Kim Yu Mi°, Lee Jae Joon, Yin Shou Yu, Hong Jin Tae, Lee Myung Koo

College of Pharmacy, Chungbuk National University, Cheongju 361-763, Republic of Korea

There is little information concerning the effects of tributyltin (TBT) compounds, which are the endocrine disrupters on living organisms. TBT compounds and L-DOPA both induce apoptosis in catecholaminergic PC12 cells. In this study, the effects of TBT compounds on L-DOPA-induced neurotoxicity were investigated. Tributyltin acetate (TBTA) and tributyltin chloride (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 42.8% and 44.9% inhibition of dopamine content. Exposure of PC12 cells to 0.1 μM TBTA, 0.5 μM TBTC or 20 and 50 μM L-DOPA neither affected cell viability, determined by MTT assay, nor induced apoptosis, tested by TUNEL technique and flow cytometry. However, at concentrations higher than 0.5 μM TBTA and 1.5 μM TBTC caused a neurotoxicity through an apoptotic process. In addition, TBTA at 0.1 μM and TBTC at 0.5μM also enhanced L-DOPA-induced neurotoxicity (L-DOPA concentration, 50 μM). These results suggest that TBT compounds stimulate L-DOPA-induced neurotoxicity in PC12 cells.
* This work was supported by the Brain Korea 21 project.

[PB3-3] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Mechanosensitive Ion Channels in Sensory Neurons

Cho HaWon°, Koo JaeYeon, Kim SangSeong, Shin JiEun, Hwang SunWook, Lee SoonYoul, Oh Uhtaek

Sensory Research Group, National Creative Research Initiatives, College of Pharmacy, Seoul National University, San 56-1, Shinlim, Kwanak-Gu, Seoul 151-742, Korea

Mechanosensitive (MS) ion channels are present in a variety of cells. However, very little is known about the ion channels that are responsible for mechanical sensitivity in sensory neurons. In this study, we have identified two distinct types of MS channels in membrane patches of cultured sensory (DRG) neurons of the neonatal rat. The two most frequently encountered MS channels were identified in 2125 membrane patches tested: one activated at low pressure (threshold: ?0 ~ ?0 mmHg, low-threshold (LT)), another channel activated only at high negative pressure (threshold: ?0 mmHg, high-threshold (HT)). In symmetrical 140 mM Na+ solution in inside-out patches, single-channel conductances of LT and HT MS channels were obtained. The current-voltage relationships of the LT and HT MS channels were outwardly-rectifying and linear, respectively. Both of the two channels were permeable to monovalent cations and Ca2+, and reversibly blocked by gadolinium. Colchicine and cytochalasin D reduced the activities of the two MS channels, indicating that cytoskeletal elements support mechanosensitivity. In DRG neurons, both types of MS channels were found primarily in neurons with diameters less than 30 ?. Our study identifies two distinct types of MS channels in sensory neurons that probably give rise to the observed mechanosensitive whole-cell current. Thus, these MS channels in sensory neurons may transduce mechanical stimuli to neural signals involved in somatosensation including pain.

[PB3-4] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Effects of cholinesterase inhibitors on neuronal injuries induced by glutamate, NMDA, Ab25-35, and oxidative insults

Cho JungSook°, Dok Go Hyang, Lee KwangHeun

School of Medicine, Dongguk University

Alzheimer's disease (AD) involves neuronal degeneration with impaired cholinergic transmission, particularly in areas of the brain associated with learning and memory. Several cholinesterase inhibitors

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

Kim HanSoo°, Oh Youn Hee, Lim DongKoo

College of Pharmacy, Chonnam National University

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

Shin ImChul°, Hong JinTea, Lim HwaKyung, Oh KiWan

충북대학교 약학대학 약물학 실험실

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