are widely prescribed to ameliorate the cognitive deficits in AD patients. In order to examine if tacrine and donepezil exhibit additional pharmacological actions, we investigated the effects on neuronal injuries induced in the primary cultured rat cortical cells by glutamate or N-methyl-D-aspartate (NMDA), β-amyloid fragment (Aβ25-35), and various oxidative insults. Both tacrine and donepezil were unable to inhibit the excitotoxic neuronal damage induced by glutamate. However, tacrine inhibited the excitotoxicity induced by NMDA in a concentration-dependent fashion. In addition, tacrine significantly inhibited the Aβ25-35-induced neuronal injury at the concentration of 50 μM. In contrast, donepezil did not reduce the NMDA- nor Aβ25-35-induced neuronal injury. Tacrine and donepezil did not affect lipid peroxidation or oxidative neuronal injuries induced by H2O2, Fe2+, and Zn2+. Thus, in addition to its anticholinesterase activity, the neuroprotective effects by tacrine against the NMDA- and Aβ25-35-induced toxicity may be beneficial for the treatment of AD. In contrast, the potent and selective inhibition of central acetylcholinesterase appears to be the major action mechanism of donepezil.

[PB3-5] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Changes in striatal dopaminergic activity after the subacute administration of physostigmine and procyclidine

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To determine the effects of physostigmine and procyclidine on striatal dopaminergic activity, physostigmine (0.1 mg/kg/h) and procyclidine (3 mg/kg/day) were subcutaneously infused via osmotic-mini pump. Seven days after the implantation, rats were sacrificed and striata were dissected out. Changes in the levels of dopamine and its metabolites and the characteristics of dopamine receptor (D-1) were determined using HPLC and receptor binding assay, respectively. The level of dopamine was decreased (9.4%) after physostigmine, while that was increased (10.9%) after procyclidine. However, the level of dopamine was not altered after the co-treatments. The level of sriatal dihydroxyphenylacetic acid was increased after the treatment with either each compound alone (9.0% and 23.7%) or co-treatment (40.4%). The level of homovanillic acid was only increased after the co-treatment (10.9%). In addition, the dopamine turnover was increased after the treatment with either each compound alone (20.6% and 11.6%) or co-treatment (33.0%). The striatal tyrosine hydroxylase activity was increased (9.1%) and decreased (13.7%) after physostimine and procyclidine treatment, respectively, but not after co-treatments. The maximum binding density of striatal dopamine-1 receptor was increased (18.7%) after physostigmine treatment, but not after procyclidine alone or co-administration with physostigmine. These results indicated that subacute exposure of physostigmine induced the alteration of striatal dopaminergic activity and suggest that procyclidine may counteract the physostigmine-induced dopaminergic alteration.

[PB3-6] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

NITRIC OXIDE INTERACTS WITH NMDA RECEPTORS ON APOMORPHINE-INDUCED CLIMBING BEHAVIOR IN MICE

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The purpose of this study was to characterize behavioral interactions between nitric oxide and N-methyl-D-aspartate (NMDA) recpetors on apomorphine(DA agonist)-induced climbing behavior in mice. *Nitric oxide (NO) donor, S-nitroso-N-acethylpenicillamine* (SNAP), enhanced the apomorphine-induced the climbing behavior. However nitric oxide snythase (NOS) inhibitor, NG-nitro-L-arginine methylester (L-NAME) inhibited apomorphine-induced climbing behavior. On the other hand, N-methyl-D-aspartate (NMDA) receptor antagonist, dextromethorphan, inhibited apomorphine-induced climbing behavior, but NMDA itself enhanced apomorphine-induced climbing behavior. In addtion, inhibition by

dextromethorphan of apomorphine-induced climbing behavior was reversed by the treatment with SNAP. The suppressive action by L-NAME of apomorphine-induced climbing behavior was also reversed by the treatment with NMDA.
These results have demonstrated that the NO system is located at down-stream of NMDA receptors involved in modulation of apomorphine-induced climbing behavior in mice. Therefore, the enhanced effect of NO donor and the inhibitory effect of NOS inhibitor on apomorphine-induced climbing behavior show experimental evidence which NO interacts with DA, NMDA receptors indicating that NO plays an important role in the glutamatergic modulation of dopaminergic function at the postsynaptic DA receptors.

[PB3-7] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Developmental Alteration in Nociceptive Threshold in Neonatally Capsaicin-treated Rats

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This study examined the effect of neonatal administration of capsaicin on nociceptive thereshold. Neonatal administration of capsaicin destroys a subpopulation of small diameter primary afferent neurons. So to find the evidence, we observed the age-dependent threshold alterations according to thermal, mechanical and chemical stimuli. Neonatal administration of capsaicin increased plantar latency (PL) in age-dependent manner between 3 week and 6 week of age. But that in 10 day or 2-week-old rats were higher than 3-week-old rats. Age-dependent alterations in tail flick latency (TFL) also occurred in capsaicin-treated rats. But, PL and TFL in capsaicin-treated rats after 2 weeks was not different form vehicle-treated values. The paw withdrawal threshold of capsaicin-treated rats was significantly different from that of vehicle-treated rats except for 3-week old rats. Although ophthalmic instillation of capsaicin in capsaicin-treated rats also evoked a wiping response, the number of wipes was significantly less than in the corresponding vehicle-treated rats at each age examined. The thermal difference of capsaicin treated rats and vehicle treated rats about hyperalgesia produced at 4hr after i.pl. carrageenan (CAR) examined by using the plantar test. The plantar latency was significantly greater after 4 weeks. As examined in thermal response about CAR-induced hyperalgesia, the mechanical difference was founded.

[PB3-8] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Hwangryun-Hae-Dok-tang (Huanglian-Jie-Du-Tang) extract and its constituents reduce ischemia-reperfusion brain injury via neutrophil infiltration in rats

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The preventive effect of Hwangryun-Hae-Dok-tang (HHDT, Huanglian-Jie-Du-Tang), a Chinese herbal medicine, and its ingredients on the ischemia/ reperfusion-induced brain injury was evaluated in the rat brain. Ischemia was induced by intraluminal occlusion of the right middle cerebral artery for 120 min and reperfusion was continued for 22 h. HHDT (200 mg/kg), Coptidis rhizoma (100 mg/kg), Scutellariae radix (100 mg/kg), Phellodendri cortex (100 mg/kg), and Gardeniae fructus (100 mg/kg) were orally administered twice, promptly prior to reperfusion and 2 h after the reperfusion. Baicalein, a component of Scutellariae radix, was also examined at a dosage of 50 mg/kg twice. Total infarction volume in the ipsilateral hemisphere of ischemia/ reperfusion rats was significantly lowered by the treatments of HHDT,