レセルピンによるマウス脳内^{3}H-Ro 15-1788の In Vivo結合の変化

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Changes in *In Vivo* Binding of ^{3}H-Ro 15-1788 in Mouse Brain by Reserpine

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ABSTRACT The effects of reserpine on the *in vivo* binding of ^{3}H-Ro 15-1788, (Ro 15-1788: ethyl 8-fluoro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo [1,5a] [1,4] benzodiazepine-3-carboxylate) a selective benzodiazepine antagonist, in the mouse brain were investigated. The biodistributions of tracer amounts of ^{3}H-Ro 15-1788 in mice were significantly altered by pretreatment with reserpine (2.5 or 5.0 mg/kg, 24h before the tracer administration). The time courses of radioactivity in the brain and the blood following i.v. injection of ^{3}H-Ro 15-1788 with carrier Ro 15-1788 were not changed by pretreatment with reserpine, which suggested that the specific binding process might be altered by reserpine. The degree of alteration in the *in vivo* binding of ^{3}H-Ro 15-1788 seemed to be dependent upon the dose of reserpine and the duration after the treatment of reserpine. The maximum changes in the biodistribution of ^{3}H-Ro 15-1788 were observed at 1 day after injection of reserpine. The body temperature and the brain monoamine contents (dopamine, norepinephrine and 5-hydroxytryptamine) in mice were measured as indicators of pharmacological effects of resepine, and good relationships to the degree of changes in the biodistribution of ^{3}H-Ro 15-1788 and either the body temperature or brain monoamine contents, were observed. Furthermore, the changes in the biodistribution of ^{3}H-Ro 15-1788 in the reserpinized mice were significantly supprtssed by antidepressant imipramine treatment. These results suggest that it would be possible to detect the *in vivo* drug interaction with brain benzodiazepine receptors in the living human brain using ^{11}C-Ro 15-1788 and positron emission tomography (PET).

抄録　ベンゾジアゼピンレセプターのアンタゴニストである^{3}H-Ro 15-1788の *in vivo* 結合に及ぼすレセルピンの影響を調べた。^{3}H-Ro 15-1788の *in vivo* 結合の変化の割合は，レセルピンの投与量および投与後の日数に依存する事がわかった。またレセルピンの薬理効果の指標としてマウスの体温および脳内モノアミン（ドーパミン，ノルエピネフリン，セロトニン）の含量を測定した。さらに，レセルピンによる^{3}H-Ro 15-1788の *in vivo* 結合の変化がイミプラミンの前投与によって有意に抑制された。以上の結果より，^{11}C-Ro 15-1788とPETを用いる事により薬物相互作用を *in vivo* で研究できることが示唆された。

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