

damage in the cerebral hemisphere was reduced by 36.3% ($p < 0.01$). Neurological scores were also significantly improved at 24 h after the surgery ($p < 0.01$). These results demonstrate the neuroprotective effect of wogonin in a rat model of permanent occlusion of MCA and provide strong pharmacological basis for the use of *Scutellaria baicalensis* or wogonin in the treatment of stroke.

[PB3-5] [10/17/2002 (Thr) 13:30 – 16:30 / Hall C]

Neuroprotective Effects of Treatment with Aloesin in Rat Model of Permanent Focal Cerebral Ischemia

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Brain injury resulting from cerebral ischemia remains a major public health problem. Aloesin, main component of aloe possesses various biological activities such as wound healing, anti-gastric ulcer, and chemopreventive activity. In this study we investigated whether treatment with aloesin could protect brain injury induced by permanent focal cerebral ischemia in rats. We also compared aloesin with other neuroprotective drugs such as MK801 and ebselen. Permanent focal cerebral ischemia was induced by occlusion of middle cerebral artery for 24 hr without reperfusion in male Sprague-Dawley rat. Neurological deficit scores were measured at 24 hr after onset of ischemia immediately before sacrifice. Coronal slices of the brain were stained 2,3,5-triphenyltetrazolium chloride at 24 hr after onset of ischemia and infarct volumes was measured. Administration of aloesin (10 mg/kg, i.v.) and MK801 (1 mg/kg, i.p.) significantly reduced total infarct volume by 63% and 41%, respectively compared with control group. Ebselen (10 or 30 mg/kg, i.p.) reduced infarct volume but not significantly. Immunohistochemical analysis was done using anti-caspase-3 antibody. DNA fragmentation was confirmed in agarose gel. Activated caspase-3 expression and DNA fragmentation was inhibited by administration of aloesin. The result suggest that aloesin can serve as a lead chemical for the development of neuroprotective agents by providing neuroprotection against permanent focal ischemic brain injury.

[PB3-6] [10/17/2002 (Thr) 13:30 – 16:30 / Hall C]

Erk activation mediates lipopolysaccharide-induced induction of matrix metalloproteinase-9 from rat primary astrocytes

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In central nervous system, matrix metalloproteinases (MMPs) are produced by neuron as well as glia and implicated in physiological events such as neurite outgrowth and myelination etc. In addition, MMPs also contribute to the pathogenesis of several CNS diseases such as multiple sclerosis, Alzheimer's disease and malignant glioma. In spite of their functional importance, little is known about the signal transduction pathways leading to the induction of MMPs in CNS. Here, we investigated whether the activation of Erk(1/2) is involved in the induction of MMP-9 in LPS-stimulated primary astrocytes. The activity, protein and mRNA level of MMP-9 but not those of MMP-2 were increased by LPS treatment, which were assessed by gelatin zymography, immunoblotting and RT-PCR, respectively. LPS treatment induced activation of Erk(1/2) within 30min, which was dose-dependently inhibited by PD98059, a specific inhibitor of the Erk(1/2) kinase (MEK). In this condition, PD98059 blocked the increase in MMP-9 protein and mRNA level as well as gelatin-digesting activity. The treatment of phorbol myristoyl acetate (PMA) activated Erk(1/2) with concomitant increase in MMP-9 production in a dose-dependent manner. The results from the present study suggest that induction of MMP-9 in rat primary astrocytes by LPS is mediated at least in part by the activation of Erk(1/2). The Erk(1/2)-mediated MMP-9 induction may provide insights into the regulation of MMP-9 production in CNS, which may occur in vivo in pathological situations such as CNS inflammation.

[PB3-7] [10/17/2002 (Thr) 13:30 – 16:30 / Hall C]

Cholinergic involvement of spatial memory impairment in μ -opioid receptor knockout mice

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The present study investigated the passive avoidance and spatial learning in the μ -opioid receptor gene knockout mice and wild type mice. In the step-through passive avoidance task, the μ -opioid receptor knockout mice did not differ from the wild type mice. In Morris water maze, however, the μ -opioid receptor knockout mice showed significant memory deficit compared to wild type mice. In the [³H]pirenzepine autoradiographic binding for the muscarinic type 1 receptor, the [³H]pirenzepine binding was selectively decreased in the dentate gyrus (10 %) of the hippocampus in μ -opioid receptor knockout mice compared to wild type. The acetylcholine level was reduced in the cortex of μ -opioid receptor knockout mice (22 %) compared to the control wild type mice. These results suggest that memory impairment in the μ -opioid receptor knockout mice may be related to the decrease of M1 receptor in dentate gyrus of the brain and reduction of acetylcholine level. Therefore, these results suggest that lack of the μ -opioid receptor is accompanied with reduction of the cholinergic system, showing an impairment of spatial memory.

[PB3-8] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Microglial activation and tyrosine hydroxylase immunoreactivity in the substantia nigral region following transient focal ischemia in rats

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The temporal profiles of the changes of dopaminergic cell and microglial activation induced by transient cerebral ischemia was investigated in the substantia nigral region which lay outside ischemic areas of rat brain after middle cerebral artery occlusion (MCAO). Transient cerebral ischemia was induced by intraluminal occlusion of the right middle cerebral artery for 2 h and reperfusion was continued for 1, 2, 3, 7, 10, 14, 30, 60, and 120 days. Activated microglial cells were visualized with immunohistochemistry using OX-42 antibody. We also examined the ischemia-induced apoptotic cell death event in the substantia nigra (SN) at 1, 2, and 3 days. Activated microglial cells, as amoeboid morphology, visualized with OX-42 antibody were increased at 1 day and dramatically increased at 7 days postischemia. Activated microglia cells became reduced in the substantia nigra from 7 days later. At 2 and 4 months postischemia, the number of activated microglia cells were similar to those of 2 weeks after ischemia/reperfusion. These results suggest that microglial cells be rapidly activated and those activated forms be sustained at least for 1 week in the substantia nigra following transient focal cerebral ischemia induced by MCAO. The temporal profiles of the changes of dopaminergic cell identified with immunohistochemistry using tyrosine hydroxylase antibody are under study.

Poster Presentations - Field B4. Immunology

[PB4-1] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Immuno-modulator effect of Cefodizime in IL-6

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