

研究报告

多巴胺D₄受体PET显像剂¹⁸F-FHTP的生物学评价

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摘要 为研究多巴胺D₄受体在精神分裂症、注意力缺乏多动症等疾病病因分析中的作用, 开展了多巴胺D₄受体PET显像剂3-(4-[¹⁸F]氟苄基)-8-羟基-1, 2, 3, 4-四氢苯并吡喃[3, 4-c]吡啶-5-酮 (¹⁸F-FHTP) 的体内外生物学评价。通过体外受体竞争抑制结合分析, 测定了FHTP对多巴胺D₂样受体的亲和性; 通过辛醇实验, 测定了¹⁸F-FHTP的脂水分配系数; 通过大鼠体内的生物分布和阻断分布实验, 测定了¹⁸F-FHTP在大鼠体内的各感兴趣区域的摄取率。实验测得FHTP对D₂, D₃受体的亲和常数*K_i*值分别大于5 800, 3 000 nmol/L; 对D_{4.2} 受体的*K_i*值为2.9 nmol/L; 测得其脂水分配系数为1.11; 大鼠生物分布实验显示, ¹⁸F-FHTP能通过血脑屏障进入脑, 并在纹状体、下丘脑、额叶皮质、海马、小脑等已知的D₄受体分布区域有较高的摄取率。体外受体结合分析、脂水分布实验、大鼠体内分布和阻断分布研究表明, ¹⁸F-FHTP可作为多巴胺D₄受体显像剂用于体内显像研究。

关键词 [多巴胺D₄受体](#); [PET显像剂](#); [¹⁸F](#); [生物学评价](#)
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Biological Evaluation of ¹⁸F-FHTP as a Potential Dopamine D₄ Receptor PET Imaging Agent

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Abstract 3-(4-[¹⁸F]fluorobenzyl)-8-hydroxy-1, 2, 3, 4-tetrahydrochromeno[3, 4-c] pyridin-5-one (¹⁸F-FHTP) was *in vitro* and *in vivo* evaluated as a potential dopamine D₄ receptor PET imaging agent. Through receptor binding assay, the *K_i* of FHTP were determined to be 2.9 nmol/L for D_{4.2} receptor, and to be greater than 3 000 and 5 800 nmol/L for D₃ and D₂ receptor, respectively. The lg*P* was measured to be 1.11 through octanol experiment. The regional biodistribution studies in rats were carried out through biological distribution and blocking biodistribution experiments. The biodistributions studies show that ¹⁸F-FHTP can penetrate through blood brain barrier and selectively accumulate in striatum, hypothalamus, frontal cortex, hippocampus, cerebellum, where the D₄ receptor is reportedly located, and among organs, lung and kidney have higher uptakes than the others. Conclusively, *in vitro* and *in vivo* biological studies demonstrate that ¹⁸F-FHTP is a potential dopamine D₄ receptor imaging agent.

Key words [dopamine D₄ receptor](#); [PET imaging agent](#); [¹⁸F](#); [biological](#)

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