[^{3}H] 6 −nitroquipazine によるマウス脳内セロトニン再吸収部位のインビボ標識

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In Vivo Labeling of 5－Hydroxytryptamine Uptake Sites in Mouse Brain with [^{3}H] 6－Nitroquipazineazine

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ABSTRACT 6－Nitroquipazine (DU 24565；6－nitro 2－piperazinylquinoline) is a very potent 5－hydroxytryptamine (5－HT；serotonin) uptake inhibitor. It has been demonstrated very recently that [^{3}H] 6－nitroquipazine is a suitable radioligand for studying 5－HT uptake sites. The present study evaluates [^{3}H] 6－nitroquipazine as a radioligand for *in vivo* labeling of 5－HT uptake sites in mouse brain. Very high uptake of radioactivity in the brain after i. v. administration of [^{3}H] 6－nitroquipazine was shown. Regional distribution of the radioactivity in mouse brain 3 hr after injection of [^{3}H] 6－nitroquipazine was in the order (highest to lowest) hypothalamus > midbrain > striatum > hippocampus > cerebral cortex > medulla oblongata > cerebellum. The regional distribution of *in vivo* [^{3}H] 6－nitroquipazine binding in mouse brain was highly correlated with that in rat brain obtained from previous *in vitro* binding studies. Coadministration of carrier 6－nitroquipazine (5 mg / kg) significantly decreased the radioactivity in the hypothalamus, whereas that in the cerebellum and cerebral cortex was increased. Because the cerebellum has very low density of [^{3}H] 6－nitroquipazine binding sites, the radioactivity in the cerebellum could, therefore, reflect the amount on nonspecific binding and free ligand. Kinetic studies showed highest *in vivo* specific binding 1 hr after injection of [^{3}H] 6－nitroquipazine and slow clearance of specific binding. Specific binding in the hypothalamus was inhibited in a stereoselective manner by the stereoisomers of norzimelidine. Furthermore, specific binding in the hypothalamus was reduced by several 5－HT uptake inhibitors, in a dose－dependent manner. In contrast, pretreatment with weak 5－HT uptake inhibitors and receptor antagonists did not reduce the specific binding. Moreover, there was a crrelation between the ED_{50}

values for inhibiting of *in vivo* binding and IC_{50} values for [^{3}H] 5－HT uptake into the rat brain synaptosomes. The present results indicate that [^{3}H] 6－nitroquipazine would be a sultable radioligand for studying *in vivo* 5－HT uptake sites in mouse brain.

抄録　マウス脳内セロトニン再吸収部位のインビボ測定用ラジオリガンドとしての［^{3}H］6－nitroquipazineの評価を行った。静注後，極めて高い放射能の集積がみられた。マウス脳におけるインビボ分布は，先に求めたインビトロの分布と類似した。視床下部における放射能分布は，6－nitroquipazineの同時投与によって有意に減少した。又，視床下部における分布は，セロトニン再吸収阻害剤によって用量依存的に減少した。さらに，インビボ結合を阻害する各種薬物のED_{50}値は，脳への［^{3}H］5－HTの再吸収に対するKi値と良好な関係にあった。本実験の結果は，［^{3}H］6－nitroquipazineがマウス脳内セロトニン再吸収部位のインビボ研究に有用なラジオリガンドである事を示している。