Inhibitor of cyclooxygenase-2 protects against amyloid β peptide-evoked memory impairment in mice

Magdalena Cąkała, Anna R. Malik, Joanna B. Strosznajder

Department of Cellular Signalling, Medical Research Centre, Polish Academy of Sciences, Pawinskiego 5, PL 02-106 Warszawa, Poland

Correspondence: Magdalena Cąkała, e-mail: magcakala@cmdik.pan.pl

Abstract:
Alzheimer’s disease (AD) results in an impairment of memory and behavior. It is accepted that amyloid β (Aβ) peptides are responsible for the etiopathology of AD, but the precise signaling pathways leading to the disease have not been elucidated. In this study, we have investigated the role of cyclooxygenase-2 (COX-2) in Aβ(1–42)-evoked memory impairment in mice. Moreover, the effect of systemic inflammation on Aβ-dependent locomotor and memory disturbances has been evaluated.

Twelve-month-old C57Bl6 mice were injected intracerebroventricularly (icv) with Aβ(1–42) alone or simultaneously with intraperitoneal (ip) administration of lipopolysaccharide (LPS). Some mice also received COX-2 inhibitor, NS-398. Another group of mice was pretreated with LPS at 4 and 7 months of age and then injected with Aβ(1–42) at 12 months of age. All mice were subjected to behavioral tests one week after Aβ administration. COX-2 protein level was analyzed in the hippocampus using immunochromic method.

Our data demonstrated that Aβ enhanced COX-2 protein level and decreased the locomotion and exploration in mice. Systemic inflammation elevated COX-2 immunoreactivity at an early stage after injection and intensified behavioral disturbances. Moreover, the object recognition in Aβ-treated mice was significantly affected compared to control mice. The administration of LPS simultaneously with Aβ worsened recognition performance. A COX-2 inhibitor protected mice against memory deficit and locomotor disturbances. In LPS-pretreated animals, Aβ induced locomotor disturbances, but had no effect on memory and COX-2 level.

Our results indicate that Aβ evokes enhancement of COX-2 protein level and memory deficit. Systemic inflammation modulates Aβ effect on the brain function. The COX-2 inhibitor protects the brain against Aβ-induced memory disturbances.

Key words:
cyclooxygenase, Alzheimer’s disease, systemic inflammation, memory