits [1].

Hydrogen sulfide (H2S) is a water-soluble gas and Tabiano's spa-waters are particularly rich in H2S (strong sulfydrometric degree, that is, more than 100 mg/l). H2S is increasingly being considered as an important signaling molecule in various body systems, and accumulating evidence demonstrates that H2S donor compounds exert significant beneficial effects in several animal models of inflammation and ischemia/reperfusion injury [2]. H2S is endogenously produced also in the brain, probably exerting a neuromodulatory role. It has been previously reported in literature that brain H2S synthesis is severely decreased in AD patients, and plasma H2S levels are negatively correlated with the severity of AD [3].

Objectives

The aim of this study was to evaluate the possible neuroprotection on cognitive processes in AD of a short- and long-term treatment with a H2S donor and Tabiano's spa-water.

Methods

I used two different animal models of AD:

- rat model of AD induced by an unique brain injection of β-amyloid 1-40 (Aβ);

- AD mouse model harboring human transgenes APPswe, PS1M146V, tauP301L (3xTg-AD mice).

In the rat model I studied an early phase of AD, in transgenic mice I evaluated the middle AD conditions.

Animals were divided into 4 experimental groups:

• Experimental group A (Aβ rats): dose-response study with a donor of H2S, 0.25, 0.5, 1 mg/Kg or saline, i.p., once daily for 15 days starting 3 hours after Aβ injection, and sacrificed at day 15;

• Experimental group B (Aβ rats): dose-response study with spa-water, 3, 6 and 12 ml/Kg or saline, i.p., administered for 15 days starting 3 hours after Aβ injection, and sacrificed at day 15;

• Experimental group C (3xTg-AD mice): spa-water, 12 ml/Kg (the most effective dose found in the rat model) or saline, i.p., administered once daily for 12 weeks starting at 12 weeks of age and sacrificed at 24 weeks;

• Experimental group D: control animals (rats without Aβ injection and wild-type mice): received an equal volume of saline by the same route of administration.

In each model I investigated the neuroprotective effects of the H2S donor or Tabiano's spa-water through analysis of cognitive tests (Morris water-maze test).

Results

In Aβ rats treated with the H2S donor (0.25, 0.5, 1 mg/Kg i.p.) or Tabiano's spa-water (3, 6 and 12 ml/Kg i.p.) there was a dose-related improvement in learning and memory performance, compared with the respective saline treated animals. The maximally effective doses of H2S donor and spa-water were 0.5 mg/Kg and 12 ml/Kg, respectively.

Improvement in cognitive performance was also found in all four sections of the Morris test carried out in 3xTg-AD mice.

Saline-treated AD control animals showed impaired ability, as compared with normal controls, in platform finding during all sessions (assay of learning and memory, respectively). Learning and memory impairment persisted thought the study.

Conclusions

These favorable results would suggest that appropriate treatments with H2S donors or Tabiano's spa-water might represent an innovative approach to slow down AD progression in humans.

References:

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