EFFECT OF ANGII-INDUCED HYPERTENSION ON BRAIN PERFUSION AND NEUROPATHOLOGY IN A MOUSE MODEL OF ALZHEIMER DISEASE

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Introduction: The Renin-Angiotensin System (RAS) is a key player in the regulation of blood pressure and many epidemiological and experimental studies link RAS to the development and progression of Alzheimer Disease (AD) and dementia.

Aims: The objective of this study is to evaluate the effects of the manipulation of blood pressure on AD and atherosclerosis (ApoE null) on cerebral blood flow (CBF), on learning and memory, and on cerebral inflammation.

Methods: Male C57Bl/6, APP/PS1 as model of AD, ApoE null mice as model of atherosclerosis will receive subcutaneously AngII (500ng/Kg/min) or saline through osmotic minipumps for two months. After four weeks some mice will receive a diuretic (Hydrochlorothiazide 7.5mg/Kg in drinking water) or an AT-1R inhibitor (Eprosartan mesylate 0.35mg/Kg in drinking water). Blood pressure is monitored daily through tail cuff plethysmography. Learning and memory deficits are evaluated through Morris Water Maze at the beginning, after one month and at the end of the treatment. CBF is measured at the end of the study through a 11.7 T Clinscan in hippocampus and cortex with continuous arterial spin labeling. Brains are collected and processed to visualize immunohistochemically β-Amyloid plaques, blood vessels and activated glial cells.

Results: The experiments are currently being performed and the results will be shown.

Conclusions: The expected outcome of this study is to observe preserved functions in those groups of mice in which hypertension is treated. Using two different lowering blood pressure strategies we hope to distinguish specific effects exerted by AngII through its receptor AT1.