Increased Transforming Growth Factor β2 in the Neocortex of Alzheimer’s Disease and Dementia with Lewy Bodies is Correlated with Disease Severity and Soluble Aβ42 Load

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Abstract.
Background: Of the three transforming growth factor (TGF)-β isoforms known, TGFβ1 deficits have been widely reported in Alzheimer’s disease (AD) and studied as a potential therapeutic target. In contrast, the status of TGFβ2, which has been shown to mediate amyloid-β (Aβ)-mediated neuronal death, are unclear both in AD and in Lewy body dementias (LBD) with differential neuritic plaque and neurofibrillary tangle burden.

Objective: To measure neocortical TGFβ2 levels and their correlations with neuropathological and clinical markers of disease severity in a well-characterized cohort of AD as well as two clinical subtypes of LBD, dementia with Lewy bodies (DLB) and Parkinson’s disease dementia (PDD), known to manifest relatively high and low Aβ plaque burden, respectively.

Methods: Postmortem samples from temporal cortex (BA21) were measured for TGFβ2 using a Luminex-based platform, and correlated with scores for neuritic plaques, neurofibrillary tangles, α-synuclein pathology, dementia severity (as measured by annual decline of Mini-Mental State Examination scores) as well as soluble and total fractions of brain Aβ42.

Results: TGFβ2 was significantly increased in AD and DLB, but not in PDD. TGFβ2 also correlated with scores for neurofibrillary tangles, Lewy bodies (within the LBD group), dementia severity, and soluble Aβ42 concentration, but not with neuritic plaque scores, total Aβ42, or monomeric α-synuclein immunoreactivity.

Conclusions: TGFβ2 is increased in the temporal cortex of AD and DLB, and its correlations with neuropathological and clinical markers of disease severity as well as with soluble Aβ42 load suggest a potential pathogenic role in mediating the neurotoxicity of non-fibrillar Aβ. Our study also indicates the potential utility of targeting TGFβ2 in pharmacotherapeutic approaches to AD and DLB.

Keywords: Alzheimer’s disease, amyloid-β, dementia with Lewy bodies, Parkinson’s disease dementia, transforming growth factor β2

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