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PET evaluation of the relationship between D_2 receptor binding and glucose metabolism in patients with parkinsonism

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Objective: To clarify the relationship between D_2 receptor binding and the cerebral metabolic rate for glucose (CMRGlu) in patients with parkinsonism, we simultaneously measured both of these factors, and then compared the results. ***Methods:*** The subjects consisted of 24 patients: 9 with Parkinson's disease (PD), 3 with Juvenile Parkinson's disease (JPD), 9 with multiple system atrophy (MSA), and 3 with progressive supranuclear palsy (PSP). The striatal D_2 receptor binding was measured by the C-11 raclopride transient equilibrium method. CMRGlu was investigated by the F-18 fluorodeoxyglucose autoradiographic method. ***Results:*** The D_2 receptor binding in both the caudate nucleus and putamen showed a positive correlation with the CMRGlu in the PD-JPD group, but the two parameters demonstrated no correlation in the MSA-PSP group. The left/right (L/R) ratio of D_2 receptor binding in the putamen showed a positive correlation with that of CMRGlu in the MSA-PSP group, while the two demonsrated no correlation in the PD-JPD group. ***Conclusion:*** Our PET study showed striatal D_2 receptor binding and the CMRGlu to be closely related in patients with parkinsonism, even though the results obtained using the L/R ratios tended to differ substantially from those obtained using absolute values. The reason for this difference is not clear, but this finding may reflect the pathophysiology of these disease entities.

Key words: D_2 receptor binding, CMRGlu, ^{11}C-raclopride, ^{18}FDG, Parkinson's disease

INTRODUCTION

PARKINSON'S DISEASE (PD) is characterized by neurodegeneration of the nigrostriatal dopaminergic system.[1] Patients with other types of parkinsonism, such as multiple system atrophy (MSA), also show neurodegeneration of this system.[2] Previous positron emission tomography (PET) studies using radioligands to measure the presynaptic dopaminergic function, such as F-18 DOPA[3] or C-11 β-CIT,[4] successfully revealed the hypofunction of the presynaptic dopaminergic system. On the other hand, both striatal D_2 receptor binding and the cerebral metabolic rate for glucose (CMRGlu) are usually normal in the early stage of PD[5]: namely, the postsynaptic dopaminergic function is preserved in this pathological condition. This finding is thought to be helpful for differentiating PD from other types of parkinsonism such as MSA,[6] in which neurodegeneration and a decrease in the CMRGlu occur more widely.[7,8] These results suggest that striatal D_2 receptor binding is closely related with the CMRGlu. However, the relationship between D_2 receptor binding and the CMRGlu in patients with parkinsonism has not yet been fully examined. To clarify this issue, we simultaneously measured the striatal D_2 receptor binding and CMRGlu in patients with parkinsonism, and evaluated the relationship between D_2 receptor binding and the CMRGlu in both the caudate nucleus and putamen. In

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addition, we also evaluated the relationship between L-dopa responsiveness and the PET findings.

MATERIALS AND METHODS

The subjects consisted of 24 patients and 19 normal subjects: 9 patients with PD (age, 62.7 ± 10.0 [mean ± SD] years), 3 with Juvenile Parkinson's disease (JPD) (age, 29.0 ± 2.7 years), 9 with MSA (age, 57.2 ± 6.4 years), 3 with progressive supranuclear palsy (PSP) (age, 73.0 ± 4.0 years) and 19 normal volunteers (age, 34.7 ± 8.3 years). The patients and their clinical features are summarized in Table 1. The diagnosis was clinically made according to the criteria proposed by the Movement Disorders Society.[9] None of the patients showed apparent dementia or neuropsychiatric symptoms. The disease duration ranged from 1 to 13 years. In the present study, these 24 patients were divided into two groups according to the predominantly affected sites, namely the PD-JPD and MSA-PSP groups. The former group shows a predominantly presysnaptic dopaminergic dysfunction,[1,10] while the latter shows both pre- and post-synaptic dopaminergic dysfunctions.[2,11] The Hoehn & Yahr stage was significantly higher in the MSA-PSP group than in the PD-JPD group (Mann-Whitney's U-test, $p < 0.005$). Nineteen of the 24 patients had unilaterally dominant symptoms. All 24 patients had been previously treated with L-dopa. Among them, 11 patients showed a good response to L-dopa, while the remaining 13 patients showed a poor response. L-Dopa was the only dopaminergic treatment in fourteen of the 24 patients, while seven patients received dopamine agonist, three received an anticholonergic drug, and one received droxidopa. All patients underwent PET studies after all medications had been suspended for at least one day. The normal volunteers (Vt) consisted of medical doctors and technicians at our institute, as well as social workers.

The PET device used in this study was the ECAT EXACT HR+ (Siemens, Knoxville, TN), which had a spatial resolution of 4.2 mm in full-width at half maximum, and 63 contiguous slices were simultaneously obtained 2.3 mm apart. The subjects were placed in the supine position on a bed in a semidark room. In the F-18 fluorodeoxyglucose (FDG) PET study, a small canula was placed in the radial artery for arterial blood sampling. A transmission scan using a Ge-68/Ga-68 rod source was obtained for each subject for attenuation correction before the emission scan. A PET scan was started 45 min after the administration of 185 to 370 MBq of FDG in the 3D data acquisition mode. Arterial blood was drawn every 15 sec

Table 1 Patients and clinical features in this study

Subjects	Diagnosis	Age (years)	Sex (male/ female)	Disease duration (years)	Hoehn & Yahr stage	Rest tremor	Rigidity	Akinesia	Dominant side	L-dopa dose/day (mg)	response
1	PD	50	m	1	2	+	+	+	lt	300	+
2	PD	53	m	1	2	+	+	+	rt	–	–
3	PD	54	m	3	2	+	+	+	rt	300	+
4	PD	60	f	1	2	+	+	–	lt	300	+
5	PD	61	f	5	4	–	++	++	lt	800	+
6	PD	64	f	13	3	+	+	+	rt	300	+
7	PD	67	f	1	3	+	++	++	lt	300	–
8	PD	77	m	2	3	+	++	+	lt	200	+
9	PD	78	f	5	3	+	++	+	rt	100	+
10	JPD	27	m	4	2	+	++	+	–	50	+
11	JPD	28	f	3	3	+	++	+	rt	150	+
12	JPD	32	f	3	2	+	++	++	lt	300	–
13	MSA	48	f	4	3	+	+	++	lt	600	–
14	MSA	53	m	2	2	±	+	+	lt	400	–
15	MSA	54	f	2	5	–	++	++	lt	100	–
16	MSA	55	m	5	4	–	–	+	–	900	+
17	MSA	57	m	4	3	–	–	+	lt	–	–
18	MSA	58	f	6	3	–	+	+	rt	–	–
19	MSA	58	f	1	3	–	+	+	lt	–	–
20	MSA	61	m	5	4	–	+	++	lt	600	+
21	MSA	71	m	2	5	–	+	+	lt	300	–
22	PSP	77	f	1	4	–	+	++	–	200	–
23	PSP	69	f	1	4	–	+	+	–	200	–
24	PSP	73	f	4	4	±	++	++	–	150	–

PD; Parkinson's disease, JPD; Juvenile Parkinson's disease, MSA; Multiple system atrophy, PSP; Progressive supra palsy, L-dopa response; +: Positive, –: Negative

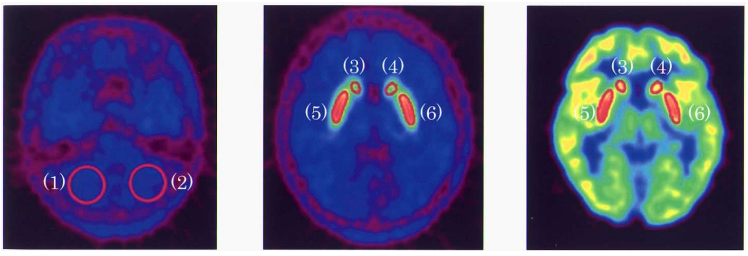

Fig. 1 ROIs were established in the cerebellum (ROIs nos. 1, 2), caudate nucleus (ROIs nos. 3, 4), and putamen (ROIs nos. 5, 6) on the PET images.

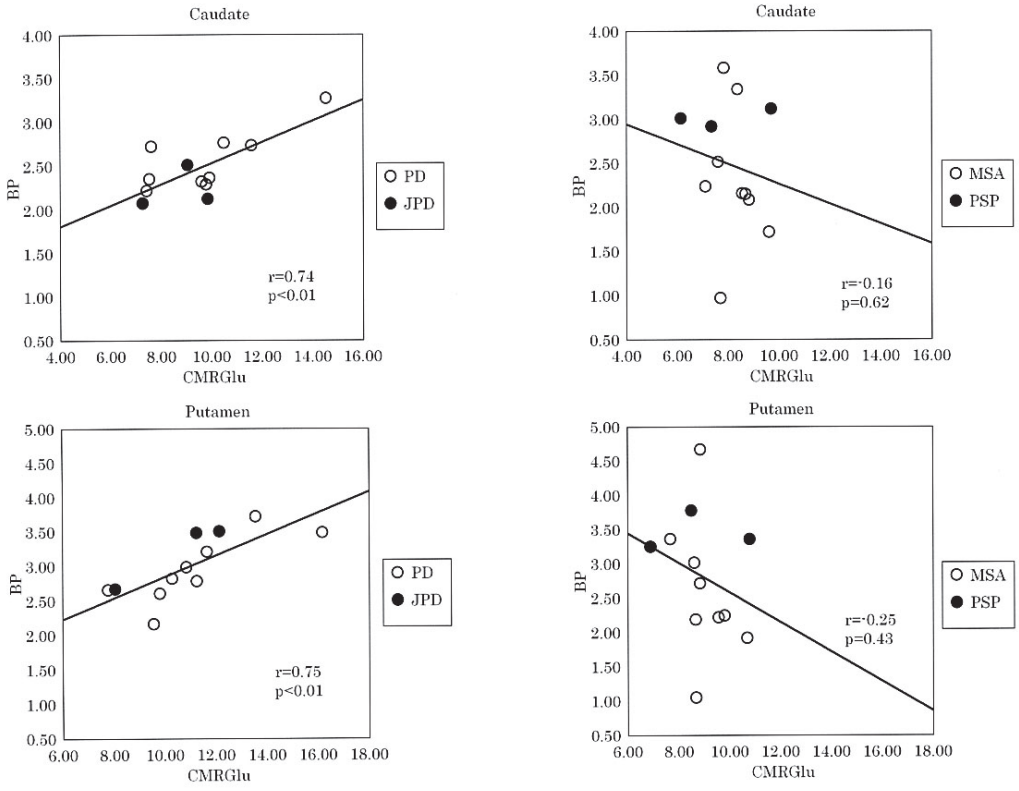

Fig. 2 Comparison of the D_2 receptor binding and CMRGlu results. A significant linear correlation was observed between D_2 receptor binding and CMRGlu in both the caudate nucleus and putamen in patients with PD or JPD, while no correlations were seen between the two in either region in patients with MSA or PSP (Spearman's rank correlation analysis).

for 2 min, every 30 sec for 4 min, every 2 min for 10 min, every 5 min for 20 min and every 10 min thereafter to quantify the CMRGlu. In the C-11 raclopride PET study, arterial blood sampling was not performed. After completing the transmission scan, 370 MBq of C-11 raclopride was intravenously administered as a bolus. The specific radioactivity of C-11 raclopride was 8–54 GBq/μmol at the time of the injection. A dynamic scan was started immediately after injection, and data were collected for 60 min in a 3D data acquisition mode. C-11 raclopride PET and F-18 FDG PET were performed on all 24 patients. Thereafter, C-11 raclopride and F-18 FDG PET studies were separately performed within a week.

Parametric images were created on an ULTRA60 workstation (SUN Microsystems, Santa Clara, USA). The CMRGlu was calculated using the F-18 FDG autoradiographic method.[12] Striatal dopamine D_2 receptor binding was measured by the C-11 raclopride transient equilibrium method based on a 3-compartment model.[13] The radioactivity of the specific binding to D_2 receptor was obtained by subtracting the cerebellar radioactivity from the striatal radioactivity. The length of time for the transient equilibrium was individually determined by observing the radioactivity curve of the specific binding. Typically, transient equilibrium was reached within 30 min after the administration of C-11 raclopride, and

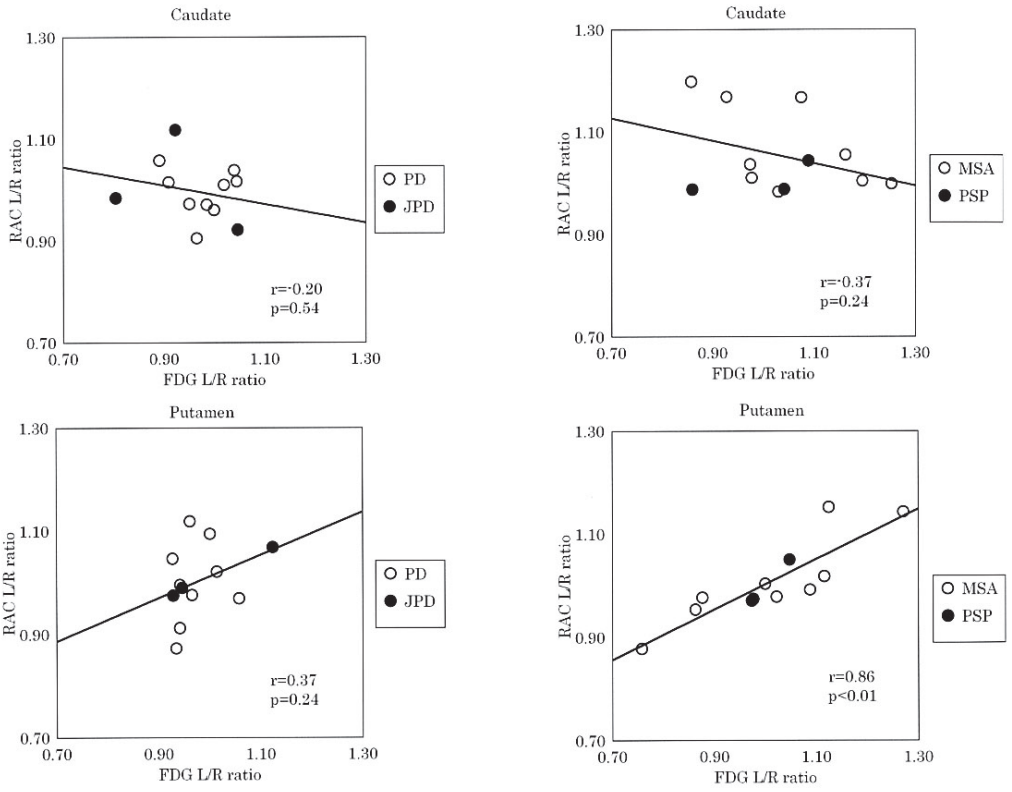

Fig. 3 Comparison of the L/R ratios between the D_2 receptor binding and CMRGlu results. Within the putamen, a significant linear correlation was observed in patients with MSA or PSP, while no correlation was seen in either the caudate nucleus or putamen in patients with PD or JPD (Spearman's rank correlation analysis).

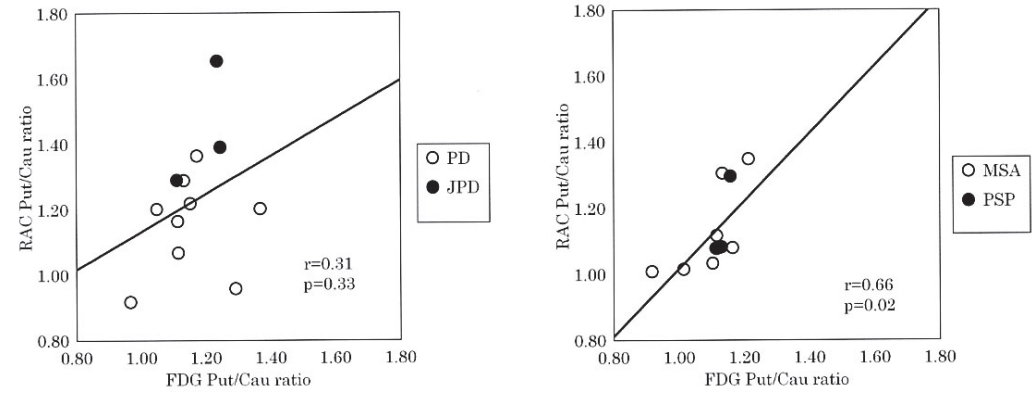

Fig. 4 Comparison of the Put/Cau ratios between the D_2 receptor binding and CMRGlu results. The Put/Cau ratios showed a significant linear correlation in the MSA-PSP group, while no correlation was seen in the PD-JPD group (Spearman's rank correlation analysis).

C-11 raclopride images were obtained during a 20-min period of transient equilibrium. The striato-cerebellar ratio at this time was measured as k3/k4, which is an index which closely parallels the binding potential (BP: Bmax/Kd).[11] Regions of interest (ROIs) were placed on the caudate nucleus, putamen and cerebellum on MRI, C-11 raclopride and F-18 FDG PET images (Fig. 1) coregistered by using SPM99 (Wellcome Department of Cognitive Neulogy, Queen Square, London, UK). The cerebellum was used as a reference region. D_2 receptor binding was calculated according to the following equation: $C_{caudate}/C_{cerebellum} - 1$, or $C_{putamen}/C_{cerebellum} - 1$.

D_2 receptor binding and the CMRGlu were corrected for age according to the following equation based on the data obtained for normal control subjects. In this correction, we assumed all subjects to be 50 years old:

$Y = -0.0137X + 3.0892$

(Y: D_2 receptor binding in the caudate nucleus, X: age)

Table 2 D_2 receptor binding and CMRGlu in each group of patients

	Age	RAC		FDG		BP/CMRGlu	
		Age corrected		Age corrected		Age corrected	
		Caudate BP	Putamen BP	Caudate CMRGlu mg/min/100 m*l*	Putamen CMRGlu mg/min/100 m*l*	Caudate	Putamen
PD (n = 9)	62.7 ± 10.0	2.6 ± 0.3	2.9 ± 0.5	9.8 ± 2.3	11.2 ± 2.5	0.27 ± 0.05	0.27 ± 0.04
JPD (n = 3)	29.0 ± 2.7	2.2 ± 0.2	3.2 ± 0.5	8.7 ± 1.3	10.5 ± 2.2	0.26 ± 0.04	0.31 ± 0.02
MSA (n = 9)	57.2 ± 6.4	2.3 ± 0.8	2.6 ± 1.0	8.2 ± 0.8	9.0 ± 0.9	0.28 ± 0.10	0.29 ± 0.13
PSP (n = 3)	73.0 ± 4.0	3.0 ± 0.1	3.5 ± 0.3	7.7 ± 1.8	8.7 ± 2.0	0.40 ± 0.09	0.41 ± 0.09
Vt RAC (n = 19)	34.7 ± 8.2	2.4 ± 0.3	2.7 ± 0.3	—	—	—	—
Vt FDG (n = 10)	40.0 ± 19.1	—	—	9.7 ± 1.7	11.3 ± 1.8	—	—

Mean ± SD

Table 3 Asymmetry index and putamen-to-caudate ratio in each group of patients

	RAC (Binding potential)			FDG (CMRGlu)		
	A.I. caudate	A.I. putamen	Putamen to caudate ratio	A.I. caudate	A.I. putamen	Putamen to caudate ratio
PD (n = 9)	0.04 ± 0.03	0.06 ± 0.05	1.2 ± 0.2	0.05 ± 0.04	0.05 ± 0.03	1.2 ± 0.1
JPD (n = 3)	0.07 ± 0.05	0.03 ± 0.03	1.4 ± 0.2	0.11 ± 0.09	0.08 ± 0.03	1.2 ± 0.1
MSA (n = 9)	0.07 ± 0.07	0.06 ± 0.06	1.1 ± 0.1	0.10 ± 0.07	0.13 ± 0.09	1.1 ± 0.1
PSP (n = 3)	0.02 ± 0.02	0.06 ± 0.02	1.2 ± 0.1	0.09 ± 0.06	0.04 ± 0.01	1.1 ± 0.0
Vt RAC (n = 19)	0.05 ± 0.04	0.04 ± 0.03	1.1 ± 0.1	—	—	—
Vt FDG (n = 10)	—	—	—	0.07 ± 0.06	0.04 ± 0.04	1.2 ± 0.1

Mean ± SD

$Y = -0.0135X + 3.4063$
(Y: D_2 receptor binding in the putamen, X: age)
$Y = -0.0642X + 12.947$
(Y: CMRGlu in the caudate nucleus, X: age)
$Y = -0.0607X + 14.317$
(Y: CMRGlu in the putamen, X: age)

Statistical analysis was done as follows. Correlations between two variables were evaluated by Spearman's rank correlation analysis. Comparisons of values between two groups or among four groups were performed by Mann-Whitney's U-test or Kruskal-Wallis test, respectively. This study was approved by the Committee for the Clinical Application of Cyclotron-Produced Radionuclides at Kyushu University Hospital and the ethics committee at the Graduate School of Medical Sciences, Kyushu University. In addition, informed consent was obtained from the normal volunteers and patients (and/or their families) before all PET studies.

RESULTS

Figure 2 shows the correlations between D_2 receptor binding and the CMRGlu in the caudate nucleus and putamen. The ratios of D_2 receptor binding in both the caudate nucleus and putamen showed a positive and close correlation with the CMRGlu in the PD-JPD group (Spearman's rank correlation analysis, $p < 0.01$), while the two parameters did not show a close correlation with the MSA-PSP group. Figure 3 shows the relationship between the left/right (L/R) ratios of D_2 receptor binding and the CMRGlu. The L/R ratio of D_2 receptor binding in the caudate nucleus was not significantly correlated with that of the CMRGlu in either group of patients. The L/R ratio of D_2 receptor binding in the putamen showed a significantly positive correlation with that of the CMRGlu in the MSA-PSP group (Spearman's rank correlation analysis, $p < 0.01$); however, no such correlation was seen in the PD-JPD group. Figure 4 shows the correlations in the putamen to caudate (Put/Cau) ratios between D_2 receptor binding and the CMRGlu. The Put/Cau ratio showed a significantly positive correlation in the MSA-PSP group (Spearman's rank correlation analysis, $p < 0.02$), while no such correlation was seen in the PD-JPD group.

Table 2 shows the mean and standard deviation (SD) of D_2 receptor binding and the CMRGlu in the caudate nucleus and putamen for each group regarding patients. There was no significant difference among these four groups in either D_2 receptor binding, the CMRGlu, or their ratio (D_2/CMRGlu), even though the PSP patients showed the highest mean values of D_2 receptor binding, the lowest CMRGlu, and thus the highest D_2/CMRGlu ratio in both the caudate nucleus and putamen (Kruskal-Wallis test). MSA patients showed slightly lower mean

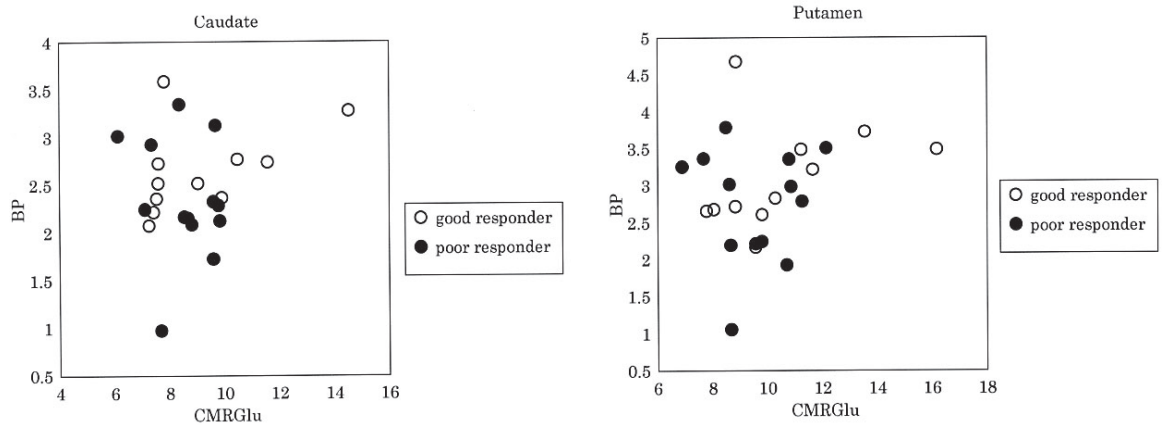

Fig. 5 Relationship between D_2 receptor binding and CMRGlu in good responders and poor responders to L-dopa therapy. The relationship between D_2 receptor binding and CMRGlu was not affected by the responsiveness to L-dopa or by the type of imaging used, i.e., RAC-PET or FDG-PET.

Table 4 Relationship among L-dopa response, binding potential, and CMRGlu

	RAC (Binding potential)			FDG (CMRGlu)		
	good responder (n = 11)	poor responder (n = 13)	p-value	good responder (n = 11)	poor responder (n = 13)	p-value
Caudate	2.6 ± 0.4	2.3 ± 0.6	N.S.	9.1 ± 2.3	8.5 ± 1.2	N.S.
Putamen	3.1 ± 0.7	2.7 ± 0.8	N.S.	10.5 ± 2.5	9.5 ± 1.5	N.S.
Putamen to caudate ratio	1.2 ± 0.2	1.2 ± 0.2	N.S.	1.2 ± 0.1	1.1 ± 0.1	N.S.
A.I. in caudate	0.04 ± 0.05	0.05 ± 0.05	N.S.	0.07 ± 0.07	0.09 ± 0.06	N.S.
A.I. in putamen	0.04 ± 0.03	0.07 ± 0.05	N.S.	0.07 ± 0.04	0.09 ± 0.09	N.S.
BP/CMRGlu in caudate	0.30 ± 0.07	0.28 ± 0.10	N.S.	—	—	—
BP/CMRGlu in putamen	0.31 ± 0.08	0.30 ± 0.11	N.S.	—	—	—

Mean ± SD

values in D_2 receptor binding and the CMRGlu than PD patients. Table 3 shows the Put/Cau ratios and respective asymmetry indices of D_2 receptor binding and CMRGlu. There were no significant differences among the subjects groups in either the Put/Cau ratios or the asymmetry indices (Kruskal-Wallis test). The mean of the Put/Cau ratios of D_2 receptor binding was slightly higher in MSA patients than in the PD patients. The asymmetry index of the caudate CMRGlu was the largest in the JPD patients, while that of the putamen was the largest in the MSA patients.

Figure 6 shows the relationship between D_2 receptor binding and the CMRGlu in good responders and poor responders to L-dopa therapy. Patients with both preserved D_2 receptor binding and a preserved CMRGlu tended to show a good response to L-dopa therapy, while patients with severely impaired D_2 receptor binding or CMRGlu showed a poor response (Table 4); however, this difference was not significant (Mann-Whitney's U-test).

Representative images of D_2 receptor binding and the CMRGlu through the putaminal level of a normal volunteer and patients with PD, JPD, MSA and PSP are shown in Figure 6. In the PD and JPD patients, both D_2 receptor binding and the CMRGlu increased in the putamen bilaterally in comparison to the levels in normal control subjects, whereas in MSA patients, D_2 receptor binding and the CMRGlu tended to decrease mainly in the putamen. The reduction pattern in putaminal D_2 receptor binding was similar to that in the CMRGlu. In the MSA and PSP patients, the CMRGlu also decreased throughout the cerebral cortices.

DISCUSSION

D_2 receptor binding decreases with age.[14,15] In a study using C-11 raclopride PET, Rinne et al.[14] reported the Bmax of the striatal dopamine D_2 receptors to decline by 4.6% per decade, while Kd did not change. Wong et al.[15] observed the same phenomenon using C-11 NMSP PET. In this study, we quantified D_2 receptor binding using the C-11 raclopride transient equilibrium method, which yields only the BP. As a result, we corrected the BP values by assuming that all subjects were 50 years old. The CMRGlu also decreases with age,[16] although the reduction rate is much smaller than that of D_2 receptor binding. Therefore,

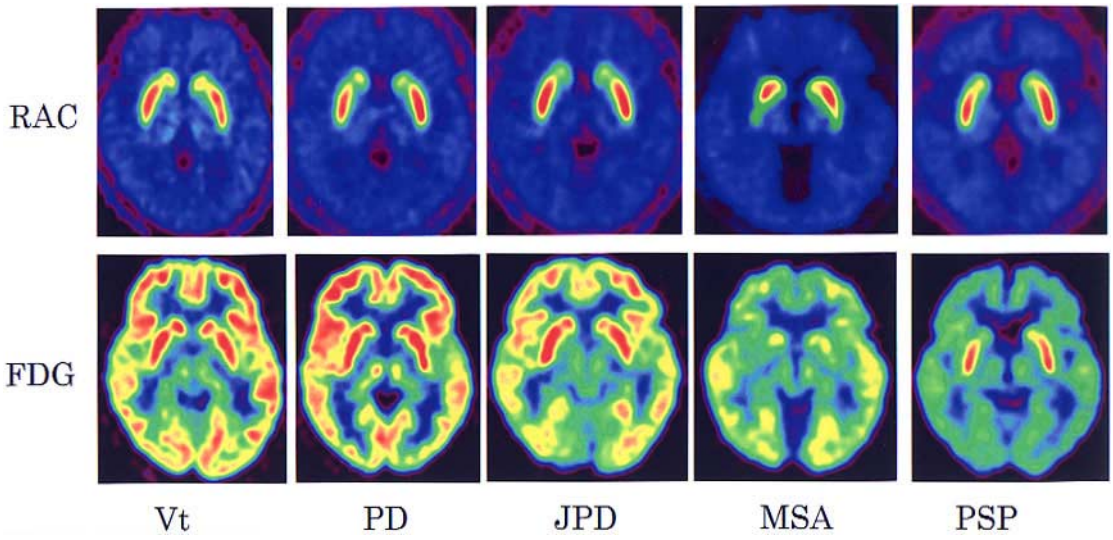

Fig. 6 PET images of RAC (*top row*) and FDG (*bottom row*) through the putaminal level in normal volunteer, PD, JPD, MSA and PSP patients. The RAC images show a pattern similar to that observed in the CMRGlu images.

the values of CMRGlu were also corrected for the ages of the patients according to the lineal function obtained by normal volunteers.

As shown in Figure 3, the caudate nucleus and putaminal D_2 receptor binding both showed a positive correlation with the CMRGlu in the PD-JPD group, while no such correlation was observed with the CMRGlu in the MSA-PSP group. There have been few reports on the relationship between striatal D_2 receptor bindings and CMRGlu. Antonini et al.[17] reported the putaminal D_2 receptor binding to not be correlated with CMRGlu as estimated by either absolute values or asymmetry indices. More recently, they described[6] D_2 receptor binding and CMRGlu to be correlated in the putamen, but not in the caudate nucleus. This and other previous findings indicated that D_2 receptor binding was either normal or slightly increased in early PD.[6, 18] This up-regulation of D_2 receptor binding was considered to be due to a decrease in the dopamine release from presynaptic neurons in the striatum. The finding of normal D_2 receptor binding and CMRGlu has also been reported in patients with JPD.[19] Glucose is mainly consumed to maintain the synaptic activity.[20] In the early stages of PD, the nigrostriatal dopaminergic system is predominantly affected, while other neuronal activities are well preserved in the striatum.[21] As a result, the change in the energy metabolism mainly depends on the alteration of the postsynaptic dopaminergic neuronal function, and striatal D_2 receptor binding may thus be positively correlated with the striatal CMRGlu.

On the other hand, in the MSA-PSP group there was no apparent correlation between striatal D_2 receptor binding and the CMRGlu, even though the L/R ratio of D_2 receptor binding correlated closely with that of CMRGlu. There seem to be several reasons for this difference between D_2 receptor binding and the CMRGlu in these patients. C-11 raclopride PET can disclose only post-synaptic dopaminergic damage,[22] while CMRGlu globally reflects the neuronal activities in the striatum.[20] D_2 receptor binding has been reported to either decrease or remain at normal levels in MSA patients[6,23] and in PSP patients.[24] Analyses by FDG PET have shown the CMRGlu to decrease in the striatum, cerebral cortices, brain stem and cerebellum in MSA patients,[25] and the CMRGlu was also observed to decrease in the striatum, cerebral cortices and brain stem in PSP patients.[26] The structural changes such as neuronal loss or gliosis occur more widely in MSA than PD.[2] In addition, the dopaminergic system accounts for only 10% of the striatal neurons, and thus it seems reasonable that D_2 receptor binding does not always correlate with the CMRGlu. Diversity of the D_2 receptor binding also may explain the difference between D_2 receptor binding and CMRGlu. The difference in the Hoehn & Yahr stage between the MSA-PSP and the PD-JPD group may also have influenced the results. Przedborski et al.[27] reported a case with Hemiparkinsonism-hemiatrophy syndrome, which showed marked reduction in the FDG uptake in the left putamen and a symmetrical uptake in F-18 fluoroethylspiperon binding to D_2 receptor.

In the present study, we found that the L/R ratio of putaminal D_2 receptor binding correlated significantly with that of the CMRGlu in the MSA-PSP group. This suggests that the distribution pattern of D_2 receptor binding is similar to that of the CMRGlu. As shown in Figure 5, the PET image of D_2 receptor binding showed the same reduction pattern as in that of the CMRGlu in the MSA-PSP group. In contrast, the L/R ratio of D_2 receptor binding did not correlate with that of the CMRGlu in the

PD-JPD group. The reason for this difference between the MSA-PSP and PD-JPD groups is not clear, but the relatively larger asymmetry in the MSA-PSP group may have played a role in the significant correlation between D_2 receptor binding and CMRGlu. In addition, the normalization of the receptor binding and the CMRGlu with the data regarding the contralateral putamen might disclose a close relationship in the distribution of these tracers, which was masked by the physiological variation or difference in absolute values of these two parameters. It has been well established that the decrease in striatal dopamine metabolism is greater in the putamen than in the caudate nucleus in the early stage of PD.[3] It has also been reported that the level of D_2 receptor binding in the putamen is higher than that in the caudate nucleus, while, in addition, the L/R asymmetries of the putaminal dopamine metabolism and D_2 receptor binding showed a negative correlation in PD patients.[17] In the present study, both D_2 receptor binding and CMRGlu were higher in the putamen than in the caudate nucleus. However, we could not find any significant correlation between the Put/Cau ratios of D_2 receptor binding and the CMRGlu in the PD-JPD group, even though the Put/Cau ratios showed a positive correlation in the MSA-PSP group. This finding may thus reflect the functional difference between the putamen and caudate nucleus.

L-Dopa is an agonist of D_2 receptor, and its effect is assumed to be dependent on the patency of the D_2 receptor in the dopaminergic postsynaptic neurons in the putamen. However, Schwarz et al.[28] reported the case of an L-dopa-resistant patient with normal D_2 receptor binding, and systems other than the dopaminergic system may thus have been affected in this patient. In Figure 5, we tried to clarify the difference in the putaminal D_2 receptor binding and the CMRGlu between good responders and poor responders to L-dopa therapy to evaluate the clinical significance of the simultaneous measurements of both putaminal D_2 receptor binding and CMRGlu, but we could not clearly separate good responders from poor responders based on the C-11 raclopride findings and FDG PET. As a result, we could not conclude that the combination of C-11 raclopride and FDG PET provided clinically significant information for prediction of the L-dopa effect. Brooks et al.[24] reported the D_2 receptor binding to be low in L-dopa-treated patients with Parkinson's disease. All of our 24 patients underwent L-dopa therapy before the PET studies. This may have led to an underestimation of D_2 receptor binding in good responders to L-dopa therapy.

In conclusion, our PET study revealed that striatal D_2 receptor binding and CMRGlu were closely related in the patients with parkinsonism, although the results obtained by absolute values were different from those obtained by L/R ratios. The reason for this difference is not clear, but this finding may reflect the pathophysiology of these disease entities.

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