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Research article

INCREASED EXPRESSION OF PAD2 AFTER REPEATED INTRACEREBROVENTRICULAR INFUSIONS OF SOLUBLE $A\beta_{25-35}$ IN THE ALZHEIMER'S DISEASE MODEL RAT BRAIN: EFFECT OF MEMANTINE

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Abstract: Peptidylarginine deiminases (PADs) convert the arginine residues in proteins into citrulline residues in a Ca^{2+}-dependent manner. We previously showed that a bilateral injection of ibotenic acid into the rat nucleus basalis magnocellularis elevated the PAD2 activity in the hippocampus and striatum. In this study, we examined whether repeated intracerebroventricular infusions of soluble $A\beta_{25-35}$ would affect the PAD2 expression in any regions of the rat brain. We also assessed the protective effect of memantine on Aβ-induced PAD2 alterations. The infusion of $A\beta_{25-35}$ increased the activity and protein level of PAD2 in the hippocampus, and co-treatment with memantine suppressed these changes. An immunohistochemical analysis showed that an increased level of PAD2 was coincident with GFAP-positive astrocytes and CD11b-positive microglia. In addition, immunofluoresecence staining revealed that citrulline-postive immunoreactivity coincided with the occurrence of GFAP-positive astrocytes. Co-treatment with memantine reversed the activation of the astrocytes and microglia, thus attenuating the PAD2 increment. These biochemical and immunohistochemical results suggest that PAD2 might play an important role in the pathology of early Alzheimer's disease, and may correlate with the changes in glial cells that are recovered by memantine treatment.

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Abbreviations used: Aβ – amyloidβ; AD – Alzheimer's disease; GFAP – glial fibrillary acidic protein; PAD – peptidylarginine deiminase