ORIGINAL ARTICLE

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Preclinical evaluation of [^{11}C]SA4503: radiation dosimetry, *in vivo* selectivity and PET imaging of sigma$_1$ receptors in the cat brain

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Our previous *in vivo* study with rats has demonstrated that ^{11}C-labeled 1-(3,4-dimethoxyphenethyl)-4-(3-phenylpropyl)piperazine ([^{11}C]SA4503) is a potential radioligand for mapping CNS sigma$_1$ receptors by positron emission tomography (PET). In the present study, we further characterized this ligand. The radiation absorbed-dose of [^{11}C]SA4503 in humans estimated with the tissue distribution in mice, was higher in the liver, kidney and pancreas than in other organs studied, but was low enough for clinical use. The brain uptake of [^{11}C]SA4503 in mice was reduced to approximately 60–70% by co-injection of carrier SA4503 and haloperidol, but not by co-injection of any of six ligands for sigma$_2$ or other receptors, for which SA4503 showed *in vitro* >100 times weaker affinity than for sigma$_1$ receptor. In the cat brain, the uptake in the cortex was higher than that in the cerebellum. The radioactivity in the cortex and cerebellum accumulated for the first 10 min and then gradually decreased until 81.5 min in the baseline measurement, but rapidly decreased in the carrier-loading condition. The receptor-mediated uptake was estimated to be approximately 60–65% of the total radioactivity in the cortex and cerebellum at 76 min after tracer injection. We have concluded that [^{11}C]SA4503 has the potential for mapping sigma$_1$ receptor by PET.

Key words: sigma$_1$ receptor, [^{11}C]SA4503, central nervous system, positron emission tomography