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Evaluation of [^{11}C]SA5845 and [^{11}C]SA4503 for imaging of sigma receptors in tumors by animal PET

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Sigma receptors are expressed in a wide variety of tumor cell lines, and are expressed in proliferating cells. A radioligand for the visualization of sigma receptors could be useful for selective detection of primary tumors and their metastases, and for non-invasive assessment of tumor proliferative status. To this end we evaluated two sigma receptor ligands, [^{11}C]SA5845 and [^{11}C]SA4503. In an *in vitro* study, AH109A hepatoma showed moderate densities of sigma$_1$ and sigma$_2$ receptors, and VX-2 carcinoma showed a high density of sigma$_2$ receptors: B_{max} (fmol/mg protein) for sigma$_1$ vs. sigma$_2$, 1,700 vs. 1,200 for AH109A hepatoma and 800 vs. 10,000 for VX-2 carcinoma. In a cell growth assay *in vitro*, neither SA5845 nor SA4503 (<10 μM) showed any inhibitory effect on proliferation of the AH109A hepatoma cells. In rats, the uptake of [^{11}C]SA5845 and [^{11}C]SA4503 in AH109A tissues was accumulated over the first 60 minutes; however, the uptake of both tracers increased by co-injection with haloperidol as a sigma receptor ligand. On the other hand, in the PET studies of rabbits, the uptake of [^{11}C]SA5845 in the VX-2 carcinoma was relatively higher than that of [^{11}C]SA4503, because of a much higher density of sigma$_2$ receptors compared to sigma$_1$ receptors in the VX-2 tissue, and the uptake of both tracers in the VX-2 tissue was decreased by carrier-loading and pre-treatment with haloperidol ([^{11}C]SA5845, 53% and 26%, respectively; [^{11}C]SA4503, 41% and 22%, respectively at 30 minutes after injection). Therefore, [^{11}C]SA5845 and [^{11}C]SA4503 may be potential ligands for PET imaging of sigma receptor-rich tumors.

Key words: sigma receptor, PET, SA5845, SA4503, tumor imaging