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Dynamics of Cerebral Metabolism in Patients with Chronic Subdural Hematoma Evaluated with Phosphorous 31 MR Spectroscopy before and after Surgery

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PURPOSE: To determine whether the depression of cerebral bioenergetic metabolism caused by chronic subdural hematomas can account for neurologic dysfunction and whether the degree of metabolic depression may be useful for clinical assessment and therapy. **METHODS:** Sixteen patients who had chronic subdural hematomas with hemiparesis and/or mental disturbances underwent phosphorous 31 MR spectroscopy before and 10 to 14 days after surgery. Phosphorous 31 MR spectroscopy was also performed on 5 patients who had chronic subdural hematomas with only slight headaches who were treated by conservative therapy and on 10 healthy volunteers. **RESULTS:** The preoperative phosphocreatine-to-inorganic phosphate ratio (2.10 ± 0.36) improved to normal values (2.69 ± 0.44) after evacuation of hematomas. This improvement was accompanied by complete disappearance of hemiparesis and/or mental disturbance. Brain tissue pH also improved from 7.07 ± 0.11 to 7.205 ± 0.13 after surgery. On the other hand, patients who had chronic subdural hematomas with only slight headaches had the same phosphocreatine-to-inorganic phosphate ratio and brain intracellular pH as healthy volunteers. **CONCLUSION:** The phosphocreatine-to-inorganic phosphate ratio may be useful for determining when to operate on patients with chronic subdural hematomas and to assess the efficacy of treatment.

Index terms: Hematoma, subdural; Brain, metabolism; Magnetic resonance, spectroscopy; Surgery; Brain, magnetic resonance

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Chronic subdural hematoma, which is a slowly expanding intracranial mass lesion, can cause neurologic dysfunction by several possible mechanisms; however, the exact mechanism by which compression and displacement of the brain cause reversible reduction of cerebral function is not clear. Reduction of cerebral blood flow recently has been reported in patients who had chronic subdural hematomas with neurologic deficits (1–5). It is not clear whether cerebral blood flow reduction is a cause of brain dysfunction or merely a result of a reduced metabolic demand in the dysfunctional brain. The relationship between cerebral metabolism and neurologic symptoms has not been determined, because one could not directly define cerebral metabolism in vivo.

The objective of this study was to determine using magnetic resonance (MR) spectroscopy whether depression of cerebral bioenergetic metabolism can cause neurologic dysfunction and whether the degree of metabolic depletion may be useful for clinical assessment and therapy. We examined the dynamics of cerebral metabolism in patients who had chronic subdural hematomas with and without neurologic dysfunction using phosphorous 31 spectroscopy. In patients with hemiparesis and/or mental disturbances, P-31 spectroscopy was performed before and after surgery. The results

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were then compared with the P-31 spectra from 10 healthy adults.

Materials and Methods

Sixteen patients (32 to 82 years old) who had chronic subdural hematomas with hemiparesis and/or mental disturbances underwent MR spectroscopy before and 10 to 14 days after surgery. P-31 MR spectroscopy was also performed on 5 patients (50 to 70 years old) who had chronic subdural hematomas with only slight headaches and were treated by conservative therapy and on 10 healthy volunteers (17 to 82 years old) who had no abnormal findings on MR.

P-31 MR spectroscopy was performed on a 1.5-T whole-body system. A saddle-type double-tuned (for hydrogen 1 and P-31), send-and-receive head volume coil, 285 mm in diameter, was used for imaging and for spectroscopy; this allowed rapid switching from H-1 MR imaging to P-31 MR spectroscopy without the need to move the patient or replace the coils. T1-weighted H-1 MR images (260/9/1 [repetition time/echo time/excitations], field-echo, 90° flip angle, 10-mm section width, and 256 × 256 matrix) were used to inspect the volume of interest. Field homogeneity was optimized by autoshimming on the water-proton signal. Then the instrument was switched to P-31 MR, and a spectrum of a volume of interest was obtained.

The method used to obtain P-31 MR spectra was one-dimensional image-selected in vivo spectroscopy (6, 7). This method avoids transverse relaxation and therefore allows short T2 signals to appear on the MR spectra. Spectra were recorded with a repetition time of 2000, a sampling decay time of 0.80, 1024 sampling points, and 300 to 800 excitations. Thickness of the volume of interest was 30 to 50 mm, and total acquisition time was 13 to 15 minutes. The volume of interest was placed in the center of the hemisphere, usually at the level of the basal ganglia, and included gray and white matter (Fig 1A). An attempt was made to exclude the hematoma itself from the volume of interest, although spectra from the hematoma consisted only of very small inorganic phosphate signals. However, all spectra obtained contained signals from extracranial structures, such as bone, muscle, and skin. It is possible that these tissues may have influenced phosphocreatine-to-inorganic phosphate (PCr/Pi) ratios and tissue pH values.

Quantification of the spectra was performed by means of area measurements using automated area analysis. The convolution difference method (8) was used to remove the broad signals derived from bone and from tissues in the inhomogeneous profiled magnetic field. In this study, we measured the β-adenosine triphosphate (β-ATP) concentration and calculated the PCr/Pi ratio. The β-ATP peak was chosen to measure the ATP concentration, because the α- and γ-ATP peaks included signals caused by adenosine diphosphate and dihydronicotinamide adenine dinucleotide, respectively (9). Tissue pH was also calculated from the chemical shift of inorganic phosphate (10, 11).

Statistical Analysis

Statistical analysis of the PCr/Pi ratios and β-ATP was performed with the paired Student's *t* test. All data are presented as means ± SDs.

Results

Example Case. A 57-year-old man presented with a headache of 3 weeks' duration. He had a

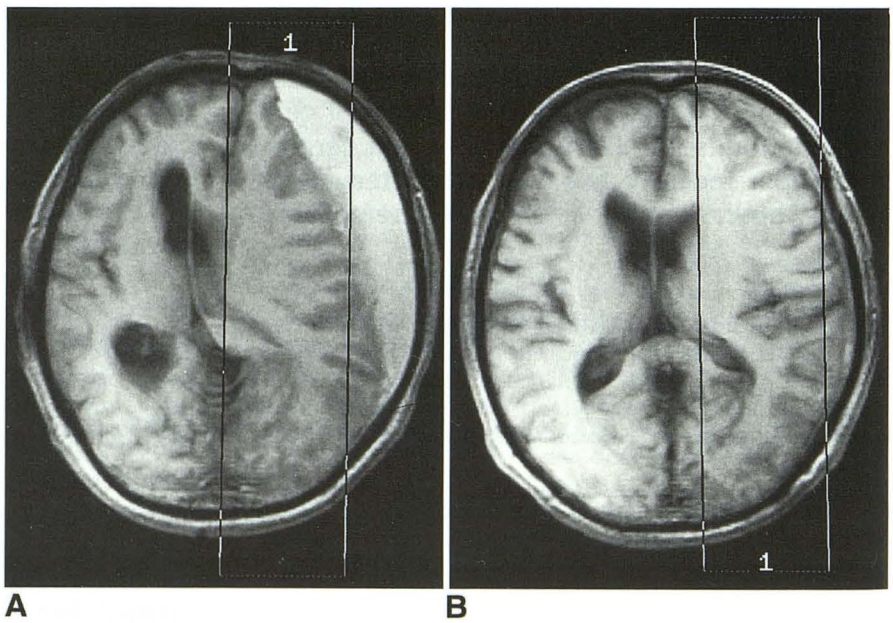

Fig 1. *A,* T1-weighted H-1 MR image (260/9) shows a chronic subdural hematoma of high signal intensity in the left frontoparietal region with a moderate degree of brain shift. The volume of interest is placed in the whole hemisphere sagittally between the horizontal lines.

B, The hematoma was almost gone after surgery.

progressive right hemiparesis and disorientation. T1-weighted MR imaging demonstrated a chronic subdural hematoma of high intensity in the left frontoparietal region with a moderate degree of brain shift (Fig 1A). After surgery, the patient was free of neurologic symptoms, and only a small hematoma without brain shift was noted (Fig 1B). Figures 2A and B show P-31 MR spectroscopy before and 1 week after surgery. The PCr/Pi value normalized from 1.80 to 2.47, and brain tissue pH increased from 6.985 to 7.149.

Patients who had chronic subdural hematomas without neurologic deficits had grossly the same PCr/Pi ratio (2.65 ± 0.15) as healthy volunteers (2.76 ± 0.19) (Table). The PCr/Pi ratio measured in patients with neurologic deficits significantly improved from 2.10 ± 0.36 to 2.69 ± 0.44 after evacuation of hematoma ($P < 0.01$). This specimen change was accompanied by complete disappearance of hemiparesis and/or mental disturbances. Brain tissue pH also improved from 7.07 ± 0.11 to 7.21 ± 0.13 ($P < 0.05$) after surgery. However, brain pH values in patients who had chronic subdural hematomas without neurologic deficits and healthy volunteers were 7.149 ± 0.14 and 7.15 ± 0.13, respectively. Figure 3 shows preoperative and postoperative PCr/Pi ratios (Fig 3A) and brain pH (Fig 3B) in patients who had chronic subdural hematomas with neurologic deficits. All preoperative PCr/Pi ratios were less than 2.6, which were below those in volunteers; pH values in all patients with chronic subdural hematomas, except one (7.345), were less than 7.15, the pH of healthy volunteers. β-ATP values showed no significant difference between groups.

Discussion

It is unclear why chronic subdural hematomas, which slowly expand and compress the brain, cause reversible reduction in cerebral function. Compression of the subjacent brain and subsequent development of focal cerebral edema may lead to cerebral dysfunction and clinical symptoms. Brain substance remote from the mass could be rendered ischemic because the compression can affect blood supply seriously. Another possible mechanism deserving examination is alteration of the electrical and chemical properties of neurons caused by damage and/or distortion of their architecture.

Many investigators have reported cerebral blood flow studies in patients with chronic subdural hematomas (1–5). Ikeda et al (2) found that cerebral blood flow reduction was more pronounced in patients with hemiparesis and/or mental disturbances than in patients with only headaches. Tanaka et al (3) suggested that pyramidal signs were caused by a local cerebral blood flow reduction not in the cortex but in the central cerebral areas at the basal ganglia level. However, observation of cerebral bioenergetic metabolism has not been reported for patients

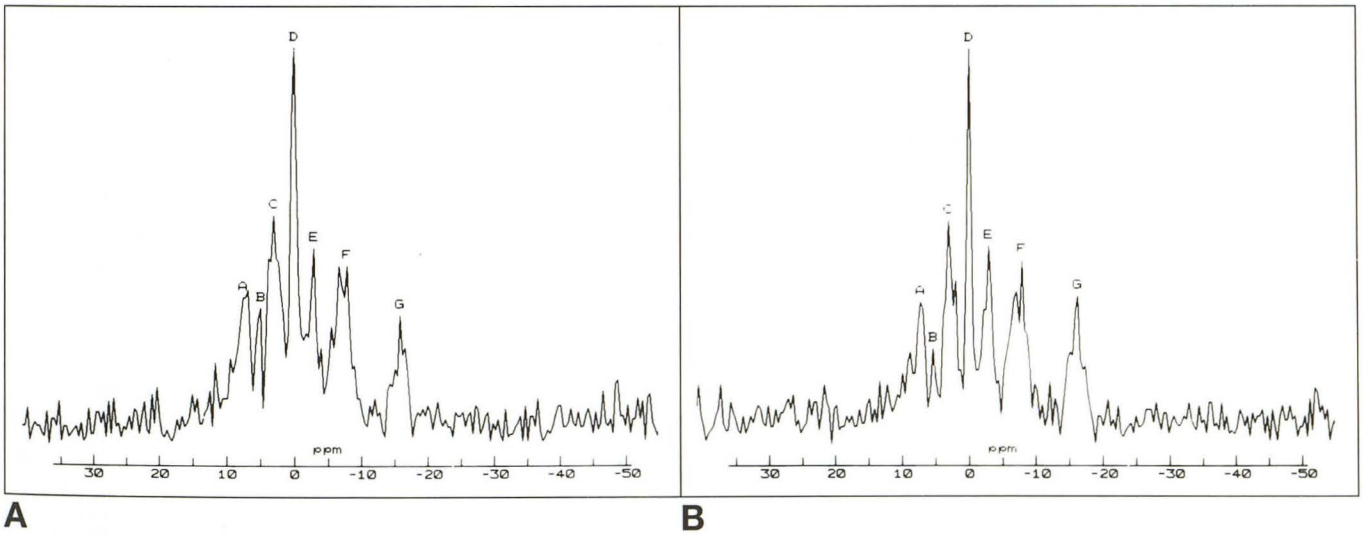

Fig 2. P-31 MR spectroscopy before (*A*) and 1 week after (*B*) surgery. Peak *A* indicates phosphomonoester; *B*, inorganic phosphate; *C*, phosphodiester; *D*, PCr; *E*, γ-ATP; *F*, α-ATP; and *G*, β-ATP. The PCr/Pi ratio normalized from 1.80 to 2.47 after surgery. Brain tissue pH increased from 6.985 to 7.149.

Metabolic Parameters

Subject	n	PCr/Pi	β-ATP	Brain pH
Healthy volunteer	10	2.76 ± 0.19	0.54 ± 0.06	7.15 ± 0.13
Chronic subdural hematoma without symptoms	5	2.65 ± 0.15	0.50 ± 0.08	7.15 ± 0.14
Chronic subdural hematoma with symptoms (preoperative)	16	2.10 ± 0.36[a]	0.50 ± 0.08	7.07 ± 0.11[b]
Chronic subdural hematoma with symptoms (postoperative)	16	2.69 ± 0.44	0.50 ± 0.08	7.21 ± 0.13

Note.—Data are means ± SDs.

[a] $P < 0.01$ compared with any other group.

[b] $P < 0.05$ compared with postoperative group.

with chronic subdural hematomas, although the cerebral metabolic rate of oxygen in one patient was measured by Gjerris and Brodersen (5). In this patient, the metabolic rate of oxygen was reduced more than cerebral blood flow. It was speculated that the cerebral blood flow reduction might be caused by a reduced metabolic demand rather than by cerebral ischemia.

In the present study, we compared the clinical symptoms with cerebral bioenergetic metabolism by P-31 MR spectroscopy. Since the initial measurement of P-31 MR spectra in biological tissues (12), a great deal of attention has been paid to the possibility that energy metabolites could be measured in vivo, without extracting or homogenizing the organs. However, various studies of in vivo MR spectroscopy have shown that quantitative evaluations are difficult to perform, particularly the measurement of absolute concentrations of metabolites. These problems are currently circumvented by calculating the ratios of metabolites. From this study, we wish to emphasize that the PCr/Pi ratio is a sensitive marker of cerebral bioenergetic depression. A major role of PCr in the brain is to buffer the ATP-to-adenosine diphosphate ratio through the creatine-kinase reaction. Because a decrease in PCr is most likely accompanied by an increase in Pi, the PCr/Pi ratio amplifies even subtle decreases in PCr (13).

Previous P-31 MR investigations in animals have shown decreased ratios of PCr/Pi in cases of experimental head trauma (13), acute cerebral infarction (14–16), hypoxia (9, 17), and convulsion (18, 19). Bottomley et al (20) reported brain tissue pH and PCr/Pi were 7.01 (± 0.05) and 7.7 (± 2.3), respectively, in healthy adults. Our data (7.15 ± 0.13 and 2.76 ± 0.19) were different, possibly because we used one-dimensional image-selected in vivo spectroscopy, and therefore, signals from the extracerebral structure, such as bone, muscle, and skin, were sampled at the same time. The pH values reviewed by Petroff et al (10) show a considerable variation (7.09 to 7.33).

Metabolic alterations after experimental traumatic head injury have been reported by many investigators. Yoshida and Marmarou (13) considered the reduction in PCr/Pi ratio without β-ATP changes after experimental brain injury to be indicative of an energy metabolism disturbance. Ishige et al (21) also observed brain acidosis and decreased PCr/Pi without ATP changes after mild head injury. In the present

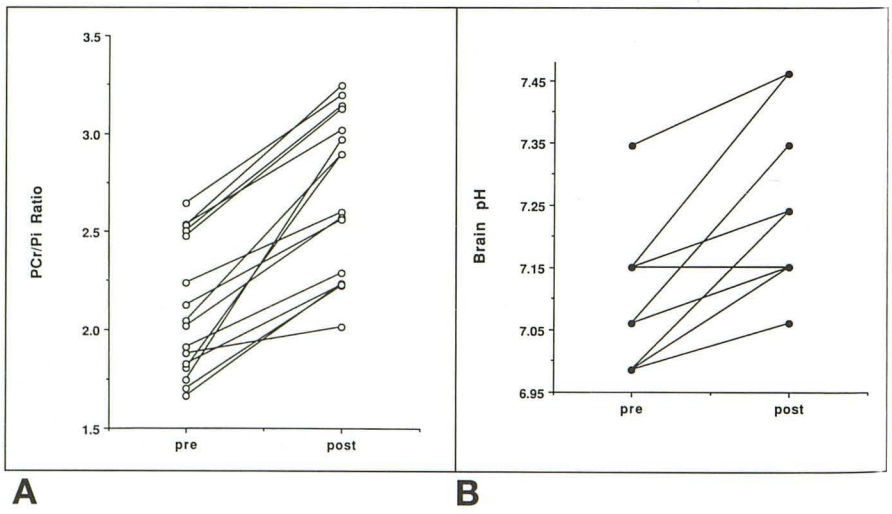

Fig 3. Preoperative and postoperative PCr/Pi ratio (*A*) and brain pH (*B*) in patients who had chronic subdural hematomas with neurologic deficits. All preoperative PCr/Pi ratios were less than 2.6, less than values in healthy volunteers. All pH values, except one (7.345), were less than 7.15, the value in healthy volunteers.

investigation, patients who had chronic subdural hematomas with neurologic symptoms had slight brain acidosis (7.07 ± 0.11). We found that the reduction of PCr/Pi ratio coincided with a reduction of cerebral function, as reflected by hemiparesis and/or decreased mental function. The preoperative PCr/Pi ratio in our patients with hemiparesis and/or mental disturbances was extremely low (2.10 ± 0.36). It was noteworthy that the ratio recovered to normal levels (2.69 ± 0.44) after evacuation of hematoma ($P < .01$), along with the disappearance of neurologic deficits. Brain tissue pH reduction was accompanied by a reduction in the PCr/Pi ratio but without any change in the β-ATP value. This phenomenon is indicative of a bioenergetic metabolic disturbance, a finding demonstrated by others (13, 21–24). We speculate that the lack of change in ATP is the reason for reversible reduction of cerebral function. It is also notable that patients who had chronic subdural hematomas without neurologic deficits had grossly the same PCr/Pi ratio as healthy volunteers. We speculate that the symptom of headache was caused by elevation of intracranial pressure, without a depression of cerebral metabolism. We believe the depression of cerebral metabolism leads to neurologic dysfunction. Therefore, the PCr/Pi ratio may be useful for determining when to operate and to assess the efficacy of treatment. When patients with chronic subdural hematomas have PCr/Pi ratios and brain pH values less than 2.6 and 7.15, respectively, they may need surgical intervention. However, the one-dimensional image-selected in vivo spectroscopy used in our studies covers the whole hemisphere and does not locate changes precisely. Further advances in MR technology may enable detection of smaller metabolic changes and better their anatomic relationships.

Reduction in cerebral perfusion pressure caused by increased intracranial pressure leads to a reduction in cerebral blood flow. However, a chronic subdural hematoma may be considered a slowly expanding intracranial mass, which allows compensatory mechanisms that prevent a marked rise in intracranial pressure. When the mass expands slowly, expression of cerebrospinal fluid from the supratentorial compartment permits accommodation of a large volume, and brain stem displacement is less (25). The exact mechanism by which compression and displacement of the brain by chronic subdural hematoma cause reversible reduction of cerebral function remains unclear. It was clear from our study, however, that the reduction of the PCr/Pi ratio indicates a reduction of the cerebral metabolic state. Possibly the cerebral metabolism is depressed by a direct compression of neural tissues by the hematoma. Tanaka et al (3) reported that the mean hemispheric cerebral blood flow decreased about 7% in patients with chronic subdural hematomas and headaches but about 35% in patients with hemiparesis and/or mental disturbances. However, Gjerris and Brodersen (5) measured the cerebral metabolic rate of oxygen in their patient and found that it was reduced more than cerebral blood flow. Therefore, it is possible that cerebral blood flow reduction (ischemia) might not be the cause of brain dysfunction but is the result of reduced metabolic demand in the dysfunctional brain (we did not measure cerebral blood flow in this study).

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