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Improvement of Glucose Metabolism in the Visual Cortex Accompanies Visual Field Recovery in a Patient with Hemianopia

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Damage to the visual cortex or the geniculostriatal pathways could cause homonymous visual field (VF) defects at the contralateral side of the lesion. In clinical practice, it is known that the VF defects are gradually recovered over months on the cases. We report a case with recovered homonymous hemianopia following an infarction in the visual cortex by positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) and ^{11}C-flumazenil (FMZ). A 58-year-old man experienced defect of left VF, and magnetic resonance imaging (MRI) revealed a localized infarction in the right occipital lobe. Goldmann VF perimetry revealed left homonymous hemianopia, but central VF was intact. Three months after the onset of infarction, we measured cerebral glucose metabolism with FDG and FMZ binding using PET. FMZ binding reflects the density of surviving neurons. Moreover, eight months after the onset, FDG-PET scan was performed. Goldmann VF perimetry was also performed at the same times of PET examinations. Decrease of cerebral glucose metabolism in the right anterior striate cortex was observed at three months after onset, while FMZ binding in the same area did not decrease in the patient. At eight months after onset, we observed recovery of VF and improvement of cerebral glucose metabolism in the anterior striate cortex. We presented change of cerebral glucose metabolism using PET accompanying improvement of VF. Evaluation of cerebral glucose metabolism and FMZ binding in the striate cortex is useful for estimating the prognosis of hemianopia caused by organic brain damage.

Keywords: homonymous hemianopia; positron emission tomography; recovery; striate cortex; visual field
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Introduction

Damage to the visual cortex or the geniculostriate pathways produce homonymous visual field (VF) defects contralateral to the side of the lesion. Stroke is the most common cause of homonymous hemianopia, and 50-70% of all hemianopia cases are caused by stroke (Zhang et al. 2006). In some cases, in clinical practice, it is known that the VF defects improve gradually over several months. Positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) has been used to study clinical-metabolic correlations in patients with ischemic lesions of the visual cortex or optic radiations (Bosley et al. 1987). However, early FDG-PET findings do not reflect a residual function of the visual cortex due to diaschisis. Recently, diffusion-weighted magnetic resonance imaging (MRI) (Kidwell et al. 1999) and ^{11}C-flumazenil (FMZ)-PET (Heiss et al. 2000) have been used to evaluate acute ischemic cerebral lesions, and they reported that FMZ binding was useful to presumption of VF prognosis. FMZ binding reflects the density of surviving neurons. Moreover, in our previous study in which we examined 8 hemianopia patients with FDG- and FMZ-PET, we showed that an evaluation of the cerebral glucose metabolism in the visual cortex more than one month after the onset is useful for estimating the VF prognosis (Suzuki et al. 2008). Here we present the case of a patient with hemianopia following an infarction in the visual cortex. Using PET, we show that cerebral glucose metabolism changes accompany improvements in the VF defect.

Materials and Methods

Case presentation

A 58-year-old right-handed man without any past history of

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serious illness experienced a defect in the left VF. His corrected visual acuity was 20/20 in both eyes, and a clinical examination of the fundi revealed no abnormality. The patient's eye movements were full and smooth. Goldmann VF perimetry revealed incomplete left homonymous hemianopia, and the central 10° of the VF was mostly maintained (Fig. 1A). Hemispatial neglect was not observed. An MRI revealed a localized infarction in the right striate cortex. Three months after the onset of hemianopia, another Goldmann perimetry as well as FDG-PET and FMZ-PET scans were performed. Goldmann perimetry and an FDG-PET scan also were performed 8 months later.

A total of 15 healthy individuals, including 6 men and 9 women (age, 54.3 ± 4.4 years), volunteered as subjects for the control group. All the subjects underwent MRI and PET with FDG, and FMZ. None of the participants exhibited any other neurologist-diagnosed neuropsychiatric diseases. Neither the control subjects nor the patient had taken any neuro-psychiatric drugs. Informed consent was obtained from all the subjects prior to their participation in the study. The study protocol was approved by the ethics committee of the Tokyo Metropolitan Institute of Gerontology. All the procedures conformed to the tenets of the Declaration of Helsinki.

Magnetic resonance imaging scans

All the participants underwent MRI scans in a 1.5-Tesla scanner (Signa Horizon, General Electric, Milwaukee, WI, USA). We obtained transaxial images with T1-weighted contrast [three-dimensional spoiled gradient recalled acquisition (3D-SPGR), repetition time (TR) = 9.2 ms, echo time (TE) = 2.0 ms, matrix size = 256 × 256 × 124, and voxel size = 0.94 × 0.94 × 1.3 mm], T2-weighted contrast (first spin echo, TR = 3,000 ms, TE = 100 ms, matrix size = 256 × 256 × 20, and voxel size = 0.7 × 0.7 × 6.5 mm), and fluid-attenuated inversion recovery (FLAIR) [TR = 10,002 ms, TE = 106.5 ms, inversion time (TI) = 2,500 ms, matrix size = 256 × 256 × 19, and voxel size = 0.86 × 0.86 × 5 mm] imaging techniques (Suzuki et al. 2012).

PET data acquisition

We acquired PET scans using a SET 2400W scanner (Shimadzu, Kyoto, Japan) at the Positron Medical Center, Tokyo Metropolitan Institute of Gerontology.

For the FDG-PET scan, we injected an intravenous bolus of 2.5 MBq/kg (body weight) FDG, and each subject was instructed to lie down with their eyes closed during the accumulation time. A 6-min emission scan in the three-dimensional mode was started 45 min after the injection of FDG, and 50 transaxial images with an interslice interval of 3.125 mm were obtained (matrix size = 128 × 128 × 63 and voxel size = 2.0 × 2.0 × 3.125 mm). The tomographic images were reconstructed using the filtered back-projection method with a Butterworth filter (cut-off frequency = 1.25 cycles/cm; order = 2) (Suzuki et al. 2012).

For the FMZ-PET scan, we injected an intravenous bolus of 6.0 MBq/kg (body weight) FMZ, and the FMZ binding data were acquired in the three-dimensional static scanning mode (matrix size = 128× 128 × 63 and voxel size = 2.0 × 2.0 × 3.125 mm) from 20 to 40 min after the FMZ injection (Mishina et al. 2000; Suzuki et al. 2012). The 20-min emission scan image was represented to reflect the FMZ-binding capacity (Mishina et al. 2000).

In each PET scan, attenuation was corrected by performing a transmission scan using a rotating $^{68}Ga/^{68}Ge$ source.

Data processing

We registered the three-dimensional PET images to the individual 3D-SPGR MRIs using the statistical parametric mapping (SPM8) software (Friston et al. 1991), which was implemented in MATLAB (MathWorks, Sherborn, MA). Further data analysis was performed using Dr. View software (AJS, Tokyo, Japan). Regions of interest (ROIs, 8-mm diameter) were interactively defined on the 3D-SPGR MRIs by visual observation with reference to the co-registered PET images (Suzuki et al. 2012). Bilateral ROIs were defined in the posterior striate cortex, anterior striate cortex, extrastriate cortex, cuneus and thalamus. We measured cerebral glucose metabolism and FMZ binding in these regions. These two parameters were compared with those recorded for the homologous regions in the contralateral hemisphere by calculating the ipsilateral/contralateral (I/C) ratio (Suzuki et al. 2008). We defined a significant change in the I/C ratio in the patient as an increase or decrease over the normal mean ± 2 SD (Suzuki et al. 2012).

Results

We observed a decrease in glucose metabolism and a reduction in FMZ binding in the area of the infarction (i.e., in the right occipital cortex) 3 months after the onset. The I/C ratio for cerebral glucose metabolism was decreased in the anterior striate cortex of the patient 3 months after the onset, but improved 8 months after the onset (Fig. 2, Table 1). The I/C ratio of the FMZ binding of the patient was not significantly changed (Table 1). Goldmann VF perimetry revealed that the VF was improved three months and eight months after the onset compared with previous measurements (Fig. 1).

Discussion

In the present case, we observed a left peripheral VF defect and a decrease in cerebral glucose metabolism in the right anterior striate cortex 3 months after onset. The patient exhibited recovery of the VF and improvement in cerebral glucose metabolism in the right anterior striate cortex 8 months after the onset. The central VF almost maintained, and cerebral glucose metabolism change in the posterior striate cortex was not observed.

The central VF representation is located at the occipital pole in the striate cortex, and the peripheral VF corresponds to the anterior parts of the striate cortex (Horton 2006). The most striking feature of the visual field map is the disproportionately large fraction of striate cortex assigned to the representation of central vision. The central 10° occupies half of the surface area of the posterior striate cortex. Lesions in the primary visual cortex do not always produce a complete loss of vision from the appropriate VF; some central vision usually remains intact (McFadzean et al. 1994) due to the fact that input from the center of the retina is spread over a large portion of the striate cortex.

Previous PET studies have observed decreased cerebral glucose metabolism in the contralateral striate cortex of patients with hemianopia following an infarction (Bosley et al. 1987; Suzuki et al. 2008), and increases in cerebral glucose metabolism in the striate cortex are associated with

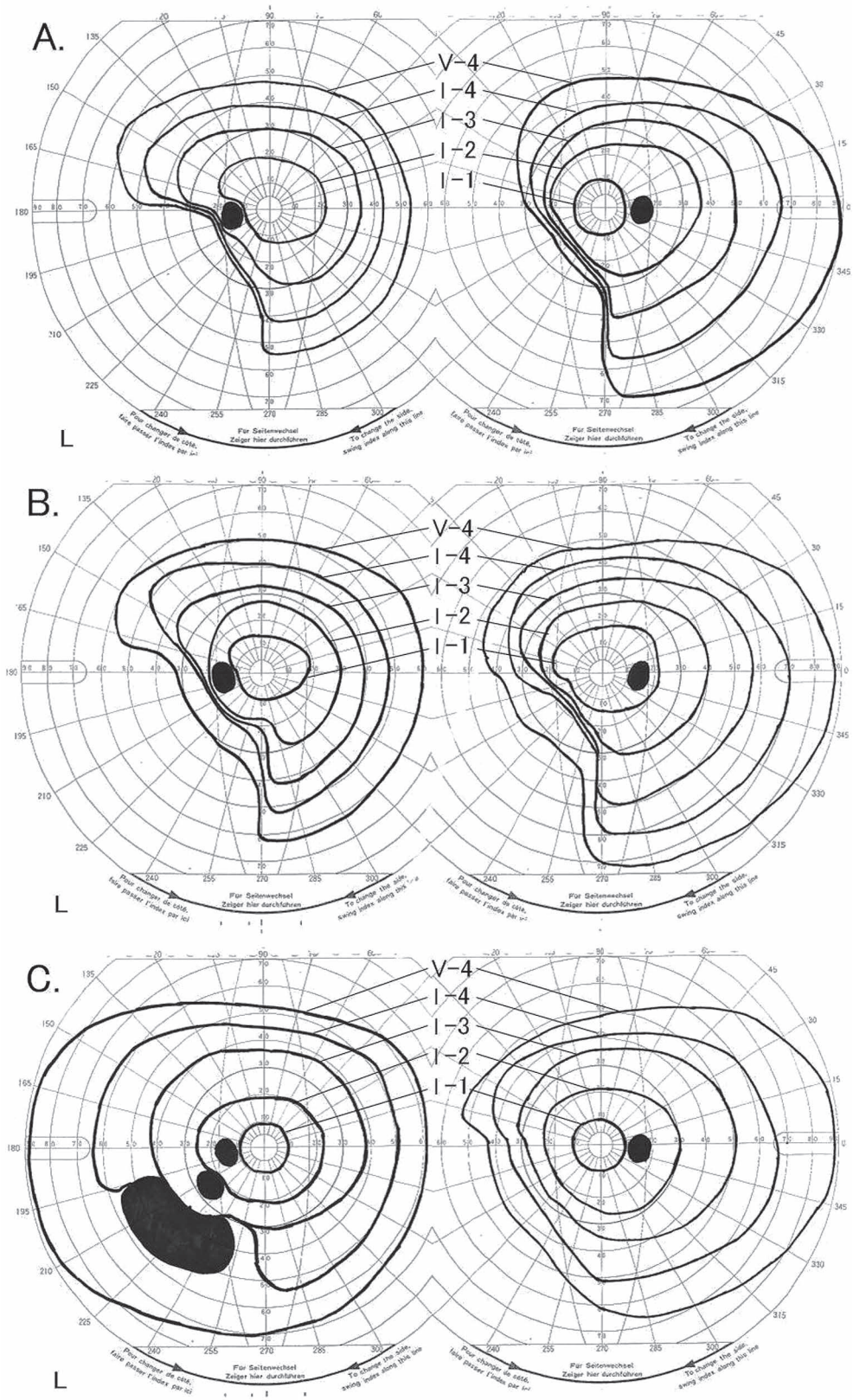

Fig. 1. Improvement of visual field.
The visual field (VF) of a patient with hemianopia one month (A), three months (B), and eight months (C) after the onset. Incomplete left homonymous hemianopia was observed. The central VF was intact from the time of the onset, and the peripheral VF improved gradually over time.

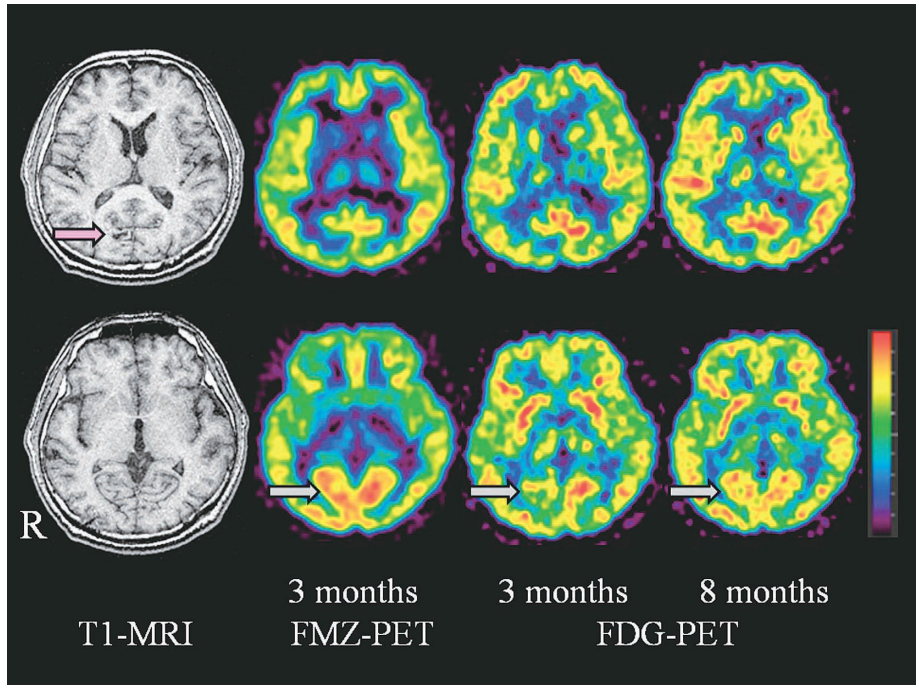

Fig. 2. Positron emission tomographic image of a patient with hemianopia.
Shown are the T1-weighted magnetic resonance image (MRI; left), ^{11}C-flumazenil (FMZ)-positron emission tomographic (PET) image (center) and ^{18}F-fluorodeoxyglucose (FDG)-PET image (right) in the patient with hemianopia. The FMZ-PET was obtained 3 months after the onset of hemianopia, and the FDG-PET was obtained three months and eight months after the onset. A cerebral infarction was observed in the right occipital cortex (pink arrow, upper). Glucose hypometabolism was observed in the right striate cortex three months after the onset (gray arrows, lower). FMZ binding was not decreased in the striate cortex. Glucose metabolism improved in the striate cortex eight months after the onset.

Table 1. The ipsilateral/contralateral (I/C) ratio for cerebral glucose metabolism using ^{18}F-fluorodeoxyglucose (FDG) and ^{11}C-flumazenil (FMZ) binding in the brain of the patient and control subjects.

Term		Area				
		Posterior striate cortex	Anterior striate cortex	Extrastriate cortex	cuneus	thalamus
FDG	3 months	0.962	0.889[a]	0.959	0.998	1.000
FMZ	3 months	0.995	0.979	1.074[b]	1.069[b]	1.107[b]
FDG	8 months	0.997	0. 998	0. 997	0.999	0.991
Average of control subjects						
FDG		0.999	0.994	1.008	0.995	1.004
		± 0.036	± 0.027	± 0.027	± 0.038	± 0.020
FMZ		1.000	1.005	1.006	1.000	0.991
		± 0.021	± 0.014	± 0.024	± 0.003	± 0.052

[a]Significant decrease in the I/C ratio (below the normal average – 2 SD).
[b]Significant increase in the I/C ratio (over the normal average + 2 SD).

recovery of the VF. On the other hand, Bosley et al. (1987) observed that 3 patients did not recover the VF and glucose metabolism did not improve. It is known that reorganization phenomena of the brain cause along with recovery of functions in patients after infarction. The reorganization phenomena represent over-activation of areas belonging to the physiological neural network for a specific task or activation of unusual areas that attempt to replace the functions of the damaged tissue (Rossini et al. 2007). However, the recovery mechanism of the striate cortex is not well known. In our previous PET study of hemianopia, we observed that adenosine A_1 receptor density on the injured side of the striate cortex was elevated in recovered patients (Suzuki et al. 2012). Elevated adenosine A_1 receptor activity may be

associated with a protective role in damaged tissues via the reduction of metabolic damage due to hypoxia or glucose-oxygen deprivation (Logan and Sweeney 1997). Moreover, in the current hemianopia patient, the I/C ratio for FMZ binding increased in the extrastriate cortex, cuneus, and thalamus. A previous animal study reported that cortical retinotopic maps are reorganized following an ischemia, and the plasticity of the functional maps is accompanied by morphological and biochemical modifications in the area surrounding the lesion (Zepeda et al. 2003). The increase of FMZ binding in the surrounding areas is in part due to the increase of $GABA_A$ receptor density following an ischemia (Zepeda et al. 2004).

It is important for the patients to predict the prognosis of their VF. However, it is difficult to estimate of prognosis of the visual field from an early evaluation of glucose metabolism (Bosley et al. 1987). Even if neurons survive in the area of the injury, glucose hypometabolism is usually observed in this area due to diaschisis during the early stage (Chu et al. 2002). Therefore, early stage FDG-PET findings may not reflect actual damage to the area. Glucose hypometabolism due to diaschisis usually improves promptly during the acute stage (Suzuki et al. 2008), and subsequent improvement of glucose metabolism in the visual cortex may accompany a recovery of the VF. However, FMZ binds to intact neurons only, and therefore FMZ binding in injured areas reflects the number of surviving neurons. Therefore, FMZ-PET may be able to detect permanent and irreversibly damaged cortex even during the acute stage (Heiss et al. 1998). Our previous study demonstrated that patients with high FMZ binding in the striate cortex (i.e., an I/C ratio > 0.85) exhibited VF recovery over time (Suzuki et al. 2008). The VF test is a subjective examination, but glucose metabolism measurement is an objective examination. Moreover, we cannot deny that the technician's skill may affect the result of VF. In the cases with a large VF defect, glucose metabolism in the visual cortex may be low trend. However, we cannot expect precise correlation between VF and glucose metabolism in the striate cortex.

In conclusion, we observed that the improvement in cerebral glucose metabolism accompanied VF recovery in a patient with hemianopia. The measurement of cerebral glucose metabolism and FMZ binding in the striate cortex is useful for estimating the damage to the visual cortex and the prognosis for VF recovery.

Conflict of Interest

The authors declare no conflict of interest.

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