P082 Oxidative stress and DNA damage in cerebral white matter lesions of the ageing human brain

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Introduction: White matter lesions (WML) are linked to dementia and depression. Ischaemia, may contribute to their pathogenesis but the exact role of glial cell pathology remains unclear.
Aims: To investigates the hypothesis that oxidative DNA damage contributes to the pathogenesis of WML and the surrounding WM through altered glial cells functioning.
Materials and Methods: Expression of 8-OHdG, a marker of oxidative stress, was investigated in WML and control WM, both from cases with WML (referred to as lesional controls) and without WML derived from the MRC-CFAS. Lesions were identified using post mortem MRI. Oxidative DNA damage was detected by immunohistochemisty and nuclear expression was quantified. Double staining was performed for GFAP, CD68 and oligodendrocyte specific protein to enable colocalisation of 8OHdG with markers of astrocytes, microglia and oligodendrocytes, respectively. Expression of Malonaldehyde (MDA) was also quantified as a marker of lipid peroxidation using Western Blotting technique on the frozen cohort.
Results: Extensive DNA damage was identified in all three groups of WM in multiple cell types. Both WML (p=0.007) and lesional control WM (p=0.011) showed significantly more 8-OHdG immunoreactive cells than control WM, whilst WML and lesional controls did not significantly differ (p=0.526). Other markers of DNA damage, including γH2AX and DNA-PK), showed a similar pattern of expression. MDA quantification did not significantly differ between the three groups of WM.
*Conclusion:*The similarity in the level of oxidative DNA damage in lesional control WM and WML suggests that oxidative damage is widespread and not confined to WML.