TITLE: ANALYSIS OF INTESTINAL MICROBIOTA DIVERSITY IN ANIMAL MODELS FOR ALZHEIMER'S DISEASE

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ABSTRACT:

The gut microbiota is composed by a huge number of microorganisms that play different functions in the host, such as modulation of immune system and of metabolic functions. Metabolomic studies have revealed that bacterial metabolites produced in gut (hormones and neurotransmitters) have a vast influence on nervous system function. From the evidence of this connection, it was suggested the existence of a signaling network called "microbiota-gut- brain axis", and that imbalances in the microbiota could influence the outcome of syndromes such as Parkinson's and Asperger's. As with other disease, the association between gut microbiota and Alzheimer's disease (AD) is still hypothetical. The aim of this study is to investigate the interplay between gut microbiota and the development of Alzheimer's symptoms. The methodology will be based on two models: timeline evaluation of bacterial gut microbiota of *APP/PS1* mice, considered a model of familial AD, compared to the microbiota of age-matched littermates. In a second model, gut microbiota dysbiosis will be induced by a cocktail of antibiotics composed by 0,5 μg/ml of metronidazole and 1 μg/ml of streptomycin in the drinking water of Swiss mice from day 10 to day 15 of pregnancy. After birth, the offspring will be accompanied through behavioral tests to evaluate locomotion, anxiety and cognitive performance, during 3 months. After this, they will receive an i.c.v. injection of amyloid-β oligomers (AβOs) before evaluation of memory in the object recognition paradigm. For both models, microbiological evaluation was performed through collection of feces and cecal content for total bacterial DNA extraction. Shifts in microbiological communities were analyzed and compared by qPCR for four bacterial phyla and 16S DNA sequencing. Dysbiosis was confirmed by the PCR analysis and behavioral tests showed no significant differences between the groups studied in the acute Alzheimer's model during the initial 3 months of life. After the injection of AβOs, we performed behavioural tests that showed significant differences in learning between the dysbiose and control groups. In Familiar Alzheimer's model, PCR analyses have shown diferences in microbiota composition between wild types and transgenic mice, but more analyses are necessary to understand these differences.

Keywords: Microbiota, Alzheimer, Brain-Gut-Microbiota axis, Dysbiosis

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