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BACKGROUND AND PURPOSE: **There is a lack of information with regard to normal metabolic ratios acquired with MR spectroscopy utilizing a long echo time technique. Our purpose was to measure metabolic ratios in healthy adults to determine whether the metabolites varied across brain regions and by sex.**

METHODS: **Single voxel proton spectra were acquired with an echo time of 135 milliseconds in 10 brain regions of 72 healthy subjects ranging in age from 20 to 44 years. Six gray matter sites in the cerebrum included four cortical areas in the frontal, parietal, temporal, and occipital lobes, and two deep nuclear sites in the basal ganglia and the thalamus. Two subcortical white matter regions were in the parietal and the frontal lobes. Two posterior fossa sites included the pons and the cerebellum. All 10 brain regions were not studied in each subject. For each spectrum, the metabolites N-acetylaspartate (NAA), creatine (Cr), and choline (Ch) were identified and ratios of NAA/Cr and Ch/Cr calculated for each brain region. A multifactorial analysis of variance was performed with the two metabolic ratios as dependent variables and with brain region and sex as independent variables. Post hoc statistical analysis consisted of the Scheffé *F* statistic for significant difference between pairs of brain regions for both metabolic ratios.**

RESULTS: **There was significant regional variation for both the NAA/Cr ratio ($P < .0001$) and the Ch/Cr ratio ($P < .0001$). The NAA/Cr ratio was consistent within cortical gray and white matter but differed between cortical gray (smaller ratio) and white matter (larger ratio). The Ch/Cr ratio was variable in the gray matter, differed between some but not all gray and white matter regions, but was consistent within subcortical white matter regions. There was no difference between men and women for either metabolic ratio.**

CONCLUSION: **There was variation of the NAA/Cr ratio and the Ch/Cr ratio across brain regions, but no sex differences were found. These findings provide the requisite normative values to use single voxel, long-echo-time MR spectroscopy in adult patients with neurologic disorders.**

MR spectroscopy is used clinically to measure brain metabolites in a variety of disorders, including neoplasms, metabolic diseases, inflammatory processes, and infections (1–4). To be accepted as a diagnostic test, it is essential to define a range of normal values against which disease will be judged, as is the case for most laboratory tests. In clinical applications of MR spectroscopy, the ratios of the various metabolites are used more often than absolute metabolite concentrations (1–3). Commonly used metabolic ratios include the ratio of N-acetylacetate asparte to creatine (NAA/Cr) and the ratio of choline to creatine (Ch/Cr). In many cases, MR spectra are obtained from affected brain tissue and contralateral unaffected tissue, because a normal reference data base may not be available. Earlier studies that defined normal metabolite values either used short echo times or studied actual metabolite concentration in a limited number of brain areas (5–12). Current clinical applications of MR spectroscopy, however, routinely include spectra obtained with long echo times (TE) in a variety of different brain regions, therefore by using normal volunteers, we set out to define a range of normal NAA/Cr and Ch/Cr ratios for both sexes in a number of brain areas by using long TE MR spectroscopy. We

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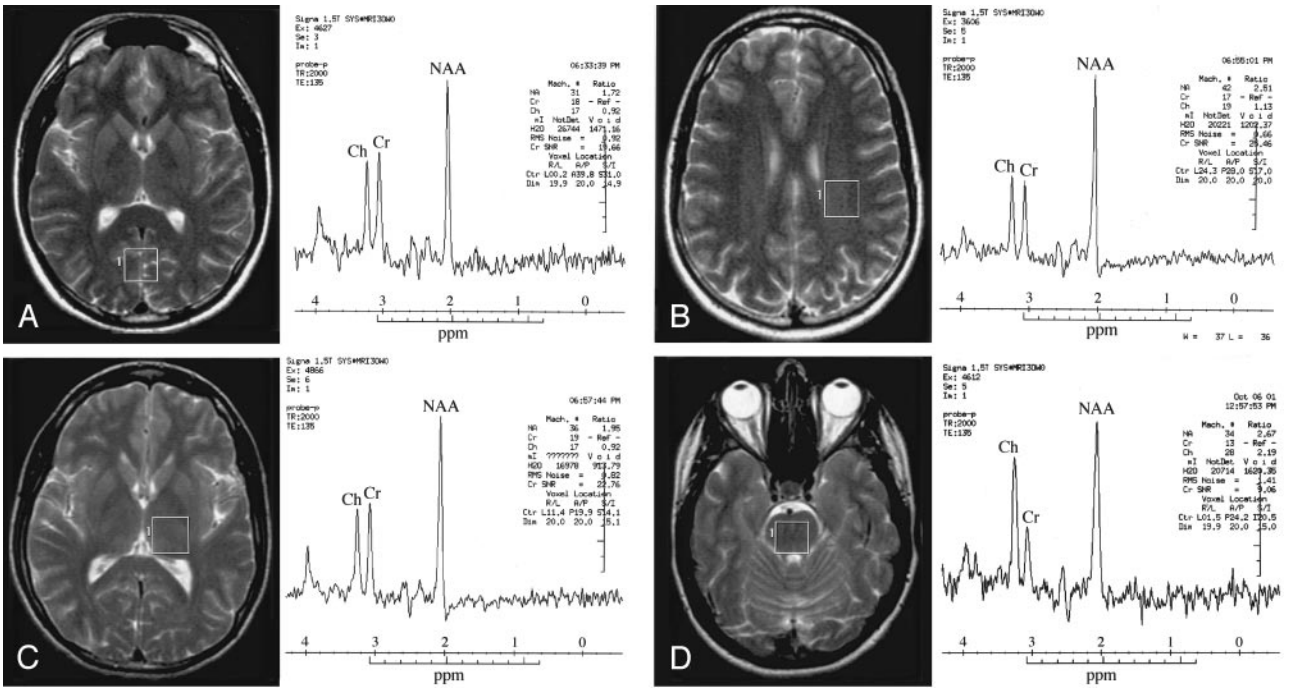

FIG 1. Single voxel PRESS proton MR spectra (TR/TE = 2000/135) demonstrate choline (Ch), creatine (Cr), and *N*-acetylaspartate (NAA) peaks from occipital gray matter (*A*), posterior white matter (*B*), thalamus (*C*), and pons (*D*). The axial T2 FSE image shows the voxel location for the acquired spectrum. The chemical shift scale is in parts per million relative to tetramethylsilane.

hypothesized that both the NAA/Cr ratio and Ch/Cr ratio would differ across brain regions.

Methods

Seventy-two healthy subjects (32 men and 40 women) participated in this study. Subjects ranged in age from 22 to 44 years. Mean age was 27 years (±6 years). Subjects were recruited from the university or medical center by word of mouth and e-mail. All subjects had attended college or were in college. Subjects filled out a questionnaire regarding past medical and surgical history. All subjects gave written informed consent, and the research was approved by the institutional review board. Exclusion criteria included claustrophobia, pregnancy, history of serious medical or neurologic illness, and failure to fulfill the safety criteria for patients undergoing MR imaging.

MR studies were performed on a 1.5-T MR imaging system. Subjects lay supine in the magnet with their heads immobilized by a neck support, foam wedges, and a restraining band drawn around the forehead. Scout images in the sagittal plane were acquired with parameters of 500/11 (TR/TE), a field of view of 24 cm, an imaging matrix of 256 × 192, and 5-mm contiguous sections. Axial T2-weighted images were acquired through the entire brain by using a fast spin-echo sequence with parameters of 3,000/80 (TR/TE), a field of view of 22 cm, an imaging matrix of 256 × 192, an echo train length of 16, and 3-mm contiguous sections.

On the basis of the T2-weighted images, voxels in 10 regions of the brain were chosen for MR spectroscopy spectra (see below). Voxels were 2 × 2 × 2 cm or 2 × 2 × 1.5 cm in size. The spectra were acquired by using a point-resolved ^{1}H spectroscopy (PRESS) technique. After the transmitter and receiver were automatically adjusted, water signal intensity was automatically shimmed to within a line width of 3–5 Hz. The parameters for MR spectroscopy were 2,000/135 (TR/TE), a field of view of 22 × 22 cm, an imaging matrix of 256 × 192, 128 total scans, and scan time of 4 minutes 56 seconds. All data processing was performed by software provided by the manufacturer. Spectral processing included zero-filling, Gaussian apodization, Fourier transformation, water reference processing, frequency shift correction, and phase and baseline correction. By using the curve-fitting software provide by the manufacturer, peak integral values were determined. NAA was assigned at 2.02 parts per million (ppm), Ch at 3.2 ppm, and Cr at 3.03 ppm. The peak areas of NAA and Ch were normalized with respect to Cr. The integral value of each peak was dimensionless and represented relative measurement of the amount of each metabolite. The ratios of NAA to Cr and Ch to Cr were calculated. Spectra and integral values were displayed next to an anatomic T2-weighted image on which a square box was overlaid to indicate the anatomic location of each voxel from which the spectra was obtained.

In the examination time available, each of the 10 brain regions could not be studied in each subject, so spectra from three or four regions were sampled in three different subject groups. In group 1, spectra were collected from three brain regions of 22 subjects (10 men and 12 women): the occipital lobe gray matter, which included aspects of the cuneus, lingual gyrus and calcarine fissure; the lentiform nuclei (basal ganglia); and the posterior white matter (primarily the subcortical white matter in the parietal lobe). In group 2, spectra were collected from the frontal gray matter (superior frontal gyri), frontal white matter (subcortical white matter bordering superior and middle frontal gyri), and pons of 31 subjects (12 men and 19 women). Spectra were also collected from the temporal gray matter (primary auditory cortex in posterior aspect of the superior temporal gyrus) of 15 group 2 subjects. In group 3, spectra were collected from the thalamus, cerebellar hemisphere, and parietal gray matter (middle aspect of the intraparietal sulcus) of 20 subjects (10 men and 10 women). As in group 2, spectra were also collected from the temporal gray matter of 13 group 3 subjects. Figure 1 illustrates the four different brain regions and their corresponding spectra.

An analysis of variance with age as the dependent variable and group as a factor demonstrated no significant difference between the mean ages of the three subject groups ($F [2, 64] = 0.95$; $P = .4$). The mean ages were 29, 27, and 27 years. An omnibus multifactorial analysis of variance (MANOVA) was

TABLE 1: Mean NAA/Cr ratio in 10 brain regions

Brain Region	Mean	Standard Deviation	Standard Error
bg	1.834	0.336	0.075
occgm	2.000	0.097	0.021
powm	2.419	0.266	0.059
fgm	1.789	0.210	0.039
fwm	2.346	0.370	0.071
pgm	2.040	0.199	0.046
tgm	2.026	0.192	0.036
pons	2.427	0.364	0.069
th	2.093	0.228	0.052
cb	1.512	0.262	0.059

Note.—bg = basal ganglia; occgm = occipital gray matter; powm = posterior white matter; fgm = frontal gray matter; fwm = frontal white matter; pgm = parietal gray matter; tgm = temporal gray matter; th = thalamus; cb = cerebellum.

TABLE 2: Mean Ch/Cr ratio in 10 brain regions

Brain Region	Mean	Standard Deviation	Standard Error
bg	1.018	0.192	0.043
occgm	0.678	0.075	0.016
powm	1.242	0.160	0.036
fgm	1.144	0.156	0.029
fwm	1.459	0.258	0.050
pgm	0.826	0.125	0.029
tgm	0.929	0.113	0.021
pons	1.914	0.302	0.057
th	1.133	0.171	0.039
cb	1.511	0.144	0.032

Note.—bg = basal ganglia; occgm = occipital gray matter; powm = posterior white matter; fgm = frontal gray matter; fwm = frontal white matter; pgm = parietal gray matter; tgm = temporal gray matter; th = thalamus; cb = cerebellum.

performed that collapsed across the three groups and examined the two metabolite ratios as the dependent measures and brain region (all 10 regions) and sex as independent variables, or factors. Post hoc analysis consisted of the Scheffé *F* statistic for any significant difference between pairs of brain regions for both the NAA/Cr ratio and the Ch/Cr ratio. To guard against the possibility that significant effects or interactions of brain region and sex could result from differences in variance among the three groups of subjects, a separate MANOVA was performed for each of the three subject groups with the metabolic ratios of NAA/Cr and Ch/Cr as the dependent variables and with brain region and sex as factors. Post hoc analysis again consisted of the Scheffé *F* statistic for significant differences between pairs of brain regions for both NAA/Cr and Ch/Cr (13).

Results

The omnibus MANOVA for the NAA/Cr ratio collapsed across the three groups and 10 brain regions revealed a main effect of brain region ($F[9, 213] = 27$; $P < .0001$), which indicates regional variation for the NAA/Cr ratio. There was no main effect of sex ($F[1, 213] = 0.123$; $P = .73$) and no interaction between brain region and sex ($F[9, 213] = 0.614$; $P = .78$). Table 1 lists the mean NAA/Cr ratio and standard deviation (SD) for the 10 brain regions, collapsed across sex. The omnibus MANOVA for the Ch/Cr ratio demonstrated a main effect of brain region ($F[9, 213] = 85$; $P < .0001$), which again indicates regional variation of Ch/Cr. There was no effect of sex ($F[1, 213] = 1.26$; $P = .26$) and no interaction between brain region and sex ($F[9, 213] = 0.742$; $P = .67$). Table 2 shows the mean Ch/Cr ratio and SD for the 10 brain regions, collapsed across sex. Figure 1 illustrates the MR spectra obtained from different brain regions.

The main effect of brain region and lack of an effect of sex were confirmed with the additional MANOVAs calculated separately for each of the three subject groups. The MANOVA for group 1 (basal ganglia, occipital gray matter, and posterior white matter) for the NAA/Cr ratio demonstrated a main effect of brain region ($F[2, 56] = 30$; $P < .0001$) but no effect of sex ($F[1, 56] = 2.384$; $P = .13$) and no interaction between brain region and sex ($F[2, 56] = 0.87$; $P = .42$). Results for the Ch/Cr ratio demonstrated a main effect of brain region ($F[2, 56] = 74$; $P < .0001$) but no effect of sex ($F[1, 56] = 1.3$; $P = .25$), and no interaction between brain region and sex ($F[2, 56] = 0.027$; $P = .97$).

The separate MANOVA for group 2 (frontal gray matter, frontal white matter, temporal gray matter, and pons) for the NAA/Cr ratio demonstrated a main effect of brain region ($F[3, 90] = 25$; $P < .0001$) but no effect of sex ($F[1, 90] = 0.109$; $P = .74$) and no interaction between brain region and sex ($F[3, 90] = 0.165$; $P = .92$). Results for the Ch/Cr ratio demonstrated a main effect of brain region ($F[2, 56] = 74$; $P < .0001$) but no effect of sex ($F[1, 56] = 1.3$; $P = .25$) and no interaction between brain region and sex ($F[2, 56] = 0.027$; $P = .97$).

The separate MANOVA for group 3 (parietal gray matter, temporal gray matter, thalamus, and cerebellum) for the NAA/Cr ratio demonstrated a main effect of brain region ($F[3, 54] = 23$; $P < .0001$) but no effect of sex ($F[1, 54] = 0.002$; $P = .96$) and no interaction between brain region and sex ($F[3, 54] = 0.165$; $P = .25$). Results for the Ch/Cr ratio demonstrated a main effect of brain region ($F[2, 56] = 74$; $P < .0001$) but no effect of sex ($F[1, 56] = 1.3$; $P = .25$) and no interaction between brain region and sex ($F[2, 56] = 0.027$; $P = .97$).

To determine which brain regions differed for a given metabolic ratio, the post hoc analysis on the omnibus MANOVA consisted of calculating the Scheffé *F* statistic for pairwise comparisons between brain regions for the NAA/Cr ratio (see www.ajnr.org for Table 3) and the Ch/Cr ratio (see www.ajnr.org for Table 4), respectively. Forty-five pairwise comparisons were made for both metabolic ratios. Twenty-one comparisons were significant for the NAA/Cr ratio (Table 3), and twenty-eight comparisons were significant for the Ch/Cr ratio (Table 4). For the NAA/Cr ratio, a direct comparison of regions containing predominately gray matter, like the four cerebral cortical regions and the gray matter nuclei of the basal ganglia and thalamus, did not show signifi-

TABLE 3: Comparison of NAA/Cr between pairs of brain regions

Regions	Mean Diff	Crit Diff	*P* Value	
bog, occgm	−0.167	0.348	.9105	
bg, powm	−0.585	0.356	<.0001	S
bg, fgm	0.044	0.327	>.9999	
bg, fwm	−0.512	0.332	<.0001	S
bg, pgm	−0.206	0.361	.7707	
bg, tgm	−0.192	0.327	.7407	
bg, pons	−0.593	0.33	<.0001	S
bg, th	−0.26	0.361	.4441	
bg, cb	0.321	0.356	.1281	
occgm, powm	−0.418	0.348	.0043	S
occgm, fgm	0.211	0.318	.5748	
occgm, fwm	−0.345	0.324	.0239	S
occgm, pgm	−0.04	0.353	>.9999	
occgm, tgm	−0.025	0.318	>.9999	
occgm, pons	−0.426	0.321	.0006	S
occgm, th	−0.093	0.353	.9988	
occgm, cb	0.488	0.348	.0002	S
powm, fgm	0.629	0.327	<.0001	S
powm, fwm	0.073	0.332	.9997	
powm, pgm	0.379	0.361	.0294	S
powm, tgm	0.393	0.327	.0044	S
powm, pons	−0.008	0.33	>.9999	
powm, th	0.325	0.361	.1277	
powm, cb	0.906	0.326	<.0001	S
fgm, fwm	−0.556	0.301	<.0001	S
fgm, pgm	−0.251	0.332	.3684	
fgm, tgm	−0.237	0.296	.2776	
fgm, pons	−0.637	0.298	<.0001	S
fgm, th	−0.304	0.332	.1146	
fgm, cb	0.277	0.327	.2007	
fwm, pgm	0.306	0.337	.123	
fwm, tgm	0.32	0.301	.0255	S
fwm, pons	−0.081	0.304	.9986	
fwm, th	0.252	0.337	.3807	
fwm, cb	0.833	0.332	<.001	S
pgm, tgm	0.014	0.332	>.9999	
pgm, pons	−0.387	0.335	.008	S
pgm, th	−0.053	0.365	>.9999	
pgm, cb	0.528	0.361	<.0001	S
tgm, pons	−0.401	0.298	.0005	S
tgm, th	−0.067	0.332	.9999	
tgm, cb	0.513	0.327	<.0001	S
pons, th	0.334	0.335	.0518	
pons, cb	0.914	0.33	<.0001	S
th, cb	0.581	0.361	<.0001	S

Note.—bg = basal ganglia; occgm = occipital gray matter; pown = posterior white matter; fgm = frontal gray matter; fwm = frontal white matter; pgm = parietal gray matter; tgm = temporal gray matter; th = thalamus; cb = cerebellum, diff = difference, crit = critical, S = significant at 5% level for Scheffe's F statistic.

TABLE 4: Comparison of Ch/Cr between pairs of brain regions

Regions	Mean Diff	Crit Diff	*P* Value	
bog, occgm	0.34	0.241	.0002	S
bg, powm	−0.224	0.246	.1199	
bg, fgm	−0.126	0.227	.7992	
bg, fwm	−0.441	0.23	<.0001	S
bg, pgm	0.192	0.25	.34	
bg, tgm	0.089	0.227	.9743	
bg, pons	−0.896	0.228	<.0001	S
bg, th	−0.115	0.25	.9313	
bg, cb	−0.133	0.246	.8253	
occgm, powm	−0.564	0.241	−.0001	S
occgm, fgm	−0.466	0.22	−.0001	S
occgm, fwm	−0.781	0.224	<.0001	S
occgm, pgm	−0.149	0.244	.6968	
occgm, tgm	−0.251	0.22	.0099	S
occgm, pons	−1.236	0.222	<.0001	S
occgm, th	−0.455	0.244	<.0001	S
occgm, cb	−0.474	0.241	<.0001	S
powm, fgm	0.098	0.227	.9531	
powm, fwm	−0.217	0.23	.0878	
powm, pgm	0.416	0.25	<.001	S
powm, tgm	0.313	0.227	.0003	S
powm, pons	−0.672	0.228	<.0001	S
powm, th	0.109	0.25	.9488	
powm, cb	0.091	0.246	.9844	
fgm, fwm	−0.315	0.208	<.0001	S
fgm, pgm	0.318	0.23	.0003	S
fgm, tgm	0.216	0.205	.0281	S
fgm, pons	−0.77	0.207	<.0001	S
fgm, th	0.012	0.23	>.9999	
fgm, cb	−0.007	0.227	>.9999	
fwm, pgm	0.633	0.233	<.0001	S
fwm, tgm	0.53	0.208	<.0001	S
fwm, pons	−0.455	0.21	<.0001	S
fwm, th	0.326	0.233	.0002	S
fwm, cb	0.307	0.23	.0006	S
pgm, tgm	−0.102	0.23	.9436	
pgm, pons	−1.088	0.232	<.0001	S
pgm, th	−0.306	0.253	.0037	S
pgm, cb	−0.325	0.25	.001	S
tgm, pons	−0.985	0.207	<.0001	S
tgm, th	−0.204	0.23	.1447	
tgm, cb	−0.223	0.227	.0591	
pons, th	0.781	0.232	<.0001	S
pons, cb	0.762	0.228	<.0001	S
th, cb	−0.019	0.25	>.9999	

Note.—bg = basal ganglia; occgm = occipital gray matter; pown = posterior white matter; fgm = frontal gray matter; fwm = frontal white matter; pgm = parietal gray matter; tgm = temporal gray matter; th = thalamus; cb = cerebellum, diff = difference, crit = critical, S = significant at 5% level for Scheffe's F statistic.

cant differences among each other. Similarly, a comparison of regions containing predominately white matter, like the frontal white matter and the posterior white matter, did not differ from each other. The white matter regions also did not differ from the pons. Each cortical gray matter had a smaller NAA/Cr ratio than each cerebral white matter region and the pons. Each cortical gray matter region except the frontal area had a larger NAA/Cr ratio than the cerebellum, with the frontal area not showing a significant difference with the cerebellum. The NAA/Cr ratio of the basal ganglia was significantly smaller than the frontal and posterior white matter regions and the pons, but it was not significantly different from the cerebellum. The thalamic NAA/Cr ratio, however, did not differ from the subcortical white matter regions or the pons, but it was larger than the cerebellum.

The Ch/Cr ratio varied widely across different brain regions (Tables 2, 4). The cortical gray matter sites showed significant differences between each other, with only the occipital gray and parietal gray matter regions having similar Ch/Cr ratios. The ratio

in the occipital gray matter was smaller than the ratio in the frontal and temporal regions. The Ch/Cr ratios in the two subcortical white matter sites were equivalent, but, unlike the NAA/Cr ratio, they had significantly different (smaller) ratios compared with the pons. The basal ganglia and thalamus had statistically similar Ch/Cr ratios. The basal ganglia showed few significant differences with other regions. The thalamus also differed with only a few regions. The post hoc Scheffé *F* statistic analyses on both the omnibus MANOVA and in the MANOVA calculated separately for each group resulted in similar findings, which suggests that the three groups of subjects had relatively homogeneous variance with regard to MR spectroscopy measurements of the metabolic ratios.

Discussion

Many MR spectroscopy data bases of normal brain metabolites and metabolic ratios published to date use stimulated echo acquisition mode (STEAM) short TE proton MR spectroscopy. In clinical practice, however, the PRESS technique, with longer echo times, is also used. We undertook this study to establish a data base of normal metabolic values obtained with the PRESS technique and a long echo time. These results provide normal reference values for comparison with spectra from adults with neurologic disease.

We studied a number of different regions of the brain because of the histologic and functional differences of cortical and subcortical areas. Cytoarchitectural studies of gray matter indicate that there are six fundamental layers of cortex that can be differentiated on the basis of geometry, attenuation, and types of cells (14). Cytoarchitectural maps like the Broadmann map demonstrate how these cortical layers also vary across brain regions (14). This variance in histology is often related to function. Functional imaging methods have confirmed clinical and electrophysiologic evidence that cortical regions can have different functions (15). Organization of the cortical gray matter differs from that of the thalamus, basal ganglia, and cerebellum, and gray matter in general is different from white matter (14). Although we expected subcortical white matter regions to be similar, we included white matter regions in the frontal and posterior areas on the possibility that metabolic ratios might vary based on the percentage of association or projection fibers. Because there are neurologic diseases that do not have a predilection for any particular brain location yet different areas of the brain vary according to function and histology, we established a data base of normal controls that included metabolic values for a number of brain regions.

Our study found significant differences in both the NAA/Cr and Ch/Cr ratios across various brain regions. The NAA/Cr ratio differed between white matter and gray matter brain regions but did not vary significantly within gray matter or within white matter regions (Tables 1, 3). There were also no significant differences in the NAA/Cr ratio of gray matter regions and cortical nuclei or in white matter regions and the pons. The white matter regions and the pons had lager NAA/Cr ratios compared with the cortical gray matter, basal ganglia, and cerebellum. The cerebellum had a smaller NAA/Cr ratio compared with the gray matter and the thalamus. The Ch/Cr ratio demonstrated greater variability across brain regions than did the NAA/Cr ratio, including variation within gray matter sites (Tables 2, 4). The Ch/Cr ratio did not differ significantly within different white matter sites.

Prior studies, most of which used short TE STEAM MR spectroscopy, also demonstrated that metabolite concentrations vary across brain regions (5–12). A report that is comparable to our study in technique rather than aim was primarily targeted at determining the reproducibility of MR spectroscopy spectra in vivo and in vitro rather than determining a normative range (16). Metabolic concentrations and ratios in a single voxel placed over the parietal white matter in both hemispheres were measured normal volunteers by using similar parameters as our study. The mean NAA/Cr ratio in parietal white matter was consistent with the NAA/Cr ratio we report in the posterior white matter.

Metabolite concentrations are also affected by age (5–7, 9, 17–20). Myoinositol is the dominant peak in short TE spectra of in neonates, choline is the dominant peak in older infants, and the adult spectrum has NAA as the major metabolite (6). Older adults show different NAA, Cr, and Ch levels compared with young adults (18–20). Our study is pertinent to MR spectroscopy in adults and is not necessarily applicable to the pediatric or geriatric population.

The effect of sex on metabolic ratios in normal individuals is less well studied, and conclusions of the few published reports have been conflicting. Some studies showed no sex differences in NAA/Cr, NAA/Ch, and Ch/Cr ratios or absolute concentration in white matter and gray matter (8, 12, 18). A study by using the STEAM technique at short TE in six brain regions reported no sex difference in four regions. Increased levels of NAA in women compared with men were found in the sensorimotor cortex and orbitofrontal cortex (5). Another study used a PRESS sequence with a TE of 135 milliseconds revealed significantly smaller NAA/Ch and larger Ch/Cr ratios in the parietooccipital white matter in males as compared with females (21). Our study, utilizing a long TE PRESS technique and sampling from 10 brain regions, showed no sex differences in the metabolite ratios.

Because only three or four regions were measured for each subject group in our study, the effect of brain region on the metabolic ratio could result from a difference in variance between groups rather than a true difference between brain regions. Measurement of metabolite ratios in all 10 regions of interest in each subject would have been ideal; however, time constraints precluded us from doing so. The Scheffé *F* statistic, the most conservative of the paired comparison procedures (13), was used in the data analysis to

account for this potential confounding variable. This procedure is useful for post hoc comparisons if samples sizes vary in size and if there is a possibility of heterogeneous variances among groups. The post hoc analysis by using Scheffé *F* statistic resulted in similar findings in both the omnibus MANOVA and in the MANOVA calculated separately for each group, which indicates that the three groups of subjects had relatively homogeneous variance within the measured metabolic ratios.

The Ch/Cr ratio varied significantly within gray matter regions. This variability could be technical in nature because of data collection and processing limitations or errors. The large voxel size inherent to single voxel MR spectroscopy means that volumes of interest do not contain only one tissue type. Other technical factors include artifacts from inadequate shimming in regions close to bone. Suboptimal shimming affects spectral quality and the metabolic ratios. Our results, as well as others reported in the literature, could be refined by additional shimming procedures, by segmenting gray and white matter to achieve a more homogeneous volume of interest, and by off-line processing of data, but these steps are rarely used in the clinical setting. The variability in Ch/Cr could also be biologic in nature. A previous study reported that choline levels changed across gray matter regions (12). We used the same collection and processing parameters for NAA/Cr and Ch/Cr, and no significant variation was observed for NAA/Cr within gray matter sites. It is unlikely that a technical problem would cause variation in the Ch/Cr ratio in gray matter and no variation in NAA/Cr ratio.

Both the PRESS and STEAM techniques are used in clinical practice today and are available on most commercially made high field scanners. Compared with PRESS, the major advantage of STEAM is that shorter echo times can be used to detect small metabolites with shorter T2 times (1–3). The main disadvantage of the STEAM sequence is its lower signal intensity–to-noise ratio compared with PRESS. PRESS was used in this study because it offers the benefits of improved signal intensity–to-noise ratio and a simpler spectrum with less peak interference from lipid signals and metabolites with short T2 values, which aids in the interpretation of the spectrum (1–3). We chose a TE of 135 milliseconds because this TE is close to an odd multiple of the inverse of the J coupling, or spin-spin coupling constant for lactate (J = 7.3 Hz; 1/J = 136 milliseconds). Lactate is inverted at this TE and can be better differentiated from lipids. Longer echo times such as 270 milliseconds or 288 milliseconds can also be used, but they do not invert lactate and can result in signal intensity loss due to T2 signal intensity decay. Disadvantages of PRESS include more modulation from J coupling and less sensitivity to metabolites with short T2 values, which can be important in the clinical evaluation of certain diseases (1–3).

Quantification of metabolites in MR spectroscopy can be difficult, so a more practical method to assess variations in metabolite levels is to calculate peak area ratios. The metabolite ratios calculated in this study are routinely employed in clinical practice. They are simple to obtain, require no technical expertise or additional software, are independent of changes in coil loading or other differences among individuals, and do not require relaxation-time measurements (1–3, 8). The metabolites of interest are in lower concentrations in CSF, so ratios are relatively unaffected by inclusion of small amounts of CSF in the voxel as compared with the use of absolute metabolite concentrations. A limitation of using metabolic ratios is that the concentration of both metabolites could be abnormally increased or decreased together, resulting in a normal ratio despite the presence of disease. If Cr is used as the reference value, the assumption that its concentration does not change is not always the case and can lead to erroneous interpretation (1, 11).

A need exists for a normal reference range of metabolite ratios for single voxel, long TE, PRESS MR spectroscopy. A data base of normal values can be referred to while reading clinical cases and also minimizes the need to perform MR spectroscopy on the brain contralateral to the area of pathology. We provide physicians who interpret an MR spectroscopy study in the clinical setting a set of reference values (Table 1, 2) to compare with the MR spectroscopy data acquired at their respective institutions.

Conclusion

The NAA/Cr ratio was consistent within cortical gray and white matter but differed between cortical gray and white matter. The Ch/Cr ratio was variable in the gray matter and differed between some but not all gray and white matter regions but was consistent within subcortical white matter regions. There was no sex difference for either metabolic ratio. The results of this study provide a reference set of normal values for MR spectroscopy studies in adults acquired with a single voxel, PRESS, long TE technique.

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