

[PA1-24] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Changes of M1 muscarinic receptor mRNA and [³H] pirenzepine receptor binding in the brain of sensitized mice by methamphetamine administration

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Methamphetamine is a powerful stimulant that appears to produce locomotor activity and behavioral sensitization. Previous study has indicated that dopaminergic receptors are implicated in the behavioral responses of methamphetamine. Recently, it has been reported that other receptors, especially, M1 muscarinic acetylcholine receptor (M1R) plays an important role in the regulation of behavioral responses, and this receptor is abundantly expressed in brain regions, including the cerebral cortex, striatum, and the hippocampus of the animal. However, there were few reports related with methamphetamine and other receptors including M1R. Therefore, the present study was investigated the role of M1R in the mouse brain which produced locomotor activity and behavioral sensitization to methamphetamine. In order to undertake the aim, we examined M1R mRNA expression and [³H] pirenzepine binding for M1R in the brain regions of mice treated with methamphetamine. Our results showed that M1R mRNA expression was increased in the cortex (117 %), striatum (112 %), and the hippocampus; CA1 (113 %), CA2 (125 %), CA3 (113 %), and DG (96 %) regions, in acute methamphetamine treated group compared to the saline treated group. In the present study, moreover, it was obvious that M1 muscarinic receptor mRNA expression was significantly increased in the cortex (117 %), striatum (130 %), CA1 (115 %), CA2 (122 %), CA3 (124 %), and DG (123 %) regions in chronic methamphetamine treated group compared to the saline treated group. On the other hand, this study exhibited that levels of binding M1R labeled with [³H] pirenzepine were increased in the cortex (112 %) at acute session and the DG region (110 %) at chronic session except other regions. Consequently, it is suggested that M1R plays a role in behavioral response of the mice resulting from methamphetamine administrations. [Supported by the Brain Korea 21 Project in 2003]

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Effect of chelidonine derivatives on atrial fibrillation

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The number of patients suffering from atrial fibrillation is increasing and many cardiologists is trying to develop the ideal antiarrhythmic drugs for atrial fibrillation. An ideal antiarrhythmic agent would selectively prolong the action potential duration more in extraordinarily depolarized cardiac myocytes than in normal cells, and show tissue selectivity. Voltage-gated K⁺ (Kv) channels represent a structurally and functionally diverse group of membrane proteins. These channels play an important role in determining the length of the cardiac action potential and are the targets for antiarrhythmic drugs. Many K⁺ channel genes have been cloned from human myocardium and functionally contribute to its electrical activity. One of these channels, Kv1.5, is one of the more cardiovascular-specific K⁺ channel isoforms identified to date and forms the molecular basis for an ultra-rapid delayed rectifier K⁺ current found in human atrium. Thus, the blocker of hKv1.5 is expected to be an ideal antiarrhythmic drug for atrial fibrillation. We reported that chelidonine isolated from *Chelidonium majus* prolonged the action potential durations of atrial, ventricular myocytes and Purkinje fibers in a dose-dependent manner. The effect of chelidonine on atrial APD was frequency-dependent whereas the effect of chelidonine on the APDs of ventricular myocytes and Purkinje fibers was not frequency-dependnet. In the present study, we synthesized the 14 compounds of chelidonine derivatives and examined their effect on the hKv1.5 current expressed in Ltk-cells using whole cell mode of patch clamp techniques. We found out that chelidonine derivatives inhibited the hKv1.5 current expressing predominantly in human atrium. Also, chelidonine was more potent than a well-known antiarrhythmic drug, dofetilide. These results strongly suggest that chelidonine derivatives could be an ideal drug for atrial fibrillation.