ラットの皮質膜に対する[^{3}H]6-nitroqupazineの高親和性結合：5-hydroxytryptamine並びに5-hydroxytryptamineの再吸収阻害剤による阻害

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Neuropharmacology, **30**(2)113－117 (1991)

HIGH AFFINITY BINDING OF [^{3}H]6-NITROQUIPAZNE TO CORTICAL MEMBRANES IN THE RAT: INHIBITION BY 5-HYDROXYTRYPTAMINE AND 5-HYDROXYTRYPTAMINE UPTAKE INHIBITORS

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ABSTRACT [^{3}H]6-Nitroquipazine is a new, suitable radioligand for studying the uptake system for 5-hydroxytryptamine (5-HT;serotonin). In the present study, inhibition by drugs of the binding of [^{3}H]6-nitroquipazine to uptake sites for 5-HT in the cerebral cortex of the rat was investigated. The inhibition of 5-HT and several inhibitors of the uptake of 5-HT (paroxetine,clomipramine, citalopram, Z-norzimelidine, fluoxetine, imipramine, desipramine and 5-methoxytryptoline) against the binding of [^{3}H]6-nitroquipazine to membranes from the cortex of the rat were the same and competition curves indicated a single population of binding sites. The addition of 5-HT and the tricyclic inhibitors of the uptake of 5-HT, imipramine, clomipramine and desipramine, all produced changes in the apparent dissociation constant (*Kd*), without changes in the number of binding sites (*Bmax*). Also, the non-tricyclic inhibitors of the uptake of 5-HT, paroxetine, citalopram, fluoxetine and Z-norzimelidine, and 5-methoxytryptoline, all produced changes in *Kd* values without changes in the *Bmax*. These results suggest that all the drugs used in this experiment exhibited competitive interactions with the binding of [^{3}H]6-nitroquipazine to uptake sites for 5-HT in the brain of the rat. These drugs may bind to common binding sites, which are likely to represent the substrate recognition sites for the uptake of 5-HT.

抄録　ラットの大脳皮質のセロトニン（5-HT）再吸収部位への[^{3}H]6-nitroquipazine(6-NQ)の結合に対する各種薬物の阻害効果について検討した。6-NQの皮質膜への結合に対する5-HT及び再吸収阻害剤（パロキセチン，クロミプラミン，Z-ノルジメリジン，フルオキセチン，イミプラミン，デシプラミン及び5-メトキシトリプトリン）の効果は同一の置換曲線を示し，結合部位は一種であることが判明した。5-HT及び三環系薬物の添加は結合点数には影響しないが，見かけの解離定数を大きく変化させた。また非三環系阻害薬も同様の影響を示した。このことから，今回実験に用いた阻害薬はラット脳の5-HT再吸収部位に対する6-NQの結合を競合的に阻害することが判明した。