

IN VIVO QUANTIFICATION OF PRESYNAPTIC DOPAMINE
TRANSPORTER BINDING PARAMETERS IN HUMAN
BRAINS WITH [I-123]IPT SPECT

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A method for quantifying the concentration of the presynaptic dopamine transporter could help identify patients at risk of developing neurodegenerative disorders. The purpose of this dynamic SPECT study was to determine the feasibility of measuring the kinetic binding parameters for a new transporter imaging agent with several highly advantageous properties, [I-123] N-(3-iodopropene-2-yl)-2 β -carbomethoxy-3 β -(4-chlorophenyl) tropane (IPT). The sample included 4 well characterized healthy volunteers with a mean age of 65 (range:60-67). About 5 mCi (185 MBq) of [I-123] IPT were injected as a bolus. Dynamic SPECT scans of the brain were then acquired on a triple headed camera (Prism 3000, Picker International) for 5 minutes each over 150 minutes. Blood samples were obtained every 8.4 seconds for the first 3 minutes with a peristaltic pump, and manually at 4, 8, 10, 15, 20, 30, 60, and 120 minutes after administration. The projection data sets were reconstructed with a count-dependent Wiener filter and corrected for attenuation with Chang's first order method. The basal ganglia (BG) time activity curves were decay corrected and converted CPM/ml into units of uCi/ml with an experimentally measured SPECT calibration factor of 0.00068 uCi/CPM. The metabolite corrected total plasma activities CPM/ml were also decay corrected and converted into units of uCi/ml with a measured well counter calibration factor of 6.3×10^{-7} uCi/CPM. The plasma activities were then fitted to a sum of three exponentials. The BG time-activity curves were fitted to a standard three compartment model. The findings are shown below for the rate constants (k_1 (ml/min/g), k_2 (/min), k_3 (/min), k_4 (/min)) and binding potential (BP(ml/g) \pm S.D). The % coefficient of variations of the parameter estimates are in parentheses.

	K_1	k_2	k_3	k_4	BP
Sub1	1.19(3.9)	0.057(11.5)	0.031(13.4)	0.007(13.9)	90.4(8.1)
Sub2	2.00(5.2)	0.074(14.2)	0.041(15.1)	0.011(10.4)	102.3(4.6)
Sub3	10.23(13.0)	0.55(17.7)	0.037(9.8)	0.015(6.8)	47.4(2.7)
Sub4	0.55(2.9)	0.019(17.7)	0.015(49.6)	0.011(47.9)	39.0(16.7)
Mean	3.49(4.53)	0.18(0.25)	0.031(0.01)	0.011(0.003)	69.8(31.3)

The parameters K_1 , k_2 , k_3 , and k_4 were well identified by the three compartment model except k_3 and k_4 for the Sub4. The outcome measure BPs for the dopamine transporter binding parameters were identifiable from the compartmental model. The results suggest [I-123] IPT SPECT can be used to quantify several kinetic parameters that reflect the functional status of the presynaptic dopamine transporter.