NUCLEAR AND MITOCHONDRIAL BASE EXCISION REPAIR ACTIVITIES IN BRAINS FROM ALZHEIMER’S DISEASE PATIENTS

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Alzheimer's disease (AD) is characterized by a progressive cognitive decline affecting the individual's social and occupational roles. Accumulation of DNA lesions and alterations in DNA repair are proposed to play a role in AD. Base Excision Repair (BER) repairs oxidized DNA lesion, which accumulate in AD patients. We investigated whether alterations in BER activities in the brain play a causative role during the development of AD. Nuclear and mitochondrial fractions were prepared from autopsy brain samples from cognitively normal, AD subjects and individuals who show neuropathological features of AD but remained cognitively normal (asymptomatic AD - asAD). BER activities were measured using a fluorescence-based in vitro assay. Mitochondrial and nuclear UDG activity were significantly reduced in both AD and asAD, when compared with control. On the other hand, APE1 activity was decreased only in nuclear extracts from the AD group, when compared with either controls or asAD. As BER contributes to maintaining mtDNA integrity, we emploed the Random Mutation Capture assay to determine the mutation rate and spectrum in the mtDNA of our samples. No significant increase in mutations was observed in any group. On the other hand, a selective mtDNA depletion was detected in AD patients. Together, our data suggest that changes in BER activity may contribute to lesion accumulation and selective degradation of damage mitochondrial genomes in AD pathology.

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

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