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Necessity of a uniform start for scanning after FDG injection in brain PET study

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The authors' goal was to show the importance of starting scanning at a uniform time after F-18 fluorodeoxyglucose injection in positron emission tomography (PET) brain study. ***Method:*** Fifteen healthy normal subjects underwent FDG-PET to obtain glucose metabolic images starting 60 min and 70 min after FDG injection, respectively. The two sets of images were compared in a voxel-by-voxel analysis. ***Results:*** In the bilateral posterior cingulate gyrus, parietal and frontal association cortices, the FDG uptakes were larger on the 70 min scan images than on the 60 min scan images; the 60 min scans resembled Alzheimer's metabolic reduction area. Similarly the FDG uptakes were larger in the pons and vermis on the 60 min scan image than on the 70 min scan image. ***Conclusions:*** Regional FDG uptake is different depending on the time scanning starts after FDG injection, even with a 10 minute difference in start time and different scanning time may lead to misdiagnosis. It is important to standardize the start time of FDG PET after FDG injection in brain PET.

Key words: positron emission tomography (PET), F-18 fluorodeoxyglucose (FDG), normal human brain, scanning time

INTRODUCTION

Uptakes of 2-[F-18]fluoro-2-deoxy-D-glucose (FDG) are different for various regions of the normal brain when scans are taken earlier and later in positron emission tomography (PET).[1] This choice of start time effects the FDG PET findings and diagnosis of Alzheimer disease (AD) with a late start for scanning returning superior findings to early scans in detecting hypometabolic regions in patients with AD.[2] The present study aimed to determine whether there are any regional differences in FDG uptake in the normal human brain in only 10 minutes different starting in scans (starting only ten minutes apart at 60 minutes and 70 minutes) after FDG injection by using voxel-by-voxel analysis with statistical parametric mapping (SPM) which is suitable for group comparison and three dimensional stereotactic surface projections (3D-SSP), which is suitable for individual evaluation.

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METHODS

Subjects

We studied 15 healthy normal volunteers (7 men, 8 women; average age ± SD, 40.0 ± 8.2 years; range: 24–53 years) who had no clinical symptoms of cognitive deficits or neurological disease and were not taking any acute or chronic medications at the time of the study. The study was approved by the Internal Ethics Committee at our institution.

PET Procedure

PET was performed with PET scanner Allegro (Philips, Cleveland, USA) under resting conditions with the subject's eyes closed and ears unplugged. All subjects had fasted for at least 4 hours before PET scanning. Emission scan was performed for 20 min starting at 60 minutes after administration of 185 MBq of FDG. Images were

reconstructed by 2.5 D-RAMLA.[3] Attenuation correction was performed by analytical attenuation correction with uniform attenuation factor (0.095/cm) inside an elliptical outline. Ninety PET slices were acquired using 128 × 128 matrix with a pixel dimension of 2 mm, and the slice thickness was 2 mm.

Data Analysis

For the 60 minute image, consecutive dynamic images 60 min after injection (from 60 min to 70 min) were summed, and for the 70 min image, consecutive dynamic images 70 min after injection (from 70 min to 80 min) were summed. To evaluate the regional differences between the 60 min and 70 min scans, statistical processing was performed with Statistical Parametric Mapping 2 (SPM2) software (Wellcome Department of Cognitive Neurology, London, UK) (http://www.fil.ion.ucl.ac.uk/spm/). Calculations and image matrix manipulations were performed in MATLAB (Mathworks Inc., Natick, MA, USA). All the individual scans were transformed into a standard stereotactic anatomical space. All images were smoothed with a 12 mm isotropic Gaussian kernel to increase the signal-to-noise ratio and to compensate for the differences between individuals in gyral anatomy. Individual FDG images were adjusted using proportional scaling to compare the effects of the early and late scans. Paired *t* test was performed between the 60 and 70 min scan groups. Significance was accepted if the voxels survived an un-

Table 1 Regions of relative hypometabolism and hypermetabolism for scans starting 60 mins after FDG injection compared with those taken after 70 mins in the same subjects. Threshold is $p < 0.001$, uncorrected. The coordinate indicates the region of peak *t* value in the significant area

		t	*x*	*y*	*z*
70 > 60	Lt. inferior parietal lobule	11.19	−38	−58	43
	Rt. inferior parietal lobule	9.87	27	−69	42
	Rt. superior frontal gyrus	8.16	17	20	50
	Rt. precuneus	8.12	3	−65	28
	Lt. medial frontal gyrus	7.95	−19	47	20
	Rt. inferior parietal lobule	6.61	48	1	30
60 > 70	Vermis	9.13	8	−52	−22
	Pons	8.06	−1	−32	−34

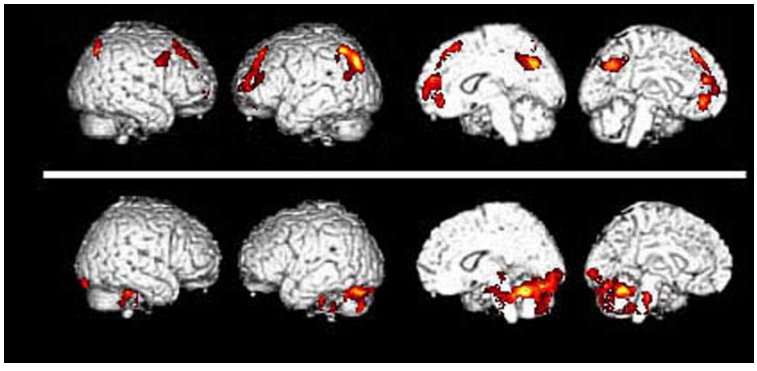

Fig. 1 Comparison of regional cerebral metabolic reductions shown by Statistical Parametric Mappings (SPM) in normal subjects obtained with 60 min and 70 min uptake scans. Regional FDG uptakes in the 70 min scan are larger than those in the 60 min scan in the bilateral parietal and frontal association cortices, and posterior cingulate gyrus (*upper row*). In the bilateral lateral upper part of the cerebellar hemisphere, vermis and the pons, regional FDG uptakes in the 60 min scan were larger than those in the 70 min scan (*lower row*).

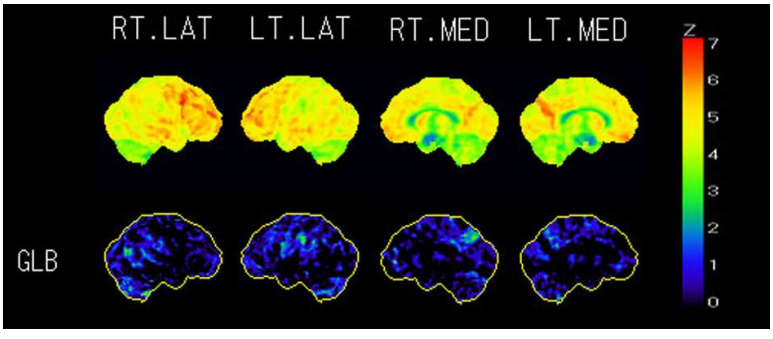

Fig. 2 Representative 60 min starting time scan of start time for FDG-PET image demonstrated by 3D-SSP. The subject was a 33-year-old normal man. FDG uptake was significantly reduced in the bilateral parietal and precuneus cortices on the Z score map (*lower row*).

corrected threshold of $p < 0.001$.

In addition, based on the group comparison study, we analyzed the pattern of metabolic changes in 60 min scan images of individual subjects using 3D-SSP[4] system, which generates voxel-by-voxel statistical images in comparison with the 70 min scan image database. Individual Z score maps at 60 min and 70 min scan were generated by "iSSP" (Nihon Medi-Physics Corp, Nishinomiya, Japan), which consists of 3D-SSP programs and was specifically designed to support clinical diagnoses, using a database consisting of 70 min and 60 min scans. On the Z score map, a visual inspection was conducted to analyze whether each subject had an Alzheimer pattern, showing posterior cingulate and/or parietotemporal association cortical metabolic reduction.

RESULTS

As shown in Table 1, in the bilateral posterior cingulate gyrus, parietal and frontal association cortices, and subcallosal cortices, FDG uptakes were larger on the 70 minute scan image than on the 60 minute scan image ($p < 0.001$, Fig. 1 *upper row*), and the FDG uptakes were larger in the pons and cerebellar hemisphere and vermis on the 60 minute scan image than on the late scan image ($p < 0.001$, Fig. 1 *lower row*). Visual inspection revealed that 4 of 15 subjects' 60 scan Z score maps derived from the 70 min scan database showed an Alzheimer metabolic pattern. Figure 2 shows the 3D-SSP image of a 33-year-old normal male. The Z score map shows significant bilateral parietal and precuneus FDG uptake reduction compared with the 70 min scan database.

DISCUSSION

Previous studies have shown that a thirty minute difference in starting time for FDG-PET brain study affects the findings.[1,2] However, while our study agreed that FDG uptake is not consistent we found there are regional uptake differences between early and late scans even within a ten minute after intravenous injection of FDG. Moreover we found that diagnoses using images which do not have a regulated scan time start might lead to misdiagnosis. Reasons for regional metabolic differences between different scan time starts have been discussed in previous reports.[1,2] It has been suggested that differences may be due to a difference in regional rate constants. For example, K4 cannot be assumed to be zero for a long period after injection. Previous researchers have also reported a tendency for higher K1 and lower K3 in the cerebellum than in the cerebrum.[5,6] Further investigation is needed using techniques such as parametric images obtained with arterial input functions.

FDG PET is considered to be useful in detecting early AD and predicting AD changes in mild cognitive impairment subjects by demonstrating parietotemporal and/or posterior cingulate and precuneal FDG uptake reduction.[7,8] However, as this study showed, scans starting only 10 minutes earlier may lead to misdiagnosis of early AD in normal subjects (Fig. 2); this is due to the previous reports that showed in later scans in normal subjects parietotemporal and posterior cingulate FDG uptake is slightly larger than other regional uptakes.[1,2,9] Therefore we think a uniform start for scanning after FDG injection would avoid misdiagnosis of this case.

CONCLUSION

In studies of brain FDG-PET, scan time starts should be strictly uniform to avoid possible misdiagnosis.

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