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Apomorphine: A potential modifier of amyloid deposition in Parkinson's disease?

Alison J Yarnall, MRCP[1], Tammaryn Lashley, PhD[2], Helen Ling, MRCP[2], Andrew Lees, MD, FRCP, FMedSci [2], Tamas Revesz, MD, FRCPath[2], David J Burn, MA, MD, FRCP[1]
[1]Institute for Ageing and Health, Newcastle University, Newcastle, UK
[2]Queen Square Brain Bank, Department of Molecular Neuroscience, University College London, UK

Objective: To determine whether ante-mortem exposure to apomorphine is associated with lower levels of amyloid-β (Aβ) in brain tissue.

Background: Dementia affects up to 80% of people with PD (PDD). Although the precise cause of PDD is unknown, evidence from clinical and pathological studies suggests a role for both α-synuclein and Aβ. A recent study demonstrated an improvement in memory and reduced Aβ burden in transgenic murine Alzheimer (AD) models given subcutaneous apomorphine injections. We therefore investigated the effect of apomorphine on Aβ plaque load in a clinicopathological study of PD subjects with and without PDD.

Methods: The case notes of donors with pathologically proven PD who had (n=36; Apo+) and had not received apomorphine (n=43; Apo-) during life for motor complications were reviewed to determine presence (CI) or absence (CN) of cognitive impairment. The severity of Aβ mature/diffuse plaque load was established together with the severity of AD development (Mirra 1991, Thal 2002). Cerebral amyloid angiopathy (CAA) was determined based on a 4-tier grading system. Tau pathology was assessed according to Braak and Braak. α-synuclein pathology was classified using the Braak and McKeith staging systems. ApoE genotype was established in 25 Apo+ and all Apo- cases.

Results: 20 Apo+CN, 16 Apo+CI, 16 Apo-CN and 27 Apo-CI cases were assessed. A trend towards reduced diffuse plaque load and overall Aβ plaque burden was found in Apo+CN when compared with the Apo-CN groups (mean Diffuse $plaque_{sum}$ scores 2.20 *vs* 4.81, p=0.077; $Plaque_{sum}$ + Diffuse $plaque_{sum}$ 3.15 *vs* 7.00, p=0.083). When the CN group were dichotomised into those who had not and had received apomorphine doses greater than the median value, there was significantly less Aβ peptide deposition in those who had received high dose apomorphine ($Plaque_{sum}$ 0.11 *vs* 2.04, p=0.047; Diffuse $plaque_{sum}$ 4.31 *vs* 0.67, p=0.005; $Plaque_{sum}$ + Diffuse $plaque_{sum}$ 6.35 *vs* 0.78, p=0.005). No significant difference in plaque burden was found between the Apo+CI and Apo-CI groups.

Conclusions: This work in progress suggests that apomorphine may have a modifying effect on amyloid deposition in non-demented PD cases. Apomorphine may therefore represent a possible therapeutic target to reduce the burden of cognitive impairment in PD.

Mirra et al. Neurology 41:479-86, 1991
Thal et al. Neurology 58:1791-80, 2002