

PET imaging of benzodiazepine receptors in the human brain: Evaluation of [¹⁸F]Flouroethylflumazenil

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Objectives:

5-(2'-[¹⁸F]fluoroethyl)flumazenil ([¹⁸F]FEF) is a ¹⁸F-labeled PET tracer for central benzodiazepine receptors. Compared to [¹¹C]flumazenil, it has the advantage of the longer half-life of the fluorine-18 label. After optimization of its' synthesis and determination of its' in vitro receptor affinities we performed first PET studies in humans.

Methods:

PET studies in four healthy volunteers were performed on a Siemens ECAT EXACT whole-body scanner. In two subjects, a second PET scan was conducted after pre-treatment with unlabeled flumazenil. A third subject was studied both with [¹⁸F]FEF (Fig. 2) and with [¹¹C]flumazenil. Brain radioactivity was measured for 60-90 min p.i. and analyzed with a ROI-oriented approach and on a pixelwise basis with spectral analysis. Plasma radioactivity was determined from arterial blood samples and metabolites were determined by HPLC.

Results:

In human brain, maximum radioactivity accumulation was observed 4±2 min p.i. with a fast clearance kinetics. [¹⁸F]FEF uptake followed the known central benzodiazepine receptor distribution in the human brain. Pre-treatment with unlabeled flumazenil resulted in significantly reduced specific tracer uptake in all brain areas except for receptor-free reference regions like the pons. Spectral analysis revealed 1.5- to 2.5-fold higher distribution volumes for [¹¹C]flumazenil compared to [¹⁸F]FEF, while relative uptake of [¹⁸F]FEF was higher in the cerebellum, which is most likely due to its' relatively higher affinity for benzodiazepine receptors containing the α6 subunit.

Conclusion:

Although [¹¹C]flumazenil has some advantages over [¹⁸F]FEF, our results indicate that [¹⁸F]FEF is a suitable PET ligand for quantitative assessment of central benzodiazepine receptors, which can be used independently of an on-site cyclotron.

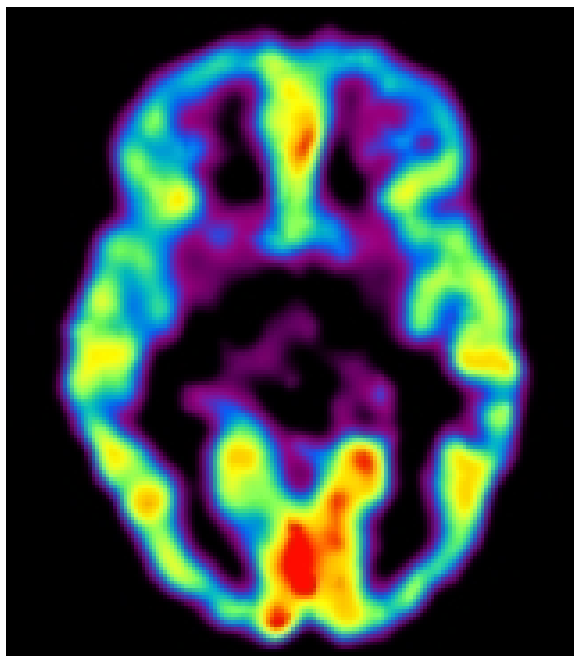


Fig. 1: N-methyl-[¹¹C]Flumazenil

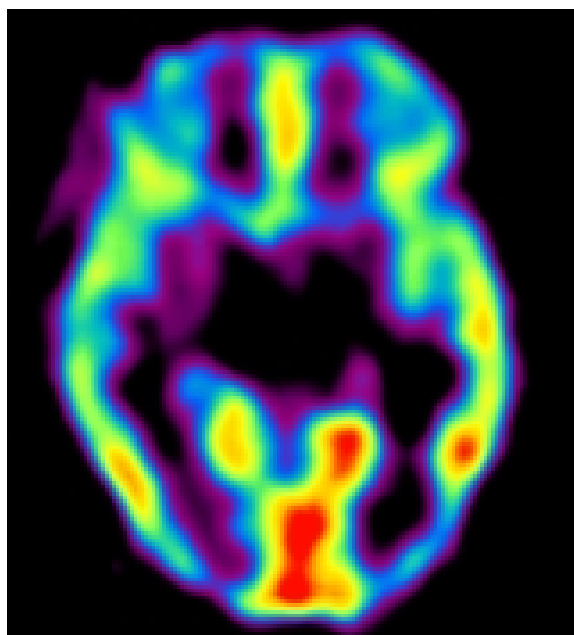


Fig. 2: 5-(2'-[¹⁸F]fluoroethyl)flumazenil