In vivo-PET evaluation of [^{18}F]PRD04-MZ in rats: A novel highly selective dopamine transporter ligand for PET

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Introduction: Dopamine reuptake mediated by the dopamine transporter DAT plays a key role in the regulation of dopaminergic signal transduction. Dopaminergic malfunctions have been observed in psychosis or attention deficit/hyperactivity syndrome ADHS. In the case of PD, a diminished dopamine DA biotransformation is buffered by a significant upregulation of available DAT binding sites in an early state of PD. Therefore ^{18}F-labelled probes for non-invasive quantitative visualisation of DAT-availability are of significant clinical relevance. Herein, the novel radioligand [^{18}F]PRD04-MZ is characterised *in vivo* in adult Wistar rats.

Methods: [^{18}F]PRD04-MZ was obtained in a radiochemical purity >99% after HPLC-purification and SPE-mediated isolation. A CEM discover® focussed microwave was used for microwave enhanced radiosynthesis. β-CFT (WIN 35,428) was used for displacement studies. 40 MBq [^{18}F]PRD04 (radiochemical purity > 99%) were injected directly into the tail vene of five adult Wistar rats at t=0 s. After recording the uptake kinetics for 60 to 90 min, 1 mg/kg β-CFT was applied as bolus, followed by the continuous application of 1 mg/kg*h via a perfusor (Fig. 1). Animals were anaesthetised with chloral hydrate. A Siemens/CTI Focus 120 Microimager was used for data acquisition.

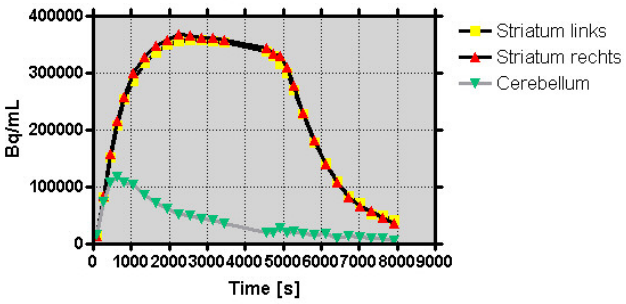

Fig. 1: time activity curve of [^{18}F]PRD04: acquisition time 2 x 3600 s, 2 mg/kg β-CFT i.v. after 4200 s

Results: [^{18}F]PRD04-MZ shows high specific uptake into the caudate putamen. Neither in cortical regions nor in the thalamus, any specific binding could be detected (Figs. 2,3). In addition, uptake into the harderian glands is remarkably low. These results display the exorbitant monoamine transporter selectivity of the novel candidate [^{18}F]PRD04-MZ.

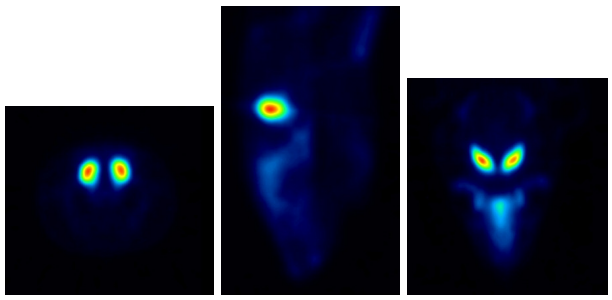

Fig. 2: transversal, sagittal and coronal view of [^{18}F]PRD04-MZ, summarised after 60 min

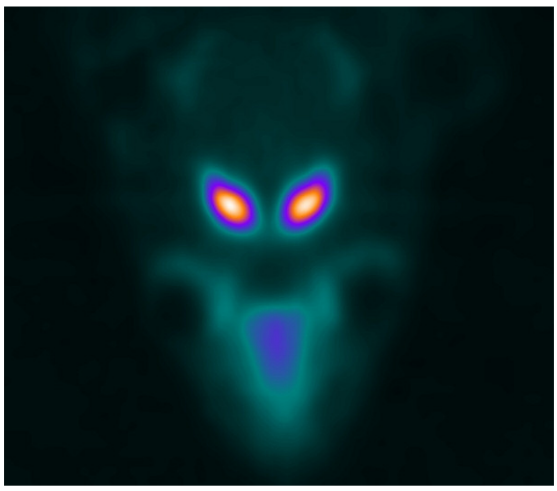

Fig. 3: coronal view, illustration of low uptake into the harderian glands

Conclusions: A novel radio-fluorinated tropane derivative was evaluated in rats. The radioligand shows outstanding selectivity and binding characteristics in DAT-rich brain regions. The cerebellum can be used as a reference region. Its characteristics facilitate comparative studies of dopaminergic signal pathways involving D_2/D_3-selective radioligands [^{18}F]FP and [^{18}F]DMFP.

References:

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