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Studies on Neuropathologic Mechanism of Alzheimer's Disease

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Epidemiologic studies show that the widely used non-steroidal anti-inflammatory drugs (NSAIDs) reduced the pathological incidence of Alzheimer's disease. The principal action of these drugs is to inhibit cyclooxygenase. Two isoforms of this enzyme have been described. Of these much attention has been devoted to COX-2, since this highly regulated isoform plays a major role in peripheral inflammation. Moreover, many studies demonstrated that Cox-2 expression was up-regulated in the brain of patients with Alzheimer's disease. To test the effect of constitutively elevated neuronal human COX-2 in pathologic processing of AD, transgenic mice were generated that overexpressed hCOX-2 in neuron. To generate animal model for AD, we will be backcross neuronal hCOX-2 transgenic mice with the APPswe/PS-2mt double-transgenic line. On the other hand, an influence of COX-2 on Aβ42-mediated neuronal responses was confirmed by *in vitro* studies showing that the overexpression of hCOX-2 in APPswe/PS-2mt constantly expressing neuronal cells induces the apoptotic damage and increases level of Aβ42, compared to the control. This study indicates that principal pathway by which neuronal Cox-2 in brain may influence Alzheimer's disease is by promoting neuronal death through mechanism involving the Aβ42 production.

Keyword : Alzheimer's disease, COX-2, Aβ42, Transgenic mice