Autoradiographic *in vivo* evaluation of [^{18}F]PRD04-MZ in mice: 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. In the case of Parkinson´s Desease (PD), a diminished dopamine (DA) biotransformation is buffered by a significant up-regulation of available DAT binding sites in an early state of PD. In this relationship, positron emitter-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 *ex vivo* in 14 µm rodent brain sections using autoradiography.

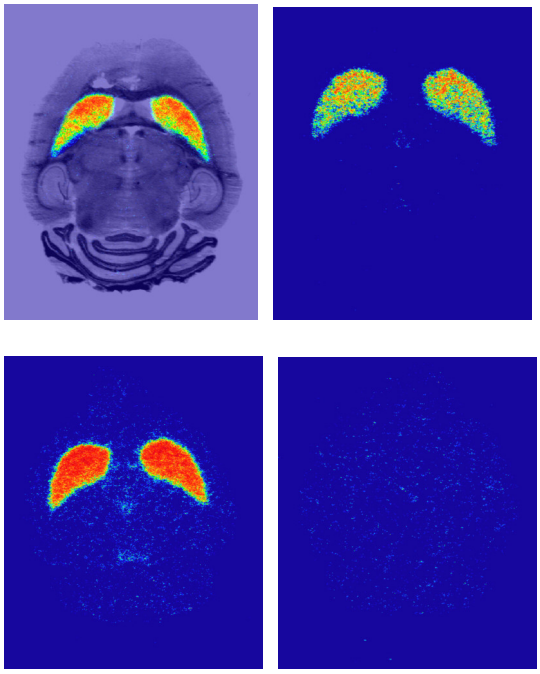

Figure 1: In vivo autoradiography on coronal sections of wild-type mice 35 min p.i., **upper left:** specific binding, coregistered with thionin coloured specimen; **upper right:** specific binding; **lower left:** total binding, **lower right:** displacement with β-CFT (i.p. application of 1 mg/kg β-CFT 20 min prior application of the radioligand)

Method: Radiosynthesis of [^{18}F]PRD04-MZ was performed in a CEM discover® focussed Microwave, purified by HPLC and isolated by SPE. Autoradiography was carried out at room temperature in reaction buffer (50 mM Tris/HCl buffer, pH 7.4 containing 120 mM NaCl and 5 mM KCl) with [^{18}F]PRD04-MZ. β-CFT (WIN 35,428) was used for displacement studies. Sections with [^{18}F]PRD04-MZ were washed 1x20 min in reaction buffer containing 0.01 % Triton X-100 and 1x20 min in reaction buffer, shortly dipped into deionized water and quickly dried in a stream of cold air. Sections were exposed to Fuji phosphor screen for 3 h.

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. These results visualise the exorbitant monoamine transporter selectivity of the novel candidate [^{18}F]PRD04-MZ.

Conclusions: A radio-fluorinated tropane derivative containing a conformational restricted C_4 chain at the nitrogen has been prepared for *in vitro* and *in vivo* evaluation. This evidence for its outstanding selectivity and binding characteristics facilitates comparative studies of dopaminergic signal pathways involving D2/D3-selective radioligands [^{18}F]FP and [^{18}F]DMFP.

References:

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