(36.2%) and hippocampus (127%). Although the levels of dopamine and serotonin were not altered, the turnover rates of serotonin were increased in entorhinal cortex (27.7%) and hippocampus (22.7%). However, the levels of dopamine (22.8%) and serotonin (13.5%) were decreased and the levels of dihydroxyphenylacetic acid were increased (76.6%) in frontal cortex. The turnover rates of dopamine were increased in frontal cortex (131.5%) and striatum (24.2%) and that of serotonin was increased (19.6%) in frontal cortex. However, the levels of total glutamate were not changed in all examined regions. These results indicate that the lesions of entorhinal cortex induced the impairments of learning and memory and the alteration of the monoamine metabolisms in various brain regions. The results suggest that serotonergic activities in entorhinal cortex and hippocampus may contribute in the memory processes.

[PB3-2] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

The effects of tributyltin compounds on dopamine content and L-DOPA-induced neurotoxicity in PC12 cells

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There is little information concerning the effects of tributyltin compounds such as tributyltin acetate (TBTA) and tributyltin chloride (TBTC), which are the endocrine disrupters on living organisms. In this study, the effects of tributyltin compounds on dopamine content and L-DOPA-induced neurotoxicity in PC12 cells were investigated. TBTA and TBTC at concentration ranges of 0.05-0.75 μM decreased dopamine content in a concentration-dependent manner in PC12 cells. TBTA (0.1 μM) and TBTC (0.5 μM) showed 57.2% and 55.1% inhibition of dopamine content for 48 hr. IC50 values of TBTA and TBTC were 0.12 μM and 0.6 μM. Treatment of PC12 cells with L-DOPA at concentration ranges of 10-50 μM increased dopamine content and the increase in dopamine levels by L-DOPA were in part inhibited by TBTA (0.05-0.5 μM) and TBTC (0.5-5.0 μM). TBTA and TBTC did not show a up to 0.25 μM and 1.0μM, respectively. However, at concentrations higher than 0.5 μM and 1.5 μM, TBTA and TBTC caused a neurotoxicity through an apoptotic process. In addition, TBTA (0.05-0.5 μM) and TBTC (0.5-5.0 μM) also enhanced L-DOPA-induced neurotoxicity (L-DOPA concentration, 10-100 μM). These results suggest that tributyltin compounds inhibit dopamine biosynthesis and stimulate L-DOPA-induced neurotoxicity in PC12 cells.
*supported by the Brain Korea 21 project.

[PB3-3] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

The effects of protoberberine alkaloids on L-DOPA-induced neurotoxicity in PC12 cells

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It has been reported that berberine and palmatine decrease dopamine content by inhibition of TH activity, and the IC50 values were 18.6 μM and 7.9 μM, respectively. In this study, the effects of berberine, palmatine and coptisine on L-DOPA-induced neurotoxicity were investigated by using PC12 cells. Berberine and palmatine showed concentration-dependent decrease in dopamine content, however, coptisine did not. L-DOPA at concentrations of 10-50 μM increased dopamine content, but, the increased dopamine levels were in part inhibited when L-DOPA (10-50 μM) were associated with berberine or palmatine. L-DOPA (20-50 μM), berberine (10-20 μM), palmatine (20-50 μM) or coptisine (10-20 μM) did not affect the cell viabilities, which were determined by the MTT

assay, while L-DOPA (100-150 μM) showed the decrease in cell viabilities. When berberine (20 μM), palmatine (50μM) or coptisine (20μM) was associated with 20-50μM L-DOPA, a concentration-dependent decrease in cell viabilities was observed by an apoptotic process, respectively. These results indicate that berberine, palmatine and coptisine enhance L-DOPA-induced neurotoxicity in PC12 cells.
*supported by the Brain Korea 21 project.

[PB3-4] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

The effects of passive administration and self-administration of methamphetamine on serotonin receptors level in rat brain

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(+)-Methamphetamine (METH) is a psychostimulant, which has been the most popular abused drug in Korea. The rewarding mechanism in METH abuse has been reported to be mediated by dopaminergic system. Recently, it has been reported that dopamine releaser (phentermine) plays a dominant role in the discriminative stimulus effects of METH, whereas 5-HT releaser (fenfluramine) can strongly modify METH self-administration. The present study is designed to assess the behavioral changes and the changes of the serotonin receptors in the brains of rats administered repeated or self-administered METH. The repeated administration of 1.0 mg/kg/day METH for 12 days increased locomotor activities, and there was no difference between i.v. and i.p. treatment. Rats had acquired actively METH self-administration for 3 weeks at 0.1 or 0.2 mg/kg/injection. Whereas, it was taken few days to acquire sucrose pellet self-administration. The binding of [3H]-8-hydroxy-DPAT (5-HT^{1A} receptors) and [3H]-5-carboxytryptamine (5-HT^{1B} receptors) to brain sections was examined. Both passive administration and self-administration of METH did not change significantly the serotonin receptors levels in hippocampus, striatum and nucleus accumbens. These results suggest that serotonin receptors may not change in the acquisition period of METH self-administration, and we are trying to investigate the serotonin receptors levels of brain in rats maintained of METH self-administration.

[PB3-5] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

The blood-brain barrier permeability of antioxidants, ebselen in rats

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Ebselen is a lipid soluble seleno-organic compound with anti-oxidate activity through a glutathione peroxidase-like action. Ebselen also have the potential effect to protect the brain against ischemic insults. In this study, we investigated the brain uptakes through the blood-brain barrier and *pharmacokinetic parameters of ebselen in SD rats by intravenous injection technique. Ebselen was* administered intravenously to rats and the concentration of ebselen in plasma and brain was determined by HPLC at various time. The plasma concentration of ebselen declined biexponentially with elimination half-life of approximately 30 min. The blood-brain barrier permeability of ebselen after IV injection at 30 min was high compared with that of morphine. This results indicated that ebselen can be uesd for neuropharmaceutical agent to stroke because it uptakes to the brain very well even though it metabolised very rapidly in blood.

[PB3-6] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]