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COMPARISON OF SINGLE VOXEL BRAIN MRS AT 3T AND 7T USING 32-CHANNEL HEAD COILS

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Abstract

Purpose—The purpose of this study was to compare magnetic resonance spectroscopy (MRS) of three different regions of the human brain between 3 and 7 Tesla, using the same subjects and closely matched methodology at both field strengths.

Methods—A semi-LASER (sLASER) pulse sequence with TE 32 ms was used to acquire metabolite spectrum along with the water reference at 3T and 7T using similar experimental parameters and hardware at both field strengths (n=4 per region and field). Spectra were analyzed in LCModel using a simulated basis set.

Results—Signal-to-noise ratio (SNR) at 7T was higher compared to 3T and linewidths (in ppm) at both field strengths were comparable in ppm scale. Of the 13 metabolites reported in the paper, most metabolites were measured with higher precision at 7T in all three regions.

Conclusion—The study confirms gains in SNR and measurement precision at 7T in all three representative brain regions using the sLASER pulse sequence coupled with a 32-channel phased-array head coil.

Keywords

Brain; Magnetic Resonance Spectroscopy; 7 Tesla

Introduction

Magnetic resonance spectroscopy (MRS) is believed to be one of the MR techniques most likely to benefit from the use of high B_0 magnetic field strengths, because of the expected

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improvements in both signal-to-noise ratio (SNR) and spectral resolution [1, 2]. Theory suggests that SNR increases linearly with field strength in biological samples, as does chemical shift dispersion [3]. However, spectral linewidths in brain tissue (measured in Hz) are also known to increase with field strength [2], so resolution improvements may not be as great as expected from simple theory [4, 5]. Nevertheless, the overall improved spectral quality at higher field strengths such as 7T has been shown to result in lower uncertainty values of metabolite concentrations [2, 6] and also to allow the estimation of various compounds that are either undetectable or require specialized pulse sequences [7, 8] for accurate quantification at lower field strengths. In particular, previous studies using surface coils have shown that the SNR, spectral resolution and measurement precision in the occipital lobe are all superior at 7T compared to lower field strengths (either 3T or 4T) [2, 6]. However, to our knowledge, there has only been one comparison MRS study [9] between field strengths that used multi-channel receiver head coils, which compared measurements made in the parietal white matter at 3T and 7T using an 8-channel head coil. The current study compared measurements made in multiple-brain regions using 32-channel head coils at 3T and 7T. This comparison is of particular importance since 32-channel coils are now being increasingly used for both research and clinical state-of-the-art neuroimaging studies.

Higher field strengths are also associated with technical challenges such as inhomogeneities in the B_0 and B_1 fields, longer T_1 and shorter T_2 relaxation times, higher radiofrequency power deposition (specific absorption rate (SAR)), and increased chemical shift displacement errors (CSDE). Some of these issues are inherent physical properties to the biochemical under investigation; whereas, others may be addressed by development of new techniques either in pulse sequence design or scanner hardware. Inhomogeneity in the B_1 transmit field causes deviations of the RF pulse flip angles from their ideal values, which may lead to decreased SNR. Also, conventional amplitude-modulated RF pulses have relatively small frequency bandwidths, leading to large CSDE artifacts at high fields such as 7T. Both of these problems may be at least partially addressed by the use of frequency-modulated adiabatic RF pulses [10], which provide uniform flip angle rotations independent of B_1 as long as the B_1 levels are high enough to fulfill the adiabatic condition [11–13]. Adiabatic pulses usually have high bandwidths, determined by the frequency sweep of the RF pulse. Usage of either fully [10, 14] or partially [15, 16] adiabatic pulse sequences have been proposed for *in vivo* MRS. The partially adiabatic semi-LASER sequence [15, 16] has become popular over the last few years, since it involves fewer RF pulses, and hence lower SAR, than fully adiabatic sequences such as SADLOVE [12] or LASER [14]. A recent study at 7T has shown a more than two-fold increase in SNR when using sLASER as opposed to the non-adiabatic STEAM sequence [17].

In this study, a systemic comparison was performed of brain MRS at 3 and 7T, using the sLASER sequence for volume selection and 32-channel receive head coils at both field strengths. Experimental parameters and pulse sequences were closely matched between systems, and the same subjects were scanned at both field strengths. The use of a volume transmit coil paired with the 32-channel receive array allowed for measurements from several brain locations.

Methods

After obtaining written consent under local IRB approval, 4 healthy subjects (age 35 ± 7 years, 2 males) were scanned at both 3T and 7T the same day using 'Achieva' scanners (Philips Healthcare LLC, Cleveland, OH) equipped with 32-channel receive head coils (7T: Nova Medical, Wilmington, MA, 3T: Invivo, Gainesville, FL). On the 7T system, a quadrature head coil was used to transmit RF pulses, while on the 3T the scanner body coil was used (nominal maximum $B_1 = 15 \mu\text{T}$ at 7T and $13.5 \mu\text{T}$ at 3T).

Imaging

Anatomical images were acquired using 3-D magnetization-prepared rapid acquisition gradient echo pulse sequence (MPRAGE) with 1 mm isotropic resolution at 3T and 0.8 mm isotropic resolution at 7T, TI = 1110 ms at 3T and 446 ms at 7T, shot interval = 1842 ms at 3T and 1534 ms at 7T, TE/TR = 3.4/13.0 ms at 3T and 1.9/4.3 ms at 7T, field-of-view (FOV) size of $240 \times 240 \times 150 \text{ mm}^3$ at 3T and $220 \times 220 \times 180 \text{ mm}^3$ at 7T, number of slices = 150 at 3T and 225 at 7T, acquisition matrix = 240×217 at 3T and 276×274 at 7T, flip angle = 9° at 3T and 7° at 7T and water-fat shift = 2.3 pixels at 3T and 2.0 pixels at 7T, scan time 4 min 20 sec at 3T and 3 min 40 sec at 7T. SENSE acceleration factor was 3.0 at 3T and 4.0 at 7T. All anatomical images were acquired in the sagittal plane and reformatted in coronal and axial views for accurate placement of the voxels.

Spectroscopy

The sLASER sequence was implemented using a non-adiabatic frequency modulated 90° excitation pulse ('fremex05', 8.7 ms, 5.3 kHz [18]) and four 3.9 ms adiabatic refocusing pulses [19] with a linear frequency sweep of 3 kHz and using the maximum B_1 available on both systems. All data were acquired with TR/TE = 3000/32 ms. A VArable Pulse power and Optimized Relaxation Delays (VAPOR) water suppression sequence was used in conjunction with a semi-LASER sequence to acquire water-suppressed metabolite spectra. Prior to data acquisition, a field-map based shimming routine was used to optimize field homogeneity using 1st and 2nd order shim coils [20], and the RF transmitter power was calibrated using a localized optimization routine [21]. With refocusing pulse bandwidth of 3 kHz, the chemical shift displacement error (CSDE) between 3.75 ppm resonance of Glu and 1.3 ppm resonance of Lac is 10% at 3T and 24% of the voxel dimension at 7T.

Water-suppressed spectra (32 averages, 16-step phase-cycle) and a non-water-suppressed reference spectrum (4 averages) were collected from each of the following regions: anterior cingulate cortex (ACC), centrum semiovale (CSO), and dorsolateral prefrontal cortex (DLPFC) with the scan duration of 1 min 54 s for each region. The voxel dimensions for ACC, CSO and DLPFC were $3 \times 3 \times 3 \text{ cm}^3$, $4 \times 2.5 \times 2.5 \text{ cm}^3$, and $3 \times 3 \times 3 \text{ cm}^3$ respectively. The representative voxel locations are shown in Figure 1. Screenshots of each anatomical region from the first scan of each subject showing the voxel locations in three planes were used as a guide to place the voxels during the subsequent scan at the other field strength, in order to ensure reproducibility of voxel placement between the 2 studies.

Spectral Analysis

Spectra were quantified using the 'LCModel' analysis software [22]. Metabolite concentrations were estimated in the LCModel using the tissue water signal as an internal intensity reference, and were reported in 'institutional units' as recommended by the LCModel manual. The term 'institutional units' reflects that not all correction factors are applied that would be necessary to convert the reported concentration values into conventional biochemical concentration units such as millimolar or micromoles per gram wet weight. The LCModel basis sets for 3T and 7T were generated using the 'VESPA' package [23]. The basis sets were calculated using full simulation of the adiabatic refocusing pulses and phase cycles used in the experiments, but did not include chemical shift displacement effects. The basis sets included the following 20 metabolites: alanine (Ala), aspartate (Asp), creatine (Cr), γ -aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glycine (Gly), glycerophosphocholine (GPC), glutathione (GSH), lactate (Lac), *myo*-inositol (mI), N-acetylaspartate (NAA), N-acetylaspartylglutamate (NAAG), phosphocholine (PCho), phosphocreatine (PCr), phosphorylethanolamine (PE), serine (Ser), scyllo-Inositol (sI), and taurine (Tau). Chemical shifts and coupling constants for each compound were taken from the literature [24]. Macromolecule (MM) resonances were fit using the standard MM spectra supplied with the LCModel, and the spectral baseline (cubic spline) was constrained with the spline knot spacing set to 0.2 ppm. Metabolite concentrations were used for further analysis only if the corresponding Cramer-Rao Lower Bound (CRLB) was less than 20% for large signals (such as NAA or Cr) or 50% for small signals (such as GABA or GSH). In total, 7 individual compounds could be estimated according to these criteria at both 3 and 7T.

Metabolite concentrations were corrected for transverse relaxation using the T_2 values given in Table 1 [25–27] with the T_2 value of NAA used for all metabolites except for water and Cr. SNRs and linewidths were calculated using in-house software. SNR was measured using the peak height of NAA singlet peak and the root-mean-square (RMS) of the noise in the –1 to –2 ppm range, and linewidths were measured from the width at half-height of the creatine peak at 3.0 ppm.

Statistical analysis included univariate regression with field strength as the independent variable and Bonferroni correction was applied to account for multiple tests.

Results

Representative spectra acquired from the ACC, CSO and DLPFC at 3T and 7T are shown in Figure 2. Good quality spectra were acquired from all subjects from all three regions at both field strengths. As expected, the appearance of spectra, for example the $^4\text{CH}_2$ resonances of Glu and Gln at 2.3–2.4 ppm are better resolved at 7T, and the Glu peak at 3T displays more multiplet structure compared to 7T, most likely because of the wider spread of the outer peaks (in ppm) of the 2.3 and 2.4 ppm resonances of Glu and Gln respectively at 3T compared to 7T. In the spectra from the CSO, the methyl peak of NAAG is also visually better resolved at 7T than at 3T.

SNR values measured at 7T were 135 ± 28 , 116 ± 33 and 138 ± 29 , and at 3T were 83 ± 12 , 97 ± 7 and 83 ± 5 (mean $\pm$ standard deviation) in the ACC, CSO and DLPFC, respectively. These resulted in average SNR improvements of factors of 1.6, 1.2 and 1.6 times higher at 7T than at 3T for ACC, CSO and DLPFC, respectively. Average linewidths (measured in ppm) of the creatine peak at 3.02 ppm were marginally better at 7T for ACC and CSO and slightly worse for the DLPFC. The average linewidths were 0.042 ± 0.005 , 0.040 ± 0.004 and 0.043 ± 0.002 ppm at 3T and 0.039 ± 0.002 , 0.039 ± 0.003 and 0.045 ± 0.006 ppm at 7T in the ACC, CSO and DLPFC, respectively. These values are comparable to other studies in the literature [25, 26].

Figure 3 shows representative LCModel fit results for spectra acquired at 3T and 7T for the three brain regions. The measurement precision of metabolite concentrations as reflected by their CRLBs is given in Table 2a. The measurement precision was better at 7T for Asp (avg. CRLB 27% at 3T vs. 15% at 7T), Glu (avg. CRLB 5% at 3T vs. 3% at 7T), and Gln (avg. CRLB 19% at 3T vs. 9% at 7T) in all three regions. Some metabolites were measured with higher precision at 7T in ACC and CSO, including mI, GSH and NAA. NAAG was also measured with higher precision in the CSO and DLPFC at 7T compared to 3T. CRLBs were comparable at both field strengths for the large signals in the spectrum (i.e. tNAA, tCr, tCho, and mI+Gly), with CRLBs less than 5% at both field strengths. PE, serine and taurine could not be accurately determined at either field strength (CRLB > 50%) so are not included the results shown. The estimated concentration values for these compounds were also very low, so had no influence on the fitted results of other metabolites.

NAA concentrations (i.u.) measured at 3T were higher than at 7T. Metabolite concentrations (Table 2b) measured at 3T and 7T for most metabolites did not show any statistical difference except for Asp ($p < 0.01$), mI, ($p = 0.039$) Gln ($p = 0.013$), mI+Gly ($p = 0.039$) and Glx ($p = 0.026$) in the CSO, NAA ($p = 0.039$) in the DLPFC and mI+Gly ($p = 0.039$) in the ACC.

Discussion

This study used a closely matched methodology between field strengths, including pulse sequence to compare the MRS measurements made at 3T and 7T more precisely. Consistent with prior studies of the occipital lobe using surface coils [2, 6] and one study of parietal white matter using an 8-channel head coil [9], this study confirms the improved SNR and generally lower metabolite CRLBs at 7T compared to 3T, across three brain regions using 32-channel receiver coil arrays. Improvements in SNR seen in the cortical regions (63–66%) in the current study were similar to those seen in reference [6], slightly lower than those reported in reference [2] and also lower than the linear prediction from simple theory (a factor of 2.3). The lowest SNR improvement in the current study was seen in the voxel placed in the deep white matter (20%). While multiple factors affect SNR in MRS, the most likely explanation for these findings is the different sensitivity profiles of the phased-array receiver coils [28]. At 7T, it is known that B_1 changes (decreases) more rapidly as a function of distance from the coil than at lower field strengths [29]; thus, the most favorable results are found at 7T when the MRS voxel is located in a superficial brain region, such as the

cortical surface. This would explain why the CSO (located furthest from the receive array) in the current study showed the smallest improvement at 7T compared to 3T.

Various other factors in the current study may have also resulted in potential signal reductions at 7T, including effects of T_2 relaxation and RF pulse miscalibration. While the sLASER sequence offers a number of advantages over STEAM and PRESS (such as better slice profiles, adiabatic performance, and smaller CSDE), it also has more RF pulses, which place a limit on the shortest attainable TE. Using relaxation time estimates from the literature [25, 26], the shorter metabolite T_2 's at 7T are estimated to cause between 2–8% more metabolite signal loss at 7T than at 3T. It is possible that there may also be some signal loss arising from longer metabolite T_1 's at 7T [30]. The sLASER sequence also only partially compensates for transmit B_1 inhomogeneity (which is also greater at 7T than 3T) because of the non-adiabatic excitation pulse. It should also be noted that simulations suggest that the frequency swept refocusing pulses used in the current experiments provide greater than 90% refocusing efficiency so long as the B_1 level is 14 μ T or higher, but are less efficient when B_1 is lower than 14 μ T. Although a localized power optimization was used for each voxel at 7T [21], in some regions, most notably the DLPFC, the B_1 field failed to reach the nominal 15 μ T even at the maximum transmitter power. This resulted in small reductions in the nominal excitation flip angle. In addition, the localized power optimization was not able to compensate for transmit B_1 field inhomogeneities within the MRS voxel itself. At 7T, actual B_1 values for the transmit radiofrequency field were only 89, 81 and 71 % of the full B_1 values required to produce 90° flip angle in ACC, CSO and DLPFC respectively resulting in the signal loss of 1, 4 and 6% respectively.

The improved SNR at 7T and also greater chemical shift dispersion translated into improved precision of metabolite concentration determinations for compounds such as Gln, Glu, Asp and mI for all three brain regions, as reflected by their lower CRLBs. The most significant improvements were for Glu and Gln, which are known to be harder to separately quantify at lower field strengths due to the high degree of spectral overlap [2]. NAAG was also more reliably determined in CSO and DLPFC, but not ACC. Interestingly, the CRLBs for the major metabolite signals in the spectra (i.e. mI+Gly, tCho, tCr, Glx, tNAA) were similar at both field strengths and were all consistently under 5%. Average CRLB for GABA was higher than 35% in all three regions at both field strengths (data not shown).

Most of the metabolite concentrations, estimated using tissue water as an internal intensity reference and corrected for T_2 relaxation effects, showed no statistically significant difference between the two fields. The exceptions were mI+Gly in the ACC which was lower at 7T than at 3T, Asp, Gln, mI, mI+Gly and Glx in the CSO which were higher at 7T than at 3T, and NAA in the DLPFC which was lower at 7T than at 3T. These discrepancies could be due to two factors: cerebrospinal fluid correction and large voxel sizes. Cerebrospinal fluid (CSF) correction was not included in the data analysis, which could account for some of the differences due to the influence from T_2 relaxation time of CSF which is different from GM and WM. In the current study, quite large voxel sizes (and relatively short scan times) by MRS standards were deliberately used since some of the compounds with smaller signals in the spectrum (Glu, Gln, GABA, GSH, NAAG) were of particular interest, and it was desired to cover multiple regions of interest in a single setting.

The data collected in this study was part of a longer protocol including multiple other sequences, hence, limited time was available for the sLASER sequences which contributed to the use of larger voxels. The use of large voxel sizes, particularly for the cortical regions of interest, probably results in significant CSF contribution to the voxel composition, and could be reduced in future studies by the use of smaller voxels and longer scan times. Another limitation of the current study was that simulated basis sets did not account for CSDE, which particularly at 7T may result in reduced accuracy of the LCModel spectral fitting.

In conclusion, this study demonstrates that improvements in SNR and measurement precision (previously shown in occipital lobe with surface coil reception, and parietal white matter using an 8-channel receive coil assembly) can be demonstrated in multiple brain regions using a volume transmit coil paired with a 32-channel receive array for whole brain imaging coverage at 7T compared to 3T. The current study also confirms that the sLASER pulse sequence works well at 7T (provided that sufficient transmit B_1 levels are available) and can at least partially ameliorate the increased chemical shift displacement effects and transmit B_1 inhomogeneity encountered at 7T. The measurement precision of Glu and Gln in all three regions was better at 7T than at 3T.

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Figure 1. Coronal and axial views of the 3 voxel locations used in this study (ACC – anterior cingulate cortex, CSO – centrum semiovale, DLPFC – dorsolateral prefrontal cortex) overlaid on top of the T₁-weighted MPRAGE images (example in one subject at 7T).

Figure 2.

Representative spectra at 3 and 7T from each of the regions illustrated in Figure 2 for one subject. Major peaks from N-acetylaspartate (NAA), creatine (Cr), choline (Cho), *myo*-inositol (mI), glutamine (Gln), glutamate (Glu) and their sum (Glx = Glu + Gln) are labeled.

Figure 3.

Results of the LCModel fitting analysis for 3 brain regions at 3 and 7T. The original spectra are shown in Figure 3. The red curve is the result of the fitting procedure, and the residual (difference of the original data minus the fit) is plotted at the top. Good fitting is apparent in all spectra, although a small residual peak at 2.6 ppm is observed at 7T which may be due to a MM resonance not included in the basis set.

T₂ Relaxation Times (ms, taken from the literature [25–27]) used to correct metabolite concentrations in white and gray matter.

Table 1

	3T			7T		
	H ₂ O	NAA	Cr	H ₂ O	NAA	Cr
Gray matter (GM)	110	247 ± 13	162 ± 16	50 ± 3	132 ± 6	95 ± 3
White matter (WM)	80	301 ± 18	178 ± 9	55 ± 4	191 ± 7	131 ± 8

Table 2

(a) Average Cramer-Rao Lower Bounds (CRLB) and (b) metabolite concentrations (expressed in 'institutional units', i.u.) for 7 individual compounds, as well as 5 composite signals (tCho = GPC+PCCho, tCr = Cr+PCr, tNAA = NAA+NAAG, Glx = Glu+Gln, and mI+Gly) estimated in three brain regions at both 3 and 7T.

a)	%CRLB	ACC		CSO		DLPFC	
		3T	7T	3T	7T	3T	7T
Asp		20.5	13.5	26.0	15.8	25.5	13.8
Gln		14.8	7.8	24.5	10.5	14.8	10.5
Glu		4.0	2.5	5.0	4.8	4.3	3.0
GSH		8.0	7.8	9.0	14.0	8.8	7.3
mI		5.3	3.3	4.3	4.3	3.8	3.3
NAA		3.0	2.0	2.5	2.5	3.0	2.0
NAAG		28.5	ND	8.5	5.5	24.8	11.8
tCho		3.5	3.3	3.5	4.3	3.8	4.5
tNAA		2.0	2.3	1.8	1.8	2.0	1.8
mI+Gly		4.0	3.3	4.3	4.3	3.8	3.3
tCr		2.0	2.0	2.0	2.3	2.0	2.0
Glx		4.3	3.0	5.3	5.0	4.8	3.5

b)	Conc. (i.u.)	ACC		CSO		DLPFC	
		3T	7T	3T	7T	3T	7T
Asp		1.8 ± 0.2	2.3 ± 0.2	1.1 ± 0.3	2.6 ± 0.1	1.5 ± 0.4	2.6 ± 0.3
Gln		2.1 ± 0.4	2.8 ± 0.2	1.0 ± 0.3	3.1 ± 0.7	2.1 ± 0.3	2.5 ± 0.6
Glu		8.1 ± 0.5	7.6 ± 0.4	5.2 ± 0.1	5.8 ± 0.4	7.1 ± 0.7	7.3 ± 0.2
GSH		1.3 ± 0.1	1.0 ± 0.2	0.8 ± 0.1	0.7 ± 0.1	1.2 ± 1.0	1.2 ± 0.2
mI		4.5 ± 0.3	3.9 ± 0.1	3.3 ± 0.2	4.0 ± 0.2	4.6 ± 0.7	4.2 ± 0.3
NAA		8.4 ± 0.5	7.4 ± 0.6	7.6 ± 0.6	7.4 ± 0.2	9.0 ± 0.3	8.1 ± 0.3
NAAG		0.7 ± 0.1	ND	1.8 ± 0.3	2.5 ± 0.2	0.8 ± 0.2	1.3 ± 0.3
tCho		1.6 ± 0.3	1.6 ± 0.3	1.3 ± 0.3	1.3 ± 0.2	1.5 ± 0.1	1.3 ± 0.2

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Conc. (i.u.)	ACC		CSO		DLPFC	
	3T	7T	3T	7T	3T	7T
tNAA	9.0 ± 0.6	7.6 ± 0.7	9.4 ± 0.7	9.9 ± 0.3	9.9 ± 0.5	9.4 ± 0.4
mI+Gly	4.6 ± 0.3	3.9 ± 0.1	3.3 ± 0.2	3.9 ± 0.2	4.6 ± 0.7	4.2 ± 0.3
tCr	5.8 ± 0.4	5.5 ± 0.3	4.7 ± 0.3	5.3 ± 0.3	5.8 ± 0.2	5.7 ± 0.2
Glx	10.2 ± 0.5	10.4 ± 0.3	6.2 ± 0.3	8.9 ± 1.0	9.2 ± 0.5	9.8 ± 0.6

ND = not determined