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Regional cerebral blood flow, blood volume, oxygen extraction fraction, and oxygen utilization rate in normal volunteers measured by the autoradiographic technique and the single breath inhalation method

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By means of a high resolution PET scanner, the regional cerebral blood flow (rCBF), cerebral blood volume (rCBV), oxygen extraction fraction (rOEF), and metabolic rate of oxygen ($rCMRO_2$) for major cerebral gyri and deep brain structures were studied in eleven normal volunteers during an eye-covered and ear-unplugged resting condition. Regional CBF was measured by the autoradiographic method after intravenous administration of $H_2{}^{15}O$. Regional OEF and $rCMRO_2$ were measured by the single inhalation of $^{15}O_2$. With MR T_1-weighted images as an anatomical reference, thirteen major cerebral gyri, caudate nucleus, lentiform nucleus, thalamus, midbrain, pons, cerebellum and vermis were defined on the $CMRO_2$ images. Values were read by using circular regions of interest 16 mm in diameter. The posterior part of the cingulate gyri had the highest rCBF and $rCMRO_2$ values among brain structures, followed by the lentiform nucleus, the cerebellum, the caudate nucleus, and the thalamus. Parahippocampal gyri had the lowest rCBF and $rCMRO_2$ values among the cortical gyri. Regional OEF for the pontine nuclei (0.34 ± 0.04), the midbrain (0.35 ± 0.05), the parahippocampal gyri (0.35 ± 0.04 for the right and 0.37 ± 0.05 for the left), and the thalami (0.37 ± 0.05 for the right and 0.36 ± 0.04 for the left) were significantly lower than the mean OEF for the cerebral cortices (0.42 ± 0.04) ($p < 0.05$ or less). The global CBF and $CMRO_2$ were consistent with those obtained by the Kety-Schmidt method. Although several limitations to the quantification derived from an inadequate spacial resolution remain unsolved, the performance of the present PET scanner and the method for the quantification employed provide regional estimates of brain circulation and oxygen metabolism more acurately than the PET system and the steady state method previously used.

Key words: rCBF, rCBV, rOEF, $rCMRO_2$, PET

INTRODUCTION

SINCE THE DEVELOPMENT of PET and the oxygen-15 steady-state (SS) technique,[1-3] regional values for cerebral blood flow (rCBF), the extraction fraction of oxygen (rOEF) and the metabolic rate of oxygen ($rCMRO_2$) have been studied in normal volunteers to obtain control values for comparison with patients and to examine the effect of age[4-8] but mean CBF values obtained by the SS technique were considerably lower than those obtained by the Kety-Schmidt (KS) method[9] and the radioactive inert gas clearance method.[10,11] Mean CBF for whole brain by the KS method was estimated to be 54 m*l*/100 g/min in adults, whereas the rCBF in the lentiform nucleus defined as "pure" gray matter and white matter by the SS method[8] was 43.0 m*l*/100 m*l*/min and 21.9 m*l*/100 m*l*/min, respectively, which may produce a mean global CBF of around 30 m*l*/100 m*l*/min by assuming that the gray to white matter volume ratio is 1. By means of a ^{133}Xe clearance method, the blood flow in cortical gray matter and deep

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white matter was reported to be 78.2 ± 9.8 ml/100 g/min and 18.7 ± 1.6 ml/100 g/min, respectively.[11] The major reason for lower values in the initial PET measurement was inadequate spacial resolution of the PET scanner employed.[12] Due to a partial volume effect, a concentration of radioactivity accumulated in a small structure or thin structure in the cortical gray matter is underestimated. In addition, the SS model itself includes the underestimation factor derived from tissue mixture.[13]

Recently, several improvements in measuring rCBF, rOEF, and $rCMRO_2$ have been made. Firstly, the autoradiographic method with $H_2{}^{15}O$ for rCBF measurement[14] and the $^{15}O_2$ single inhalation for $rCMRO_2$ measurement[15] were developed instead of the SS technique. Secondly, a Headtome IV scanner with an improved spacial resolution[16] was employed for clinical use. Thirdly, MR images which clearly depict cortical gyri are available as an anatomical reference instead of CT. Although anatomical regions had been defined by CT in our previous report on normals,[6] it was still difficult to identify some major cerebral gyri such as the angular gyrus and supramarginal gyrus.

The normal values obtained with a high resolution tomograph by the autoradiographic technique and the single inhalation method have not yet been published. Here we give the normal rCBF, rCBV, rOEF, and $rCMRO_2$ values estimated by means of these improved methods. The values are compared with values in the literature obtained by the KS method and the SS technique.

MATERIALS AND METHODS

Subjects

Eleven normal volunteers (nine males and two females) were studied. Their age ranged from 24 to 68 years (mean and 1 SD: 42.5 ± 18.2 years). All of them had always been free from neurological and psychiatric abnormalities. No organic lesions were found in an examination of brain MR imaging (T_1-weighted images) before a PET study. All the subjects gave written informed consent. This project was approved by the PET Research Committee of the Institution.

MRI

Prior to PET measurements, the subjects were studied with a 0.5 T whole body MR scanner (Magnex 50; Shimadzu, Kyoto). After taking midsagittal images, sixty T_1-weighted sequence axial images (TR 300 msec/TE 9 msec) were obtained parallel to an anterior commissure–posterior commissure (AC-PC) line with an axial interval of 2 mm. Axial T_1-weighted images were used as an anatomical reference.

Setting of scan slice in PET

All the PET images were obtained parallel to the AC-PC line. The AC-PC line in the PET measurement was first identified in a mid-sagittal image of T_1-weighted MRI as follows. Each patient was lying on a bed for the PET study. A lateral cranial X-ray photograph was taken with a metal line landmark placed parallel to the scanning slices. By fitting the cranial X-ray photograph to the MR-mid sagittal image and by measuring the angle produced by a metal line landmark and the AC-PC line of the MRI, the tilting angle of the PET gantry was determined.

PET measurements

PET scans were performed with a whole body 4 ring-7 slice positron tomograph (Headtome IV, Shimadzu, Kyoto).[16] The spacial resolution in the tomographic plane and axial resolution were 8 mm (FWHM) and 10 mm, respectively. The center to center spacing of slices was 15 mm. By moving the detector ring 7.5 mm in the axial direction, two different positions were scanned. A total of 14 axial images with 7.5 mm spacing were produced in each measurement.

The regional cerebral blood flow (rCBF), regional extraction fraction for oxygen (rOEF), regional metabolic rate for oxygen ($rCMRO_2$) and regional cerebral blood volume (rCBV) were measured by administering oxygen-15 labeled water,[14] and by inhaling oxygen-15 labeled molecular oxygen[15] and oxygen-15 labeled carbon monoxide,[15] respectively. The subject lay on the PET bed in the supine position, and the catheter was inserted into the radial artery. The catheter end was connected to a manometer tube of 0.5 mm inner diameter. The manometer tube was coiled two turns 20 cm from the catheter end and was taped on the face of the beta-ray detector. The other end of the manometer tube was connected to a Harvard pump to withdraw arterial blood during the $^{15}O_2$ and $H_2{}^{15}O$ study. After setting the tilting angle of the gantry, transmission scan was performed to correct tissue attenuation. The subjects inhaled trace doses of oxygen-15 labelled $C^{15}O$ through a small plastic face mask. The tracers were delivered continuously in a constant flow of air (0.5 l/min) and at a constant concentration of $C^{15}O$. The radioactive doses in the air delivered were 100 to 140 mCi/min or 3700 to 5180 MBq/min. The static scans for two positions were initiated at 3 min after $C^{15}O$ inhalation for 1 min to measure rCBV. The data aquisition time was 2 min for each position. Arterial blood was taken three times during the $C^{15}O$ study to measure the radioactivity in whole blood. Following a 15-min period to allow for the decay of ^{15}O radioactivity in the brain to the background level, the patient inhaled $^{15}O_2$ gas delivered through the face mask. The radioactive doses in the air delivered were 150 to 180 mCi/min (5550 to 6660 MBq/min). At 15 sec after starting inhalation, a dynamic scan with 5 sec data aquisition was repeated 24 times for each position. The arterial radioactivity concentration during $^{15}O_2$ inhalation was monitored by detecting β-rays with a plastic scintillator. The arterial blood was withdrawn at a constant rate of 5 ml/min. The arterial plasma concentration

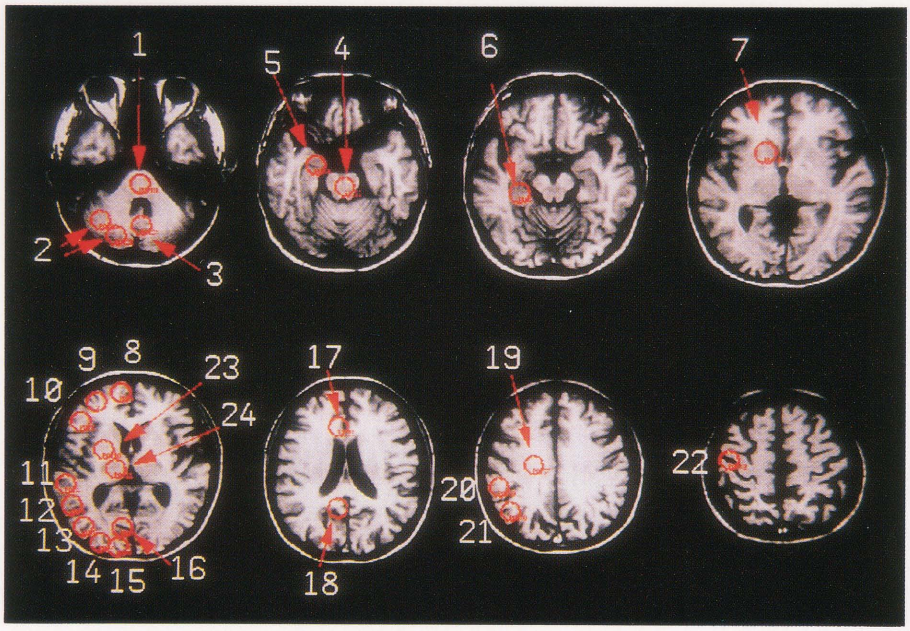

Fig. 1 Reference MR images corresponding to the PET images and the location of regions of interest. Sixty images of MR T_1-weighted sequence were obtained in each subject with 2 mm axial spacing. The nearest MR images were chosen as an anatomical reference. According to the human brain atlas by Duvernoy,[17] cortical gyri and deep brain structures were identified in the following regions; 1: pons, 2: cerebellar cortices (2 ROI), 3: cerebellar vermis, 4: midbrain, 5: entorhrinal area of parahippocampal gyrus, 6: parahippocampal gyrus, 7: caudate nucleus, 8: superior frontal gyrus, 9: middle frontal gyrus, 10: inferior frontal gyrus (pars orbitalis), 11: superior temporal gyrus, 12: middle temporal gyrus, 13: middle occipital gyrus, 14: superior occipital gyrus, 15: occipital cuneus, 16: precuneus, 17 and 18: cingulate gyrus (anterior part and posterior part), and 19: semioval center, 20: supramarginal gyrus, 21: angular gyrus, 22: somato-sensory cortex, 23: lentiform nucleus, 24: thalamus. These ROIs were manually set on the $CMRO_2$ images by visual inspection.

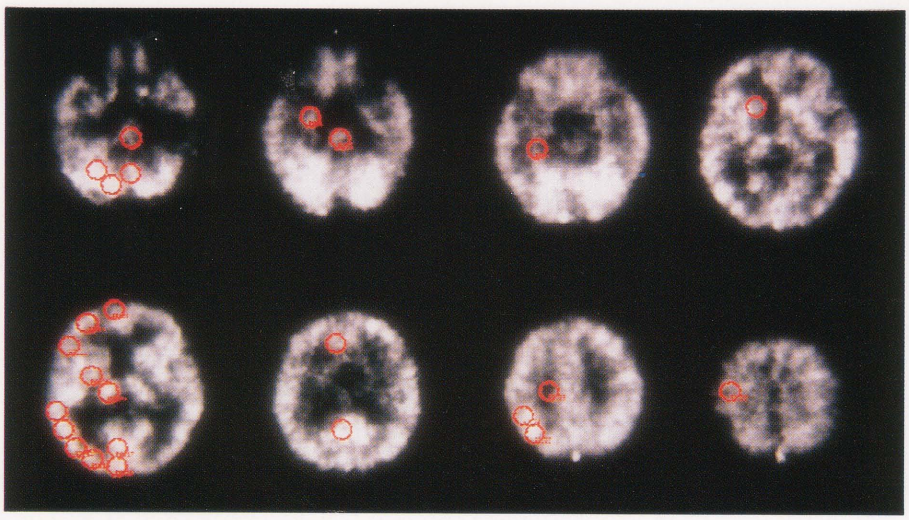

Fig. 2 The $CMRO_2$ images with the regions of interest located on the major cortical gyri and the deep brain structure corresponding with the region of interests in MR images.

of ^{15}O labeled metabolic water was calculated according to the method previously described by Iida et al.[17]

Following the $C^{15}O$ and $^{15}O_2$ inhalation study, oxygen-15 labeled water was administered intravenously as a bolus. The usual amount of the tracer was 5 m*l* and the dose of radioactivity was 30 to 40 mCi. Sequential scanning of 5 sec data aquisition repeated 9 times for each position was started at 10 to 20 sec after injection when

the radioactivity was detected in the brain. The arterial radioactivity concentration was monitored in the same way as in the $^{15}O_2$ study. The dispersion was corrected by deconvolving the beta probe curve with a fixed dispersion time constant of 3 sec.[18] Beta probe curve delay in comparison with radiotracer appearance in the brain was corrected by adjusting the initial rise in radioactivity in the blood and brain. The delay was 3 to 8 sec among the subjects.

Arterial partial pressure of O_2 and CO_2, hematocrit, and pH were measured in a blood gas tension analyzer (IL-1303, Instrumental Laboratory, USA). Mean values were 87.5 ± 7.2 mmHg, 38.5 ± 2.1 mmHg, $39.5 \pm 3.0\%$, and 7.412 ± 0.112, respectively. The arterial hemoglobin concentration was measured with a hemoglobin analyzer (MLK-1100, NIHON KODEN Ltd., Japan). The mean value was 12.0 g/d*l*. Systemic blood pressure and heart rate were monitored with a 2300 Finapress BP monitor (Omeda, USA) during the study.

Data analysis

Regional CBF, rCBV, rOEF, and $rCMRO_2$ were calculated by using tissue radioactivity and radioactivity of the blood input function, and the model equations. The blood to tissue partition coefficient of water was set at 1.0 for the CBF calculation. The functional data were transfered to a conventional unix work station system (TITAN 750, Kubota Computer, Tokyo) for further analysis.

The first step is to identify cerebral gyri in the MR images of individual subject by comparing them with the human brain atlas by Duvernoy.[19] Although the rectal gyri, orbital gyri, inferior temporal gyri, and fusiform gyri were easily found in MR images, these cortical gyri were not always depicted in the PET images, and were excluded from the analysis. The second step is to set regions of interest on the $CMRO_2$ images. The circular regions of interest (ROI) with a 16 mm diameter were manually located in the following regions on the PET images with MR reference: pons, midbrain, cerebellar cortices (2 ROIs), cerebellar vermis, caudate nucleus, lentiform nucleus, thalamus, superior frontal gyrus, middle frontal gyrus, inferior frontal gyrus (pars orbitalis), superior temporal gyrus, middle temporal gyrus, entorhrinal area of parahippocampal gyrus, parahippocampal gyrus, supramarginal gyrus, angular gyrus, middle occipital gyrus, superior occipital gyrus, occipital cuneus, precuneus, cingulate gyrus (anterior part and posterior part), and semioval center. Except for midline structures such as pons, midbrain, and vermis, ROIs were set on both hemispheres. The location of ROI in the reference MRI and the $CMRO_2$ image are shown in Figure 1 and Figure 2, respectively. The mean values for rCBF, rCBV, rOEF and $rCMRO_2$ in 11 subjects were calculated for each brain structure. Student's t-test was employed for the statistics.

Estimation of global CBF and $CMRO_2$

We calculated the global CBF and $CMRO_2$ by using the "pure" gray matter and white matter values in the PET measurement comparable with the Kety-Schmidt values. The values for the lentiform nucleus defined as "pure gray matter" and semioval center defined as white matter were combined with the 57 : 43 mass ratio for gray and white matter reported by Miller et al.[20]

RESULTS

Averages of regional values for rCBF, rCBV, rOEF, and $rCMRO_2$ in 11 subjects are shown in Table 1. The mean cortical CBF, CBV, OEF, and $CMRO_2$ were 55.4 ± 8.9 m*l*/100 m*l*/min, 4.80 ± 0.51 m*l*/100 m*l*, 0.42 ± 0.04 and 3.86 ± 0.42 m*l*/100 m*l*/min, respectively. The posterior part of the cingulate gyri showed the highest values for rCBF and $rCMRO_2$ among the brain structures, followed by the lentiform nucleus, the cerebellum, the caudate nucleus, and the thalamus. The parahippocampal gyri showed the lowest values among cortical gyri. Right-left asymmetry was not significantly found among the supratentorial structures. Regional CBV showed a high value in areas neighboring the venous sinuses, such as the transverse sinus, superior sagittal sinus and cavernous sinus.

Regional OEF values in the pontine nuclei, the midbrain, the parahippocampal gyri and the thalami were significantly lower than the mean OEF for cerebral cortices (0.42 ± 0.04) ($p < 0.05$ or less). There was no significant difference in rOEF among the cortical gyri.

The regional CBF of "pure" gray matter (lentiform nucleus, mean for right and left) and white matter (semioval center, mean of right and left) in this study was 73.5 m*l*/100 m*l*/min and 22.8 m*l*/100 m*l*/min, respectively. The $CMRO_2$ for the lentiform nucleus and semioval center were 5.22 m*l*/100 m*l*/min and 1.54 m*l*/100 m*l*/min, respectively. The global CBF and $CMRO_2$ calculated with these values were 51.7 m*l*/100 m*l*/min and 3.63 m*l*/100 m*l*/min, respectively.

DISCUSSION

The oxygen-15 steady state technique has been widely employed to measure rCBF, rOEF, and $rCMRO_2$ in clinical studies. It is based on a simple model and the procedure is not complicated[1-3] but it is not suitable for measuring the vasoreactivity to $PaCO_2$ and physiological stimulations because it takes 15 to 20 min for a single measurement. On the other hand, the ARG method is a quick way to measure rCBF which provides multiple measurement in a single study. However, as will be indicated below, the ARG method is sensitive to the dispersion and the delay of the arterial input function.[18,21,22]

The rCBF and $rCMRO_2$ values in the present study were higher in most gray matter structures than those

Table 1 Mean values of rCBF, rCBV, rOEF, and $rCMRO_2$ for 11 normal volunteers measured by means of Headtome IV PET scanner and the autoradiographic technique and the single breath inhalation method

Regions		rCBF (ml/100 ml/min)	rCBV (ml/100 ml)	rOEF	$rCMRO_2$ (ml/100 ml/min)
Posterior Fossa Structures					
Cerebellum	right	65.4 ± 10.9	5.49 ± 2.06	0.44 ± 0.06	4.78 ± 0.74
	left	67.2 ± 9.8	6.90 ± 3.94	0.44 ± 0.05	4.92 ± 0.85
Cerebellar vermis		54.7 ± 10.5	4.97 ± 2.65	0.42 ± 0.04	3.74 ± 0.87
Pontine nuclei		49.5 ± 8.2	2.72 ± 1.20	0.34 ± 0.04	2.77 ± 0.39
Midbrain		45.3 ± 6.0	3.08 ± 1.44	0.35 ± 0.05	2.62 ± 0.28
Supratentorial Structures					
Cortical gray matter					
Superior frontal gyrus	right	50.7 ± 12.3	3.90 ± 1.10	0.40 ± 0.06	3.35 ± 0.53
	left	53.5 ± 11.4	3.58 ± 0.87	0.40 ± 0.04	3.38 ± 0.46
Middle frontal gyrus	right	48.2 ± 8.8	4.23 ± 1.04	0.42 ± 0.06	3.38 ± 0.46
	left	44.7 ± 7.9	3.34 ± 0.63	0.43 ± 0.05	3.22 ± 0.61
Inferior frontal gyrus	right	52.8 ± 17.4	3.65 ± 0.67	0.42 ± 0.04	3.67 ± 1.20
	left	49.2 ± 13.0	3.22 ± 0.60	0.42 ± 0.05	3.43 ± 0.09
Superior temporal gyrus	right	71.8 ± 20.11	4.53 ± 1.05	0.41 ± 0.04	4.88 ± 1.07
	left	61.2 ± 18.4	4.23 ± 1.04	0.41 ± 0.04	4.16 ± 0.98
Middle temporal gyrus	right	61.5 ± 14.7	4.23 ± 1.04	0.42 ± 0.05	4.23 ± 0.70
	left	56.5 ± 12.6	3.97 ± 0.69	0.43 ± 0.05	4.19 ± 0.81
Parahippocampal gyrus entorhrinal area	right	39.8 ± 7.91	8.23 ± 5.50	0.37 ± 0.07	2.42 ± 0.34
	left	40.3 ± 6.33	3.86 ± 2.14	0.38 ± 0.04	2.59 ± 3.65
Parahippocampal gyrus	right	47.5 ± 7.6	5.79 ± 2.61	0.35 ± 0.04	2.80 ± 0.40
	left	45.8 ± 10.7	5.02 ± 2.46	0.37 ± 0.05	2.84 ± 0.60
Middle occipital gyrus	right	55.2 ± 12.1	3.96 ± 0.59	0.46 ± 0.07	4.15 ± 0.68
	left	51.6 ± 9.9	3.97 ± 0.92	0.43 ± 0.05	3.70 ± 0.54
Superior occipital gyrus	right	63.6 ± 16.3	6.56 ± 1.98	0.42 ± 0.05	4.39 ± 0.78
	left	62.4 ± 13.8	5.25 ± 1.29	0.45 ± 0.04	4.56 ± 0.61
Occipital cuneus	right	62.4 ± 13.8	12.7 ± 84.8	0.45 ± 0.08	4.56 ± 0.84
	left	54.8 ± 12.0	7.98 ± 3.00	0.44 ± 0.05	3.97 ± 0.55
Precuneus	right	40.5 ± 6.7	3.77 ± 0.70	0.44 ± 0.06	2.99 ± 0.32
	left	41.7 ± 8.7	4.20 ± 1.92	0.44 ± 0.05	3.03 ± 0.42
Supramarginal gyrus	right	57.5 ± 11.0	3.36 ± 0.59	0.42 ± 0.06	4.07 ± 0.69
	left	53.4 ± 9.7	3.81 ± 0.83	0.42 ± 0.06	3.79 ± 0.46
Angular gyrus	right	57.1 ± 13.4	3.95 ± 1.29	0.44 ± 0.04	4.18 ± 0.63
	left	56.4 ± 9.7	4.06 ± 0.87	0.43 ± 0.06	4.05 ± 0.46
Somato-sensory cortex	right	59.4 ± 15.9	4.03 ± 1.07	0.40 ± 0.03	3.89 ± 0.77
	left	55.5 ± 9.4	3.60 ± 0.73	0.42 ± 0.05	3.93 ± 0.72
Cingulate gyrus	anterior part	64.3 ± 9.1	6.40 ± 5.20	0.37 ± 0.04	3.97 ± 0.52
	posterior part	74.4 ± 14.7	8.52 ± 2.24	0.43 ± 0.04	5.14 ± 0.52
Central gray matter					
Caudate nucleus	right	65.3 ± 17.2	4.03 ± 1.65	0.39 ± 0.06	4.18 ± 0.87
	left	65.1 ± 13.7	3.71 ± 1.19	0.43 ± 0.06	4.62 ± 1.11
Lentiform nucleus	right	73.8 ± 23.3	3.56 ± 2.09	0.43 ± 0.05	5.22 ± 1.43
	left	73.2 ± 21.4	4.00 ± 0.90	0.42 ± 0.04	5.08 ± 1.14
Thalamus	right	61.2 ± 11.9	4.16 ± 1.50	0.37 ± 0.05	3.85 ± 0.50
	left	63.7 ± 8.8	4.16 ± 1.18	0.36 ± 0.04	3.74 ± 0.41
White matter					
semioval center	right	22.8 ± 3.1	1.83 ± 0.73	0.40 ± 0.06	1.54 ± 0.27
	left	22.8 ± 2.9	2.40 ± 0.95	0.40 ± 0.06	1.54 ± 0.25

obtained in previous PET measurements.[4–8] For example, the mean rCBF of lentiform nucleus was 53.1 ml/100 ml/min with the Headtome III and the SS technique[6] but 73.8 ml/100 ml/min with the Headtome IV and the autoradiographic method in this study. In early studies, the scanner employed was the ECAT II[4,7,8] or Headtome III[5,6] which had a spacial resolution as great as 12 mm in FWHM in the tomographic plane. For example, in-plane and axial spa-

cial resolution of Headtome IV were 8 mm and 10 mm respectively in FWHM but those of Headtome III were 10.5 mm and 13.1 mm respectively.[23] The improved spacial resolution of the present scanner may contribute most to the high values for rCBF and $rCMRO_2$ by reducing a partial volume effect in the transaxial and axial directions. Another reason for the increased CBF values is the difference in the method employed. As shown previously, the SS method inherently underestimates rCBF owing to tissue heterogeneity.[13] In the area of an equal mixture of gray and white matter, underestimation may reach around 18%.[14] Kanno et al.[24] demonstrated that this underestimation is less for the autoradiographic method (9% in the same situation). The cortical mean CBF with the SS technique and Headtome III was 43.0 ml/100 ml/min for the cerebrum, and 52.0 ml/100 ml/min for the cerebellum.[5] In the present study, the values were 55.4 ml/100 ml/min for the cerebrum and 66.3 ml/100 ml/min (mean of right and left) for the cerebellum. In the cortical ROI where a mixture of gray and subcortical white matter is expected, the autoradiographic measurement is much less affected by underestimation due to tissue heterogeneity especially in high flow areas.[24]

Correction for the dispersion and the delay of the arterial input function is critically important in measuring rCBF accurately. We previously reported that rCBF by the ARG method was equal to that by the SS technique when a dispersion time constant was around 10 sec.[21] The study also predicted that a smaller constant produced a higher CBF value by the ARG method. Later, we estimated the dispersion time constant to be 3 sec in the present beta probe system with a manometer tube 20 cm in length and 0.5 mm inner diameter.[18] The employment of a dispersion time constant of 3 sec in the present study may be another reason for the systematic increase in rCBF compared with that obtained by Headtome III and the SS method.

Relatively high rCBF and $rCMRO_2$ values were found in the cingulate gyri, cerebellar hemisphere, lentiform nucleus, caudate nuclei, superior temporal gyri, superior occipital gyri, and occipital cuneus. In contrast, parahippocampal gyri had the lowest values among the cortical gyri measured. Although the results might be greatly affected by the condition of the study (i.e., eye-covered or not), this distribution of high rCBF and $rCMRO_2$ was consistent with previous reports.[4,5,8]

In contrast to the remarkable increase in rCBF and $rCMRO_2$, rCBV values for most brain structures were not changed compared with previous results. For example, mean cortical CBV was 4.8 ml/100 ml in the present study but 4.3 ml/100 ml in the study by Yamaguchi et al.[5] and 4.7 ml/100 ml in the territory of the middle cerebral artery as reported by Leenders et al.[8]

Regional OEF for cerebral cortices and the caudate and the lentiform nuclei was simillar to that in previous reports. The values ranged from 0.40 to 0.45 although there were remarkable regional changes in rCBF and $rCMRO_2$ among structures. This confirmed the coupling of rCBF and $rCMRO_2$ under physiological conditions. It is interesting that the pontine nuclei, midbrain, parahippocampal gyri, and thalami had lower OEF than the cerebral cortices. This was not found in previous reports. Although we do not have an explanation for this, it is noteworthy that the perfusion of these areas is maintained by the posterior circulation through vertebro-basilar arteries (pons, mid brain, thalamus) and the branches of the posterior cerebral artery (parahippocampal gyrus).

The global CBF and $CMRO_2$ for the whole brain were originally estimated by Kety and Schmidt[9] to be 54 ml/100 ml/min and 3.30 ml/100 ml/min, respectively. Their values were confirmed by many studies using the radioactive inert gas method. It is now considered that normal CBF for the whole brain is between 45 and 60 ml/100 g/min, and normal $CMRO_2$ is between 2.9 and 4.0 ml/100 g/min.[25,26] The calculated values for global CBF (51.7 ml/100 ml/min) and $CMRO_2$ (3.63 ml/100 ml/min) in this study were in close agreement with these estimates.

Each region of interest was set on the PET image by using a corresponding T_1-weighted image. In a previous study, Yamaguchi et al. used the CT scan and standard brain atlas as an anatomical reference[5] but it was still difficult to identify some gyri, especially the marginal and angular gyri in the parietal lobe. By using MR images, it is easier to find the gyral structure.

In conclusion, the rCBF and $rCMRO_2$ estimated by means of Headtome IV and the autoragiographic and the single inhalation method were higher in most of the brain structures than those measured by means of a PET scanner with lower spacial resolution. The global rCBF and $rCMRO_2$ estimated by using the "pure" gray matter and white matter values for the present PET measurements were consistent with the KS method. Although several limitations to the quantification derived from inadequate spacial resolution remain to be clarified, the performance of the present PET scanner and the method employed in measurements may provide rCBF, rCBV, rOEF, and $rCMRO_2$ values with anatomical and physiological accuracy.

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