

Accepted Manuscript

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PII: S0197-4580(16)30064-1

DOI: [10.1016/j.neurobiolaging.2016.05.003](https://doi.org/10.1016/j.neurobiolaging.2016.05.003)

Reference: NBA 9605

To appear in: *Neurobiology of Aging*

Received Date: 24 September 2015

Revised Date: 3 May 2016

Accepted Date: 4 May 2016

Please cite this article as: Phipps, A.J., Vickers, J.C., Taberlay, P.C., Woodhouse, A., Neurofilament-labelled pyramidal neurons and astrocytes are deficient in DNA methylation marks in Alzheimer's disease, *Neurobiology of Aging* (2016), doi: [10.1016/j.neurobiolaging.2016.05.003](https://doi.org/10.1016/j.neurobiolaging.2016.05.003).

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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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