

Cerebral Glucose Metabolic Rate in Visual Cortices Associated with Visual Dysfunction in Multi-Infarct Dementia

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IV. 6. Cerebral Glucose Metabolic Rate in Visual Cortices Associated with Visual Dysfunction in Multi-Infarct Dementia

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Abstract

Cerebral metabolic rate for glucose (CMRGlc) of twelve patients with multi-infarct dementia (MID) as well as age-matched controls were evaluated with positron emission tomography and ^{18}F -fluoro-deoxyglucose technique. Primary visual function (visual acuity), as well as higher visual function (color vision, stereopsis, and figure copying) were also evaluated. We found that all the MID patients showed impaired higher visual function and CMRGlc of the primary as well as the associate visual cortices of the patients were lower than those of the controls, and that CMRGlc of the primary visual cortices of the patients with impaired visual acuity was lower than that of the patients with unimpaired visual acuity, whereas CMRGlc of the associate visual cortices was not different. Dementing process may directly affects metabolism and function in the associate cortices.

Introduction

It is clinically well known that patients with senile dementia, especially those with Alzheimer's disease, suffer from "visual" dysfunction. Early in the course of the illness, they complain of poor vision with symptoms such as difficulty in reading (alexia), disorientation at home (environmental agnosia), difficulty in recognizing faces (prosopagnosia), and in interpreting complex visual scenes (simultanagnosia)¹⁾. Kiyosawa et al.¹⁾ examined Alzheimer's disease patients with or without such visual symptoms using positron emission tomography (PET) and the fluoro-deoxy-glucose (FDG) method. They found that patients with visual symptoms had a lower cerebral glucose metabolic rate in the visual association cortices compared with that of the patients without visual symptoms, while the cerebral glucose metabolic rate in the primary visual cortices was not statistically different between the two groups.

However, there have been no metabolic studies on multiinfarct dementia (MID) involving visual symptoms. Therefore, we examined the correlation between visual function and glucose metabolism in MID.

Patients and Methods

1. Patients

Eight normal aged subjects and twelve MID patients were studied. Regarding the normal group, which consisted of 4 males and 4 females, ages ranged from 64 to 83 years with a mean age of 73. As to the MID group, which consisted of 8 males and 4 females, ages ranged from 68 to 87 with a mean age of 77.

2. Neuro-ophthalmologic examination

Visual acuity was checked with full correction. Visual field was checked by confrontation testing or Goldmann's kinetic perimetry. Fundi were examined with an indirect ophthalmoscope under conditions of pupil dilation. The grade of sclerosis of the retinal artery was determined based on a modification of Keith Wagener's ³⁾ and Sheie's ⁴⁾ classifications. Stereopsis was examined by the random dot E (RDE) stereotest ⁵⁾. The double pentagon figure copying test included in the Mini Mental Status Examination (MMSE)⁶⁾ was also administered, as was color vision test employing a Ishihara isochromatic plates (ISH). For acquired color blindness, more than half of the misreadings were considered as test failures. Pupillary light reaction and ocular motility were also examined.

MID patients were classified into two groups based on corrected visual acuity, i.e., the group with unimpaired visual acuity and the group with impaired visual acuity. The former was composed of patients with more than 20/100 in both eyes.

3. Measurement of Cerebral Glucose Metabolism

Cerebral metabolic rates for glucose (CMRGlc) of the subjects were examined with positron emission tomography (PET) and the F-18-fluoro-deoxy-glucose (FDG) technique. The type of PET tomography used was a PT 931 (CTI Inc. USA) which has a resolution of 7 mm and 8 mm (FWHM) in the trans-axial and axial planes, respectively. Transmission scan was not performed since patients in this study could not tolerate lengthy examination, CMRGlc was calculated according to the method of Phelps et al.⁷⁾ The lumped constant used was 0.42. Two emission scans were performed 40 to 60 min after injection of 2 to 6 mCi FDG. One scan consisted of 7 slices, each slice being 7 mm in thickness with 1 mm gaps between the slices. One scan was done 30 mm above the orbitomeatal line (OM)+30 mm and the other, OM+77 mm.

Regional values of CMRGlc (rCMRGlc) were obtained for regions of interest (ROI) from the tomographic images on the computer screen. The rCMRGlc in the following bilateral regions were measured: upper frontal, anterior frontal, inferior frontal, parietal, temporo-

parietooccipital, Heschl (primary auditory), inferior temporal, basal ganglia, cerebellum, white matter (foramen centrum semiovale) and the visual cortices. The visual cortices consisted of the primary visual cortices (anterior calcarine cortices and posterior calcarine cortices) and the association visual cortices (the peristriate cortices and the lateral occipital cortices).

The average value of the entire grey matter CMRGlc was calculated based on values of all the regions except for that of the white matter. Statistical analysis (Student's t test) was performed to compare the total average values of MID patients with those of normal controls, as well as compared the values of MID patients with unimpaired visual function.

Results

1. Neuro-ophthalmologic Examinations

Eight patients were classified as having unimpaired visual acuity and four were classified as having impaired visual acuity. The results of neuro-ophthalmologic examinations are shown in Table 2 as follows:

1) In the unimpaired visual acuity group, corrected visual acuity ranged from finger counting (FC) to 20/20. The causes of low visual acuity were unilateral residual occlusion of a branch of the retinal vein (#8), age-related macular degeneration (#1, #3), residual narrow angle glaucoma (#4), and incipient cataract in other cases. In the group with impaired visual acuity, incomplete cerebral blindness or double hemianopsia with poor central visual acuity was suspected in four patients. They had similarly shaped visual field defects, and normal pupils and fundi.

2) Unilateral or bilateral hemianopsia was found in 3 patients in the group with unpaired visual acuity and in all 4 patients in the group with impaired by exudates, hemorrhages, or apparent crossing phenomena of retinal vessels. The severity of retinal changes, however, did not correspond to visual acuity so long as the macula was not involved.

4) As for the group with unimpaired visual acuity, stereopsis was impaired in 7 of the 8 patients. Only one of these 7 patients had a retinal problem, and stereopsis in the other 6 was suspected of being due to central nervous system disorders.

5) As for the group with impaired visual acuity, all patients failed stereopsis and figure copying tests. The Ishihara plate could not be used with three patients.

2. Cerebral Metabolic Rate for Glucose

1) MID patients had a decreased average value for the entire grey matter CMRGlc compared with that of normal subjects as well as a decreased average rCMRGlc in all the regions measured, including the primary visual cortices and the association visual cortices.

2) In MID patients, the group with impaired visual acuity showed a lower rCMRGlc in the primary visual cortices (the anterior calcarine cortices and the posterior calcarine cortices) compared with those of the group with unimpaired visual acuity. As for the CMRGlc of the

association visual cortices (the peristriate cortices and the lateral occipital cortices), as well as that of other regions, no statistical differences were found (Fig. 1).

Discussion

1. Neuro-ophthalmologic Findings in MID Patients

There were cases with unimpaired visual acuity and with impaired visual acuity. As for the causes of impairment, ocular disease, and lesions in the higher levels were indicated. The former included senile cataracts, glaucoma and other intraocular changes such as branch retinal vein occlusion and age-related macular degeneration. The latter included cortical blindness.

Hemianopsia is the most common macroscopic sign in MID. It may be caused by a lesion in the area ranging from the optic tract to the primary visual cortices. Hemianopsia can be caused by a deep branch infarction of the middle cerebral artery and can also result from the involvement of the optic radiation and/or calcarine cortices in the area supplied by the posterior cerebral artery. Five of our 12 patients had hemianopsia. As for Alzheimer's disease, hemianopsia is rare, and therefore the presence of hemianopsia is a standard reason for ruling out the disease.

Incomplete cerebral blindness or double hemianopsia with poor vision was suspected in four patients with bilaterally impaired visual acuity. Although unilateral homonymous hemianopsia was suspected in two of these patients, contralateral hemianopsia might have been overlooked at the time of the bedside confrontational test for demented patients. Despite their poor acuity, they had similarly shaped visual field defects on corresponding sides of the vertical midline for each eye, normal pupils and fundi, and ocular motility. These observations indicated double homonymous hemianopsia^{8,9}) Miller suggested that the loss of visual acuity was a result of diffuse involvement of occipital lobes without specific visual field defect other than concentric, usually mild, constriction¹⁰).

In the visual perception system in the primates, segregation of form, color, and stereopsis, has been proposed by Livingstone and Hubel¹¹). Disturbances of higher visual functions, especially of movement and depth perception in Alzheimer's disease have been reported¹²⁻¹⁴). The incidence of disturbed higher visual functions in MID, however, is still unclear.

To test stereoscopic depth perception, which is believed to be processed by way of magnocellular pathways¹¹), we used the random dot "E" test. The patients were to detect the prominent "E" with both eyes through Polaroid glasses. This test is superior to the Titmus stereo test because in the latter, subject cannot respond when they do not have stereopsis. Only one patient (#7) could pass this test. More than 20/100 visual acuity is needed and at least 5 patients had defective stereopsis with good visual acuity (#1-5).

Patients could pass the double pentagon figure copying test if they had good spatial perception and good visual acuity enabling them to see the figure at least in one eye. Nine of our 12 patients, failed the test and at least 7 of them (#2-4, 7, 8, 9, 11) had reasonable visual acuity.

2. Cerebral Metabolic Rate for Glucose

We found that MID patients had significantly lower CMRGlc in the entire grey matter than did normal subjects. We also observed that in MID patients, the group with impaired visual acuity had significantly lower rCMRGlc in the primary visual cortices than did the group with unimpaired visual acuity.

In the MID patients, impaired visual acuity affected rCMRGlc in the primary visual cortices rather than that of the associate visual cortices. A previous study by Kiyosawa et al¹⁾ reported that Alzheimer's disease patients with visual symptoms had decreased rCMRGlc in the association cortices rather than in the primary cortices. However, all patients in this study showed impaired higher visual functions related to the association cortices; as for visual acuity associated with the primary cortices, some patients showed impairment. All Alzheimer's patients studied by Kiyosawa et al. had unimpaired visual acuity, and as for higher visual functions, some patients showed impairment. Therefore, the difference between the two studies was not due to MID and Alzheimer's disease but rather to the brain regions involved.

Visual signals were projected from the retina to the primary visual cortices through the optic tract and the lateral geniculate body and integrated in the association cortices in the brain. In our study, the MID patients with impaired visual acuity showed statistically greater decreased metabolism in the primary visual cortices than did subjects with unimpaired visual acuity. The dementing process in MID, therefore, may directly affect function and metabolism in the association visual cortices.

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Table 1. Clinical characteristics of the Multi-Infarct Dementia (MID) Patients

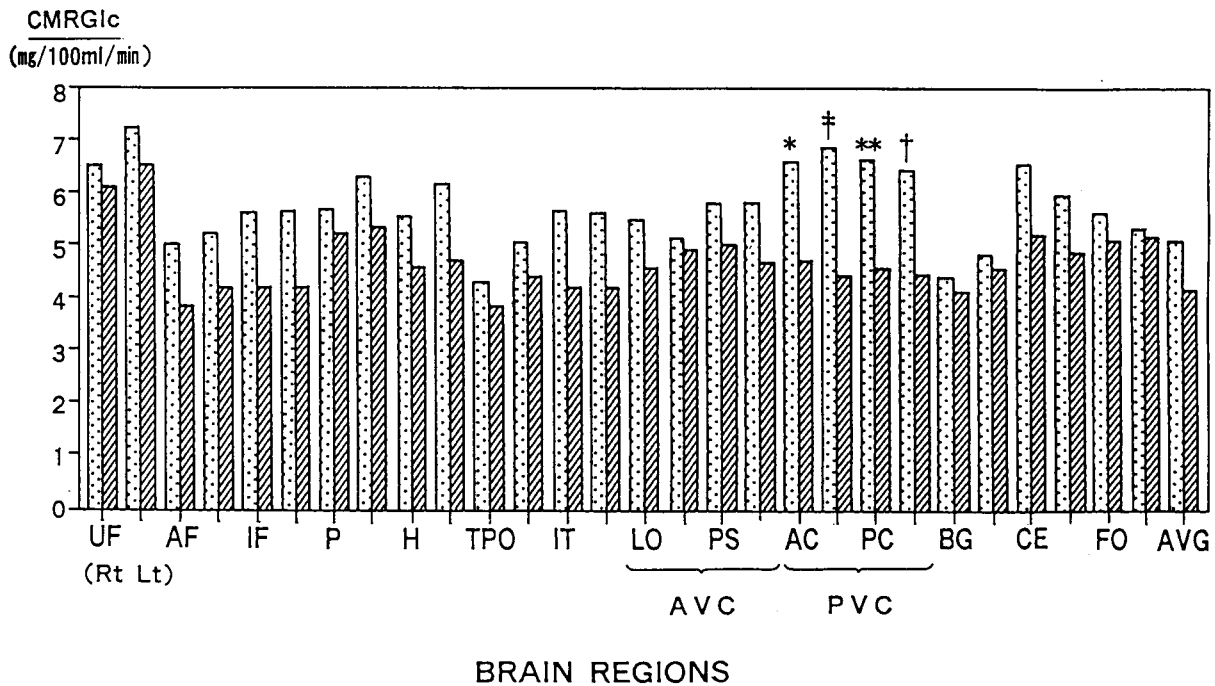
	Age	Sex	MMS	CT findings	Hemiparesis
unimpaired VA					
ID.					
# 1	80	M	22	lacunar	No
# 2	81	F	23	PVL+rt. basal ggl. infarction	lt.
# 3	81	M	16	lacunar + rt. parietal infarction	rt.
# 4	85	F	5	lacunar	No
# 5	83	M	16	lacunar	No
# 6	66	M	14	PVL+lacunar	No
# 7	77	F	19	PVL	No
# 8	87	M	14	lacunar	No
impaired VA					
# 9	77	F	12	lacunar	No
# 10	61	M	8	PVL+lacunar + blt. occipital infarctions	lt.
# 11	80	M	13	lacunar	No
# 12	71	M	13	lacunar	lt.

MID, multi-infarct dementia
 VA, visual acuity
 MMS, Mini-Mental Status
 PVL, periventricular lucency
 lt, left
 rt, right

Table 2. Neuro-ophthalmologic Findings of Multi-Infarct Dementia (MID) patients

	Fundus	VD/VS	VF	ISHI	stereopsis	Figure copy
unimpaired VA						
ID.						
# 1	IIb	0.8/0.6	Normal	11/15 12/15	No	OK
# 2	IIa	0.8/0.6	Lt.	13/15 11/15	No	No
# 3	IIb III	0.6/0.4	Lt.	11/15 7/15	No	No
# 4	IIb	0.1/0.5	Rt.	10/15 15/15	No	No
# 5	IIa	0.9/0.5	Normal	15/15 15/15	No	OK
# 6	IIa	1.2/1.0	Normal	1/15 1/15	No	OK
# 7	IIb	0.5/1.0	Normal	7/15 10/15	OK	No
# 8	IIb	0.3/FC	Fds	8/15 0/15	No	No
impaired VA						
# 9	IIa	0.05/0.05	Blt.	12/15 12/15	No	No
# 10	IIa	HM/HM	Blt.	0/15 0/15	No	No
# 11	IIa	0.05/0.1	Lt.	1/15 1/15	No	No
# 12	IIa	FC/FC	Lt.	0/15 0/15	No	No

MID, multi-infarct dementia
 VA, visual acuity
 VD, visual acuity dextra
 VS, visual acuity sinistra
 HM, hand movement
 FC, figure counting
 VF, visual field
 Lt, left hemianopsia
 Rt, right hemianopsia
 Blt, bilateral
 ISHI, Ishihara isochromatic plates



MID with unimpaired VA
 impaired VA

* $P < 0.05$ (welch-M)

** $P < 0.005$

† $P < 0.05$ (t-test)

‡ $P < 0.01$

Fig. 1. Regional Cerebral Metabolic Rate for Glucose (CMRGlc) of Multi-infarct Dementia (MID) Patients

The primary visual cortices of the patients with impaired visual acuity shows significantly lower values compared to those of the patients with unimpaired visual acuity.

CMRGlc, cerebral metabolic rate for glucose

MID, multi-infarct dementia

UF, upper frontal

AF, anterior frontal

IF, inferior frontal

P, parietal

H, Heschel (primary auditory)

TPO, temporo-parieto-occipital

IT, inferior temporal

AVC, associate visual

LO, lateral occipital

PS, peristriate

PVC, primary visual

AC, anterior calcarine