3，4－Methylenedioxymethamphetamine によるラット脳内[^{3}H]6－Nitroquipazine 標識セロトニン再吸収部位の減少

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Reduction of [^{3}H] 6－nitroquipazine－labelled 5－hydroxytryptamine uptake sites in rat brain by 3，4－methylenedioxymethamphetamine

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ABSTRACT 3，4－Methylenedioxymethamphetamine (MDMA；Ecstasy) is a known neurotoxin to 5－hydroxytryptamine (5－HT；serotonin) never terminals. It has recently been demonstrated that [^{3}H] 6－nitroquipazine is a new radioligand for studying the 5－HT transporter system in brain. Therefore, we examined the effects of repeated systemic administration (10 mg／kg ip, twice daily for 3 d) of MDMA on 5－HT uptake sites in rat brain. Marked reductions in the concentrations of 5－HT and its major metabolite 5－hydroxyindoleacetic acid (5－HIAA) were observed in the cerebral cortex 1 week after the last injection of MDMA. In addition, the density of [^{3}H] 6－nitroquipazine－labelled 5－HT uptake sites was significantly decreased by MDMA. Furthermore, the reduction of 5－HT and 5－HIAA content and the density of [^{3}H] 6－nitroquipazine－labelled 5－HT uptake sites by MDMA were significantly prevented by coadministration of 6－nitroquipazine (5 mg／kg), a very potent and selective 5－HT uptake inhibitor. The present results indicate that the 5－HT uptake carrier plays an important role in the neurotoxic action of MDMA.

抄録　MDMA はセロトニン神経終末に対して神経毒として作用する事が知られている。今回，[^{3}H]6－nitroquipazine 結合に及ぼす MDMA の影響を調べた。MDMA を投与すると大脳皮質におけるセロトニンおよび代謝物である5－ヒドロキシインドール酢酸の含量が著明に減少した。又，[^{3}H]6－nitroquipazine によってラベルされるセロトニン再吸収部位の密度も有意に減少した。MDMA によるこれらの減少は，セロトニン再吸収阻害薬である6－nitroquipazine の同時投与によって有意に抑制された。本実験の結果は，セロトニン再

吸収過程がMDMAの神経毒作用に重要な役割を担っている事を示している。