マウスにおける［^{3}H］3，4－メチレンジオキシメタンフェタミンの分布に及ぼす併用薬物の影響

橋本謙二、前田晴美、平井克己、五郎丸　毅

Europ. J. Pharmacol., **228** (5－6) 247－256(1993)

Drug effects on distribution of [^{3}H]3,4－methylenedioxymethamphetamine in mice

Kenji Hashimoto, Harumi Maeda, Katsumi Hirai and Tsuyoshi Goromaru

Abstract The present study was undertaken to examine the drug interactions between 3,4-methylenedioxymethamphetamine (MDMA) and paroxetine or several compounds including the 3,4-methylenedioxybenzyl (piperonyl) group in mice. The time course of radioactivity in the mouse brain after i.v. administration of the tracer amount (approximately 70 ng/kg) of [^{3}H]MDMA was altered significantly by coinjection of carrier MDMA (15 mg/kg) or by pretreatment with paroxetine (10 mg/kg, i.p., 5 min). Furthermore, the radioactivity in the brain 60 min after injection of [^{3}H]MDMA was increased significantly by pretreatment with paroxetine, but not by pretreament with 6-nitroquipazine, fluoxetine, clomipramine, GBR 12909 or desipramine, indicating that paroxetine-induced alteration of the brain radioactivity was not due to the inhibitory effect of 5-hydroxytryptamine (5-HT) uptake of paroxetine. The radioactivity in the brain 60 min after injection of [^{3}H]MDMA was increased significantly by pretreatment with 3,4-methylenedioxyamphetamine (MDA), MDMA, 1-piperonylpiperazine and N, α-dimethylpiperonylamine, but not by pretreatment with piperonylacetone, piperonyl butoxide and piperonyl isobutyrate. HPLC analyses indicated that the alteration of brain radioactivity 60 min after injection of [^{3}H]MDMA was, in part, due to inhibition in the metabolism of [^{3}H]MDMA to radioactive metabolite(s). The present results suggest that a specific mechanism for the 3,4-methylenedioxyphenyl group which rapidly alters the disposition and metabolism of [^{3}H]MDMA may exist in brain and peripheral

organs of mice.

3，4—メチレンジオキシメタンフェタミン(MDMA)とパロキセチンなどのピペロニル基を有する薬物との相互作用をマウスを用いて検討した。^{3}H標識MDMAを投与後のマウス脳内の放射能は非標識MDMAおよびパロキセチンの併用により大きく変化した。この変化はセロトニン再吸収阻害効果とは無関係であることが6—ニトロキパジン等との併用により明らかとなった。またピペロニル基を有する他の薬物の前処理により脳内放射能は明らかに増加し、これはMDMAの代謝阻害によることが示唆された。