RELATIONSHIP BETWEEN RNA OXIDATION ADDUCTS AND Aβ IN ALZHEIMER’S DISEASE


Sanders-Brown, University of Kentucky, Lexington, KY, USA

Introduction: While many researchers support the idea of amyloid-β (Aβ) as the etiologic agent of Alzheimer's Disease (AD), the mechanism of action remains unclear. Growing evidence indicates certain adducts of RNA caused by oxidation also represent an early phenomenon in AD. The extent that these two observations coincide remains controversial.

Aims: We examined the relationship between RNA oxidation and other known measures of AD pathology.

Methods: Post-mortem samples were collected from five brain regions (Superior and Middle Temporal Gyrus, Inferior Parietal lobe, Hippocampus, Brodmann's Area 9, and Cerebellum) from AD cases (N = 12) and age matched controls (N = 10). For each brain region, we quantified five markers of oxidative damage (8-OHG, 8-OHA, 5-OHC, FapyA, and FapyG) of RNA using gas chromatography / mass spectrometry with selective ion monitoring and stable labeled internal standards. Levels of Aβ in PBS-soluble, SDS-soluble, and formic acid-soluble fractions were quantified by ELISA. We used these data, demographic statistics (such as age and gender) and neuropathological markers used to diagnose AD (such as plaque and neurofibrillary tangle counts), in the analysis.

Results: RNA oxidation as measured by 8-OHG (8-hydroxyguanine) content is predicted only by PBS-soluble Aβ42 peptide (adj-R²=0.773). This relationship was found only in control subjects, and not in late stage AD cases. No other RNA adducts significantly correlated with Aβ.

Conclusions: Oxidation of RNA, specifically formation of 8-OHG, may be an early indicator of AD progression prior to any memory deficit and is possibly related to the amount of PBS-soluble Aβ42.