Amyloid Beta1-42 Induced Glial Activation and Cell Death in Corpus Callosum in Vivo

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Abstract

White matter degeneration is a frequent phenomenon found in Alzheimer's disease (AD) apart from the well-known lesions in certain grey matter areas such as cortex and hippocampus. However its pathogenesis has not been fully established. Therefore, the aim of this work was to assess the effects of Aβ1-42 in rat corpus callosum from 6 hr upto 2 weeks using immunocytochemistry since amyloid deposits can be found in CC of AD patients. Administration of 1 nmol of Aβ1-42 into corpus callosum resulted in considerable damage to axons, as evidenced by the loss of neurofilament-immunoreactive fibers at time points of 6 hrs and 7 days post-injection. Significant damage was also evident to myelin (using Luxol fast blue myelin staining) and oligodendrocytes (using CC1 immunocytochemistry); in the latter case marked caspase-3 immunoreactivity was demonstrated in the CC1-immunoreactive oligodendrocytes. Additionally, the numbers of GFAP-immunoreactive astrocytes and OX-42/OX-6-immunoreactive microglia were markedly increased following $A\beta_{1-42}$ injection. These findings suggest that Aβ1-42 plays an important pathophysiological role in white matter damage and one possible mechanism of oligodendroglial death is through activation of caspase-3. This is the first finding on Aβ1-42-induced toxicity in corpus callosum in vivo which could provide a potential new model for the study of white matter damage in AD.

Keywords: Amyloid beta; Corpus callosum; Glia; Oligodendrocytes; Astrocytes; Microglia; Neurofilament; Myelin