EPILEPSY: A MODEL FOR STUDYING EARLY EVENTS IN THE EVOLUTION OF ALZHEIMER´S DISEASE AND PARKINSON´S DISEASE

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Introduction: Epilepsy, a condition characterized by neuronal hyperexcitability, is associated with precocious development of Alzheimer´s disease (AD). In epilepsy, AD, and Parkinson's disease (PD) neuronal levels of the β-amyloid precursor protein (βAPP) and glial activation with interleukin-1 (IL-1) overexpression are common. IL-1 elevates the expression of both βAPP and ApoE, which itself elevates neuronal βAPP expression in a genotype-specific manner (ApoE ε3>ε4).

Aim: As IL-1 induces the precursors of Aβ plaques, hyperphosphorylated neurofibrillary tangles, and Lewy bodies and each is elevated in epilepsy, we aim to show that epilepsy provides a paradigm for studying the development of the neuropathological changes observed in AD and PD.

Methods: Frozen and paraffin-embedded tissues from temporal lobes resected from 95 patients (3 mo - 71yrs) with intractable temporal-lobe epilepsy (ApoE and IL-1 genotype specified). Tissue levels and cellular expression of IL-1, ApoE, βAPP, and Aβ were analyzed, using western immunoblot and RT-PCR and semi-quantitative immunohistochemistry, respectively.

Results: Glial activation with IL-1 overexpression was prominent in the first decade, as was a neuronal impact indicated by elevated expression of βAPP and of ApoE. In addition, dense Aβ deposition was an early event in epilepsy (9 yrs).

Conclusion: Early overexpression of IL-1, ApoE, βAPP and Aβ plaque deposition is consistent with the idea that early, excess IL-1 expression in epilepsy amplifies the neuropathological changes associated with AD, suggesting that epilepsy may provide a human condition for studying early events in neuropathogenesis. Support: NIA-AG12411 and the Windgate Foundation.