DNA Base Excision Repair Activities are Reduced in Brains from Alzheimer’s Disease Patients

Soltys, D.T.\textsuperscript{1}, Pereira, C.P.M.\textsuperscript{1}, Farfel, J.M.\textsuperscript{2}, Souza-Pinto, N.C.\textsuperscript{1}

\textsuperscript{1}Department of Biochemistry, Institute of Chemistry, and \textsuperscript{2}Department of Pathology, Faculty of Medicine, University of São Paulo, São Paulo, SP, Brazil.
e-mail: soltys@usp.br

Introduction: Alzheimer's disease (AD) is a progressive cognitive deterioration, which affects the social and occupational roles of the individual. Studies suggest that the accumulation of oxidized lesions in DNA and changes in the pathways that remove these lesions may have a role in the progression of AD. These lesions are primarily removed by the Base Excision Repair (BER) pathway. The main objective of this study is to determine whether alterations in BER activities in the brain are involved with the development of AD.

Material and Methods: The subjects of this study are normal individuals versus individuals with AD, and a third group of individuals who show neuropathological features of AD, but remained cognitively normal (asymptomatic AD). To measure BER capacities, we developed a novel fluorescence-based \textit{in vitro} assay.

Results and Discussion: As the biological material available is \textit{post mortem} (PM), we tested the effect of PM interval in the activities of the proteins UDG and APE1 in the murine brain, and found no change up to 24 hours after the sacrifice. Mitochondrial and nuclear proteins were isolated from the cerebellum of human brains. UDG activities were significantly reduced in both AD and asymptomatic AD, when compared with control. These activities were inversely correlated with CERAD and Braak stages, suggesting that the presence of neurofibrillary tangles and amyloid plaques negatively modulate UDG activity. On the other hand, APE1 activity was decreased only in the AD group, when compared to controls and asymptomatic. We will extend these investigations to brain regions that are directly related to the pathophysiology of AD (hippocampus and temporal cortex), nonetheless is remarkable that we have already detected differences in the cerebellum.

Conclusion: An impairment of the BER capacities could sensitize to the sequence of molecular events leading to neuronal death associated with the development of AD.

Keywords: DNA repair; Alzheimer's disease; DNA damage.