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Synthesis and biological evaluation in rat and cat of [^{18}F]12ST05 as a potential 5-HT$_6$ PET radioligand☆

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Abstract

Introduction: 5-hydroxytryptamine (5-HT)$_6$ receptors represent one of the more recently discovered serotoninergic receptor family. However, no 5-HT$_6$ positron emission tomography (PET) radiotracer is currently used in clinical imaging studies. The purpose of this study was to propose the first fluorinated PET radiotracer for this brain receptor.
Methods: A new compound presenting in vitro high affinity towards the serotoninergic 5-HT$_6$ receptor, *N*-[2-(1-[(4-fluorophenyl)sulfonyl]-1*H*-indol-4-yloxy)ethyl]-*N*,*N*-dimethylamine, was labelled with fluorine 18 via a nitro-/fluoronucleophilic substitution. Biological evaluations included (i) in vitro and ex vivo autoradiographies in rat brain and (ii) a PET scan on anaesthetized cat.
Results and Conclusion: Although the radioligand showed excellent brain penetration, it did not reveal any specific binding to the 5-HT$_6$ receptors indicating that this radiotracer is not suitable for mapping 5-HT$_6$ receptors using PET.

Keywords: 5-HT$_6$ receptors; Radioligand; Positron emission tomography; Rat; Cat