Quantification of D_2-like dopamine receptors in the human brain with [^{18}F]Desmethoxyfallypride

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Substituted benzamides such as [^{11}C]raclopride or [^{123}I]iodobenzamide are selective radiotracers for PET and SPECT imaging of D_2-like dopamine (DA) receptors. [^{18}F]Desmethoxyfallypride ([^{18}F]DMFP) is a benzamide tracer with the advantage of a fluorine-18 label. We optimized the synthesis and evaluated [^{18}F]DMFP in PET studies in healthy human volunteers.

Methods: The affinity of DMFP for D_2-like DA receptors was characterized *in vitro* using membrane preparations from rat striatum and the DA receptor ligand [^{3}H]spiperone. PET studies in ten healthy human volunteers were performed on a Siemens ECAT EXACT camera after injection of 214 ± 54 MBq (mean ± SD) [^{18}F]DMFP. Brain images were acquired dynamically over 124 min and metabolite-corrected plasma activity was used as input function. Data analysis was performed utilizing several different approaches (compartmental, graphical, equilibrium methods).

Results: The mean inhibition constant (K_i) of DMFP was 15 ± 9 nM. In human brain, the striatum-to-cerebellum ratio reached a maximum of about four between 60 and 120 min. When specific binding in the striatum was expressed as the difference between binding in the striatum and the cerebellum, it reached a maximum at approximately 60 min post injection (p.i.) and remained almost constant until the end of data acquisition. The ratio of specific striatal to non-specific cerebellar binding was about 3:1 at 120 min p.i. A small, but significant specific tracer binding could also be detected in the thalamus. Treatment of a schizophrenic patient with a high dose (1000 mg/day) of another substituted benzamide, amisulpride, resulted in a reduction of specific tracer uptake of about 90% in striatal regions. With regard to measured distribution volumes and binding potentials, there was an excellent agreement between all applied analytical methods (Table 1).

Conclusion: Our study demonstrates that [^{18}F]DMFP is a highly reliable tracer for PET imaging of D_2–like DA receptors. It offers the major advantage that it can be used independently of an on-site cyclotron within a PET satellite network. Non-invasive analytical methods without blood sampling provide valid measurements of receptor quantities in human striatum. Due to the fluorine-18 label and the favorable imaging properties, [^{18}F]DMFP could become an efficient substitute for [^{11}C]raclopride in a clinical context.

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Table 1

	Cerebellum	Thalamus	Caudate	Putamen
VD 2-Compartment	3.11 ± 0.94	3.83 ± 1.33	8.74 ± 3.00	10.76 ± 3.58
BP 2-Compartment *	--	0.22 ± 0.08	1.80 ± 0.41	2.44 ± 0.40
VD 3-Compartment	--	3.73 ± 1.41	8.73 ± 3.01	10.74 ± 3.59
BP 3-Compartment	--	0.18 ± 0.12	1.79 ± 0.41	2.44 ± 0.40
VD Logan Invasive	3.29 ± 0.92	3.92 ± 1.37	8.87 ± 3.00	10.97 ± 3.61
BP Logan Invasive *	--	0.18 ± 0.10	1.67 ± 0.37	2.30 ± 0.32
BP Logan Noninvasive	0	0.19 ± 0.10	1.61 ± 0.34	2.21 ± 0.31
BP RTM	--	0.20 ± 0.07	1.68 ± 0.37	2.33 ± 0.31
BP Equilibrium	--	0.22 ± 0.14	1.65 ± 0.22	2.19 ± 0.32