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^{1}H MR Spectroscopic Patterns of Normal Adult Brain[1]

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Purpose : To evaluate regional differences of ^{1}H magnetic resonance(MR) spectral patterns in normal adult human brains.

Materials and Methods : A total of 44 ^{1}H MR spectra in 25 volunteers aged 27−45 were obtained in five regions including the frontal lobe(10), parietal lobe (10), temporal lobe(5), basal ganglia(10) and thalamus(9). ^{1}H MR spectroscopy (MRS) was performed using a PRESS sequence with a TR of 2000 ms and a TE of 270ms from a volume of cm on a 1.5T clinical MR unit. Relative metabolite ratios of NAA/Cho, NAA/Cr and Cr/Cho in each region were measured and compared.

Results : A total of 44 reliable spectra were successfully obtained in all regions. NAA/Cho, NAA/Cr and Cr/Cho ratios varied considerably, ranging from 1.09 ± 0.2 to 2.46 ± 0.25, from 1.72 ± 0.35 to 2.45 ± 0.25 and from 0.64 ± 0.1 to 1.01 ± 0.12, respectively. Significant regional differences in metabolite ratios were observed; higher NAA/Cho and NAA/Cr ratios in the parietal lobe, lower NAA/Cho ratios in the temporal lobe, and lower Cr/Cho ratios in the temporal lobe compared to those of other regions($p<0.05$). Differences in metabolite ratios between the right and left frontal lobes, and between the right and left basal ganglias were not significant.

Conclusion : ^{1}H MR spectra of the normal adult human brains using in vivo single voxel ^{1}H MRS represented significant regional differences in metabolite ratios of NAA/Cho, NAA/Cr and Cr/Cho. Our ^{1}H MR spectroscopic results are a useful reference for assessing the ^{1}H MRS pattern of various intracranial diseases.

Index Words : Magnetic resonance (MR), spectroscopy

INTRODUCTION

In vivo single voxel ^{1}H magnetic resonance spectroscopy(MRS) techniques have recently been developed, which allow us to obtain a reliable in vivo ^{1}H MRS data on a 1.5T MR unit. The ^{1}H MR spectral pattern of the normal human brain is very important, because it is used as a reference for the evaluation of various intracranial diseases, and so the accumulation of much more normal reliable spectral data is required. In most studies, however, ^{1}H MR spectral patterns of normal human brain have been obtained only as control data that were not systematic for assessing the brain diseases(1−3). In all studies on the normal human brain, ^{1}H MR spectra have shown high N-acetylaspartate (NAA) signals compared to creatine complex(Cr) and choline complex(Cho) signals that were at almost the same intensity. Several authors have reported regional differences in both metabolite ratios and absolute metabolite concentration in the human brain(4, 5); other studies, however, have demonstrated a variety of regional differences in ^{1}H MR spectral patterns. To our knowledge, only a few systematic reports have been published(4−13); moreover, ^{1}H MR spectral data on the normal brains of domestic adults have not been reported. The purpose of the present study is to evalu-

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ate regional differences in relative metabolite ratios in various regions of normal adult brains.

MATERIALS and METHODS

Twenty-five normal volunteers(15 males and 10 females) were studied with ^{1}H MRS. Forty-four spectra from five regions — the frontal lobe on both sides (n=10), the basal ganglia on both sides(n=10), the parietal lobe(n=10), the thalamus(n=9) and the temporal lobe(n=5) — were obtained(Table 1).

All investigations of normal human brain were performed on a 1.5T MR unit(Magnetom SP, Siemens, Germany) operating at about 63MHz for proton. A commercial, circular polarized(CP) head coil was used for imaging and spectroscopy. PRESS sequence with a TE of 270ms and a TR of 2 seconds were used resulting in a total acquisition time of 4min 16 s for 128 scan. A single chemical shift selective(CHESS) pulse with a spoiler gradient was applied for water suppression. Only the second half of the echo was acquired and 1024 data points were sampled with a sampling frequency of 1000 Hz. T1-weighted MR imagings in three orthogonal planes or often T2-weighted images in the transverse plane preceded ^{1}H MRS to define the volume of interest(VOI) as cm. Before spectroscopic measurements, field homogeneity was optimized over the selected VOI by observing the ^{1}H MR signal of tissue water with the spatially selective PRESS sequence. Typical full widths at half maximum(FWHM) of 4—8Hz were achieved in all investigations.

Following the zero-filling of 4096 points in all free induction decay(FID) data, an exponential line broadening(center : 0ms, half time : 150ms) was applied before Fourier transformation ; zero-order phase correction was applied to all spectra. Insufficient water suppression made other small intensity signals sit on the slope of the residual water signal. An interactive baseline correction carried out by calculating the second-

Table 1. Distribution of Regions Examined for All Normal Volunteers

Location	No.
Frontal lobe	10/5
parietal lobe	10/10
Basal ganglia	10/5
Thalamus	9/10
Temporal lobe	5/5
Total	44/25

Notes. Both right and left sides were examined in the basal ganglias and the frontal lobes in 5 volunteers.
Two regions, one parietal lobe and one thalamus, were examined in each of 10 volunteers.
No. =number of regions examined/number of volunteers

Table 2. NAA/Cho Ratios in Various Regions of Normal Brains

mean ± SD

Location	Peak Height	Peak Area
Frontal lobe(n=10)	1.94 ± 0.28	1.99 ± 0.37
Parietal lobe(n=10)	2.46 ± 0.25 *	2.17 ± 0.25
Basal ganglia(n=10)	1.57 ± 0.27	1.46 ± 0.32
Thalamus(n=9)	1.94 ± 0.36	2.18 ± 0.63
Temporal lobe(n=5)	1.09 ± 0.20 **	1.17 ± 0.51

* NAA/Cho ratios of the parietal lobe are significantly higher than those of all other regions($p < 0.05$)
** NAA/Cho ratios of the temporal lobe are significantly lower than those of all other regions($p < 0.05$)

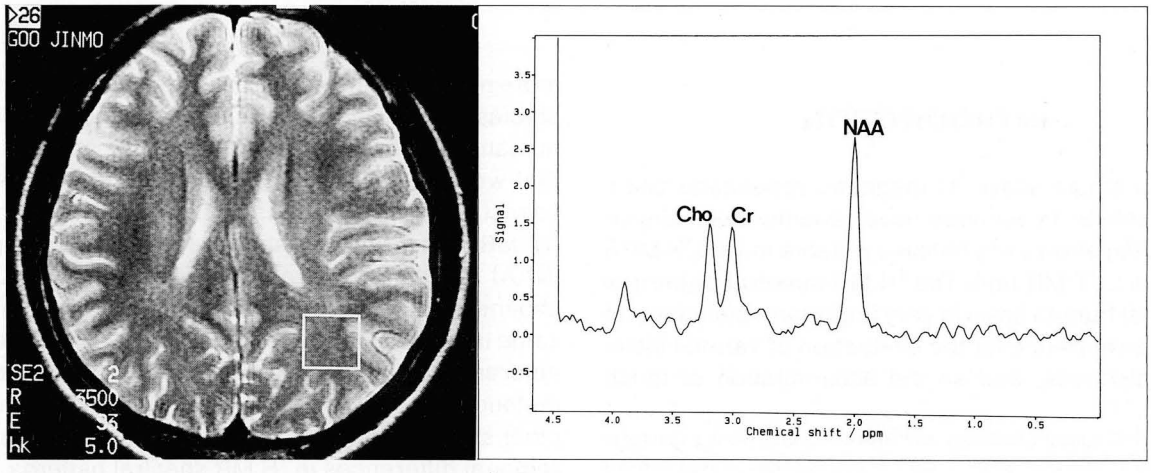

Fig. 1. A characteristic in vivo ^{1}H MR spectrum obtained in VOI of 2×2×2cm in the parietal lobe (a) of the normal brain by using PRESS sequence(TR/TE=2000/270ms). Typical three signals are well seen as followings (b) ; N-acetylaspartate(NAA, 2.02ppm), creatine-containing compound(Cr, 3.02ppm) and choline-containing compound(Cho, 3.20ppm). Peak assignments were based on the previous literatures.

order polynomial of the baseline defined manually reestablished a flat baseline in those spectra with large residual water signal. In all subjects, total measurement time taken in each ^{1}H MRS study, including the formation of MR images, was about 1 or 1.5 hours.

Identification of NAA(2.02 and 2.6ppm), Cho(3.20 ppm), Cr(3.0 and 3.9ppm) and lipid(1.30 and 0.8ppm) was based on the previous literatures(4). All spectra were evaluated by comparing the peak heights and the peak areas of resonance. Peak areas were calculated by multiplying the peak heights by FWHMs of resonances assuming spectra line shapes were Lorentzian type. Following the measurements of each peak height and peak area through three repeated baselines and phase corrections, in order to minimize operator measurement errors, their mean values were calculated. After calculating the metabolite ratios of NAA/Cr, NAA/Cho and Cr/Cho ratios in various regions of the brain, these were compared in order to evaluate the regional differences of metabolite levels and ratios. The right and left sides of both the frontal lobe and the basal ganglia were compared in order to evaluate the asymmetry of metabolite distribution.

Student unpaired t-tests(SPSS/PC+ver 4.01) were used for statistical analyses.

RESULTS

For all human brains, a total of 44 analyzable spectra were obtained. Metabolites detected by ^{1}H MRS were primarily NAA, Cr, and Cho, as shown in Fig. 1. Lipid signals were detected on some spectra of the temporal lobes.

Results of the NAA/Cho, Cr/Cho and NAA/Cr ratios are summarized in Tables 2, 3 and 4. The NAA/Cho ratios were significantly higher in the parietal lobe(2.46 ± 0.25) than in all other regions($p<0.05$); these ratios in the temporal lobe(1.09 ± 0.2) were significantly lower than those in all other regions($p<0.05$). Fig. 2 shows the scatter plots of NAA/Cho ratios in five regions of normal adult brains.

Cr/Cho ratios were significantly lower in the temporal lobe(0.64 ± 0.1) than in all other regions($p<0.05$). There were no significant differences in these ratios among the other four regions(Fig. 3).

NAA/Cr ratios in the parietal lobe(2.45 ± 0.25) were significantly higher than in the other regions except the thalamus($p<0.05$), whereas there were no significant

Table 3. Cr/Cho Ratios in Various Regions of Normal Brains

mean ± SD

Location	Peak Height	Peak Area
Frontal lobe(n=10)	1.98 ± 0.13	1.09 ± 0.18
Parietal lobe(n=10)	1.01 ± 0.12	1.02 ± 0.19
Basal ganglia(n=10)	0.88 ± 0.11	0.90 ± 0.15
Thalamus(n=9)	0.88 ± 0.08	0.93 ± 0.15
Temporal lobe(n=5)	0.64 ± 0.10*	0.71 ± 0.26

* Cr/Cho of the temporal lobe are significantly lower than those of all other regions($p<0.05$)

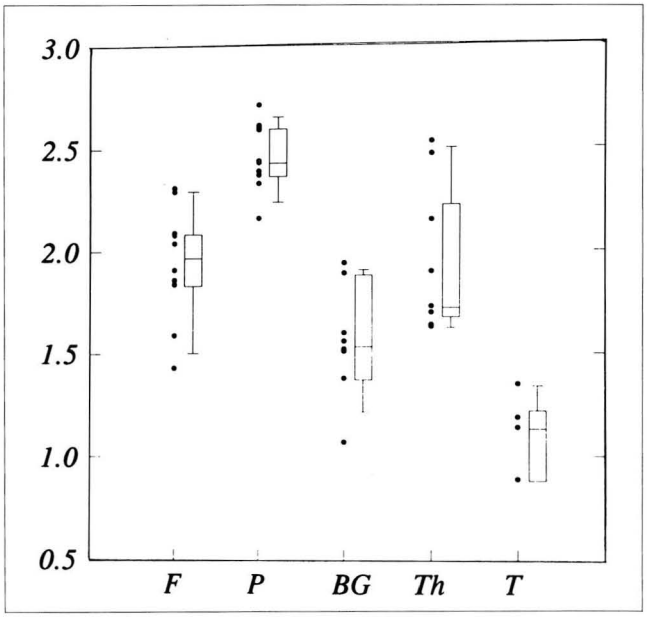

Fig. 2. NAA/Cho ratios of various regions in the normal brains. NAA/Cho ratios of the parietal lobe and the temporal lobe are significantly higher and lower than those of all other regions($p<0.05$, for all), respectively.
Notes. The ratios were based on the peak heights of resonances. F=frontal lobe, P=parietal lobe, BG=basal ganglia, Th=thalamus, T=temporal lobe

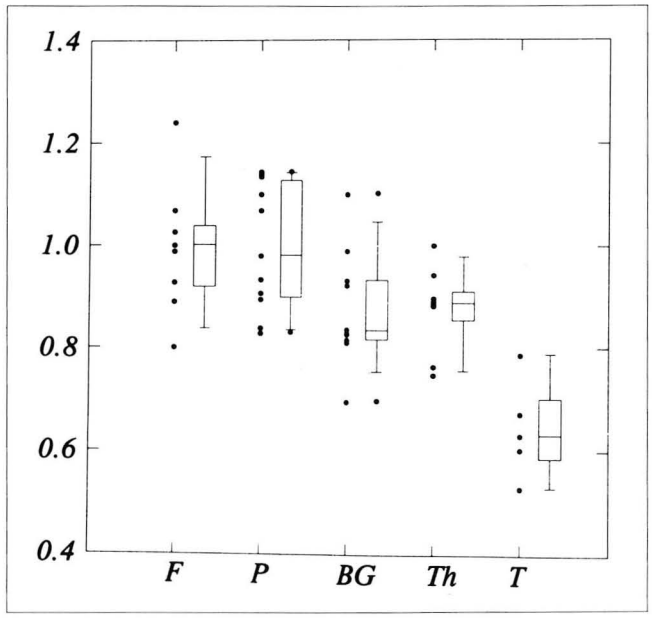

Fig. 3. Cr/Cho ratios of various regions in the normal brains. Cr/Cho ratios of the temporal lobe are significantly lower than those of other regions($p<0.05$).
Note. The ratios were based on the peak heights of resonances.

differences in these ratios among all four other regions(Fig. 4).

Table 5 shows no significant differences in NAA/Cr, Cr/Cho and NAA/Cho ratios between the right and left frontal lobes, and between the right and left basal ganglia.

There were no significant differences in the metabolite ratios between the peak height and the peak area in a given spectrum, but ranges of variation were smaller at peak height than at peak area.

DISCUSSION

The results of the present study indicate that metabolite ratios differ depending on the region of the normal adult brain.

Metabolite ratios in a given region, however, showed large inter-individual variation at peak height and at peak area ; of all five regions, thalamus showed the largest variation. A recent study of localized phased-array ^1H MRS of the temporal lobe addressed the potential importance of the partial volume effect on metabolite ratios(14) ; the study stated that for ^1H MR spectral data to be reproducible, reliable and reproducible protocols regarding voxel positioning, voxel volume and intravoxel tissue composition are required, since variation in these factors might result in a wide range of metabolite ratios in the various regions. As the thalamus is located near the third ventricle, the inclusion of cerebrospinal fluid in the ROI might markedly effect metabolite ratios with different voxel positioning.

This fact might cause metabolite ratios in the thalamus to vary more than in other regions. Meyerhoff et al (15) reported that white matter NAA levels were higher than those of gray matter, and that Cho levels of the white matter or mesial gray matter of the frontal brain were higher than those of the posterior brain. Thus, the degree of combination of white and gray matter in each ROI also might contribute to a large variation in metabolite ratios.

In the literature, the general pattern reported is that NAA levels in the normal adult brain are higher than those of Cho and Cr, and this was so in our study ; we found, though, that metabolite ratios were different from those of other authors'(1 −3). Toft et al(5) showed that NAA/Cho ratios of the parietal lobe measured by using PRESS(TR/TE=1600/272) were significantly higher than those of other regions including the basal ganglia, the temporal lobe and the frontal lobe in the brains of adolescents aged 10−15. Their results are in accordance with the results of the present study, though our NAA/Cho ratios were generally lower than theirs(2.46 ± 0.25 versus 3.56 ± 0.35). In addition, they found that NAA/Cho ratios in the frontal lobe, basal ganglia and temporal lobe were 1.96 ± 0.23, 2.21 ± 0.30 and 1.71 ± 0.16, respectively. Even in the basal ganglia and temporal lobe, NAA/Cho ratios in their study were higher than those of the present study. These differences might be due to different experimental procedures such as the selection of localized pulse sequences and postprocessing algorithms. As explained above, Strauss et al(14) showed significant variation of NAA levels in the temporal lobe due to partial volume effects, thus relative NAA levels were shown to change

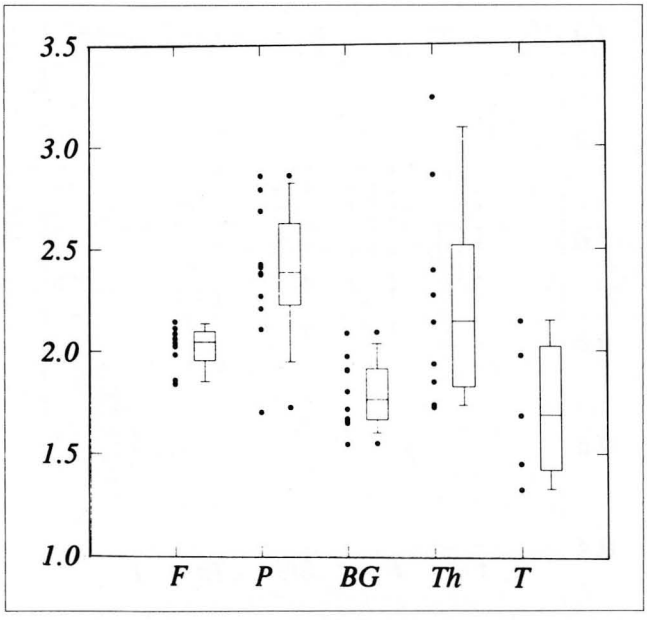

Fig. 4. NAA/Cr ratios of various regions in the normal brains. NAA/Cr ratios of the parietal lobe and the thalamus are significantly higher than those of all oter regions($p < 0.05$).
Note. The ratios were based on the peak heights of resonances.

Table 4. NAA/Cr Ratios in Various of Normal Brains

mean ± SD

Location	Peak Height	Peak Area
Frontal lobe(n=10)	1.99 ± 0.14	1.79 ± 0.34
Parietal lobe(n=10)	2.45 ± 0.25	2.95 ± 0.29
Basal ganglia(n=10)	1.79 ± 0.17	1.58 ± 0.20
Thalamus(n=9)	2.25 ± 0.52	2.37 ± 0.64
Temporal lobe(n=5)	1.72 ± 0.35	1.73 ± 0.51

Table 5. Metabolite Ratios of the Right and Left Sides in the Frontal Lobes and the Basal Ganglias

mean ± SD

	Frontal lobe		Basal ganglia	
	Right(n=5)	Left(n=5)	Right(n=5)	Left(n=5)
NAA/Cr	2.00 ± 0.18	1.97 ± 0.11	1.73 ± 0.21	1.86 ± 0.12
NAA/Cho	1.86 ± 0.35	2.03 ± 0.19	1.56 ± 0.36	1.59 ± 0.19
Cr/Cho	0.92 ± 0.11	1.03 ± 0.13	0.90 ± 0.15	0.86 ± 0.08

Notes. The values were based on the peak heights of resonances.

with varying VOIs. Voxel size, therefore, seems to be another important factor which can result in different authors reporting metabolite ratios.

To overcome partial volume effects, MRS techniques that allows smaller regions to be investigated will be developed, and the precise evaluation of ^{1}H MR spectral patterns in various regions of the normal human brain will be possible. These technical factors will allow the precise and reliable comparison of ^{1}H MR spectral data between all authors, and should be carefully taken into account.

The previous literature has addressed controversial differences of NAA/Cho ratios between the right and left temporal lobes(16−18). In the present study, average NAA/Cho and NAA/Cr ratios between the right and left frontal lobes, and between the right and left basal ganglias were symmetrical ; our study did not, however, evaluate the symmetry of metabolite levels and ratios between the right and left sides in other various regions of the brain. Further evaluation on the symmetry of metabolite ratios between the right and left sides in other brain regions is therefore required.

In conclusion, analyzable and reproducible ^{1}H MR spectra were obtained by in vivo ^{1}H MRS in all subjects. ^{1}H MR spectral patterns were different among various regions of the brain. The mean NAA/Cr and NAA/Cho ratios were significantly higher in the parietal lobe than in other regions, and lower in the temporal lobe. However, the differences in metabolite ratios between both frontal lobes and between both basal ganglias were not significant.

The results of the present study can be used as a reference for assessing ^{1}H MRS studies of other intracranial diseases.

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정상 성인 뇌의 수소자기공명분광 양상[1]

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목 적 : 정상 성인의 뇌 여러 부위에서 측정한 수소자기공명분광(^{1}H MR Spectroscopy, MRS) 양상이 부위별 차이를 보이는 지를 밝히는 것이다.

대상 및 방법 : 뇌 여러 부위에서의 ^{1}H MRS 양상 차이를 알아 보기 위해 25명의 한국 정상 성인을 대상으로 하였다. 1.5T MR 장치를 이용하여 총 44개의 스펙트럼을 뇌의 다섯 부위(전두엽 10, 두정엽 10, 측두엽 5, 기저핵 10, 시상 9)에서 PRESS 방법(TR/TE=2000/270ms, voxel 용적 =2×2×2cm)을 사용하여 얻었다. 각 부위에서 N-acetylaspartate(NAA), creatine를 포함하는 복합 물질 (Cr) 및 choline을 포함하는 복합물질(Cho) 등 세가지 물질의 크기를 측정하여 NAA/Cho과 NAA/Cr 그리고 Cr/Cho의 상대적 비를 계산하여 비교하였다.

결 과 : 총 44개의 분석 가능한 스펙트럼을 얻을 수 있었다. NAA/Cho비와 NAA/Cr비 그리고 Cr/Cho비는 각각 1.09±0.2부터 2.46±0.25까지, 1.72±0.35부터 2.45±0.25까지, 그리고 0.64±0.1부터 1.01±0.12까지의 다양한 분포를 보였다. 대사 물질의 농도비에 있어서는 뇌의 부위에 따라 통계적으로 의미있게 차이가 있었다 : 두정엽은 다른 네 부위보다 NAA/Cho 및 NAA/Cr비가 가장 높았고, 측두엽에서 가장 낮았다. 그리고, 측두엽은 다른 네 부위보다 낮은 Cr/Cho비를 보였다 ($p<0.05$). 좌우 전두엽과 좌우 기저핵간에 있어서 대사 물질의 농도비 차이는 없었다.

결 론 : 정상 성인 뇌에서 얻은 ^{1}H MRS 양상은 NAA/Cho과 NAA/Cr 그리고 Cr/Cho 등의 대사 물질의 농도비가 뇌의 부위에 따라 다르게 나타났다. 본 연구의 ^{1}H MRS 결과는 여러 뇌질환의 ^{1}H MRS 양상을 평가하는데 있어서 유용한 참고 자료로 사용될 수 있을 것이다.