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研究报告

NMDA受体显像剂$^{99}Tc^{m}$-NCAM的制备和受体结合分析

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摘要 用$^{99}Tc^{m}$标记新的美金刚胺（memantine）衍生物*N*-[2-(N-(2-巯基乙基))氨基乙酰基]-N-(2-巯基乙基)3,5-二甲基金刚烷胺基乙酰胺（N_2S_2-memantine，简称NCAM），并通过优化标记条件获得放射化学纯度达95%以上的标记化合物$^{99}Tc^{m}$-NCAM。脂溶性实验测得其脂水分配系数lg P=1.90。放射性受体结合分析显示，其与 N-甲基-D-门冬氨酸（NMDA）受体结合具有饱和性，根据受体B区理论编制的计算机程序求出NMDA受体结合参数最大结合容量B_{max}=56.8 μmol/g，平衡解离常数Kd=706.3 nmol/L，特异性NMDA受体拮抗剂能阻断其与NMDA受体的结合。结果显示$^{99}Tc^{m}$-NCAM与NMDA受体结合具有中等程度的亲和力和结合特异性，具有较好的脂溶性，易透过血脑屏障，有可能成为一种新的NMDA受体显像剂。

关键词 NCAM； NMDA受体；放射性受体结合分析；显像剂

分类号 R817

Radiochemical Synthesis and Radio-Ligand Receptor Binding Assay of $^{99}Tc^{m}$-NCAM as a Potential NMDA Receptor Imaging Agent

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Abstract A new radio-ligand $^{99}Tc^{m}$-NCAM was synthesized by labeling a derivative of memantine N_2S_2-memantine (N[2-(*N*-(2-mercapotoethyl))aminoformylmethyl] *N*-(2-mercapotoethyl)-3, 5- dimethyladamantyl aminoacetamide, NCAM), and its radiochemical purity was greater than 95% determined by TLC under optimized labeling conditions. The radio-ligand receptor binding assay was shown that the binding of radio-ligand $^{99}Tc^{m}$-NCAM to NMDA receptor was saturable with a dissociation constant K_d of 706.3 nmol/L and a B_{max} of 56.8 μmol/g calculated by a computer program written based on the receptor theory in B region. The competitive analysis show that such specific binding could be inhibited by specific inhibitors of NMDA receptor. Its oil/water partition coefficient is 1.90. In conclusion, the new radio-ligand $^{99}Tc^{m}$-NCAM, which was systhesized by the method of directly labelling NCAM with $^{99}Tc^{m}$, has a moderate affinity and specific binding to NMDA receptor, and can easily transported through the blood-brain barrier(BBB). Therefore, it may be a potential NMDA receptor imaging agent.

Key words N_2S_2-memantine NMDA receptor radio-ligand receptor binding assay; imaging agent

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