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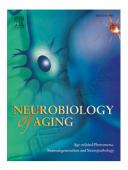
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ACCEPTED MANUSCRIPT

Neurofilament-labelled pyramidal neurons and astrocytes are deficient in DNA methylation

marks in Alzheimer's disease

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There is increasing evidence that epigenetic alterations may play a role in Alzheimer's disease (AD),

yet there is little information regarding epigenetic modifications in specific cell types. We assessed

DNA methylation (5mC) and hydroxymethylation (5hmC) marks specifically in neuronal and glial

cell types in the inferior temporal gyrus of human AD cases and age-matched controls. Interestingly,

neurofilament (NF)-labelled pyramidal neurons that are vulnerable to AD pathology are deficient in

extranuclear 5mC in AD cases compared to controls. We also found that fewer astrocytes exhibited

nuclear 5mC and 5hmC marks in AD cases compared to controls. However, there were no alterations

in 5mC and 5hmC in disease-resistant calretinin-interneurons or microglia in AD and there was no

alteration in the density of 5mC or 5hmC labelled nuclei in near-plaque versus plaque-free regions in

late-AD cases. 5mC and 5hmC were present in a high proportion of neurofibrillary tangles,

suggesting no loss of DNA methylation marks in tangle bearing neurons. We provide evidence that

epigenetic dysregulation may be occurring in astrocytes and NF-positive pyramidal neurons in AD.

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