Proton MR Spectroscopy Evaluation of Brain Metabolism in Patients with Steno-occlusive Carotid Artery Disease : Correlation with Cerebral Blood Flow and Oxygen Metabolism by PET

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Purpose

Carotid occlusive diseases may cause ischemic change both in the gray matter and in the centrum semiovale as a result of hemodynamic compromise [1] . Metabolic changes in the white matter which is easily measured by MR spectroscopy (MRS) may be another indicator of ischemic conditions. The purpose of the present study was to evaluate the relationship between the metabolic changes in the centrum semiovale measured by proton-MRS and the changes in hemodynamics and ogygen metabolims of the cerebral cortex measured by PET in carotid occlusive diseases.

Materials and Methods

Patients

Ten patients with unilateral steno-occlusive carotid artery disease (6 men, 4 women; age range of 56-84 yrs; mean age 68±8.5) were involved. Four patients had unilateral internal carotid artery (ICA) occlusion and three patients had ICA stenosis. Two others showed MCA stenosis on the M1 portion. They were diagnosed by digital subtraction angiography. All patients had transient or minor persistent symptoms of ischemic attack. All patients were examined within 12 weeks after the onset of symptoms. All patients had no cortical infarction other than minimal subcortical abnormality on MR images. In all patients, common carotid arteriography showed unilateral stenosis (>70% reduction) or occlusion. All patients with internal carotid artery (ICA) occlusion had collateral circulation through the anterior portion of the circle of Willis. In all patients with ICA or middle cerebral artery (MCA) stenosis, the affected hemisphere was mainly perfused through the stenosed carotid or middle cerebral artery.

Ten age-matched control subjects underwent MRI/MRS examination (3 men, 7 women; age range of 46-74 yrs; mean age 64.3±8.9). All of them were found to be normal on neurological examination, without any history of ischemic event. MRI revealed no abnormality.

PET Measurement

A PET study was performed using a whole-body PET scanner, ADVANCE (GE, Waukesha, WI, USA). The spatial resolution of the reconstructed clinical PET images was 6 mm in FWHM at the center of the field of view and axial resolution was 4 mm. Regional cerebral blood flow (rCBF), regional cerebral metabolic rate for oxygen ($rCMRO_2$), regional oxygen extraction fraction (rOEF) images were obtained by the steady-state method after inhalation of ^{15}O labeled gas.

The regions of interest (ROIs) were located on the affected and unaffected cortices in the territory of the middle cerebral artery, anterior watershed, and posterior watershed regions. At least 80 circular ROIs, of which the radius was 6 mm, were placed on each side. Hemispheric value was calculated as the averaged value.

MR spectroscopy

MR imaging and spectroscopy were performed with a 1.5 T system (GE Horizon). Spectroscopy was performed using the point-resolved spectroscopy pulse sequence (2000/28) with 8cm^3 voxel size. The area of three major peaks including choline (Cho;3.2ppm), the sum of creatine and phosphocreatine (Cr; 3.0ppm), and N-acetylaspartate (NAA;2.0ppm) were measured. All results are given as relative values with respect to the intensity of the Cr peak. Volumes of interest (VOIs) were located in the white matter of centrum semiovale where MR imaging had shown no apparent infarction. In the patients group, two VOIs were placed in the affected and one in the unaffected centrum semiovale. The averaged value of the two VOIs was used as the value for the affected side. For the control group, a VOI was placed in the centrum semiovale of one side.

Data Analyses

For linear correlative analyses between the relative MRS data and PET value we used asymmetry index (AI).
AI was defined as follows :
Asymmetry index
=(Ipsilateral-Contralateral)/(Ipsilateral+Contralateral)×2×100%
$p < 0.05$ was considered significant.

Results

The AI of the NAA/Cr ratio correlated significantly with that of $rCMRO_2$ ($r=0.809$, $p<0.01$; Fig.1) and rCBF ($r=0.783$, $p<0.01$). No significant correlation was found between the AI of the NAA/Cr ratio and that of rOEF. The AI of the Cho/Cr ratio showed significant correlation with that of rOEF ($r=0.844$, $p<0.01$; Fig.2) but didn't correlate with that of $rCMRO_2$ and rCBF.

In all but one patient with an ipsilateral Cho/Cr ratio > 1.03, the mean + 2SD of normal Cho ratio, PET showed a high rOEF value on the ipsilateral side (> 0.56).

Discussion and Conclusion

Our results suggest that the Cho/Cr ratio of centrum semiovale with MRS can predict hemispheric rOEF with PET which is in turn a good indicator of cerebral revascularization [2] . The Cho signal *in vivo* proton spectra consists predominantly of glycerophosphocholine and phosphocholine, both of which are involved in membrane synthesis and degeneration pathway [3] . The increase of Cho/Cr ratio in centrum semiovale in the state with elevated rOEF may indicate membranous damage due to ischemia. Moreover, the NAA/Cr ratio with MRS can reflect the hemispheric $rCMRO_2$ with PET which is a marker of brain tissue viability [4] . The NAA/Cr ratio correlated significantly with both $rCMRO_2$ and rCBF, consistent with the fact that the majority of patients in this study showed matched perfuson, and oxygen metabolism was depressed in accord with decreased rCBF. We conclude that the metabolic change in centrum semiovale evaluated by proton MRS is able to indicate a hemodynamically compromised state with elevated OEF and brain tissue viability in patients with unilateral steno-occlusive carotid artery disease.

References

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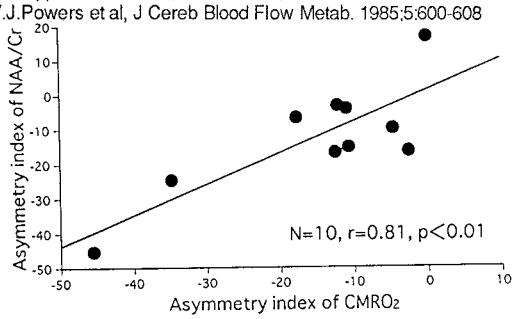

Figure1. Two-dimentional plots of AI of the NAA/Cr ratio in centrum semiovale versus AI of cortical averaged CMRO 2. There is a significant linear relationship between them.

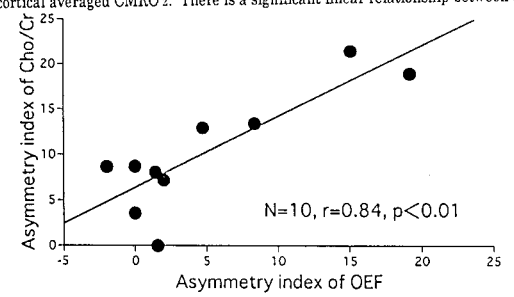

Figure2. Two-dimentional plots of AI of the Cho/Cr ratio in centrum semiovale versus AI of cortical averaged OEF. There is a significant linear relationship between them.