ORIGINAL ARTICLE

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Further characterization of a CNS adenosine A_{2a} receptor ligand [^{11}C]KF18446 with *in vitro* autoradiography and *in vivo* tissue uptake

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PET assessment of the adenosine A_{2a} receptors localized in the striatum offers us a potential new diagnostic tool for neurological disorders. In the present study, we carried out *in vitro* receptor autoradiography of a newly developed PET ligand [^{11}C]KF18446 ([7-methyl-^{11}C]-(*E*)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine) with rat brain sections. [^{11}C]KF18446 showed a high striatum/cortex binding ratio (5.0) and low nonspecific binding (<10%), suggesting that [^{11}C]KF18446 has characteristics comparable or slightly superior to [^{3}H]CGS 21680 or [^{3}H]SCH 58261, which are currently available representative A_{2a} receptor ligands. Scatchard analysis indicated a K_d of 9.8 nM and a B_{max} of 170 fmol/mm^3 tissue in the striatum and a K_d of 16.4 nM and a B_{max} of 33 fmol/mm^3 tissue in the cortex. Seven xanthine-type and four nonxanthine-type adenosine receptor ligands with an affinity for the adenosine A_{2a} receptors significantly reduced the *in vitro* binding of [^{11}C]KF18446 to the brain section. The blocking effects were much stronger in the striatum than in the cortex, but did not necessarily parallel their affinity. On the other hand, four xanthine-type ligands and one nonxanthine-type ligand (SCH 58261) of the 11 ligands studied reduced the *in vivo* uptake of [^{11}C]KF18446 in mice, but other ligands, including A_1-selective and nonselective ligands and three nonxanthine-type A_{2a}-selective antagonists did not. We conclude that [^{11}C]KF18446 is a promising adenosine A_{2a} receptor ligand for PET study.

Key words: [^{11}C]KF18446, adenosine A_{2a} receptor, striatum, PET