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Cerebellar granule and glial cells prepared from 8-day rat pups were used to investigate the effects of dehydroevodiamine (DHED) on the glutamate release and uptake. The subacute DHED exposure retarded the growth of granule cells and their LC50 was 718.3 μM. However, the viability of glial cells were not affected. The basal release of glutamate from cultured granule cells was decreased (16.1%) by 5 μM of DHED. Also NMDA-induced release of glutamate was inhibited. However, the basal and NMDA-induced release of glutamate from DHED-exposed granule cells (5 μM) for 9 days were not affected by DHED. In addition, DHED (5 μM) significantly inhibited (31%) the glutamate uptake from cultured glial cells. Although DHED did not affect the glutamate uptake from DHED-exposed glial cells (5 μM) for 9 days, DHED potentiated the inhibitory response of L-pyrollidine-2,4-dicarboxylic acid (PDC). In the cAMP-treated glial cells, DHED (5 μM) slightly inhibited (7.8%) and potentiated the inhibitory response of PDC. Although DHED did not affect the glutamate uptake from DHED and cAMP-exposed glial cells, DHED reduced the inhibitory response of PDC. These results indicate that DHED inhibited the glutamate uptake and release. Also the result suggest that DHED might modulate the glutamatergic nervous system.

[PB3-3] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Changes in the glutamatergic nervous system of cerebellum after pre - or post-natal nicotine exposure in rats

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To determine changes in the glutamatergic nervous system in cerebellum after the chronic nicotine exposure, nicotine was supplied from the mating through drinking water (25ppm). After delivery, each group was divided into two groups. Groups were continuously exposed to either deionized water or nicotine. Eight week old rats were sacrificed and cerebella were rapidly dissected. The various parameters of glutamatergic nervous activities were measured. The total levels of glutamate in post-natally nicotine exposed rats were only significantly increased (26%), compared with the control. However, those of glutamine (24%) and GABA (14%) in pre-natally nicotine exposed rats were increased. The activitiy of glutaminase was increased (15-19%) in both pre-natally and continuously nicotine exposed rats. And that of glutamine synthetase was also increased (27-87%). While those of glutamate dehydrogenase was decreased (10-37%) in all nicotine-treated rats. In addition, alteration of these enzymatic activities after nicotine exposure was similar with those of previous studies using cultured cerebellar cells prepared from eight day old pups exposed to nicotine with the same dose schedule. These results indicate that the glutamatergic nervous system in cerebellum are changed after the nicotine exposure and suggest that either pre- or post-natal nicotine exposure might affect the excitatory amino acid system during the development. Furthermore, the results suggest that the model of cell culture may be useful for the determination of the alteration by the exogenic agents.

[PB3-4] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Impairments of learning and memory following intracerebroventricular administration of AF64A in rats

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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