European Journal of
Nuclear
Medicine

Original article

Validation of quantitative brain dopamine D2 receptor imaging with a conventional single-head SPET camera

Päivi Nikkinen[1], Kristian Liewendahl[1], Sauli Savolainen[2], Jyrki Launes[3]

[1] Department of Clinical Chemistry, Division of Nuclear Medicine, Helsinki University Central Hospital, Helsinki, Finland
[2] Department of Physics, University of Helsinki, Helsinki, Finland
[3] Department of Neurology, Helsinki University Central Hosptial, Helsinki, Finland

Received 1 February and in revised form 10 April 1993

Abstract. Phantom measurements were performed with a conventional single-head single-photon emission tomography (SPET) camera in order to validate the relevance of the basal ganglia/frontal cortex iodine-123 iodobenzamide (IBZM) uptake ratios measured in patients. Inside a cylindrical phantom (diameter 22 cm), two cylinders with a diameter of 3.3 cm were inserted. The activity concentrations of the cylinders ranged from 6.0 to 22.6 kBq/ml and the cylinder/background activity ratios varied from 1.4 to 3.8. From reconstructed SPET images the cylinder/background activity ratios were calculated using three different regions of interest (ROIs). A linear relationship between the measured activity ratio and the true activity ratio was obtained. In patient studies, basal ganglia/frontal cortex IBZM uptake ratios determined from the reconstructed slices using attenuation correction prior to reconstruction were 1.30 ± 0.03 in idiopathic Parkinson's disease ($n=9$), 1.33 ± 0.09 in infantile and juvenile neuronal ceroid lipofuscinosis ($n=7$) and 1.34 ± 0.05 in narcolepsy ($n=8$). Patients with Huntington's disease had significantly lower ratios (1.09 ± 0.04, $n=5$). The corrected basal ganglia/frontal cortex ratios, determined using linear regression, were about 80% higher. The use of dual-window scatter correction increased the measured ratios by about 10%. Although comprehensive correction methods can further improve the resolution in SPET images, the resolution of the SPET system used by us (1.5–2 cm) will determine what is achievable in basal ganglia D2 receptor imaging.

Key words: Dopamine D2 receptors – Iodobenzamide – Single-photon emission tomography – Scatter correction

Eur J Nucl Med (1993) 20:680–683

Paper presented in part at the European Association of Nuclear Medicine Congress, 22–26 August 1992, Lisbon, Portugal

Correspondence to: P. Nikkinen, Division of Nuclear Medicine, Meilahti Hospital, SF-00290 Helsinki, Finland

Introduction

Brain dopamine receptors have previously been studied in humans with positron emission tomography, but now in vivo imaging of dopamine D2 receptors can also be performed with single-photon emission tomography (SPET) using iodine-123 iodobenzamide (IBZM) as the ligand [1]. Verhoeff et al. [2] studied the specific binding of ^{123}I-IBZM in vitro and in vivo in the rat and human brain, and Seibyl et al. [3] investigated the uptake and washout of this radiopharmaceutical in human subjects. Brücke et al. [4] reported striatum/frontal cortex uptake ratios for IBZM in control subjects and various patient groups.

Although dedicated multidetector brain SPET cameras are now available, most of the routine clinical work is still performed with rotating single-head gamma cameras. Therefore phantom measurements were performed in this study in order to validate the accuracy of basal ganglia/frontal cortex (BG/FC) ^{123}I-IBZM uptake ratios measured in patients with a conventional gamma camera. The phantom measurements were also used as a basis for identification of the optimal reconstruction protocol for clinical studies. Brain dopamine D2 receptors are involved in a number of neurological disorders, some of which were studied by us.

Materials and methods

Studies on phantoms. An 18-cm-high cylindrical phantom with a diameter of 22 cm was used. Inside the phantom two cylinders with diameters of 3.3 cm, simulating the basal ganglia, were inserted. The activity concentrations of the cylinders varied from 6.0 to 22.6 kBq/ml. The cylinder/background activity concentration ratios varied from 1.4 to 3.8. Scatter correction measurements with the dual-window method [5] were performed for six concentration ratios varying from 0 to 2.35.

Studies on patients. Twenty-nine patients with various neurological disorders were studied. The diagnoses were idiopathic Parkinson's disease, Huntington's disease, infantile or juvenile neuronal ceroid

lipofuscinosis (INCL or JNCL) and narcolepsy. During the study five parkinsonian patients received levodopa and/or selegiline treatment, but not dopamine agonists. Four patients with recently diagnosed Parkinson's disease received no medication at the time of the study. Patients with Huntington's disease were treated with haloperidol, but this medication had been discontinued at least 4 weeks prior to the study. INCL/JNCL and narcoleptic patients were not on dopaminergic medication. Imaging was performed with a Picker DDC4096 square detector gamma camera equipped with a PDP11/73 computer. Acquisition was started 1–1.5 h after injection of 40–260 MBq ^{123}I-IBZM (iodobenzamide; Cygne, University of Technology, Eindhoven, The Netherlands). The energy window was 159 keV ± 10%. In all studies data – 64 40 s frames – were collected into a 64 × 64 matrix. In order to assess the effect of scatter correction, phantom measurements and four patient studies were also performed using the dual-window acquisition method (130 keV ± 10% and 159 keV ± 10%).

Data analysis. Reconstruction of cross-sectional images was performed by filtered backprojection using NUD-SPETS software (Nuclear Diagnostics Ltd., Kent, UK). Various filters were tested for the reconstruction of phantom studies in order to find the optimal filter for processing of patient data. Pre-attenuation correction was performed in all studies using the method described by Larsson [5]. For measurements with one window an attenuation correction coefficient of 0.07 cm^{-1} was used. Using a homogeneous water phantom a flat profile was obtained. This low attenuation coefficient also includes the first-order scatter correction [6]. In the dual-window studies the contribution of the scattered counts were accounted for by subtraction using a scaling factor of 0.5 [6]. Pre-attenuation correction with an attenuation coefficient of 0.11 cm^{-1} was performed [5].

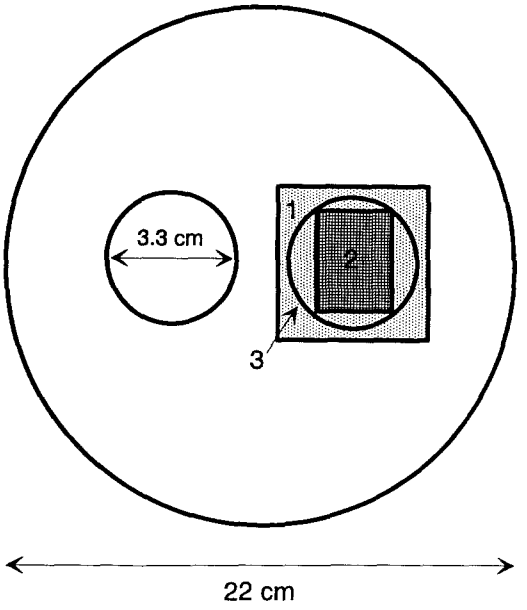

Fig. 1. Dimensions of the phantom and three different ROIs used in the determination of activity ratios

Results

Phantom studies

After testing various reconstruction filters the modified Shepp-Logan filter [5], which provided the best contrast, was selected and transversal slices (thickness 2 pixels) were reconstructed. Mean counts/pixel values were obtained by drawing ROIs on the cylinders and the background. Three different ROIs were tested as shown in Fig. 1: (1) a rectangular ROI covering the whole cylinder, (2) a rectangular ROI inside the cylinder and (3) a circular ROI simulating the anatomy of basal ganglia. The relationships between the true cylinder/background specific activity ratios and the measured ratios are presented in Fig. 2. Only values >1, having clinical relevance, were considered.

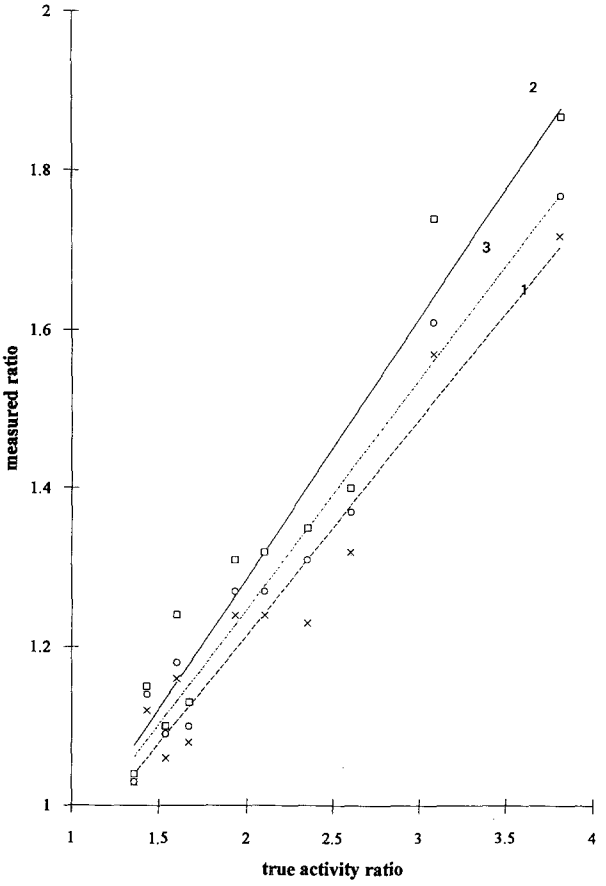

Fig. 2. Measured phantom cylinder/background activity ratio versus true activity ratio. Linear regression for three ROIs: ROI 1 (×): slope 0.27, constant 0.67, r=0.95; ROI 2 (□): slope 0.33, constant 0.63, r=0.95; ROI 3 (○): slope 0.29, constant 0.67, r=0.96

Patient data

One 1.4-cm-thick (2 pixels) transversal slice through the basal ganglia parallel to the orbitomeatal line was selected. Rectangular ROIs covering the whole basal ganglia and manually drawn anatomical ROIs on basal ganglia were tested. ROIs were also drawn on the lateral

Table 1. Basal ganglia/frontal cortex (BG/FC) ^{123}I-IBZM uptake ratios measured and corrected by linear regression in various patient groups

Diagnosis		Measured BG/FC		Correct BG/FC[a]	
		Right	Left	Right	Left
Parkinson's disease ($n=9$)	Mean	1.30	1.30	2.31	2.31
	SD	0.02	0.04	0.07	0.16
Huntington's disease ($n=5$)	Mean	1.10	1.07	1.58	1.47
	SD	0.03	0.04	0.10	0.14
Infantile and juvenile neuronal ceroid lipofuscinosis ($n=7$)	Mean	1.33	1.32	2.42	2.38
	SD	0.08	0.09	0.28	0.32
Narcolepsy ($n=8$)	Mean	1.33	1.34	2.42	2.45
	SD	0.05	0.05	0.15	0.15

[a] Correction equation $y=3.66x-2.45$

frontal cortex. From the counts /pixel values of the ROIs the BG/FC ratios were calculated for the right and left hemispheres. For this calculation we used the average counts/pixel value for the right and left frontal cortex. The measured values were corrected using the linear regression equation corresponding to ROI 1 in Fig. 2. Results for the various patient groups are shown in Table 1.

In patients the measured BG/FC ratios derived from an anatomical basal ganglia ROI were about 3% higher than the values obtained using a rectangular ROI covering the whole basal ganglia. In the phantom studies the measured cylinder/background activity ratios obtained using a circular ROI were 1.8%–3.7% higher than ratios obtained using the rectangular ROI 1. This difference can be corrected for with the linear regression equation, enabling the use of rectangular basal ganglia ROIs in patient studies.

Discussion

For quantitative SPET analysis the relationship between counts detected in the organ studied and the true organ radioactivity must be determined. This relationship is affected by many factors including attenuation and scatter corrections and the reconstruction protocol. Therefore the uptake ratios obtained with different equipment in different laboratories are not directly comparable. A comprehensive review of the physical elements of quantitative SPET has recently been published by Blokland et al. [7].

The use of dual-window scatter correction can improve results [6, 8]. However, the optimal value of scaling factor k in scatter image subtraction is difficult to determine [6]. According to Yanch et al. [9], in SPET reconstruction first-order correction for attenuation and scatter using an artificially low attenuation correction coefficient can improve the result. In the dual-window measurements the "true" attentuation coefficient 0.11 cm^{-1} was used. In the phantom studies dual-window scatter correction improved the contrast in both cold and hot areas, and for concentration ratios >1 the measured ratios increased by about 5%. In the patient studies the measured ratios increased on average by 10%. Similar values were obtained in a preliminary report by Berding et al. [10] regarding SPET imaging of basal ganglia uptake of ^{123}I-IBZM. The use of correction based on phantom measurements must therefore be regarded as essential when performing quantitative or semiquantitative measurements.

The activity concentration in the brain is quite low, about 5 kBq/ml, and therefore determination of the basal ganglia ROI using objective algorithms is difficult and in many patients with low uptake of tracer even impossible; in six of our patients the BG/FC ratio measured was below 1.2. From the results of the phantom studies it is apparent that calculation of the corrected activity ratio is not dependent on how the ROI is determined. However, to achieve comparable results in patient studies we recommend the use of rectangular ROIs covering the whole basal ganglia. A fixed ROI technique was also preferred by Axelsson et al. [11] in bone marrow scintigraphy and by Valkema et al. [12] in dual-photon absorptiometry. The system resolution of the gamma camera used at 10 cm depth is about 1 cm in planar imaging. Resolution in SPET, which depends on the reconstruction algorithms, is 1.5–2 cm or about half the size of the basal ganglia. However, the protocol employed for SPET reconstruction in the present study can be regarded as having clinical utility as patients with normal and subnormal receptor activities can be clearly distinguished. Apparently, for accurate determination of specific receptor activities in the subnormal range dedicated multidetector SPET cameras should be employed.

Brücke et al. [4] reported a mean BG/FC ratio of 1.38 in Huntington's disease, 1.67 in untreated idiopathic Parkinson's disease and 1.74 in controls. In the study of Costa et al. [13] the BG/FC ratio was 1.52 for normal controls and 1.32 for unmedicated patients with Gilles de la Tourette syndrome. According to findings by Tatsch et al. [14], the average BG/FC ratio in patients with idiopathic Parkinson's disease (1.51) was not significantly different from that in controls (1.55). Although our investigation does not include a healthy control group, comparison with these earlier studies is possible because patients with Parkinson's and Huntington's disease were studied; the marked reduction in striatal D2 receptor density observed in Huntington's disease is in accordance with earlier data, as is the normal or near-normal D2 receptor density observed in Parkinson's disease [4]. In INCL/JNCL patients and patients suffering from narcolepsy, diseases not previously studied with ^{123}I-IBZM, no apparent dopamine D2 receptor binding abnormality could be found.

References

1. Kung HF, Alavi A, Chang W, et al. In vivo SPECT imaging of CNS D-2 dopamine receptors: initial studies with iodine-123 IBZM in humans. *J Nucl Med* 1990;31:573–579.
2. Verhoeff NPLG, Bobeldijk M, Feenstra MGP, et al. In vitro and in vivo D2-dopamine receptor binding with (^{123}I)*S*(-)iodobenzamide (^{123}I-IBZM) in rat and human brain. *Int J Rad Appl Instrum [B]* 1991;18:837–846.
3. Seibyl JP, Woods SW, Zoghbi SS, et al. Dynamic SPECT imaging of dopamine D2 receptors in human subjects with iodine-123-IBZM. *J Nucl Med* 1992;33:1964–1971.
4. Brücke T, Podreka I, Angelberger P, et al. Dopamine D2 receptor imaging with SPECT: studies in different neuropsychiatric disorders. *J Cereb Blood Flow Metab* 1991;11:220–228.
5. Larsson SA. Gamma camera emission tomography. *Acta Radiol* 1980;Suppl 363:1–75.
6. Koral KF, Wang X, Rogers L, Clinthorne NH, Wang X. SPECT Compton-scattering correction by analysis of energy spectry. *J Nucl Med* 1988;29:195–202.
7. Blokland KAK, Reiber HHC, Pauwels EKJ. Quantitative analysis in single photon emission tomography. *Eur J Nucl Med* 1992;19:47–61.
8. King MA, Hademenos MA, Glick SJ. A dual-photopeak window method for scatter correction. *J Nucl Med* 1992;33:605–612.
9. Yanch JC, Flower MA, Webb S. Improved quantification of radionuclide uptake using deconvolution and windowed subtraction techniques for scatter compensation in single photon emission computed tomography. *Med Phys* 1990;17:1011–1022.
10. Berding G, Gratz KF, Kolbe H, Hundeshagen H. Dopamine D-2 receptor imaging with (I-123) IBZM SPECT: methodological aspects and clinical results [abstract]. *Eur J Nucl Med* 1992;19:735.
11. Axelsson B, Kalin B, von Krusenstierna S, Jacobsson H. Comparison of In-111 granulocytes and Tc-99m albumin colloid for bone marrow scintigraphy by the use of quantitative SPECT imaging. *Clin Nucl Med* 1990;15:473–479.
12. Valkema R, van der Berg R, Camps JAJ, et al. Precision of dual photon absorptiometry measurements: comparison of three different methods of selection of region of interest. *Eur J Nucl Med* 1989;15:183–188.
13. Costa D, George MS, Ell PJ, Verhoeff NPLG, Robertson MM. D2 dopamine receptor studies in patients with Gilles de la Tourette syndrome [abstract]. *Eur J Nucl Med* 1991;18:563.
14. Tatsch K, Schwarz J, Oertel WH, Kirsch CM. SPECT imaging of dopamine D2 receptors with ^{123}I-IBZM: initial experience in controls and patients with Parkinson's syndrome and Wilson's disease. *Nucl Med Commun* 1991;12:699–707.