receptor supersensitivity, as shown by the enhanced ambulatory activity after administration of apomorphine (2 mg kg^{-1} s.c.). Glycine inhibited the development of postsynaptic dopamine receptor supersensitivity induced by repeated administration of morphine.
Opiate sensitization models demonstrate enhanced activating and rewarding effects of subsequent treatments which highlights the potential role of this phenonmena in drug addiction. Accordingly, the inhibition of glycine on the morphine-induced hyperactvity, reverse tolerance and dopamine receptor supersensitivity suggests that glycine might be useful for the treatment of morphine addiction.

[PA1-57] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of adenosine on the development of tolerance to and physical dependence on morphine in mice

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This study was performed to investigate the effects of adenosine on the development of tolerance to and physical dependence on morphine. Repeated adminstration of morphine developed tolerance and physical dependence. Adenosine (1, 2 and 4 mg kg^{-1} i.p.) was administered intraperitoneally to mice for 7 days once a day 30 minutes prior to the morphine (10 mg kg^{-1} s.c.). Analgesic resposes were estimated at 0. 30. 60. 90, 120 minutes by the tail flick methods 24 hours after the final injection of morphine. The inhibitory degree of morphine tolerance development of the test morphine (10 mg kg^{-1} s.c.) by i.p. administration of adenosine was evidenced by the increase in analgesic response to morphine (5 mg kg^{-1} s.c.). Adenosine inhibited the development of tolerance to morphine. In addition, we separately measured the naloxone (5 mg kg^{-1} i.p.)-precipitated withdrawal sign (jump) in mice that had received the same morphine (10 mg kg^{-1} s.c.) for 7 days. Adenosine (1, 2 and 4 mg kg^{-1} i.p.) inhibited naloxone-precipitated withdrawal in morphine dependent mice.
These results sugest that adenosine might be useful the prevention or treatment of morphine tolerance and physical dependence.

[PA1-58] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Alternation and significance of calcium signalings through ryanodine receptor in neuronal cell death

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Pathophysiological elevation of intracellular calcium concentration ($[Ca^{2+}]_i$) in the neuron has been considered as an important responsible factor in the neuronal cell damages. However, the mechanism of increase of $[Ca^{2+}]_i$ through ryanodine receptor (RyR), the relationship between $[Ca^{2+}]_i$ level and cell damages have not been fully demonstrated. We now report that PC12 cells and primary hippocampal neuron cells exhibit greatly increased levels of RyR and enhanced

calcium release following stimulation with glutamate. Glutamate dose dependently decreased cell viability and increased the level of $[Ca^{2+}]_i$. However, the cells pretreated with dantrolene, an inhibitor of calcium release through RyR located in endoplasmic reticulum (ER), substantial lowered glutamate-induced increase of $[Ca^{2+}]_i$ and cell damages in neuronal cells. Moreover, dantrolene also inhibited $[Ca^{2+}]_i$ released through RyR in PC12 cells expressing mutant presenilin-2, which seems to be a modulator of calcium signal in ER. Our data therefore suggest that alternation of $[Ca^{2+}]_i$ through RyR in ER could be significantly important in neuronal cell damages by glutamate.

Poster Presentations - Field A2. Therapeutics

[PA2-1] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

An improved method to determine hydroxyproline in an immortalized rat liver stellate cell line (HSC-T6)

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Hydroxyproline (HYP) is a post-translational product of proline hydroxylation catalyzed by an enzyme prolyl 4-hydroxylase which plays a crucial role in the synthesis of all collagens, because the 4-hydroxyproline residues are essential for the folding of the newly synthesized collagen polypeptide chains into triple-heical molecules. Considering the role of collagen and its significance in many clinically important diseases such as liver cirrhosis, a great deal of attention has been directed toward the development of an assay at cell-based system.
The numerous assay procedures described for HYP are laborious, time-consuming and not feasible for the massive-screening. Here, we report the cell-based assay of prolyl 4-hydroxylase using HSC-T6 cells. To improve the sensitivity of assay for HYP content, ascorbate in hypoxic condition or lactate were added to the media. HOE 077 or pyridine 2,4 dicarboxylic acid, inhibitors of prolyl 4-hydroxylase, exhibited the 75% and 70% of enzyme activity compared to control, respectively. The assay procedure took only 3 days after treatment with agents, while assays from the primary stellate cells or liver tissues have taken several weeks. Considering the time, expenses and trends in assay design from biochemical method to cell-based method, this assay method could be useful tool to screen the compounds for the inhibitor of prolyl 4-hydroxylase.(Supported by The Center for Biological Modulators, 21C Frontier)

[PA2-2] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

DW1350, a Newly Synthetic Anti-osteoporotic Agent : 1. DW-1350 Inhihited Bone Resorption and Promoted Bone Formation.

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