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BRAIN RESEARCH

Research Report

Neuronal expression of vimentin in the Alzheimer's disease brain may be part of a generalized dendritic damage-response mechanism

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ABSTRACT

Early pathological features of Alzheimer's disease (AD) include synaptic loss and dendrite retraction, prior to neuronal loss. How neurons respond to this evolving AD pathology remains elusive. In the present study, we used single- and double-label immunohistochemistry to investigate the relationship between neuronal vimentin expression and local brain pathology. Vimentin was localized to neuronal perikarya and dendrites in AD brain, with vimentin-immunopositive neurons prevalent in regions exhibiting intra- and extracellular beta-amyloid$_{1\text{-}42}$ (Aβ42) deposition. Neuronal co-localization of vimentin and Aβ42 was common in the cerebral cortex, cerebellum and hippocampus. Additionally, neurons in affected brain regions of AD transgenic (Tg2576) mice and in brain tissue subjected to mechanical injury expressed vimentin, while those in comparable regions of control mouse brain did not. Finally, we show that neurons in human fetal brain express vimentin concurrently with periods of rapid neurite extension. Overall, our results suggest that neurons express vimentin as part of an evolutionarily conserved, damage–response mechanism which recapitulates a developmental program used by differentiating neurons to establish dendrites and synaptic connections.

1. Introduction

Alzheimer's disease (AD) is the most common neurodegenerative disorder and is characterized by progressive memory loss, cognitive decline, behavioral changes, and eventual death (Braak and Braak, 1991; Felician and Sandson, 1999; Mirra et al., 1993; Sanders and Morano, 2008; Wisniewski et al., 1985). Pathological hallmarks include neurofibrillary tangles, amyloid deposits in cells and plaques, inflammation, synaptic loss, and neuronal degeneration (Clifford et al., 2007, 2008; Dickson, 1997;

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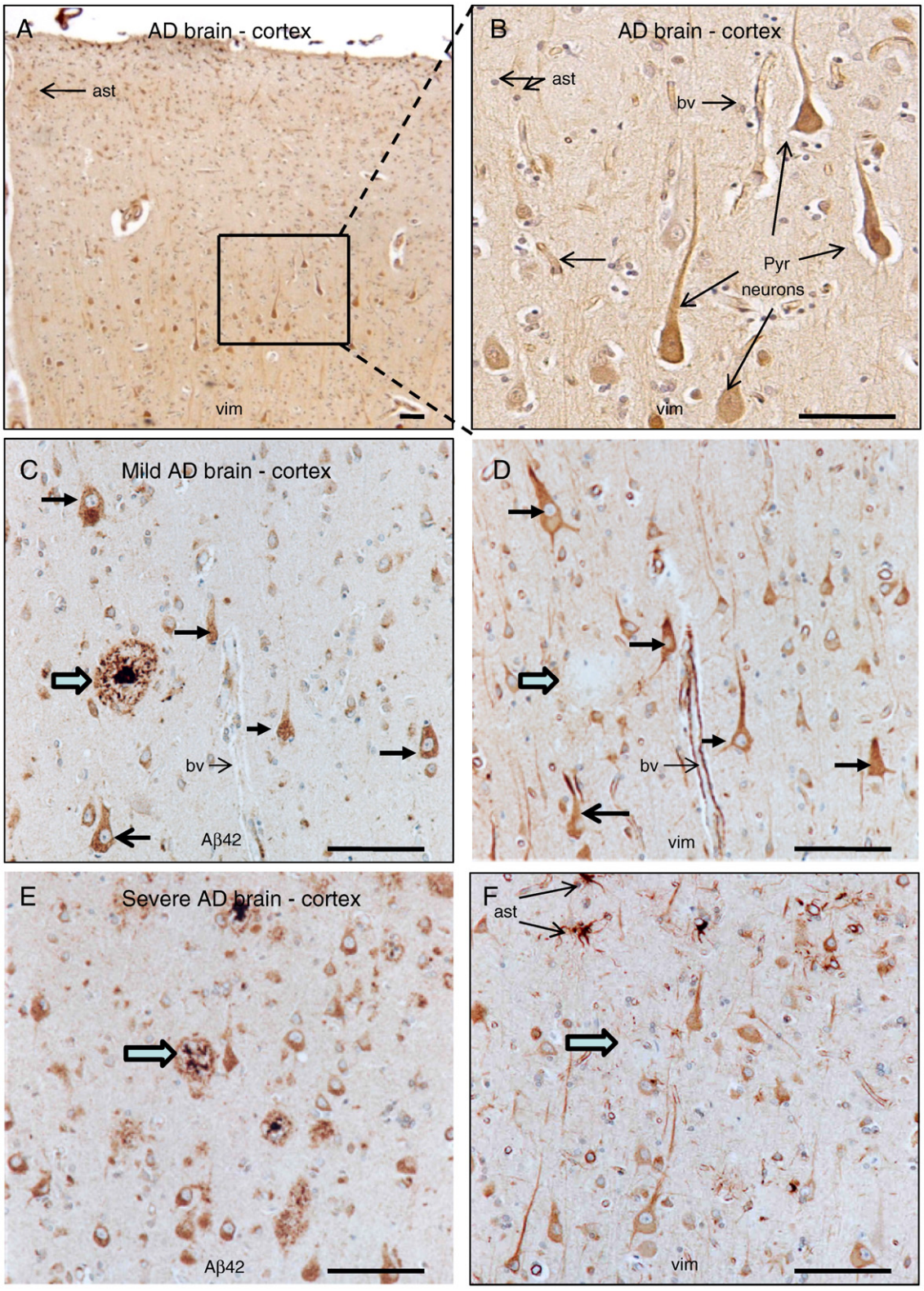

Fig. 1 – Vimentin is expressed in neurons in brain regions exhibiting typical AD pathology. (A) Low magnification view of the cerebral cortex of an AD patient showing numerous vimentin-positive neurons. ast, astrocytes. (B) Higher magnification image showing great variation in the intensity of vimentin immunoreactivity among pyramidal (Pyr) neurons. bv, blood vessel. (C, D) Consecutive sections of the AD cerebral cortex with mild pathology immunostained with Aβ42 and vimentin, respectively. Vimentin expressed by neurons burdened with intracellular Aβ42 (solid arrows). Consecutive sections of the cerebral cortex of an AD brain with more advanced pathology showing intense vimentin immunostaining in many Aβ42-burdened neurons (E, F). Open arrow, amyloid plaque. Bar = 100 μm.