

439 - Sex-dependent increase of cerebral blood flow in cortex and hippocampus as a compensatory mechanism in end-of-life dementia: A MRI-ASL translational approach in models of normal and pathological aging.

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Alzheimer's disease (AD) is associated with brain oxidative stress, inflammation, and cerebrovascular disease. Structural and functional abnormalities in cerebral microvasculature have been described in both patients and animals models. New tools and biomarkers for the detection of the disease are still emerging, such as Arterial Spin Labeling (ASL), a magnetic resonance imaging (MRI) technique for non-invasive measurements of cerebral blood flow (CBF) whose alteration may be involved in AD-pathogenesis. Nevertheless, more studies in the field are needed since both hypoperfusion and hyperperfusion in different brain areas are reported and can be involved in different brain functions. Recently, we reported in our colony of 3xTg-AD mice modeling Alzheimer's disease a higher number of β -amyloid plaques in the hippocampus and entorhinal cortex in middle-aged females and extensive regions of hypoxia which were not seen in males. In the present study, we evaluated CBF in five different brain regions (hippocampus, cortex, striatum, caudate putamen and amygdala) in older male and female surviving until very advanced-stages of disease and as compared with age-matched counterparts with normal aging. AD-phenotype was evaluated by a comprehensive screening of three main functional impairments: physical (frailty), BPSD-like and cognitive deficits. CBF was measured using MRI-ASL and meaningful correlations between AD-phenotype and CBF were performed to better understand the relation between the level of perfusion and frailty, the BPSD-like behaviors and cognitive impairments. The results indicated sex- and brain region-associated changes in CBF. Among all, 3xTg-AD female mice survivors had increased CBF in cortex and hippocampus as compared with their wildtype counterparts. Here, we also report, for the first time, asymmetry between left-right hemispheres in the female's cortex, in the hippocampus of control males and 3xTg-AD females, as well as in the striatum of control females. Cortex was the area that better correlated with behavior, with asymmetry being associated with worse memory performance. Moreover, hemisphere CBF asymmetry in limbic system was related with copying-with-stress strategies and associated locomotor activity in anxiety tests. The present study suggests a potential compensatory hemodynamic mechanism in end-of-life dementia which is sex- and brain region dependent and can be target for pharmacological and non-pharmacological interventions.