ROLE OF SSAO/VAP-1 IN THE VASCULAR OXIDATIVE DAMAGE AND INFLAMMATION IN ALZHEIMER'S DISEASE (AD) AND CEREBRAL AMYLOID ANGIOPATHY (CAA)

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Introduction: Oxidative stress and inflammation are key events in the pathogenesis and progression of Alzheimer's disease (AD) and cerebral amyloid angiopathy (CAA). The enzyme semicarbazide sensitive amine oxidase (SSAO) has been found increased in cerebrovascular tissue and in blood plasma of AD patients. This enzyme, through the metabolism of primary amines, generates hydrogen peroxide and aldehyde products that contribute to the oxidative stress. Moreover, it also behaves as vascular adhesion protein 1 (VAP-1) participating in the inflammatory leukocyte recruitment.

Aims: To study the role of SSAO/VAP-1 on the cerebrovascular pathogenesis observed in AD and CAA, mainly focused on its inflammatory activity and on the effects of its metabolic products.

Methods: To use endothelial cell lines overexpressing or not the human SSAO/VAP-1 protein treated with the Dutch mutated beta amyloid peptide (Aβ) as in vitro CAA model. To perform leukocyte-endothelium adhesion and enzymatic activity assays, and to determine the aggregation of Aβ to assess the effects of Aβ and the SSAO products on these cell lines.

Results: An SSAO/VAP-1-dependent leukocyte adhesion was observed in endothelial cells after Aβ treatment. Moreover, the Aβ presence induced an increase of the toxic effects induced by SSAO activity products, which were able also to affect to the Aβ aggregation process.

Conclusions: The elevated SSAO activity observed in AD and CAA conditions could be in part responsible of the oxidative stress and enhanced inflammation present in these pathologies. Therefore, its cronical inhibition could be considered as potential therapeutic target adressed to counteract the disease progression.