Cerebral Glucose Metabolic Rates After 30 and 45 Minute Acquisitions: A Comparative Study

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This study was undertaken to determine if measurements of absolute regional cerebral metabolic rate for glucose (rCMRglc) and variance of rCMRglc are independent of time between 30 and 45 min following injection of the radiotracer. Sixteen subjects received two sets of ^{18}FDG PET scans commencing 30 and 45 min following intravenous injection of ^{18}FDG. No statistically significant differences were detected in either absolute rCMRglc or rCMRglc variance between the two sets of scans. These data demonstrate that for most FDG PET studies, scanning can commence 30 min after injection of the radiotracer without compromising the metabolic data.

J Nucl Med 1992; 33:2103–2105

Positron emission tomography (PET) using 18-fluoro-2-deoxy-D-glucose (^{18}FDG) is used to measure glucose metabolism across a wide range of neuropsychiatric conditions (*1,2*). FDG PET is based on the 2-deoxy-D-glucose (2DG) autoradiographic technique developed by Sokoloff and collaborators (*3,4*). This was extended to measure glucose metabolism in humans using ^{18}FDG (*5,6*). PET studies using ^{18}FDG have added considerably to our understanding of diverse behavioral and neurologic disorders such as Alzheimer's disease, major depressive disorder and brain tumors (*1,2,7–9*).

PET data collection, to estimate regional cerebral metabolic rates for glucose, is conventionally begun 45 min following the injection of ^{18}FDG (*8,10*). Forty-five minutes is traditionally utilized because it is the time that was originally chosen for killing animals in the 2-deoxyglucose autoradiographic technique (*3,4*). Forty-five minutes after intravenous injection of 2DG, plasma tracer values fall to very low levels and the terms containing the rate constants fall to levels too low to influence the final result (*3,4*). Glucose metabolic rates estimated at 45 min, rather than earlier, are therefore thought to be less dependent on errors in the rate constants employed in their calculation.

Received Mar. 12, 1992; revision accepted Jul. 21, 1992.

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There is a logistical advantage in human PET studies to begin data collection earlier as some scan subjects are unable to stay in the scanner for prolonged periods of time. This occurs when transmission scans are performed prior to FDG injection to correct for attenuation (*10*). Because the subject may be in the scanner from the start of transmission scanning, shortening the FDG uptake period decreases the overall time spent in the scanner. It may also decrease the possibility of head movement between the transmission and emission scans. Although it is possible to perform transmission scans after injection of FDG (*11*), this technique is not widely available. However, if calculated rather than measured attenuation correction is performed, shortening the uptake period would be less beneficial because the subject does not have to be restrained in the scanner during the uptake period. The increased accuracy of measured attenuation correction (*10*) is frequently desirable, however, and shortening the uptake period is advantageous.

Various groups using ^{18}FDG PET commence scanning anywhere from 30 to 45 min following tracer injection (*1,8,10*). Metabolic data from studies using different time collection protocols are frequently compared with little attention paid to time of data collection as a potential source of variance. This study was initiated to determine whether measured cerebral metabolic rates for glucose (rCMRglc) are independent of time for scans starting between 30 and 45 min. Additionally, we were interested in assessing to what degree increased dependence upon the value of the rate constants at 30 min affects the variance of measured rCMRglc.

SUBJECTS AND METHODS

Sixteen subjects (8 men and 8 women) aged 20 to 82 (mean age ± s.d. = 43 ± 17) were chosen from subjects already undergoing FDG PET studies at the National Institute on Aging. All subjects were participating in research protocols conducted by the Laboratory of Neurosciences (LNS). Eight were healthy normal volunteers and the other eight met DSM-3-R criteria (*12*) for childhood onset Obsessive Compulsive Disorder (OCD). Both groups of subjects were free of other significant medical, neurologic or psychiatric disorders and had all laboratory values within the normal range. Subjects with OCD were free of psychotropic medication for at least two weeks before the scan. Detailed clinical

TABLE 1A
Cerebral Glucose Metabolism mg/(100 g × min) After 30 and 45 Minute Uptake (means ± s.d.)

Region	Rater 1			Rater 2		
	30-min scan	45-min scan	Absolute difference*	30-min scan	45-min scan	Absolute difference*
R. Front	8.21 ± 1.34	8.43 ± 1.26	0.23 ± 0.20	8.53 ± 1.33	8.68 ± 1.27	0.15 ± 0.32
L. Front	8.39 ± 1.59	8.54 ± 1.48	0.16 ± 0.28	8.75 ± 1.65	8.76 ± 1.63	0.01 ± 0.20
R. Temp	7.93 ± 1.05	8.17 ± 1.04	0.24 ± 0.23	8.28 ± 1.01	8.35 ± 0.95	0.07 ± 0.26
L. Temp	8.26 ± 1.30	8.26 ± 1.36	0.00 ± 0.28	8.71 ± 1.36	8.58 ± 1.29	−0.13 ± 0.29
R. Par	8.80 ± 1.33	8.94 ± 1.30	0.14 ± 0.27	8.81 ± 1.40	8.81 ± 1.43	0.00 ± 0.31
L. Par	8.57 ± 1.88	8.71 ± 1.74	0.14 ± 0.33	8.70 ± 1.86	8.82 ± 1.85	0.12 ± 0.24
R. Senmt	8.86 ± 1.23	9.10 ± 1.22	0.24 ± 0.40	8.73 ± 1.36	8.65 ± 1.31	−0.08 ± 0.36
L. Senmt	8.85 ± 1.64	8.95 ± 1.59	0.11 ± 0.37	8.62 ± 1.65	8.67 ± 1.63	0.05 ± 0.26
R. Cal	7.74 ± 0.91	7.85 ± 0.91	0.11 ± 0.25	8.12 ± 1.06	8.07 ± 1.01	−0.05 ± 0.18
L. Cal	7.89 ± 1.10	7.97 ± 1.10	0.09 ± 0.26	8.31 ± 1.31	8.24 ± 1.23	−0.07 ± 0.24
R. Orbfr	6.62 ± 1.12	6.83 ± 1.17	0.22 ± 0.30	7.11 ± 1.39	7.10 ± 1.21	−0.01 ± 0.31
L. Orbfr	6.91 ± 1.24	7.09 ± 1.15	0.18 ± 0.45	7.18 ± 1.22	7.21 ± 1.19	0.02 ± 0.45
R. Basgn	9.08 ± 1.69	9.32 ± 1.43	0.24 ± 0.71	9.49 ± 1.62	9.30 ± 1.48	−0.19 ± 0.39
L. Basng	9.00 ± 1.48	9.35 ± 1.36	0.35 ± 0.55	9.20 ± 1.60	9.25 ± 1.50	0.05 ± 0.45

* No significant difference ($p > 0.01$).

Table 1 shows the absolute regional cerebral metabolic rate for glucose (rCMRglc), global gray CMRglc and variance of rCMRglc after 30 and 45 min acquisitions.

R = right side, L = left side, Front = frontal, Temp = temporal, Par = parietal, senmt = sensorimotor, Cal = calcarine, Orbfr = orbitofrontal, Basng = basal ganglia.

characteristics of both groups of subjects have been previously reported (*10,13*).

PET scans were performed on a Scanditronix PC 1024-7B tomograph (Uppsala, Sweden, in plane resolution = 6 mm, axial resolution = 10 mm). All subjects were studied in the resting state with eyes patched and ears occluded, with room noise kept to a minimum. A thermoplastic mask was used to maintain head position during the scan. Two multi-slice transmission scans offset by 6.9 mm in the z-axis were performed to provide an interleaved set of 14 slices extending from 10 to 100 mm above the inferior orbito-meatal line. Five millicuries of ^{18}FDG were injected intravenously and arterial blood samples were obtained over a 60-min period following the injection to obtain plasma for measurement of radioactivity and glucose. Each subject received two 10-min scans, the first one commencing 30 min and the other 45 min following the injection of FDG.

Gray matter rCMRglc was calculated using Brook's modification of the Sokoloff equation (*14*) with the following rate constants: k1 = 0.102, k2 = 0.13, k3 = 0.062 and k4 = 0.0068. A lumped constant of 0.418 was used to estimate rCMRglc. A standard anatomical template developed at the LNS, consisting of multiple circular regions of interest 8 mm in diameter, was used to analyze the metabolic images (*10*). CMRglc from these multiple small regions was averaged to yield lobar metabolic values (*10*). Regions of interest examined included the frontal, orbitofrontal, temporal, parietal, sensorimotor, calcarine regions and the basal ganglia bilaterally. All images were independently analyzed by two raters (AK and AB). Rater 1 (AK) independently placed regions of interest on the 30-min images. These regions were subsequently transferred to the 45-min images without modification. Rater 2 (AB) independently analyzed the 45-min images and subsequently transferred the regions of interest, without any modification to the 30-min images. This process of randomization eliminates the introduction of rater bias into the analysis.

Multiple paired t-tests were performed on rCMRglc values from cortical and subcortical regions in order to identify any significant differences between values estimated at 30 and 45 min by both raters. The F statistic was computed to examine variance in rCMRglc estimates at 30 and 45 min.

RESULTS

Table 1A lists the rCMRglc for all major gray matter structures estimated after 30 and 45 min uptake of 18 ^{18}FDG. The global mean gray (Table 1B) is the mean rCMRglc of the following gray matter structures: right and left-frontal, temporal, parietal, sensorimotor, calcarine, orbitofrontal regions (*10*) and the right and left basal ganglia. There were no statistically significant differences in

TABLE 1B
Mean Global Mean Gray Glucose Metabolic Rates

	mg/100 g × min)		
	30 min	45 min	Absolute difference*
Rater 1	7.99 ± 1.13	8.16 ± 1.07	0.17 ± 0.14
Rater 2	8.35 ± 1.17	8.34 ± 1.13	−0.02 ± 0.14

Coefficient of variation of rCMRglc at 30 and 45 min

	30 min	45 min	Absolute difference
Rater 1	15.04	13.90	−1.14
Rater 2	14.0	13.50	−0.5

See Table 1A for definitions.

rCMRglc between the 30 and 45 min scans in any of the individual gray matter regions examined. The difference in global mean gray CMRglc between the two scans, as obtained by both raters, was also minimal and statistically insignificant. Table 1B also shows the coefficient of variation in rCMRglc in all 16 subjects, after the 30 and 45 min uptake periods. While rCMRglc shows slightly more variance at 30 min when compared to the 45-min scan (as determined by both raters independently), the differences were minor and statistically insignificant (F statistic).

CONCLUSIONS

These data demonstrate that under stable experimental conditions potential errors in rate constants, as a function of time, do not significantly influence estimates of rCMRglc. Fluorine-18-FDG PET scans can therefore be reliably performed 30 min after intravenous injection of the radiotracer. This can reduce the total scan time by about 15 min, without any compromise of the physiologic information. In neuropsychiatric conditions such as Alzheimer's disease, this can be a major logistical advantage and will help minimize patient discomfort. The shorter scan time also allows patients to void 15 min earlier after the scan, thereby reducing radiation exposure to the bladder (*15*). The variance of rCMRglc estimates, though marginally greater after 30 min of uptake, is also statistically insignificant between the two uptake time points. This provides additional corroboration that estimated metabolic values are independent of time of acquisition of data between 30 and 45 min following injection of radiotracer.

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