Local cerebral glucose utilisation in treated and untreated patients with Parkinson's disease*

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SUMMARY Using the ^{18}F -fluoro-2-deoxy-d-glucose technique and positron emission tomography (PET), the local cerebral glucose utilisation (ICMRGlc) was measured in four non-demented patients with early-onset, bilateral Parkinson's disease characterised by the predominance of akinesia. The study was done twice, first in the untreated condition, and then after levodopa had been resumed. Despite a marked clinical improvement, we found no alteration in ICMRGlc between the first and second studies in any of the brain structure analysed. Compared to control values, ICMRGlc in the basal ganglia was moderately increased in both studies. These essentially negative findings agree with most previous human or animal studies, and indicate that the functional alterations in the central dopaminergic systems of patients with Parkinson's disease have metabolic correlates that are too small to be demonstrated by current PET devices.

The typical symptomatic triad of Parkinson's disease, that is akinesia, rigidity, and tremor, implies that functional alterations take place in certain cerebral structures. Since energy metabolism in the brain has been shown to be coupled to function,¹ changes in regional energy metabolism specific to the functional abnormalities of Parkinson's disease might be expected to occur. Such changes should be found in the structures deprived of their normal dopaminergic afferences, principally the striatum² and the cortico-limbic areas³ and, as a secondary effect, in the structures receiving projections from these structures.

In the attempt to use local energy metabolism as a marker of disordered dopaminergic transmission systems, several studies of the local cerebral glucose utilisation (ICMRGlc) using ^{14}C -2-deoxy-D-glucose (^{14}CDG) autoradiography in rats with unilateral destruction of the dopaminergic systems have failed to show any consistent pattern of changes,⁴⁻⁹ although some reported striking alterations.^{4,5} Human studies of Parkinson's disease patients have been, for methodological reasons, restricted to 2-dimensional $^{133}\text{xenon}$ regional cerebral blood flow (rCBF)¹⁰⁻¹² or

oxygen-15¹³ investigations, but again have provided discrepant results.

Because it allows non-invasive 3-dimensional quantitative measurement of ICMRGlc in humans, positron emission tomography (PET) was used in the present work to investigate further this issue. Our protocol was essentially designed to see whether, in a small series of levodopa responders acting as their own controls, levodopa therapy would have any discernible effect on ICMRGlc.

Patients

Four severely affected non-demented male patients volunteered for the study (table 1). They were asked to participate in the investigation because of expected severe degeneration of central dopaminergic systems as suggested by: early onset of the disease, marked severity of akinesia with varying degree of rigidity and tremor, excellent response to levodopa therapy, and early occurrence of levodopa-induced adverse reactions such as on-off phenomena and abnormal involuntary movements. Each patient underwent in the fasting state two PET studies, the first 48 hours after all treatment had been stopped, and the second the next day, after treatment had been resumed for about 22 hours. In order to ensure reproducibility, repositioning of the patient's head under the field of the positron camera was as accurate as possible, using laser beams projected on external landmarks on the forehead. Just prior to each study, a Parkinson's disease clinical score was obtained,¹⁴ grading the severity of the symptoms so that the more severe the symptoms the higher the grade.

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Table 1 Clinical data

Patient	Sex	Age (yr)	Age at onset of disease (yr)	Clinical stage*	Treatment (mg/day)
1	M	54	40	4	Levodopa 600 mg, Benserazide 150 mg, Trihexyphenidile 9 mg
2	M	51	43	4	Levodopa 150 mg, Benserazide 37.5 mg, Bromocriptine 45 mg
3	M	53	46	3	Levodopa 500 mg, Benserazide 125 mg, Domperidone 15 mg, Trihexyphenidile 6 mg, Bromocriptine 9 mg
4	M	54	43	3	Levodopa 600 mg, Benserazide 150 mg, Pergolide mesylate 4 mg

*From Hoehn and Yahr³²

Methods

We used the ¹⁸f-fluoro-2-deoxy-d-glucose (¹⁸FDG) method to measure ICMRGlc¹⁵⁻¹⁶, as applied to PET,^{16,17} using the ECAT II single slice positron tomograph,¹⁸ the resolution of which is ~16 mm in the lateral plane and ~19 mm in the axial one (slice thickness), with medium resolution filter. The studies were performed in dim light, and the environment was kept as silent as possible (except for the sound of moving gantry of the detectors); the patient was asked to keep the eyes closed and not to move.

After iv injection (over about 20 seconds) of ¹⁸FDG (3-6 mCi), blood samples were collected using the time-frame advocated by Phelps *et al.*¹⁶ and the heated-hand vein procedure was employed to obtain arterialised blood while avoiding arterial catheterisation.¹⁶ Injection of ¹⁸FDG was started only after proper arterialisation of venous blood was achieved, by comparing its oxygen content to that of arterial blood (single femoral puncture). The samples were immediately put on ice, and subsequently centrifuged to measure the ¹⁸F plasma concentrations in a well-counter calibrated for ¹⁸F and cross-calibrated with the ECAT system to ensure proper quantitation of ICMRGlc.¹⁹ Five samples were also used to measure the plasma glucose content, and the average value (Cp) was used thereafter.

Two different approaches were carried out simultaneously to measure ICMRGlc. One approach was the classic *in vivo* autoradiographic paradigm,^{15,16} which uses the ¹⁸FDG blood history (Cp*), Cp and the regional tissue ¹⁸F concentration (C*t) determined in the PET quantitative images obtained at times >45 min after iv injection. In this approach, we used the operational equation of Huang *et al.*,¹⁷ which includes the 4 FDG rate-constants (that is, k*, to k*) measured by these authors in young healthy adults, and the lumped constant (LC = 0.42) derived empirically from the same studies.¹⁷ To do this, PET images of three contiguous head levels (OM +1.5 cm, OM +3.5 cm, OM +5.5 cm) parallel to the OM Line were obtained in each study at times >55 min, with routine care for accurate quantitation being taken,¹⁹ and were subsequently transformed pixel by pixel into quantitative ICMRGlc images. In this approach, however, the assumption is made that the real k* values of our Parkinson's disease patients do not deviate much from the standard k* values used in the autoradiographic operational equation. It has been shown²⁰ that inaccurate ICMRGlc may obtain if this assumption is not true. We therefore chose to measure regionally the real

k* values and hence the "true" ICMRGlc in our Parkinson's disease studies, using the method originally described for ¹⁴CDG in rats by Sokoloff *et al.*,²¹ and subsequently applied to human PET studies by Huang *et al.*¹⁷ and Reivich *et al.*²² To apply this so-called "kinetic" approach, both the Cp* curve and the ¹⁸F regional cerebral accumulation curves (decay-corrected) are needed. The latter were obtained by scanning repeatedly the midcut (basal-ganglia) level from time of injection to t = 56 min; this was a 12-scan sequence with mid-scan times of 0.5, 1.7, 2.9, 4.2, 5.4, 6.7, 9.0, 12.5, 18.9, 29.6, 42.4 and 56.2 min. (The rapid initial sampling was carried out to allow a better determination of k*,.) Subsequently, the ¹⁸F accumulation curve in each selected region of interest (see below) was fitted, using an original mathematical iterative algorithm,²³ to a 3 exponential model, thus allowing to measure regionally each of the 3 k* values (that is, k*, to k*, k*, being ignored in this relatively short scanning time²²). With the set of measured k* values, the "true" ICMRGlc was computed using the equation $ICMRGlc = [Cp/Lc] \cdot [k^*/k^*_2 + k^*_3]$ proposed by Huang *et al.*,¹⁷ where LC = 0.42. One potential inaccuracy in the kinetic method results from the presence of significant amounts of intra-vascular ¹⁸FDG in the initial PET scans. To avoid the increase of both dosimetry and examination time of an additional cerebral blood volume PET scan, we devised a standardised, time variable percent correction of the elementary ¹⁸F tissue curves for vascular ¹⁸F activity (using published data¹⁶), a correction which should be quite acceptable for the present purposes. Generally, excellent fitting of the corrected ¹⁸F curves was achieved within 20-30 iterations. Occasionally, however, statistical fluctuations due to low count-rates in the initial ¹⁸FDG scans induced slower convergence and/or less optimal fit. Nevertheless, the final ICMRGlc value depended very little on the exact individual fitting values, a fact previously stressed by Huang *et al.*¹⁷

To investigate the validity of our kinetic method, we compared the ICMRGlc values (expressed in mg Glc/100 g/min) obtained by both approaches in various cerebral structures of seven controls (mean age 57 yrs) (table 2). As expected the kinetic values were ~20% lower than the autoradiographic values, an effect of using the k*, FDG constant in the latter paradigm but not in the former.^{17,22} Nevertheless, the regional pattern of CMRGlc was identical in both studies (correlation coefficient r = 0.979, kinetic CMRGlc = 0.815, autoradiographic CMRGlc +

Table 2 Mean ($\pm$ SD) CMRGlc values obtained by both methodological approaches in various brain structures in 7 control subjects, as well as the FDG rate constants (k^*_1 , k^*_2 and k^*_3) measured by the kinetic approach in these structures.

	CMRGlc autoradiographic mg/100 g/min	CMRGlc kinetic mg/100 g/min	$k^*_1 \text{ min}^{-1}$	$k^*_2 \text{ min}^{-1}$	$k^*_3 \text{ min}^{-1}$
Caudate nucleus	6.43 $\pm$ 0.67	5.40 $\pm$ 0.44	0.097 $\pm$ 0.01	0.112 $\pm$ 0.013	0.038 $\pm$ 0.006
Thalamus	5.67 $\pm$ 0.81	4.73 $\pm$ 0.58	0.095 $\pm$ 0.009	0.122 $\pm$ 0.011	0.034 $\pm$ 0.005
Frontal cortex	6.56 $\pm$ 0.67	5.48 $\pm$ 0.52	0.098 $\pm$ 0.009	0.112 $\pm$ 0.013	0.038 $\pm$ 0.006
Temporal cortex	7.0 $\pm$ 0.78	5.85 $\pm$ 0.52	0.102 $\pm$ 0.012	0.111 $\pm$ 0.01	0.039 $\pm$ 0.005
Temporo-occipital cortex	6.69 $\pm$ 0.91	5.45 $\pm$ 0.55	0.1 $\pm$ 0.014	0.116 $\pm$ 0.01	0.037 $\pm$ 0.005
Visual cortex	8.41 $\pm$ 1.11	6.57 $\pm$ 0.84	0.120 $\pm$ 0.01	0.116 $\pm$ 0.014	0.037 $\pm$ 0.007
White matter	4.63 $\pm$ 0.63	3.48 $\pm$ 0.50	0.079 $\pm$ 0.018	0.125 $\pm$ 0.012	0.032 $\pm$ 0.005

Fig. 1 Analysis of regional CMRGlc by means of several regions of interest (ROIs), placed on the three head levels studied parallel to the OM line (from left to right, OM + 1.5 cm, OM + 3.5 cm, OM + 5.5 cm). Circular ROIs were first placed on the right hemisphere and then mirror-copied over the left side with reference to a vertical axis; medially-positioned ROIs were also used. They were placed on the cerebellum (plane 1); the head of caudate nucleus (ROIs 5 and 9), the lenticular nucleus (7 and 11), the thalamus (8 and 12), the medial (15) and lateral frontal (16 and 19) cortex, the occipito-visual cortex (14), and the temporal cortex (remaining ROIs) on plane 2; and the superior frontal (1 and 4) and parietal (remaining ROIs) cortex on plane 3. Since only the basal-ganglia level (plane 2) could be subjected to a kinetic analysis, only the corresponding ROIs provided "kinetic" 1CMRGlc data; because potentially affected by the large vascular space of the superior sagittal and straight sinuses, the occipito-visual area (14) was analysed only with the autoradiographic method.

Fig. 2 Autoradiographic CMRGlc images at the basal-ganglia level obtained in patient 2 in the untreated (left) and treated (right) conditions. Whiter shades of gray indicate higher metabolic rate. Left hemisphere is shown on left side of each image. The regional metabolic pattern appears essentially unchanged despite clinical improvement, and does not differ from that seen in control subjects.

0.002). Furthermore, the rate constants k^*_2 and k^*_3 , found in our controls closely agree with those reported by Phelps *et al.*¹⁶ although k^*_3 was moderately lower in our study presumably because these authors¹⁶ introduced a dephosphorylation rate constant (k^*_4) in their curve fitting algorithm.

On the whole, therefore, each study yielded autoradiographic 1CMRGlc images of the three head-levels, and kinetic 1CMRGlc data of the basal-ganglia level only.

Data analysis Using a standardised protocol,²⁴ regional CMRGlc values were obtained in circular (4 cm²) regions of interest (ROIs) placed symmetrically in the caudate (head), lenticular and thalamic nuclei, and in the cerebellar, temporal, parietal, occipito-visual, medial-frontal and lateral frontal cortex (see fig 1). It is recognised that the anatomical positioning of the ROIs, which followed the ¹⁸FDG atlas of Mazziotta *et al.*²⁵ remained only approximate.

Table 3

		Lenticular nucleus		Caudate nucleus		Thalamus		Medial frontal cortex		Lateral frontal cortex		Temporal cortex		Visual occipital cortex	
		Δ (%)		Δ (%)		Δ (%)		Δ (%)		Δ (%)		Δ (%)		Δ (%)	
Patient 1	I	7.33		6.97		5.21		5.89		5.25		7.31		6.15	
	II	7.18	-2.0	7.53	+8	5.53	+6.1	7.41	+25.8	5.93	+12.9	7.17	-1.9	7.70	+25.2
Patient 2	I	6.07		6.08		5.63		6.37		6.13		6.95		9.37	
	II	7.63	+25.7	6.96	+14.5	5.76	+2.3	6.83	+7.2	5.79	-5.6	7.79	+12	9.68	+3.3
Patient 3	I	9.26		8.17		7.86		8.13		7.25		8.40		11.43	
	II	8.29	-10.5	8.20	+0.4	7.21	-7.9	7.70	-5.3	7.20	-0.7	8.43	+0.3	11.86	+3.8
Patient 4	I	9.22		7.99		7.67		7.38		6.92		9.84		11.73	
	II	8.59	-6.8	7.51	-6	7.17	-6.5	6.98	-5.4	6.25	-9.7	9.07	-7.8	10.25	-12.6
Mean variation (%)		+1.6		+4.2		-1.5		+5.6		-7.8		+0.7		+4.9	
		± 16.4		± 8.9		± 6.8		± 14.7		± 9.8		± 8.3		± 14.4	
		NS		NS		NS		NS		NS		NS		NS	

Values given are local autoradiographic CMRGlc values; Δ (%) is the percent difference in local CMRGlc between study I (untreated) and Study II (treated); NS = no significant difference (paired t-test).

Table 4

	Clinical score	Lenticular nucleus	Caudate nucleus	Thalamus	Medial frontal cortex	Lateral frontal cortex	Temporal cortex	Parietal cortex	Visual occipital cortex
Controls (n = 7)	0	a 6.92 $\pm$ 0.49	6.43 $\pm$ 0.67	5.67 $\pm$ 0.81	7.11 $\pm$ 0.84	6.02 $\pm$ 0.57	7.0 $\pm$ 0.78	7.64 $\pm$ 0.64	8.41 $\pm$ 1.11
	b	5.67 $\pm$ 0.37	5.40 $\pm$ 0.44	4.73 $\pm$ 0.58	5.79 $\pm$ 0.65	5.15 $\pm$ 0.47	5.85 $\pm$ 0.52	—	6.57 $\pm$ 0.84
Study I	31	a 7.97 $\pm$ 1.55	7.30 $\pm$ 0.97	6.54 $\pm$ 1.42	6.94 $\pm$ 1.0	6.39 $\pm$ 0.89	8.12 $\pm$ 1.30	7.44 $\pm$ 1.89	9.67 $\pm$ 2.57
	b	6.58 $\pm$ 0.98*	6.06 $\pm$ 0.71	5.55 $\pm$ 0.65	5.86 $\pm$ 0.48	5.55 $\pm$ 0.33	6.73 $\pm$ 0.70*	—	—
Patients (n = 4)		a 7.92 $\pm$ 0.64†	7.55 $\pm$ 0.51‡	6.42 $\pm$ 0.90	7.23 $\pm$ 0.40	6.29 $\pm$ 0.63	8.12 $\pm$ 0.82	8.74 $\pm$ 0.87	9.87 $\pm$ 1.72
Study II	18	b 6.18 $\pm$ 0.58	6.01 $\pm$ 0.37	5.39 $\pm$ 1.05	6.0 $\pm$ 0.85	5.36 $\pm$ 0.77	6.30 $\pm$ 0.77	—	—
Comparison II/I		NS	NS	NS	NS	NS	NS	NS	NS

Mean and one SD of local CMRGlc values in 7 controls and 4 patients with Parkinson's Disease studied in the untreated (study I) and treated state (Study II). Subtypes a and b mean CMRGlc values obtained by the autoradiographic and the kinetic approach, respectively; NS = no significant variation between Study I and Study II.

*p < 0.05

†p < 0.01

‡p < 0.001, with respect to controls.

Results

Visual inspection of the CMRGlc autoradiographic images did not disclose any conspicuous difference between controls and Parkinson's disease patients, or between the untreated and treated state in any Parkinson's disease patient (fig 2). Significant right-left asymmetry in ICMRGlc was not observed in any Parkinson's disease patient.

Despite a dramatic clinical improvement from first to second study (mean Parkinson's disease scores 35 and 18, respectively), we found no significant change in ICMRGlc (both methodological approaches) in any brain area analysed (table 3). As found in controls, and for reasons explained above, the "kinetic" method yielded ICMRGlc values about 15% lower than corresponding "autoradiographic" values.

Compared to ICMRGlc values from controls of

roughly similar age, the kinetic ICMRGlc values of lenticular and temporal areas of first study were found significantly higher ($p < 0.05$), and the autoradiographic ICMRGlc values of caudate and lenticular areas of second study were found significantly higher ($p < 0.01$ and $p < 0.001$, respectively) (table 4, fig 3).

Discussion

Interpretation of the increases in ICMRGlc found in Parkinson's disease patients relative to controls (table 4, fig 3) is complicated by the fact that the two methodological approaches used for measuring ICMRGlc provided discrepant results. In the untreated state, only the kinetic values in the lenticular nucleus and temporal cortex were significantly higher than controls; in the treated state, on the other hand, only the autoradiographic values of the

Fig. 3 Mean and one standard deviation of ICMRGlc values obtained in various cerebral structures by the *in vivo* autoradiographic approach (top) and the kinetic method (bottom) in seven controls C, shaded boxes) and Parkinson's disease patients in the untreated (a, first study) and treated (b, second study) conditions.

caudate and lenticular nuclei were significantly higher than controls. Although these discrepancies would appear to weaken the pathophysiological relevance of such findings, the lenticular and caudate values in both the treated and the untreated conditions and using both methods, were consistently higher than controls values, albeit not always significantly so (table 4, fig 3). Perhaps studying larger series of Parkinson's disease patients and using a PET device of improved spatial resolution (to minimise the partial volume effect²⁶) would confirm this impression of higher metabolism in the basal ganglia of Parkinson's disease patients. It must be stressed, however, that the basal ganglia ICMRGlc was not influenced by levodopa (table 3), and hence that the relationship between the above changes and the clinical condition appears at best marginal.

The main goal of the present study was to investigate the effects of levodopa on ICMRGlc in our patient sample. Despite dramatic clinical improvement afforded by reinstitution of therapy, no alteration in ICMRGlc was found in any of the brain structures analysed. Having used both the autoradiographic method and the presumably more reliable kinetic method¹⁷ further supports this negative finding.

Although no other study of ICMRGlc in Parkinson's disease patients has been published yet, our negative findings are consonant with previously published studies of rCBF in Parkinson's disease patients. In 26 Parkinson's disease patients, two weeks of levodopa therapy induced no modification of rCBF (¹³³Xe inhalation technique).¹⁰ In another study, using the same technique, a moderate but significant diffuse reduction in rCBF in 60 Parkinson's disease patients (both treated and untreated) compared to aged-matched controls was reported, but this reduction was not seen in the young, early-onset Parkinson's disease patients subgroup.¹¹ Recently, a similar reduction in rCBF (preferentially affecting the frontal cortex) was reported, but again early-onset Parkinson's disease patients were spared.¹² If the normal couple between CBF and energy metabolism¹⁹ is maintained in Parkinson's disease, the above studies would indicate that cortical metabolism is unaffected in early-onset Parkinson's disease patients, and hence would agree with our findings, but that, on the other hand, late onset Parkinson's disease is associated with diffuse or preferentially frontal hypo-metabolism.

In a semiquantitative study of relative cerebral perfusion and oxygen metabolism using oxygen-15 and 2-dimensional scintigrams, Lenzi *et al*¹³ found a

decreased metabolism in the parietal lobe contralateral to the affected limbs in several patients with hemi-Parkinsonism. Although we did not study similar cases, our data suggest preserved ICMRGlC in the parietal cortex in bilateral Parkinson's disease.

Our essentially negative findings in human Parkinson's disease are also consonant with one quantitative autoradiographic study, showing no asymmetry of ^{14}CDG retention in the brain of rats after unilateral 6-hydroxy-dopamine (6-OHDA) destruction of the substantia nigra.⁶ Likewise, in the same rat model of unilateral Parkinson's disease, no alteration in rCBF²⁷ or cytochrome oxydase redox shifts²⁸ were observed in any part of the brain. However, four more detailed studies of ^{14}CDG uptake in brain autoradiograms of rats with unilateral 6-OHDA lesions of the substantia nigra or of the ventral tegmental area provided fairly consistent results suggesting a small (3–9%) reduction in CMRGlC in the ipsilateral striatum, and a larger CMRGlC increase in the ipsilateral pallidum (10–40%) and lateral habenular nucleus (8–24%), while smaller changes were inconsistently seen in other structures.^{5,7–9} That these alterations in ICMRGlC resulted from lesions of the DA systems was shown by their absence in 6-OHDA lesioned rats treated with the DA agonist apomorphine.^{5,7} (Only after extensive 6-OHDA or electrolytic lesions of the mesencephalic tegmentum or lateral hypothalamus were marked decreases in ipsilateral frontal cortex ICMRGlC, unaltered by treatment with apomorphine, observed.^{4,5}) To the best of our knowledge, there has been no study of the acute effects of levodopa on ICMRGlC in rats with unilateral 6-OHDA lesions of the substantia nigra. When administered to normal rats, levodopa-induced changes in the relative pattern of ^{14}CDG distribution in brain that were difficult to interpret.²⁹ Apomorphine, however, when given to normal rats, increased ICMRGlC in the caudate nucleus in a dose-dependent manner—an effect opposite to that of 6-OHDA nigro-striatal lesion—and decreased ICMRGlC in the anterior cingulate cortex.³⁰ Taken together, therefore, the above animal studies suggested that ascending dopaminergic systems have presumably direct effects chiefly on striatal and lateral habenula glucose utilisation (stimulation and deprivation of dopaminergic transmission increasing and decreasing ICMRGlC, respectively) and presumably indirect metabolic effects on the pallidum (most likely though the striato-pallidal projections). These metabolic effects, however, remain relatively small.

No such changes were found in the present PET study of Parkinson's disease patients. This discrepancy may result from several differences between

our human study and the above animal experiments. First, the relevance of the rat model of Parkinson's disease to the real human disease may be questioned, if only because of extensive biochemical defects other than those affecting the nigrostriatal dopaminergic systems.³¹ Second, the ICMRGlC changes reported in rats were either too small (for example, in striatum) or too circumscribed (for example, in pallidum and lateral habenula) to be reliably detected in humans by our PET detection device, even if they did occur.²⁶ Third, as yet another effect of partial volume averaging, any putaminal decrease in CMRGlC would have been obscured, in our single "lenticular" ROI (see Methods), by the expected pallidal CMRGlC increase. Fourth, the levodopa therapy withdrawal and reinstitution intervals in our study (48 and 22 hrs, respectively) may have been too short to induce maximal effects on the dopaminergic content at terminal sites, and, in turn, on ICMRGlC.^{9,9} Irrespective of the magnitude of changes in dopaminergic content, the clinical effects were nevertheless quite dramatic but did not result in any detectable alteration in ICMRGlC.

Despite the above-mentioned problems and additional limitations such as small patient sample and potential repositioning inaccuracies, the present study failed to detect changes in ICMRGlC that could be attributable to the clinical features of early-onset Parkinson's disease, or to modifications of the latter by levodopa therapy. This suggests that the marked functional alterations that must underlie the clinical symptoms of Parkinson's disease have metabolic counterparts that are either too small in magnitude or too localised, or both, to be reliably demonstrated by most current PET devices. However, it remains to be seen whether or not abnormalities in ICMRGlC occur in patients with late-onset or unilateral Parkinson's disease, and whether positron tomographs of improved spatial resolution are capable of detecting more localised changes in the energy metabolism of the Parkinsonian brain.

Note added in proof: Since this study was completed, two quantitative PET studies of cerebral metabolism in Parkinson's disease patients have been published in abstract form. Kuhl *et al* (*J. Nucl. Med.*, 1983;24:21) found no alteration of ICMRGlC in nine treated and two untreated patients. Leenders *et al* (*J. Cereb. Blood Flow Metabol.*, 1983;3,Suppl.1:S488–9) found the regional cerebral oxygen consumption (rCMRO₂) essentially unaltered in the untreated state, save for relatively increased values in the affected basal ganglia of patients with unilateral disease; acute levodopa challenge increased the overall rCMRO₂, although this was presumably a methodological artifact, while the basal ganglia rCMRO₂ was found increased after several weeks of treatment.

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