Effects of hydrogen sulfide on progression of experimental Alzheimer's disease

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Alzheimer's disease (AD) is a chronic disorder characterized by progressive neurodegeneration associated with cognitive decline and several behavioral deficits.
It has been previously reported that brain hydrogen sulfide (H_2S) synthesis is severely decreased in AD patients, and plasma H_2S levels are negatively correlated with the severity of AD.
In this study we evaluated the possible neuroprotective effects of a short- and long-term treatment with sodium hydrosulfide - an H_2S donor - and Tabiano's spa-waters, which are particularly rich in H_2S, to counteract the progression of AD. For this purpose, two animal models were used: a rat model of AD induced by brain injection of β-amyloid1-40 (Aβ) and an AD mouse model harboring the human transgenes APPswe, PS1M146V, tauP301L (3xTg-AD mice).
The animals from both models were significantly protected against impairment in learning and memory by treatment with H_2S and spa-water. This improvement in behavioral performance was associated with the hippocampus size of β-amyloid (Aβ) plaques and the preservation of brain morphology. Furthermore, lowered concentration/phosphorylation levels of amyloid precursor protein(APP), presenilin-1 (PS1), $A\beta_{1-42}$ and tau phosphorylated at Thr181, Ser396 and Ser202 were detected in 3xTg-AD mice treated with spa-water. These proteins, in fact, are considered the central events in AD pathophysiology. Also, in 3xTg-AD mice, the levels of malondialdehyde and nitrites were decreased, showing that oxidative and nitrosative stress were counteracted. In the hippocampus, we found a reduction of activity of c-jun N-terminal kinases, extracellular signal-regulated kinases and p38, which have an important role not only in phosphorylation of tau protein but also in inflammation and apoptosis. Consequently, levels of tumor necrosis factor-Î± (TNF-Î±) were decreased, while Bcl-2 was up-regulated and BAX and caspase-3 were down-regulated in the hippocampus of 3xTg-AD mice treated with Tabiano's spa-water. This suggests that it is able to modulate inflammation and apoptosis.
In conclusion, an appropriate treatments with H_2S donors or Tabiano's spa-water might represent an innovative approach to slow down AD progression in humans by targeting multiple pathophysiological mechanisms.