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