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