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A feasibility study of [^{11}C]SA4503-PET for evaluating sigma$_1$ receptor occupancy by neuroleptics: the binding of haloperidol to sigma$_1$ and dopamine D$_2$-like receptors

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We investigated feasibility of positron emission tomography (PET) with [^{11}C]SA4503 for evaluating the sigma$_1$ receptor occupancy rate by neuroleptics. Haloperidol, which is well known to bind dopamine D$_2$-like receptor (D2R) as well as to be a representative non-selective antagonist for sigma$_1$ receptor (σ1R), was selected as a model drug. Three healthy male subjects underwent 60-min [^{11}C]raclopride-PET and 90-min [^{11}C]SA4503-PET scans successively at a 120-min interval twice in a day for baseline measurement and on another day for haloperidol-loading measurement 16 hours after peroral administration of 3 mg of haloperidol. Binding potential (BP) of [^{11}C]raclopride and [^{11}C]SA4503 was quantitatively evaluated and the σ1R and D2R occupancy rates were determined. D2R occupancy rates by haloperidol were 64% and 62% in the caudate and putamen, respectively, 16 h after the administration, while σ1R occupancy rates were approximately 80% in all seven regions investigated including the caudate, putamen and cerebellum 18 h after the administration, suggesting that the σ1R receptor occupancy rate by haloperidol was slightly larger than the D2R receptor occupancy rate. We concluded that [^{11}C]SA4503-PET can be used for evaluating the σ1R occupancy rates by neuroleptics or other drugs.

Key words: [^{11}C]SA4503, sigma$_1$ receptor, receptor occupancy, haloperidol, positron emission tomography