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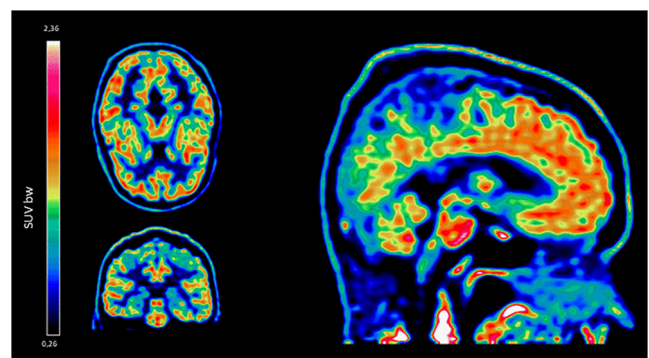
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^{18}F -F13640 PET imaging of functional receptors in humans

Matthieu Colom^{1,2} · Nicolas Costes³ · Jérôme Redouté³ · Frédéric Dailier¹ · Florent Gobert^{1,2} · Didier Le Bars^{1,3,4,5} · Thierry Billard^{3,5} · Adrian Newman-Tancredi⁶ · Luc Zimmer^{1,2,3,4} 

The vast majority of PET radiopharmaceuticals used for receptor neuroimaging are antagonists. This is particularly true for 5-HT_{1A} receptor radiopharmaceuticals such as ^{18}F -MPPF or ^{11}C -WAY100635. These radiolabeled antagonists allow PET neuroimaging of the total pool of receptors, regardless of their functional state. In contrast, agonists bind preferentially to the functionally active state of receptors, a pharmacological property that has not yet been exploited for PET imaging of functional 5-HT_{1A} receptors [1]. To this end, we have developed a highly selective 5-HT_{1A} receptor agonist, ^{18}F -F13640, and validated it in animal models [2]. A postmortem study in Alzheimer subjects showed that the *in vitro* binding of ^{18}F -F13640 differs from that of ^{18}F -MPPF, the prototypical radiopharmaceutical [3].

Here we show the first human brain image obtained *in vivo* with ^{18}F -F13640 (study registration, EudraCT 2017-002722-21). A summed brain PET image was obtained in a 32-year-old healthy man after IV injection of the radiopharmaceutical (90-min scan). ^{18}F -F13640 brain distribution, expressed by the standardized uptake value with the body weight (SUV bw), showed a binding pattern different from that seen with conventional antagonist 5-HT_{1A}



radiopharmaceuticals. Although the binding regions are well correlated to the density of 5-HT_{1A} receptors, the ROIs are mainly cortical, indicating that these brain regions are enriched in functionally active receptors.

^{18}F -F13640 is the first radiopharmaceutical that enables *in vivo* investigation of functional 5-HT_{1A} receptors that are likely to be altered in pathological conditions such as neurodegenerative diseases or psychiatric disorders. The development of this agonist PET radiopharmaceutical opens new opportunities for nuclear medicine.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Informed consent Written informed consent was obtained from the spouse of the subject for publication of this case report and accompanying images.

✉ Luc Zimmer
luc.zimmer@univ-lyon1.fr

- ¹ Hospices Civils de Lyon, Lyon, France
- ² Lyon Neuroscience Research Center, Bron, France
- ³ CERMEP-imaging platform, Lyon, France
- ⁴ Université de Lyon, Lyon, France
- ⁵ Institute of Chemistry and Biochemistry, Villeurbanne, France
- ⁶ Neurolix Inc., Dana Point, USA

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