

hours (UI = 1), it was decreased below the basal level in 6 hours. The activity of JNK was increased with accordance with the progression of esophagitis. The level of phosphorylation of p44/42 MAP kinase was increased in 1 hour and decreased in 4 hours. After 6 hours, it was recovered to the basal level. With these results, we suggest that the each type of MAP kinases shows different features of activation and deactivation in experimental esophagitis models.

Poster Presentations - Field B3. Neuroscience

[PB3-1] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

METHAMPHETAMINE SELF-ADMINISTRATION INDUCED C-FOS AND GFAP EXPRESSION IN RAT BRAINS.

Park KiSook, Lee SangMin^o, Jung HaeKwan, Park ChangWon, Oh JaeHo, Song ChiWon, Hong JinTae, Chung SooYoun

Dept. of General Toxicol., Natl. Inst. Toxicol. Res., Korea FDA, College of Pharmacy, Chungbuk National University

(+)-Methamphetamine (METH) is a psychostimulant, which has been the most popular abused drug in Korea. In this study, we investigated the behavioral changes in rats administered repeated or self-administered METH, and the effects of METH self-administration on the expression of c-fos, glial fibrillary acidic protein (GFAP) and tyrosine hydroxylase (TH) in brain. 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 dose-response relationship for METH demonstrated a typical inverted U-shaped function. Rats were injected about 1.0 mg/kg/day for 27~53 days in intravenous self-administration training course. METH self-administration increased dose-dependently the protein expression of c-fos in prefrontal cortex, hippocampus, striatum and ventral tagmental area (VTA). GFAP expression was also increased dose-dependently in hippocampus, striatum and VTA. However, TH expression was not changed in striatum and VTA. These results suggest that low dose of METH may induced neurotoxicity in rats self-administrated for long periods.

[PB3-2] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Inhibitory Effects of Aporphine Alkaloids on Dopamine Biosynthesis in PC12 cells

Jin Chun Mei^o, Shin JeongSu, Park HeeDong, Yang YouJong, Ryu SiYong, Hong JinTae, Lee MyungKoo

College of Pharmacy, and Research Center for Bioresource and Health, Chungbuk National University

The effects of aporphine isoquinoline alkaloids such as boldine, isocorydine, liliodenine, anonaine and asimilobine on dopamine biosynthesis in PC12 cells were investigated. Treatment of PC12 cells with boldine, liliodenine, anonaine and asimilobine showed 5~50 % inhibition of dopamine content at a concentration of 1~20 μ M for 24 h. However, Isocorydine did not show an inhibitory effect. The IC50 values of boldine, liliodenine, anonaine and asimilobine were 19.6 μ M, 7.7 μ M, 0.35 nM and 0.13 nM, respectively. Dopamine content decreased at 6 h and reached minimal level at 24h after the exposure to aporphine isoquinoline alkaloids described above. Tyrosine hydroxylase (TH) activities were also inhibited by aporphine alkaloids. Treatment of PC12 cells with aporphine alkaloids showed 60~85 % inhibition of TH activities at a concentration of 1~20 μ M for 6 h. However, Aromatic amino acid decarboxylase activities did not. TH activities reached minimal level at 6~12h following the treatments of boldine, liliodenine, anonaine and asimilobine (84.0 % at 24.4 μ M, 85.4 % at 12 μ M, 67.4 % at 1.51 μ M, 87.5 % at 1.48 μ M, respectively), and maintained at a reduced level for up 36 h in PC12 cells. These results suggest that the inhibition of TH activities by each aporphine isoquinoline alkaloids might be involved in at least one component of the reduction of dopamine biosynthesis in PC12 cells. Intracellular mechanisms need further studies of

aporphine alkaloids.

[PB3-3] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

β -Hydrastine derivatives inhibit dopamine biosynthesis in PC12 cells

Yin ShouYu^o, Lee JaeJoon, Kim YuMi, Shin JeongSoo, Oh KiWan, Lee MyungKoo

College of Pharmacy, and Research Center for Bioresource and Health, Chungbuk National University

The effects of (+)- β -hydrastine hydrochloride and (-)- β -hydrastine on dopamine biosynthesis in PC12 cells were investigated. (+)- β -Hydrastine hydrochloride and (-)- β -hydrastine significantly decreased the intracellular dopamine content in dose- and time-dependent manner, and the IC50 values were 9.3 μ M and 20.7 μ M, respectively. Dopamine content was lowered at 6 h and reached a minimal level at 18 h and 12 h after the exposure to 10 μ M (+)- β -hydrastine hydrochloride and 20 μ M (-)- β -hydrastine. The decreased dopamine content was maintained for up to 48 h, and then dopamine content completely recovered to the control level at about 72 h. Intracellular tyrosine hydroxylase (TH) activity was also inhibited by these compounds and reached the minimal level at about 6 h and 12 h, respectively. Intracellular cAMP and Ca⁺⁺ concentrations were also decreased by β -hydrastine derivatives. These results indicate that β -hydrastine derivatives contributes partially to the decrease in dopamine content by the inhibition of TH activity in PC12 cells.

[PB3-4] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

EVALUATION OF ABUSE LIABILITY OF EPHEDRINE IN RATS.

Park KiSook^o, Lee SangMin, Jung HaeKwan, Park ChangWon, Oh JaeHo, Song ChiWon, Hong JinTae, Chung SooYoun

Dept. of General Toxicol., Natl. Inst. Toxicol. Res., Korea FDA, College of Pharmacy, Chungbuk National University

Ephedrine is a main component of ma huang, *Ephedra sinica*, which has been used as a medicinal agent to treat hay fever or asthma. Nowadays, this sympathomimetic drug is abused in many countries. In this study, we investigated the abuse liability of ephedrine by measuring locomotor activities (LA) and self-administration (SA) profiles in Sprague-Dawley rats. LA was determined in rats treated i.p. with 3, 10 and 30 mg/kg ephedrine once a day for 14 days. Intravenous SA by ephedrine (0.23, 1 and 2.3 mg/kg) was examined in food-trained rats, and the changes of ephedrine-induced SA by treating dopamine receptor antagonist, spiperone (30 μ g/kg, s.c. 1 hr before testing) were examined. We also tested the reinforcing effect of ephedrine in rats maintained to self-administer 0.1 mg/kg/inj. Methamphetamine (METH, i.v.). Body weight was not changed, but LA was dose-dependently increased in ephedrine-treated group. Saline substitution for ephedrine increased SA rates. The SA of ephedrine was decreased by spiperone. And SA rates of 1.15, 2.3 and 4.6 mg/kg/inj. ephedrine were similar to that of saline in rats trained SA by METH. These findings suggested that ephedrine may have abuse liability, partially related to dopaminergic system, but it may not substituted for METH self-administration.

[PB3-5] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Activation of p38 MAP kinase and AP-1 during the promotion of neurite extension of PC-12 cells by 15-deoxy- Δ 12,14-prostaglandin J2

Song YS^o, Oh JH*, Park KS*, Jung KM*, Lee MK, Jung HK*, Jung SY*, Hong JT

College of Pharmacy, Chungbuk National University, *National Institute of Toxicological Research, KFDA