Three types of learning tasks (morris water maze, active avoidance and passive avoidance) were tested in rats following intracerebroventricular infusion of ethylcholine aziridium (AF64A). In morris water maze test, AF64A-treated rats showed longer latencies to find the submerged platform from 7th day after the infusion. Also, in pretrained rats, AF64A caused the significant delay of latency at 7th day but not 8th day. In the active avoidance test, the escape latency times were significantly delayed in AF64A-treated rats. The percentages of no response and avoidance in AF64A-treated rats were increased and decreased, respectively, compared with those of the control. Especially, the percentage of no response in the AF64A-treated rats was markedly increased in the first half trials of the test. In the passive avoidance test, AF64A-treated rats showed shorter latencies 1.5 hours after the electronic shock but not 24 hours after. AF64A also caused the pretrained rats to be shortened in the latency 7th day after the infusion but not 8th day.
These results indicate that AF64A might impair the learning and the consolidated memory. Also, these results indicate that the disturbed memory by AF64A might rapidly recover after the first retrain. Furthermore, the results suggest that AF64A maybe a useful agents for the learning for spatial cognition.

[PB3-5] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

In vivo studies of anti-TfR monoclonal antibody for brain drug targeting in disease model mouse

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The delivery of peptide or proteins such as antisense oligodeoxynucleotides, neurotrophic factors through the blood-brain barrier (BBB) in vivo, may be facilitated by receptor-mediated transcytosis via the transferrin receptor (TfR) located on the BBB. For example, OX26 monoclonal antibody was studied in rats as a transport vector in this system. This delivery strategy is adaptable to transgenic and knockout mice are available as models of human disease.
We studied whether anti murine TfR monoclonal antibody, 8D3 is suitable for brain delivery in Balb/C mice. Brain uptake of [^{125}I]8D3 was studied with a common carotid artery perfusion/capillary depletion method. pharmacokinetics parameters in plasma and organ uptakes of [^{125}I]8D3 were also measured by single intravenous injection technique. Brain uptake of 8D3 was 0.50 ± 0.09 percent of the injected dose per g brain after 2 hours intravenous injection. Plasma concentrations declined biexponentially with elimination half-life of approximately 2.2 hours. After perfusion 5 min the apparent volume of distribution in brain was 22.3 ± 2.7 $\mu\ell$/g, which was 4.8 fold higher than the intravascular volume.
It is concluded that a murine anti-TfR monoclonal antibody, 8D3 is transported through the BBB by the TfR and the antibody could be used for targeting the brain with the potential neuropharmaceuticals.

[PB3-6] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Brain uptake and pharmacokinetics of [3H]taurine in senescence -accelerated mouse.

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We reported about decreased brain uptake of [^{3}H]taurine in spontaneously hypertensive rat (SHR) showed compare than that of normal rat, because high blood presure or sodium concentration of

brain interstitial fuid may be changeable to transport activity. In the present study, we examined whether aging shows any effect on the brain uptake of [^{3}H]taurine. The aging model animal, senescence-accelerated mouse (SAM) strains show senescence acceleration and age-associated pathological phenotypes similar to geriatric disorders seen in humans.

The blood-brain barrier (BBB) transport of [^{3}H]taurine was compared with senescence accelerated prone mice (SAMP8), senescence resistant mice (SAMR1)and normal mice. To evaluate of BBB permeability, we used intravenous injection technique and common carotid artery perfusion method (CCAP).

In result of CCAP method, [^{3}H]taurine PS product in SAMR1 reduced by 35.1% compared with that in normal mice. And [^{3}H]taurine PS product in SAMP8 reduced by 74.8% compared with that in normal mice. In case of intravenous injection technique, the plasma clearance of [^{3}H]taurine in SAMP8 was almost compararable with that of normal mice.

These results suggest that aging may have an effect on the brain transport activity of taurine in disease state model animal.

[PB4-1] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Inhibitors of Nitric Oxide in Raw 264.7 Macrophages treated with Linarin: The main compound of Chrysanthemum zawadskii

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Linarin is the name given to the main compound from Chrysanthemum zawadskii. The herb of Chrysanthemum zawadskii, which is called Gu-Jul-Cho, has been used in traditional medicine for pneumonia, bronchitis, cough, common cold, pharyngitis, bladder-related disorders, women's diseases, gastroenteric disorders, and hypertension. This study was set up to elucidate the ability of macrophage activation of Linarin. Nitric oxide(NO), derived from L-arginine, is produced by two types(constitutive and inducible) of nitric oxide synthase(NOS). The NO produced in large amounts by the inducible NOS is known to be responsible for the vasodilation and hypotension observed in septic shock. We have found Linarin, compound of Chrysanthemum zawadskii and its MeOH extract, which inhibited the production of NO in LPS-activated Raw 264.7 cells. The Linarin may be useful candidates for the development of new drug to treat endotoxemia and inflammation accompanied by the overproduction of NO. Linarin-treated total Lymphocyte showed cytotoxicity in dose dependent manner between 10 ㎍/㎖ and 40 ㎍/㎖.

[PB4-2] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Effects of Lectin-conjugated Ellagitannin on Antitumor Activity

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Recently, studies which selectively cure tumor cell, are proceeding sprightly. Generally, antitumor durgs are strong toxicity and result in damage in normal cells. We studied antitumor activity with lectin-conjugated ellagitannin(lectin: carbohydrate-binding protein: tumor cell specific binding protein, Wheat Germ Agglutinin: melanoma specific binding protein, ellagitannin: praecoxin A: excellent antitumor effect). In this study, we injected mouse melanoma cell, B16-F10, on right the femoral region of C57BL/6 mouse and after administration with drugs, observed the live period of mouse and tumor size.