Cerebral Metabolic Abnormalities in COPD Patients Detected by Localized Proton Magnetic Resonance Spectroscopy*

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Study objectives: To investigate changes in the cerebral metabolism of patients with COPD, using localized in vivo proton magnetic resonance spectroscopy (1H MRS), and to evaluate the clinical significance of cerebral metabolic abnormalities in COPD patients.

Patients and methods: Seventeen symptomatic COPD patients and 21 age-matched healthy volunteers participated in this study. All subjects underwent 1H MRS, and neuropsychological tests (Wechsler memory scale-revised [WMS-R], color trail test, and grooved pegboard test) were performed by COPD patients. Magnetic resonance spectra were obtained from localized regions of parietal white matter (PWM) and occipital gray matter (OGM). Absolute levels of N-acetyl aspartate (NAA), creatine (Cr), choline (Cho), and myo-inositol (mI) were calculated.

Results: In COPD patients, the mean (± SD) FEV1 was 38 ± 10% predicted, the PaCO2 was 39 ± 7 mm Hg, and the PaO2 was 89 ± 18 mm Hg, and these values did not exhibit statistical correlation with the levels of cerebral metabolites. NAA, Cr, and Cho levels in PWM were all significantly lower in COPD patients than in control subjects (p < 0.0125 [Bonferroni adjusted]). Neuropsychological parameters were lower in COPD patients compared with standardized values. However, they were not correlated with the levels of cerebral metabolites except for a positive correlation between the Cho level in PWM and the general memory quotient of WMS-R (r = 0.52; p < 0.05).

Conclusions: Our results demonstrate that the cerebral metabolism is significantly altered in symptomatic COPD patients. The relationship between decreased Cho levels and memory dysfunction, and the clinical significance of other cerebral metabolic changes in COPD patients need to be further investigated.

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Key words: cerebral metabolism; cognitive function; COPD; proton magnetic resonance spectroscopy

Abbreviations: Cho = choline; CHF = congestive heart failure; Cr = creatine; CTT = color trail test; GPT = grooved pegboard test; 1H MRS = proton magnetic resonance spectroscopy; mI = myo-inositol; NAA = N-acetyl aspartate; OGM = occipital gray matter; PWM = parietal white matter; WMS-R = Wechsler memory scale-revised

Cognitive deficit is a common problem in patients with COPD. Many studies have evaluated the correlation between neuropsychological dysfunction and pulmonary function or arterial blood gas parameters in COPD patients. Depressed FEV1 is an independent predictor of neuropsychological dysfunction.1 Cognitive disturbance is common in patients with hypoxemic COPD2 oxygen therapy re- lieves neuropsychological deficits,3−5 and arterial hypercapnia characterizes the severity of cognitive dysfunction.6 However, to date and to our knowledge no study has evaluated direct metabolic changes in the brain, which might well have a direct relationship to the cognitive deficit in COPD patients.

Proton magnetic resonance spectroscopy (1H MRS) is a sensitive technique with which to detect metabolic changes of the brain in vivo. It has been
convincingly used to assess metabolic changes of the brain in various clinical disorders.7–11

In this study, we hypothesized that the cerebral metabolism was disturbed in COPD patients and that the levels of cerebral metabolites could have some clinical meanings. To address this hypothesis, cerebral metabolites were measured using 1H MRS, and the results were compared with neuropsychological parameters and other laboratory parameters.

Materials and Methods

Subjects

Seventeen symptomatic COPD patients who were <70 years of age, who visited the Asan Medical Center between March 1999 and October 1999, and 21 age-matched healthy volunteers were recruited for this study. COPD was defined as a disease state characterized by the presence of airflow obstruction (i.e., FEV1 < 80% predicted and FEV1/FVC ratio < 70%) due to chronic bronchitis or emphysema.12 All patients had been in clinically stable condition without an oxygen supply for at least 1 week before their participation in this study. Patients who had a history of or current chronic alcoholism, renal failure, chronic liver disease, cerebrovascular disease, or other diseases that might affect neuropsychological function were excluded. Serum osmolarity and sodium concentration were measured on the same day as the 1H MRS was performed to rule out the possible influence of osmolytes on the cerebral metabolism.13 Serum osmolarity, serum sodium concentration, and arterial blood gas levels were measured in nine healthy control subjects. To investigate the influence of hypercapnia, the 17 COPD subjects were divided into a hypercapnia group (n = 6) and a normocapnia group (n = 11) for comparison. Regardless of respiratory illness, 25 subjects with normal MRI findings and 13 subjects with MRI abnormalities also were compared.

The institutional review board of the Asan Medical Center approved this study, and informed consent was obtained from all participants.

1H MR Spectroscopy

All MRI scans and localized in vivo 1H MRS procedures were performed on a system equipped with shielded gradients (GE 1.5T Signa; General Electric Medical Systems; Milwaukee, WI) from 9 AM to midday. Spectroscopy was performed following a routine brain MRI analysis, and the T2-weighted images were used for localization. Image-guided stimulated echo acquisition mode spectra were obtained from the parietal white matter (PWM) and the occipital gray matter (OGM) regions (with proton brain examination) with the following acquisition parameters: echo time, 30 ms; repetition time, 3.0 s; number of averages, 36; spectral width, 2,500 Hz; spectral size, 2,048 points (General Electric Medical System) (Fig 1). The voxels used in this study had volumes of 7 to 9 mL, and a three-pulse chemical shift selective sequence was used for the suppression of the H2O signal. One experienced person undertook the careful placement of the localization voxel in the same region for all subjects, thereby increasing the consistency of region selection.

Spectroscopic raw data were processed according to the method described by Kreis et al.8 The major metabolites detectable in 1H MRS are N-acetyl aspartate (NAA), creatine (Cr), choline (Cho), myo-inositol (mI), lactate, glutamate, and other molecules if their intracellular concentrations are ≥ 2 mmol. Peaks were identified with known chemical shifts of NAA at 2.02 ppm, Cr at 3.03 ppm, Cho at 3.22 ppm, and mI at 3.56 ppm. The raw spectroscopic data were transferred to a computer workstation (SUN Sparc 10; SUN Computers; Mountain View, CA) and were processed by special software (SA/GE; General Electric Medical Systems) with the following procedure: left shift, 1 point; zero filling, 8,192 points; and exponential apodization, 0.5 Hz followed by Fourier transformation and zero order phasing. The areas under the peaks were measured by Lorenzian line-shape fitting. The absolute concentrations of NAA, Cr, Cho, and mI were calculated from the processed spectrum using the brain water as an internal reference, according to the method described by Soher et al.14 All concentrations were expressed as millimoles per kilogram of wet weight. The reference brain water signals used in our calculation were 64% in the PWM and 76% in the OGM, as calculated according to the method described by Ernst et al15 for healthy volunteers.

Figure 1. Brain MRI scan. Image-guided stimulated echo acquisition mode spectra were obtained from regions of the PWM (top, A) and the OGM (bottom, B). The volumes of the voxels were 7 to 9 mL.
Neuropsychological Function Tests

To assess the cognitive function that is known to be impaired in COPD patients, the following three neuropsychological tests were applied: Wechsler memory scale-revised (WMS-R); the color trial test (CTT); and the grooved pegboard test (GPT).

The WMS-R is a widely used neuropsychological test for memory and learning ability, which yields age-adjusted and education-adjusted standardized scores in the following five subcategories: general memory; visual memory; verbal memory; attention/concentration; and delayed recall. The CTT is used for the evaluation of attention and visuospatial scanning ability and is an improved version of the previously well-known trail-making test with less effect from cultural or educational background. The GPT test is a pin-inserting motor task that demands high levels of performance in visuomotor coordination and fine motor control of each hand.

Statistical Analysis

Statistical analyses were performed using a software package (SPSS for Windows, version 7.5; SPSS Inc; Chicago, IL). Categoric values were compared between groups using the $\chi^2$ test. Continuous values, such as age and the concentrations of metabolites, were compared between two groups using the independent sample $t$ test and the nonparametric Wilcoxon rank sum test. A Bonferroni correction was applied in multiple comparisons between the COPD and control groups. In performing the Bonferroni correction, we divided the variables into the following three groups: group 1: FEV$_1$ % predicted, FEV$_1$, PaCO$_2$, PaO$_2$, serum sodium, and serum osmolarity; group 2: NAA, Cr, Cho, and mI levels in the PWM; and group 3: NAA, Cr, Cho, and mI levels in the OGM. A Bonferroni correction was applied in each group. Spearman correlation coefficients ($r$) were calculated to test the correlations between parameters. Two-way analysis of variance was performed in order to analyze the relationships among cerebral metabolite changes, COPD, and smoking. The data are expressed as the mean ± SD, and statistical significance was achieved at $p < 0.05$. In the case of performing the Bonferroni correction, statistical significance was defined as $p < 0.05/k$, where $k$ is the number of parameters for the Bonferroni correction in each set of three variable groups.

RESULTS

Clinical Parameters

The baseline clinical characteristics are presented in Table 1. The mean age of COPD patients was 62 ± 4 years (age range, 53 to 69 years). All COPD patients had dyspnea on exertion, and all but three were current smokers or ex-smokers. Fourteen patients were being treated with theophylline, 1 patient with diuretic, and 12 patients with ipratropium bromide inhaler. Of the 21 control subjects, 8 were current smokers or ex-smokers.

The mean FEV$_1$ of COPD patients was significantly lower than that of healthy control subjects ($p < 0.008$ [Bonferroni adjusted]). The degree of airway obstruction was mild in 3 patients, moderate in 10 patients, and severe in 5 patients. All patients had a PaO$_2$ of > 60 mm Hg at the resting state. The measured PaCO$_2$ for the patients was > 45 mm Hg in 3 patients, between 40 and 45 mm Hg in 3 patients, and < 40 mm Hg in the other 11 patients. Serum osmolarity was significantly lower in COPD patients than in healthy control subjects (288 ± 9 vs 300 ± 7, respectively; $p < 0.008$ [Bonferroni adjusted]).

$^1$H MRS

The results of MRI scans of the brain were normal in 14 control subjects and 9 COPD patients ($p > 0.05$). Changes consistent with findings of lacunar infarction, ischemic change, or brain atrophy were seen on MRI scans in the remaining 15 subjects, but none of these lesions were within the localized areas for $^1$H MRS. The $^1$H MRS data and the typical $^1$H MR spectra are shown in Table 2 and Figure 2, respectively. The NAA, Cr, and Cho levels of the PWM were lower in patients with COPD than in control subjects (p < 0.0125 [Bonferroni adjusted]). The levels of mI in both the PWM and the

<table>
<thead>
<tr>
<th>Table 1—Clinical Characteristics of the Subjectsa</th>
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<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>Age, yr</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Female 7</td>
</tr>
<tr>
<td>Smoking, pack-yr†</td>
</tr>
<tr>
<td>FEV$_1$, % predicted†</td>
</tr>
<tr>
<td>FEV$_1$, L/min†</td>
</tr>
<tr>
<td>PaCO$_2$, mm Hg</td>
</tr>
<tr>
<td>PaO$_2$, mm Hg</td>
</tr>
<tr>
<td>Serum sodium, mEq/L</td>
</tr>
<tr>
<td>Serum osmolarity, mOsm/L↓</td>
</tr>
</tbody>
</table>

aValues given as mean ± SD, unless otherwise indicated.
†Statistical significance was defined as $p < 0.008$ using Bonferroni correction.

<table>
<thead>
<tr>
<th>Table 2—Absolute Concentration of Brain Metabolites Measured by $^1$H MRSb</th>
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<tbody>
<tr>
<td>Area</td>
</tr>
<tr>
<td>PWM</td>
</tr>
<tr>
<td>Cr†</td>
</tr>
<tr>
<td>Cho†</td>
</tr>
<tr>
<td>mI</td>
</tr>
<tr>
<td>OGM</td>
</tr>
<tr>
<td>Cr</td>
</tr>
<tr>
<td>Cho</td>
</tr>
<tr>
<td>mI</td>
</tr>
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</table>

bValues are given as mean ± SD.
†Statistical significance was defined as $p < 0.0125$ using Bonferroni correction.
OGM showed a decreased tendency in COPD patients compared with the control subjects ($p = 0.05$ and $p = 0.08$, respectively). According to two-way analysis of variance, the direct cause of the decreased NAA and Cr levels in the PWM was revealed to be COPD, not smoking. There were no statistically significant differences in cerebral metabolite concentrations between the hypercapnic group (ie, $\text{PaCO}_2 > 40 \text{ mm Hg}$) and the normocapnic group. There were no significant differences in cerebral metabolite concentrations between 23 subjects with normal findings on MRI scans and 15 subjects with abnormal findings on MRI scans, irrespective of their having COPD.

Neuropsychological Function Tests

The neuropsychological function tests were not carried out in two patients, and the results obtained from the 15 patients tested are listed in Table 3. The mean values of all parameters examined were decreased compared with the standardized values. Most of the COPD patients had at least one neuropsychological function parameter that was 2 SDs below the standardized values.

Correlation Between Cerebral Metabolites and Clinical Variables

The clinical parameters that showed significant correlations with the level of cerebral metabolites are listed in Table 4. Age showed an inverse correlation with NAA levels in both brain regions and with mI levels in the PWM. The serum sodium concentration was positively correlated with the level of NAA in the PWM. Among the nine neuropsychological function parameters examined, only the general memory quotient showed a positive correlation with the level of Cho in the PWM.

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**Table 3—The Results of Neuropsychological Function Tests in COPD Patients**

<table>
<thead>
<tr>
<th>Neuropsychological Function Tests</th>
<th>COPD (n = 17)</th>
<th>Standard Values†</th>
</tr>
</thead>
<tbody>
<tr>
<td>WMS-R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gen</td>
<td>62 ± 15</td>
<td>100 ± 15</td>
</tr>
<tr>
<td>Verb</td>
<td>66 ± 14</td>
<td>100 ± 15</td>
</tr>
<tr>
<td>Vis</td>
<td>71 ± 21</td>
<td>100 ± 15</td>
</tr>
<tr>
<td>Att-con</td>
<td>83 ± 19</td>
<td>100 ± 15</td>
</tr>
<tr>
<td>Del</td>
<td>67 ± 13</td>
<td>100 ± 15</td>
</tr>
<tr>
<td>CTT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTT1</td>
<td>35 ± 11</td>
<td>50 ± 10</td>
</tr>
<tr>
<td>CTT2</td>
<td>35 ± 14</td>
<td>50 ± 10</td>
</tr>
<tr>
<td>GPT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dom</td>
<td>31 ± 24</td>
<td>50 ± 10</td>
</tr>
<tr>
<td>Non-D</td>
<td>33 ± 18</td>
<td>50 ± 10</td>
</tr>
</tbody>
</table>

*Gen = general memory; Verb = verbal memory; Vis = visual memory; Att-con = attention/concentration; Del = delayed recall; Dom = dominant hand; Non-D = nondominant hand.

†Standard values are age-adjusted and education-adjusted standardized scores.
Table 4—Correlation Between the Level of Cerebral Metabolites and Clinical Parameters in 17 Patients With COPD*

<table>
<thead>
<tr>
<th>Determinants</th>
<th>Cerebral Metabolites, mmol/kg</th>
<th>r Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>NAA (PWM)</td>
<td>−0.52</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td>NAA (OGM)</td>
<td>−0.49</td>
<td>0.046</td>
</tr>
<tr>
<td></td>
<td>mI (PWM)</td>
<td>−0.49</td>
<td>0.047</td>
</tr>
<tr>
<td>Serum Na, mEq/L</td>
<td>NAA (PWM)</td>
<td>0.51</td>
<td>0.035</td>
</tr>
<tr>
<td>Gen</td>
<td>Cho (PWM)</td>
<td>0.52</td>
<td>0.049</td>
</tr>
</tbody>
</table>

*See Table 3 for abbreviations not used in text. Only variables with significant correlation coefficients were listed.

DISCUSSION

To our knowledge, this is the first demonstration of cerebral metabolism being significantly altered in symptomatic COPD patients. Although further investigation of the mechanisms and clinical significance of cerebral metabolic changes in COPD patients is required, these findings provide a neurochemical basis for the cerebral dysfunction in COPD patients.

1H MRS of the Brain

In this study, we measured the absolute concentrations of NAA, Cr, Cho, and mI in the brains of COPD patients. NAA is a neuronal marker the concentration of which decreases with neuronal cell death. Cr consists of Cr and phosphocreatine, and it participates in energy metabolism. Cho is associated with myelination, and mI is suggested to participate in the control of osmolarity, although the exact function of these metabolites is not yet known. A general decrease in cerebral metabolites was noted in the PWM of the COPD patients. This finding may be attributed to the regional difference of susceptibility to the specific changes that occurred in COPD patients. These cerebral metabolic changes are different from those in other diseases such as congestive heart failure (CHF),9 diabetes mellitus,7 or hepatic encephalopathy.8 In contrast to patients with COPD, who showed more dramatic decreases in cerebral metabolites in the PWM, patients with CHF have shown a more prominent decrease of brain metabolites in the OGM. In patients with diabetes mellitus, the Cho level increases in both the PWM and the OGM, whereas a significant reduction of NAA is found in the parietal cortex.7 In patients with chronic hepatic encephalopathy, the mI and Cho levels in the PWM are decreased.8 Therefore, it is proposed that different pathophysiologic abnormalities associated with various diseases may induce their own characteristic changes in the brain. Thus, these changes in cerebral metabolites may be characteristic findings of COPD patients, although they are not pathognomonic.

We can easily assume that hypoxemia and/or hypercapnia may influence the level of metabolites in the brains of COPD patients. However, none of the brain metabolites showed any correlation with PaO2 level in this study. Furthermore, the PaCO2 level did not correlate with the levels of any other brain metabolites. One possible explanation for our result is that, because only nonhypoxic subjects in a resting condition were included, there were not enough variances in the resting PaO2 levels that could predict the metabolic changes. Considering that all patients had dyspnea on exertion and that most of them had moderate-to-severe airflow obstruction, although they had resting normoxemia, it is highly probable that they had hypoxemia during exercise or normal activity. In addition, the nocturnal desaturation that occurs in COPD patients may play a role in the cerebral metabolite changes. One patient who performed an exercise pulmonary test in this study showed hypoxemia after completion of the test. This suggests that an important determining factor of cerebral metabolism would not be the measurement of resting PaO2 or FEV1, but the measurement of PaO2 or O2 delivery to the brain during sleep or during the activities of daily living. This finding is supported by the study of Kamba et al20 for patients with obstructive sleep apnea. Those patients showed a decreased NAA/Cho ratio in the cerebral white matter, indicating an altered cerebral metabolism for patients with moderate-to-severe obstructive sleep apnea, although the investigators did not measure the absolute concentrations of the cerebral metabolites as we did in our current study. However, in order to confirm this, we would need to perform arterial blood gas analyses during sleep or exercise in COPD patients and investigate the relationship between PaO2 levels and the levels of cerebral metabolites.

Most previous observations with 1H MRS strongly support the fact that NAA is a neuronal marker.21 The reduction of NAA generally has been reported in patients who have prominent neuronal losses, for example, glioma, stroke, dementia, and hypoxic encephalopathy. Although the NAA level of the control group did not show a significant correlation with aging in our study, the COPD group’s NAA level was inversely correlated with aging. These data suggest that hypoxemia and/or hypercapnia might have accentuated the effects of neuronal death by aging. Neuronal cell death is generally considered to be an irreversible process accompanying aging, and decreases of NAA in healthy aged persons frequently are reported.22,23 Although the possibility of cerebral
NAA restoration might be expected using long-term oxygen therapy for these COPD patients, as in the case with heart-transplanted CHF patients,9 further studies are needed to confirm whether these increases represent actual neuronal regeneration.21

Cr participates in cerebral energy metabolism and reserves. Therefore, decreased Cr levels in the PWM indicate that COPD patients undergo cerebral energy deficits in the PWM. Cho is associated with myelin, and therefore the level is higher in the PWM than in the OGM.

Although the major components of myelin, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol, are probably entirely immobile and invisible, their putative breakdown products, phosphorylcholine, glycerophosphorylcholine, Cho, and mI, are visible in 1H MRS. Therefore, decreased levels of Cho in the PWM but not in the OGM, as shown in this study, might well suggest decreased myelin levels in the PWM of COPD patients.

mI is a marker of reversible cerebral organic osmolytes.13 In this study, the tendency toward lowered mI levels seems to be related more to the lower serum osmolarity found in COPD patients compared to healthy control subjects. Lee et al9 also reported that both serum osmolarity and sodium concentrations are significantly lower in CHF patients than in healthy control subjects and that the mI level in the OGM is independently correlated with serum osmolarity. In our study, however, there was no correlation between the mI level and serum osmolarity or sodium concentration. In addition, we could not attribute the differences in serum osmolarity to serum sodium concentration, as found in the study by Lee et al.9 The primary plasma osmoles are sodium, glucose, and urea. Because there is no difference in sodium concentration between groups, healthy control subjects may have higher glucose or urea concentrations compared with COPD patients, even in the absence of symptoms or medical histories compatible with diabetes mellitus or renal dysfunction. Although it is well-known that hyponatremia, which is the main cause of hyposmolarity, is present in COPD patients with advanced disease,24 this seems not to be the case in this study. In summary, although serum osmolarity was significantly different between control subjects and COPD patients in this study, we could not determine how it affected the concentration of cerebral metabolites.

Neuropsychological Function Tests

Because the neuropsychological tests were performed only by COPD patients, a direct comparison in neuropsychological performance with the control subjects is not possible. However, as suggested in Table 3, we could find global impairment in memory, attention, visuospatial scanning ability, and motor function, as described in previous studies on neuropsychological functions of COPD patients.2,25–27 Although attentional dysfunction was demonstrated in COPD patients by the poor performance score on the attention/concentration subscale of the WMS-R, impairment was more exaggerated in the results of the CTTs. This suggests a specific difficulty in complex perceptual-motor integration, as shown in other studies.5,28

Although 87% of the patients (13 of 15 patients) showed various forms of memory impairment in the results of the WMS-R, we cannot conclude in this study that actual memory loss is the result of chronic hypoxemia. As memory is a complex integrative end-result of higher cortical functions of attention, language, visual processing, and information processing, it is likely that the combination of various cognitive deficits caused the poor performance in the memory tasks of the WMS-R in this study. This view also is supported by other studies29 showing that memory dysfunction parallels global cognitive impairment. Such studies suggest that one could expect some improvement of memory function with long-term oxygen therapy,26 which seems improbable if it was due to memory impairment per se.

Clinical Significance of Cerebral Metabolic Abnormalities

In this study, we found that the levels of cerebral metabolites of COPD patients were significantly altered, and especially that the Cho level in the PWM correlated with memory function. This correlation is compatible with previous findings that the cholinergic nervous system plays an important role in memory.30,31 Dementias, especially of the Alzheimer’s type, are characterized by a depleted cholinergic neuronal system,32 but 1H MRS findings of dementia patients do not always show a decrease in the Cho/Cr ratio, as would be expected.30,33,34 This may be due to the involvement of multiple neurotransmitter systems or to advanced brain atrophy in these patients. However, the correlation between parietal Cho level and memory function that was revealed in the COPD patients in our study provides further direct evidence for the deficit of memory function and a possible link to the cholinergic system. This is particularly true in these subjects, as we measured the absolute concentration of metabolites and excluded subjects with apparent brain atrophy from this aspect of the study.

Although we noted a reduction in NAA and Cr concentration within the PWM, these levels did not
show any correlation with neurocognitive function, in contrast to Cho-containing metabolites. The neuropsychological tests applied in this study are generally considered to be measures of global higher cognitive function. Thus, changes in the levels of brain metabolites that are detected by \(^1\)H MRS from a focal region may not fully reflect the changes that have occurred in the whole brain. Other tests for whole-brain activity or function are required for future studies.

Although we tried to exclude any subjects with conditions affecting cerebral functions, many of the COPD patients had received theophylline therapy, which is known to have a cerebral stimulatory effect, and many also had used an ipratropium bromide inhaler. However, previous reports\(^{35,36}\) have shown that neither theophylline nor ipratropium bromide has any deleterious effects on cognitive function.

Smoking may induce cerebral metabolic abnormalities independently of its influence on lung function. Although there is some evidence that cigarette smoking is a risk factor for stroke or other cerebral changes,\(^{37,38}\) interestingly, the result of this study showed that the main cause of the decreased NAA and Cr levels in PWM was COPD, not smoking. Healthy control subjects who smoke also had normal levels of cerebral metabolites compared with the patients with COPD who smoked. However, we need a further study to investigate more clearly the direct effect of smoking, and of the amount of smoking, on the brain metabolism, irrespective of whether the patient has COPD. Many patients with COPD showed ischemic changes, lacunar infarctions, or brain atrophy on MRI scans. Being uncertain of the association of such lesions with COPD, we excluded COPD patients whose MRI findings were abnormal in the area employed for spectroscopic measurement. Patients with diffuse brain atrophy shown on MRI scans also were excluded.

In conclusion, most of the symptomatic COPD patients were found to have cognitive dysfunction and cerebral metabolic abnormalities, which were confirmed for the first time in this study using \(^1\)H MRS. Although the Cho level in the PWM is correlated with the general memory quotient derived from the WMS-R, other cerebral metabolic changes did not correlate with physiologic parameters, such as pulmonary function and resting PaO\(_2\) or PaCO\(_2\) levels, or with neuropsychological performances. Further studies will be required to document the mechanism and clinical significance of cerebral metabolic abnormalities in COPD patients and to confirm the effect of therapeutic interventions on the cerebral metabolism.

References