Reproducibility and Discriminating Ability of Fluorine-18-6-Fluoro-L-Dopa PET in Parkinson's Disease

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Fluorine-18-fluorodopa (F-Dopa) PET assesses the integrity of the nigrostriatal dopaminergic neurons in Parkinson's disease. It has been used in longitudinal studies to measure the progression of Parkinson's disease and the effects of medications and intracerebral transplants. The significance of changes in PET indices in such studies depends largely on the reproducibility of the F-Dopa PET measurements. **Methods:** We performed repeated F-Dopa PET scans in 12 subjects with Parkinson's disease (between Hoehn and Yahr stages I and III) to measure scan-to-scan variations. Data were analyzed using five methods comprising two sets of regions of interest (ROIs) (total striatum and substriatal), the striatum-to-cortex ratio and two graphical methods (one using plasma radioactivity, the other using cortical radioactivity as the input function). We also studied the effectiveness of each method in discriminating between patients with Parkinson's disease and normal subjects using data obtained from a similar study in 10 normal subjects. **Results:** We found reliability coefficients between 66% and 93%; the scan-to-scan intrasubject standard deviation ranged from 2% to 16% of the mean value depending on the method of analysis and the size of the ROIs. All methods discriminated significantly between patients with Parkinson's disease and normal subjects. The ability to discriminate, as reflected by the intergroup/intragroup ratio of variance, ranged from 2 to 18. **Conclusion:** These results permit selection of the best method of analysis for studies of nigrostriatal dopaminergic function.

Key Words: fluorodopa; PET; Parkinson's disease

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Fluorine-18-6-fluorodopa (F-Dopa) PET is an accepted method of assessing dopaminergic function in Parkinson's disease (*1*). Studies of the natural evolution of the nigrostriatal lesion (*2,3*) and the effects of medication (*4–6*) and intracerebral transplants (*7–9*) have been performed using this technique. The significance of changes in the F-Dopa PET indices reported in such longitudinal studies depends on the reproducibility of the F-Dopa PET results (*10*). Until now, this reproducibility has only been assessed in nonhuman primates (*11*) and in normal humans (*12*). Patients with Parkinson's disease have a significant reduction in striatal F-Dopa accumulation compared with normal subjects. This reduction in count statistics may alter the reproducibility of the F-Dopa PET results. We performed repeat F-Dopa PET scans in patients with Parkinson's disease to measure the scan-to-scan variation in the PET indices. We also compared the reproducibility of various methods of analyzing the F-Dopa PET data and their ability to discriminate between patients with Parkinson's disease and normal subjects.

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MATERIALS AND METHODS

Patients

Twelve patients with Parkinson's disease (7 men, 5 women; mean age 57.4 ± 10.9 yr) were studied. All patients met the criteria for clinically confirmed Parkinson's disease (*13*). Mean duration of disease from the time of first symptoms to first assessment was 5.7 ± 3.0 yr. Hoehn and Yahr scores (*14*) were between I and III. All antiparkinsonian medications were withdrawn at least 12 hr before each assessment (18 hr for Sinemet CR). The patients fasted overnight and had a standard low-protein breakfast on the morning of the scanning. Each patient was assessed twice within 2 mo (46.9 ± 7.6 days). Patients gave written informed consent before each scan. These studies were authorized by the Ethics Committee of the University of British Columbia.

PET Studies

PET studies were performed using a tomograph in two-dimensional mode, permitting simultaneous acquisition of 31 axial planes with a center-to-center separation of 3.4 mm. The average reconstructed resolution is 5.5 mm in-plane and 5 mm axial, FWHM. The patient was positioned with the image plane parallel to the orbitomeatal line. A thermoplastic face mask was molded on each subject to restrain head movement. Tissue attenuation of 511 keV gamma radiation was measured for 15 min with three ^{68}Ge rotating rod sources. Carbidopa (150 mg) was given orally over the 1 hr preceding tracer injection. Fluorodopa (*15*) (181 ± 19 MBq; specific activity 0.75–2.00 Ci/mmole) was injected intravenously as a bolus of less than 30 sec duration at the beginning of the scan. Twelve sequential emission scans, each lasting 10 min, were performed starting at the midpoint of the injection. The tomograph was calibrated so that plasma and regional brain radioactivities were expressed in the same units (microcuries per milliliter).

Sequential whole-blood samples (2 ml each) were obtained from the radial artery using an indwelling catheter, as previously described (*12*). Each sample was centrifuged, and the total plasma radioactivity was determined in 0.5-ml samples with a well counter. The results were corrected for radioactive decay. Plasma metabolites of F-Dopa were measured from 5-ml samples drawn at 15, 30, 60, 90 and 120 min. The fractions of F-Dopa were determined by high-performance liquid chromatography (HPLC) (*16*).

Each subsequent scan was performed with the same protocol and with the subject in the same position.

Fluorodopa PET Data Analysis

The F-Dopa PET data were analyzed by five different methods comprising two different sets of regions of interest (ROIs), two graphical methods and a target-to-background ratio. Image data collected from 60 to 120 min after F-Dopa administration were summed to produce an integral image. The ROIs were placed on this image using two different methods (*12*).

Total Striatum (TS) Set. We used a standard set of ROIs manually drawn on images from normal subjects, as previously reported (*12*). The set consisted of two irregular ROIs (717 ± 36 mm^2) encompassing the whole striatum on the seven slices where the striata were visible and two background ROIs (908 ± 4 mm^2) located on the posterior temporoparietal cortex of the same slices, avoiding the midline and ventricles. The ROI locations were positioned by inspection. Measures of total striatal radioactivity were obtained separately for the left and right sides. Striatal radioactivity was summed both within each plane and over the seven axial planes. Summed radioactivity values in the background regions on each side were rescaled on the basis of the relative volumes of the striatal and background regions. This process was repeated in each time frame to yield total striatal and cortical radioactivity time courses. Results were recorded in units of becquels per striatum.

Caudate and Putamen (CP) Set. One circular ROI of 61.2 mm^2 (diameter 8.8 mm) was positioned by inspection on each caudate nucleus of the integral image and adjusted to maximize the average ROI radioactivity. Three circular ROIs of 61.2 mm^2 (diameter 8.8 mm) were placed along the axis of each putamen and were similarly adjusted to maximize the radioactivity without overlap. Three background circular ROIs of 296 mm^2 (diameter 19.4 mm) were placed on each side of the temporooccipital lobes. This process was repeated for the five slices where the caudate and the putamen were most clearly seen. The 70 ROIs were replicated over the 12 time frames. For each frame, ROIs of like structures were averaged, culminating in separate measurements for the left and right caudate; left and right anterior, middle and posterior putamen; and background. For the putamen, further averaging over the three ROIs gave measurements for the left and right putamen. To differentiate radioactivity concentrations in tissue more clearly from those in plasma, the results were recorded as becquerels per cubic centimeter. Correction for F-Dopa and 3-O-methyl-fluorodopa (3OMFD) in the striatal signal was performed by subtracting the background from striatal radioactivity, leaving the specific striatal radioactivity (*17*).

Tissue and plasma data were analyzed by the graphical method described by Patlak and colleagues (*17–19*) for both sets of ROIs on data from 20 to 120 min. Results are presented as the uptake constant Kip. For the TS method, the units of Kip_{TS} are milliliters of plasma per minute per striatum. For the CP method, the units of Kip_{CP} are milliliters of plasma per minute per cubic centimeter.

The TS and CP data were also analyzed by a graphical method using the parieto-occipital background radioactivity concentration as the input function (*20,21*). Results are presented as the uptake constants Kio. For the TS method, the units of Kio_{TS} are cubic centimeters of cortex per minute per striatum. For the CP method, the units of Kio_{CP} are uptake per minute.

The ratio of target-to-background (ratio method) was calculated on the integral image using the TS method (*2,7,22,23*). After correction for the areas of the ROIs, the striatal radioactivity was divided by the background radioactivity.

Control Subjects

To allow comparison of F-Dopa PET results from the patients with Parkinson's disease with those from 10 normal subjects (4 men, 6 women; mean age 51.0 ± 16.5 yr) studied previously (*12*), the F-Dopa PET data from the normal subjects were reanalyzed with the same set of ROIs and the same methods of analysis as in the present study.

Statistical Analysis of F-Dopa PET Results

One-way analysis of variance (ANOVA) was performed to estimate the standard deviations between (SDB) and within (SDW) subjects. Reliability coefficients were then estimated (*24*). The reliability coefficient measures the intraclass correlation; that is, the correlation between two measurements observed in the same subject by the same method at different times. It is thus an indication of the reproducibility of measurements over time. The analysis was performed on the Ki values and ratios resulting from the five methods.

For Kip_{TS}, similar analyses were performed on the components of the graphical analysis (PET measurements of radioactivity, blood radioactivity and metabolite correction). To allow intersubject comparison, the measurements were normalized to the group average weight and amount of F-Dopa injected and were divided by (Amount of F-Dopa injected/Group mean injected dose) and multiplied by (Weight of subject/Group average weight). For metabolite correction, the slopes of the 3OMFD/F-Dopa ratio versus time were compared. This function has been shown to be linear for times up to 2 hr after injection (*16,25,26*).

To determine the correlations among the different methods, a correlation matrix was calculated from the results of the different methods on the basis of all observations from all subjects. For each method, a nested ANOVA was carried out on the replicate measurements from each subject in the normal and Parkinson's disease groups to estimate the net variance between the two groups (V_b) and the net variance within each group (V_w). The ratio V_b/V_w was used as an index of the capability of each method to discriminate between patients with Parkinson's disease and normal subjects.

RESULTS

Reproducibility of F-Dopa PET Indices

The Kip_{TS} values calculated from the TS data gave an SDW of 11% of the group mean value (Fig. 1). The SDB was 22%, resulting in a reliability coefficient of 78%. Table 1 presents detailed results of Kip_{TS} from the two sets of ROIs.

As expected, the Kip_{CP} values calculated from the CP data varied from region to region in the patients with Parkinson's

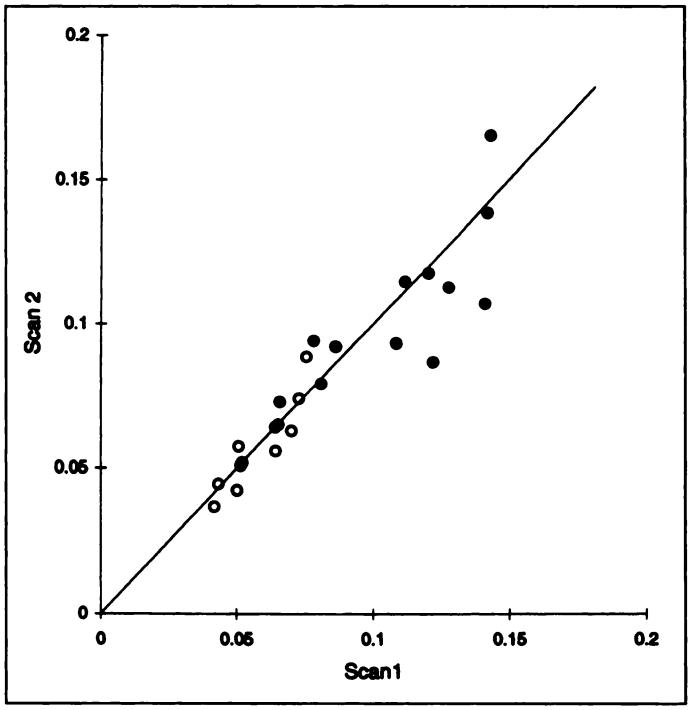

FIGURE 1. Bilateral Ki interscan correlation (using TS data). Values of Kip (solid circles) and Kio (open circles) from scan 2 are plotted against the corresponding results from scan 1. Diagonal line = line of identity (line of 100% reproducibility). The greater the scattering of the measured points around the line of identity, the lower the reproducibility of the method.

TABLE 1
Results of F-Dopa PET Analysis Methods

Constant	Mean value	SDB (% mean)	SDW (% mean)	R value
TS Kip*				
PD				
Right	1.07	0.263 (24%)	0.121 (11%)	82%
Left	1.09	0.248 (23%)	0.140 (13%)	76%
N (bilateral)	2.33	0.548 (23%)	0.233 (10%)	85%
TS Kio†				
PD				
Right	0.58	0.145 (25%)	0.041 (7%)	93%
Left	0.59	0.116 (20%)	0.059 (10%)	80%
N (bilateral)	1.04	0.048 (5%)	0.036 (3%)	64%
TS ratio				
PD				
Right	1.50	0.099 (7%)	0.046 (3%)	82%
Left	1.48	0.093 (6%)	0.032 (2%)	90%
N (bilateral)	1.82	0.087 (5%)	0.049 (3%)	76%
CP Kip				
Caudate‡				
PD				
Right	1.36	0.285 (21%)	0.163 (12%)	75%
Left	1.35	0.270 (20%)	0.145 (11%)	78%
N (bilateral)	2.15	0.471 (22%)	0.221 (10%)	82%
Putamen‡				
PD				
Right	0.78	0.181 (23%)	0.104 (13%)	75%
Left	0.80	0.183 (23%)	0.115 (14%)	72%
N (bilateral)	2.02	0.435 (22%)	0.180 (9%)	85%
CP Kio				
Caudate§				
PD				
Right	0.70	0.115 (16%)	0.053 (8%)	83%
Left	0.69	0.115 (17%)	0.083 (12%)	66%
N (bilateral)	0.95	0.097 (10%)	0.070 (7%)	66%
Putamen§				
PD				
Right	0.36	0.094 (26%)	0.058 (16%)	72%
Left	0.36	0.103 (29%)	0.040 (11%)	87%
N (bilateral)	0.84	0.082 (10%)	0.062 (7%)	64%

*$10^{-1} \cdot ml \cdot min^{-1} \cdot striatum^{-1}$; see text for explanation of units.
†$10^{-1} \cdot cc \cdot min^{-1} \cdot striatum^{-1}$.
‡$10^{-2} \cdot ml \cdot min^{-1} \cdot cc^{-1}$.
§$10^{-2} \cdot min^{-1}$.
Data presented are mean value, estimates of standard deviation (SDB, SDW) and reliability coefficient (R).
PD = patients with Parkinson's disease; N = normal subjects.

disease, with highest values in the caudate nucleus and lowest in the posterior putamen (*27,28*). The absolute values of the corresponding SDW also declined from anterior to posterior regions but far more slowly (regression analysis of the SDW for Kip_{CP} yielded the equation: SDW = 0.0011 + 0.037 Kip; r = 0.75; $p < 0.05$) (Fig. 2). Therefore, the SDW represented an increasing percentage of the Kip_{CP} values for the more posterior regions: from the caudate (12.1% left, 7.5% right) to the anterior (8.6% left, 12.6% right), middle (12.7% left, 25.0% right) and posterior putamen (32.2% left, 36.8% right). This in turn led to a progressive decrease in the reliability coefficients from the caudate (74% left; 78% right) to the anterior (73% left, 66% right), middle (71% left, 54% right) and posterior putamen (45% left, 64% right).

The Kio_{TS} values estimated from the TS data gave an SDW of 7%, an SDB of 21% and a reliability coefficient of 89% (Table 1). The Kio_{CP} values calculated from the CP data

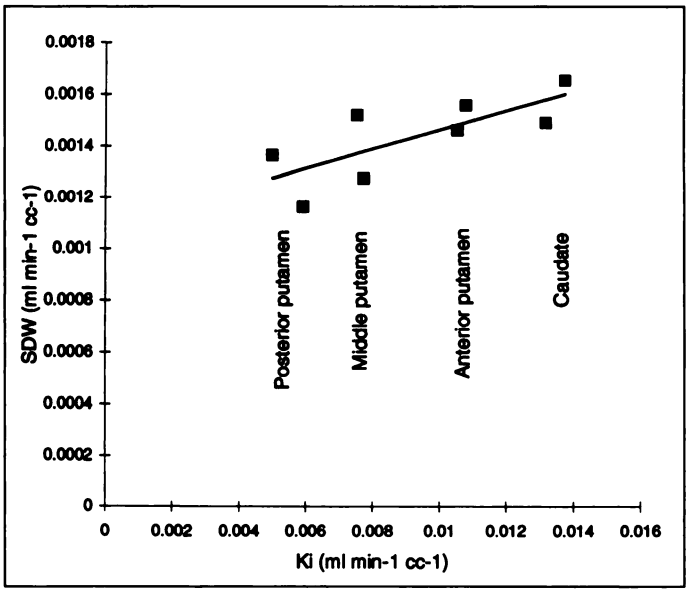

FIGURE 2. Correlation between average Kip and SDW (absolute values) for results from each ROI of CP. Diagonal line = regression line.

showed a relationship between SDW and a group mean value similar to that seen for Kip values. The ratio method gave an SDW of 2%, an SDB of 6% and a reliability coefficient of 87% (Table 1).

In keeping with the absence of significant evolution of Parkinson's disease over the 2-mo period of the study, the results of the first scans did not differ significantly from those of the second scans (p = 0.24–0.99; two-sided paired Student's t-test). Similarly, the regression line from scan 1 to scan 2 (Fig. 1) did not differ significantly from the line of identity (p = 0.23–0.85; two-sided *z*-test on slopes and intercepts). The apparent difference in the slopes of the data is expected because the second measurement in data with any error tends to regress toward the mean value.

Reproducibility of Emission, Blood and Metabolite Data

For the TS method, the SDW of the emission measurements varied between 7% and 9% of the mean value, with SDB from 18% to 20% and reliability coefficients from 83% to 89%. For the background radioactivity these values were, respectively, 6%–8%, 18%–20% and 86%–93%. The values at 115 min are presented in Table 2; the R values at other times were similar.

The SDW of the plasma radioactivity varied from 5% to 6% of the measured values at 25, 55, 85 and 115 min. The SDB varied from 8% to 13% and reliability from 69% to 89%.

The mean slope of 3OMD/F-Dopa versus time was 0.0418 min^{-1}; the SDB was 16% of the mean value, the SDW 14% and the reliability coefficient 55% (for normal subjects these values were, respectively, 0.0621 min^{-1} and 16%, 11% and 70%).

Correlations between F-Dopa PET Indices

The correlation coefficients between F-Dopa PET indices ranged between 0.61 and 0.98. The various methods based on plasma input function gave Ki values that were highly correlated with each other, with coefficient values ranging from 0.92 to 0.98. Similarly, the ratio method and all the methods based on the cortical input function were correlated with coefficients that ranged between 0.86 and 0.97. In contrast, when results from these two subgroups of methods were compared, the correlation coefficients were in general smaller, with values ranging from 0.61 to 0.90.

TABLE 2
Normalized Brain (from TS Data) and Plasma Radioactivity Concentrations (PA) 115 min After Injection

Region	Mean value	SDB (% mean)	SDW (% mean)	R value
Striatum*				
PD	69.87	13.67 (20%)	5.30 (8%)	87%
N	59.86	14.92 (25%)	5.46 (9%)	88%
Background*				
PD	45.86	9.08 (20%)	3.00 (7%)	90%
N	30.99	8.44 (27%)	3.20 (10%)	87%
PA†				
PD	715.60	93.99 (13%)	33.34 (5%)	89%
N	429.36	63.60 (15%)	37.74 (9%)	74%

*10^3 Bq/striatum.
†CPS/ml.
Data presented are mean value, standard deviation (SDB, SDW) and reliability coefficient (R).
PD = patients with Parkinson's disease; N = normal subjects.

TABLE 3
Power of Different Methods of Analysis to Discriminate between Normal Subjects and Patients with Parkinson's Disease (V_b/V_w)

ROIs	Graphical analysis		Ratio method
	Kip	Kio	
TS Ki	5.2	8.1	7.6
CP (caudate) Ki	2.4	3.0	
CP (putamen) Ki	9.6	18.0	

Discriminating Ability of F-Dopa PET Indices

All methods discriminated between the Parkinson's disease group and the normal group, with significant p values ranging from 10^{-13} to 10^{-15} (Fig. 3, Table 3). The best discrimination between patients with Parkinson's disease and normal subjects was obtained by using the Kio_{CP} method with a V_b/V_w value of 18 for the putamen. The Kio_{TS} and ratio methods gave similar V_b/V_w values of 8.1 and 7.6, respectively, whereas the Kip_{TS} method produced the smaller value of 5.1.

DISCUSSION

We showed that F-Dopa PET measurements in patients with Parkinson's disease yield reliability coefficients ranging from 66% to 93%, depending on the method of analysis. These results are similar to those previously found in normal subjects (*12*). The SDW represented 11% of the mean value for a graphical analysis using a plasma input, 7% using a cortical input and 2% for the ratio method.

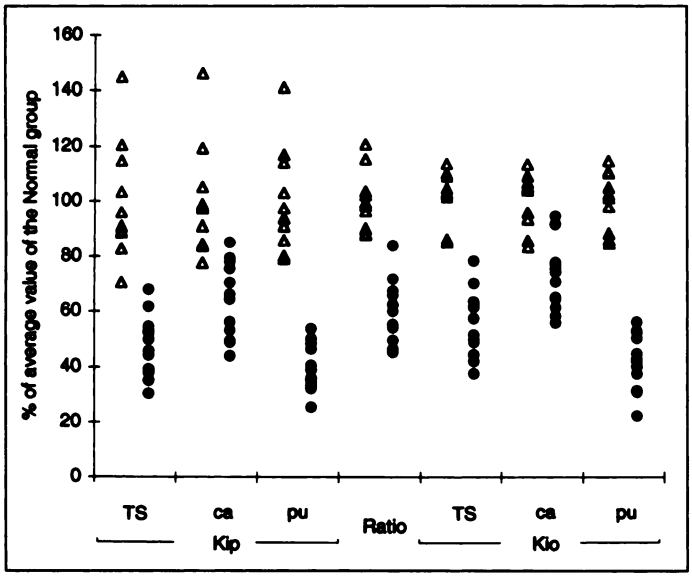

FIGURE 3. Discrimination between normal subjects (triangles) and patients with Parkinson's disease (circles). TS = total striatum ROI; ca = CP ROIs (caudate); pu = CP ROIs (putamen); Kip = graphical method, plasma input; Kio = graphical method, occipital input. Results were normalized to allow comparison.

In absolute terms, the SDW of the Kip method in patients with Parkinson's disease was smaller than that in normal subjects despite a lower striatal uptake (Table 1). Although the lower signal from the diseased striatum might be expected to add noise to the measurements, we previously showed that the SDW from the emission measurements contributes little to the overall variation (*12*). In addition, patients with Parkinson's disease received a larger bolus of radioactivity than normal subjects (182 versus 111 MBq). This larger bolus compensated for the reduced striatal F-Dopa uptake and preserved the reliability of the striatal emission measurements at the level of that in normal subjects (Table 2).

In contrast to the emission data, the SDW in the plasma radioactivity measurement is a major factor responsible for the intrasubject scan-to-scan variation (*12*). The larger bolus of radioactivity increased the reliability of the plasma radioactivity measurement, especially during the last hour of analysis (Table 2). This increased reliability of the blood radioactivity measurement was probably the major factor responsible for the decrease in the absolute value of SDW of the Kip method in patients with Parkinson's disease (*12*). The SDW of the Kio_{CP} method for patients with Parkinson's disease was also reduced relative to that in normal subjects. There was an improvement in the late cortical emission measurements similar to that observed in the plasma radioactivity measurements (Table 2). This improvement suggests a similar mechanism of error propagation in the K_{ip} and K_{io} methods, inherent to the graphical analysis itself, allowing a similar improvement in reliability from the increased bolus of radioactivity.

In keeping with our previous study in normal subjects (*12*), the reliability of the results was affected by the size of the ROI, with a lower reproducibility for the CP method than for the TS method (Table 1). This result is due to: (a) the decreased relative variation in the emission counts for larger regions, (b) less degradation of data by subject movement with larger ROIs and (c) less sensitivity to small differences in repositioning. Thus, for a study evaluating a generalized effect, such as disease progression, or a trial of medication, use of the TS method will result in higher reliability than the smaller CP method and is therefore preferable.

Smaller ROIs have the advantage of allowing the study of regional changes, as in the case of focal tissue grafting. When single, small ROIs were individually studied from the caudate to the posterior putamen (most affected striatal part in Parkinson's disease [*27,28*]), however, the SDW represented an increasing proportion of the Ki value, leading to decreasing reliability. Particular caution should therefore be used in the interpretation of variations in Ki values from small ROIs placed on the posterior putamen.

The reliability of the results differed between methods of analysis. In patients with Parkinson's disease, the ratio and Kio_{TS} methods were more reproducible than the Kip_{TS} method, with reliability coefficients between 80% and 93% versus 76% and 82%. This finding suggests that the ratio and Kio_{TS}

methods may be the best methods for evaluating changes over time in nigrostriatal dopaminergic function. Their main drawback is that they do not account for variations in peripheral F-Dopa metabolism (*6*). Despite the close correlation between the ratio and Kio_{TS} methods (Table 3) (*22*), the Kio_{TS} method, based on compartmental theories (*18,19*), should more closely reflect the underlying physiological mechanisms (*29*) and is the preferred method. However, when the background radioactivity measurement is not optimal (e.g., with low yields or with low scanner spatial resolution), the ratio method may be preferable because it is, by averaging the background radioactivity over 60 min, less sensitive to errors that appear at the end of the scanning time when the radioactivity is low (Table 1).

The final F-Dopa PET results were influenced more by the type of input function (i.e., use of blood analysis or not) than by the method of analysis (i.e., type of ROIs, graphical versus ratio). The ratio and Kio results were highly intercorrelated, as were all the results using the Kip method. The correlation between the two subgroups that did or did not use the blood input was lower than that within each group despite the use of identical ROIs. This difference underlines the fact that, even if correlated, the Kio and Kip methods are not equivalent (*30*). The Kip method is the only one able to control for the peripheral metabolism of F-Dopa and therefore is preferred in longitudinal studies when the metabolism of F-Dopa may be altered (e.g., with the use of COMT inhibitors). The method requires precise blood sampling and reproducible analytical methods to correct for metabolism of F-Dopa (*12*).

The graphical CP methods had the highest discriminating power between patients with Parkinson's disease and normal subjects and therefore may be the best method for preclinical diagnosis in cross-sectional studies. For both TS and CP data, the Kio method had a greater ability to discriminate between normal subjects and patients with Parkinson's disease than did the Kip method. In the present study, there was a difference in the method of analyzing metabolites of F-Dopa between normal subjects (batch-contact alumina-extraction method) and patients with Parkinson's disease (HPLC). Although the two methods were previously reported to give similar results (*16*), recent refinements to the HPLC analysis may have contributed to the decline in the slope of 3OMD/F-Dopa versus time seen in patients with Parkinson's disease relative to that in normal subjects. If, however, the normal subjects had a systematically lower slope, similar to that in the patients with Parkinson's disease, then their Kip values would be lower, and the discriminant power of the Kip method would be even less. The better discrimination achieved by using the Kio method instead of the Kip method has been reported previously (*22*) but is in contrast with the results of two recent studies (*30,31*) in which better discrimination with the Kip method was reported. A more probable explanation for the different pattern of results obtained from different sites might lie in differences in the reliability of the blood or cortical radioactivity measurements, or both. This would propagate to differences in the variance of the Kip or Kio results and thus affect the discriminating power of these methods. Future data on the reproducibility of the F-Dopa PET measurements from other centers may help resolve this issue (*32,33*).

CONCLUSION

Each method of analysis has its own inherent advantages for different applications. For cross-sectional studies, Kio_{TS} values give the best discrimination between normal subjects and patients with Parkinson's disease. If sufficiently accurate background region time-course data are not available, the ratio method may be a better alternative. When regional changes have been described in relation to the pathologic findings, as in Parkinson's disease, the use of small ROIs increases the discriminant power. This graphical method with small ROIs should therefore be the best for the early detection of Parkinson's disease (*31,34*).

For longitudinal studies dealing with the natural evolution of the disease, the ratio method, which has the smallest SDW, may be the best method (*2,35*). Its main drawback, as for the Kio_{TS} method, is its uncontrolled potential sensitivity to peripheral metabolism of F-Dopa, which may spuriously affect the results (*6*).

When treatments that may affect the peripheral metabolism of F-Dopa are considered, the Kip_{TS} method may perform best because it is the only method that takes into account such metabolism.

The use of small ROIs in longitudinal studies should be restricted to the search for regional changes (e.g., after tissue transplantation). Particular caution should be used in the interpretation of changes in severely affected regions because the reliability of Ki measurements in small ROIs decreases dramatically in the areas of very low uptake (e.g., in the posterior putamen, where the SDW represents up to 36.8% of the measured value, and the reliability is only 45%).

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Increased Contralateral Cerebellar Uptake of Technetium-99m-HMPAO on Ictal Brain SPECT

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Crossed cerebellar diaschisis (CCD) is a well-known brain SPECT finding in stroke patients. Two reports, however, have described supratentorial and contralateral cerebellar hyperperfusion (crossed cerebellar hyperperfusion) on ictal brain SPECT in epileptic patients. The purpose of this study was to assess the usefulness of crossed cerebellar hyperperfusion (CCH) for the detection of epileptic foci on ictal scan. **Methods:** Twelve patients with complex partial seizures having characteristic clinical, electroencephalographic (EEG) and brain SPECT findings were included. Fifteen to 20 mCi ^{99m}Tc-HMPAO were injected intravenously during the seizure period or the aura for the ictal SPECT study. The SPECT findings were visually assessed to determine whether the finding of CCH was valuable in the localization of ictal foci. **Results:** Epileptic foci were found in the right temporal (n = 6), left temporal (n = 4), right occipital (n = 1) and left frontal (n = 1) areas. CCH was observed in 8 (75%) of the 12 patients. In two patients, contralateral cerebellar uptake was more obvious than that in the epileptic foci. In the interictal scans, cerebellar activity, which was increased in ictal period, was equalized in seven of eight patients, while perfusion was diminished in the remaining patient. **Conclusion:** CCH is a frequent finding of ictal brain SPECT and may aid in the lateralization of epileptic foci.

Key Words: epilepsy; SPECT; crossed cerebellar hyperperfusion
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Seizure disorder is classified into partial and generalized forms. Partial seizures begin in a part of one hemisphere. Generalized seizures, on the other hand, are those in which the first clinical changes indicate initial involvement of both hemispheres (*1*). Partial seizures are classified as simple when consciousness is not impaired and as complex when consciousness is impaired (*1*). Medically intractable complex partial seizure is a good indication for surgical treatment; therefore, identification of epileptic focus in complex partial seizures is essential for surgical treatment (*2*). EEG, electrocorticography (ECoG) and MRI have all been used for the lateralization of epileptic foci (*2,3*). SPECT and PET have also proved to be important diagnostic tools (*4–6*). Recently, cerebral perfusion SPECT studies are widely available in conjunction with EEG data, which show high corresponding diagnostic rates in the localization of epileptic foci (*6–9*). In general, hyperperfusion or hypermetabolism is detected ictally and hypoperfusion or hypometabolism is detected interictally in ictal focus (*6,7,9*).

Crossed cerebellar diaschisis (CCD), the phenomenon of reduction of blood flow in the contralateral cerbellum due to supratentorial lesion in stroke patients, was first described by Baron et al. in 1980 using PET (*10*). Much the same as CCD in the mechanism of cerebral and cerebellar metabolic connection, supratentorial and contralateral cerebellar hyperperfusion (crossed cerebellar hyperperfusion, CCH) was sporadically reported in patients with seizures during the ictal phase (*11,12*).

The aim of our study was to evaluate the characteristic findings of CCH and to assess the usefulness of the finding for the localization of epileptic foci on the ictal scan.

MATERIALS AND METHODS

Twelve patients (9 men, 3 women; aged: 4–52 yr; mean 20 yr) with medically intractable complex partial seizures having congruent clinical, EEG and brain SPECT findings were studied.

Seven patients underwent surgical therapy: temporal lobectomy in five and occipital cortisectomy and callosotomy (anterior 2/3) in

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