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Frame-by-Frame PRESS ^{1}H-MRS of the Brain at 3 T: The Effects of Physiological Motion

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^{1}H-MRS at high field has been increasingly utilized to study brain metabolism in healthy and pathological states. The aim of this work was to determine the effects of physiological motion on the results of this exam in the presence of the increased susceptibility differences at high field. Single voxel spectra of various regions in the human brain were acquired using frame-by-frame PRESS ^{1}H-MRS at a 0.5 Hz sampling rate. The frame-by-frame variations of the FID phase and the frequency and fractional amplitude variations of the residual water-signal were analyzed. In the human brain the standard deviations of these variations were 3.9 ± 0.5°, 0.83 ± 0.32 Hz, and 0.028 ± 0.013 of the mean amplitude (n = 15). In a motionless phantom, smaller phase and frequency variations were detected in water-suppressed acquisitions. However, the end effects of physiological motion on PRESS ^{1}H-MRS of the brain at 3 T were negligible. Magn Reson Med 51:184–187, 2004. © 2003 Wiley-Liss, Inc.

Key words: 3 T; proton MR spectroscopy; brain; frame-by-frame

Brain proton MR spectroscopy (^{1}H-MRS) is a noninvasive method to study brain metabolism in healthy and pathological states (1). Although most studies have been performed at a field of 1.5 T, studies at high field (3 T and up) have been increasingly reported (2–7). The factors which might influence the results of brain ^{1}H-MRS at high field are not fully explored. Physiological motion, in the presence of increased susceptibility differences, might influence the results of brain ^{1}H-MRS at high field.

Physiological motion of the brain or in the body has been previously shown to lead to line-shape deterioration and reduced signal-to-noise ratio (SNR) of the ^{1}H-MRS signals at 1.5 T (8–10). The effects of motion on MRS include 1) voxel misregistration; 2) phase and frequency variations, caused by movement of the tissue through an inhomogeneous B_0 field; 3) phase dispersion caused by motion of the spins during the pulsed field gradients used for MRS voxel localization; 4) amplitude variation caused by movement of the tissue through inhomogeneous B_0 and B_1 fields; and 5) out-of-voxel contamination that may or may not be apparent in the spectra. Different strategies may be used to determine the effects of motion on the MRS results. These include prospective and retrospective cardiac/respiratory gating of the spectra as well as breath pacing. In the present study we explored the end effects of motion on the MRS results by acquiring the spectra frame-by-frame. Previously, we found frame-by-frame acquisition and processing useful for detecting (and correcting) the adverse effects of respiratory motion on ^{1}H-MRS of the abdomen and thorax (11).

Susceptibility differences are linearly dependent on the field, leading to an increase in B_0 inhomogeneity over anatomical scales at higher fields. For this reason, it may be important to investigate the effects of motion on the MRS results at high fields. Motion-induced phase, frequency, and amplitude variations may be apparent in a frame-by-frame investigation of the spectra. Frame-by-frame phase variations may lead to some signal cancellation in the summation of uncorrected spectra. Frame-by-frame frequency variations could result in overall line broadening in the summation of the unregistered frames. Frame-by-frame amplitude variations would suggest signal loss that may not be fully corrected for by postprocessing methods. If the results of ^{1}H-MRS of the brain at high field were to be found significantly deteriorated due to physiological motion, the use of cardiac gating and breath pacing/gating might be required.

In order to detect the effects of physiological motion such as breathing and cardiac/arterial pulsation that occurs at a frequency of about 0.2–1 Hz, we sampled the ^{1}H-MRS frame-by-frame at a frequency of 0.5 Hz (repetition time of 2 sec). The motion of brain parenchyma as well as the flow of cerebrospinal fluid have been previously shown to be correlated with the cardiac cycle (12–14). The ^{1}H-MRS data were sampled from three brain regions: centrum semiovale, cerebellum, and occipital cortex. These regions may have varying degrees of motion induced by arterial blood and cerebrospinal fluid pulsation. In order to reduce phase dispersion of the signal due to motion during the application of pulsed gradients, we used the point-resolved spectroscopy (PRESS) sequence (15). This sequence employs an even (two) number of refocusing (π) pulses which are given at equal time intervals. These conditions lead to refocusing of phase shifts that are induced by constant-velocity throughout the duration of the scan, as previously described ("even echo rephasing" (16)).

MATERIALS AND METHODS

Volunteers

Seven subjects, all right-handed, underwent ^{1}H-MRI/MRS of the brain. ^{1}H-MRS examinations were performed in the

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centrum semiovale, cerebellum, and occipital cortex (each location was examined in five subjects). Informed consent was obtained in accordance with the guidelines of the institutional review board of the Beth Israel Deaconess Medical Center.

MRI and Spectroscopy

The studies were performed on a 3 T scanner (Signa LX, GE, Waukesha, WI) equipped with a birdcage head coil. Anatomical T_2-weighted images of the brain were recorded using a low flip angle RARE sequence (17). The MRS voxel was localized using the anatomic images. Single voxel ($2 \times 2 \times 2$ cm^3) PRESS ^{1}H spectra were acquired with a repetition time of 2 sec, time to echo of 35 msec, spectral width of 5000 Hz, 2048 time points, and 32 or 128 frames (1.1 and 4.3 min, respectively). The crusher gradients applied in this sequence were with an amplitude of 32 mT/meter (80% of the full scale system gradient amplitude), a spacing of 10 msec, and a duration of 4 msec (maximum crusher width).

By acquiring the spectra in a frame-by-frame mode each frame was stored individually and was then amenable to individual processing (PRESS-CSI, GE Medical Systems). The standard head spectroscopy phantom (GE Medical Systems) was used for experiments in a motionless phantom.

Water suppression was adjusted manually. The residual water signal was kept larger than the NAA signal and at the same phase as that of the metabolite signals. Spectra in which the line shape of the water signal was distorted were excluded. Linear shims were used to correct the B_0 inhomogeneity across the investigated voxel. Optimization of the linear shimming was performed using an automatic algorithm (18) (GE Medical Systems).

Data Analysis

Spectral analysis was performed using SAGE, a spectra analysis software provided by GE Medical Systems. For frame-by-frame acquisitions, the phase variations were calculated using a phase regularization algorithm embedded in SAGE. This algorithm uses the first point of the FID to determine the phase of each frame. The in vivo and in vitro FIDs were then zero-filled to 8192 and 32,768, respectively, to allow for representation of the in vivo and in vitro signals by a similar number of points per peak. The frequency and amplitude variations were determined from the peak of the water signal in the frequency domain of magnitude spectra. Magnitude spectra were used in order to avoid the contributions of misphasing. Statistical analysis of the distribution of phase, frequency, and amplitude variations was performed with IDL 5.4 (Research Systems, Boulder, CO).

The standard deviation (SD) of the phase variations is reported in degrees and the SD of the frequency variations is reported in Hz. The SD of the amplitude variation is reported as a fraction of the mean amplitude. Since multiple studies were performed in vivo and in vitro, the average $\pm$ SD of these SDs is reported.

Further postprocessing of frame-by-frame spectra (in the real channel) was carried out using two methods: 1) global processing, all of the frames were corrected with the same zero order phase correction factor, and the frequency was not registered; 2) individual processing, each frame was corrected with an individual zero order phase correction factor, and the frequency of the water signal in all of the frames was registered to 4.7 ppm. Following each postprocessing method the frames were summed and the amplitude and the width (at half height) of the creatine signal were determined. Throughout, n represents the number of measurements in vitro or in vivo.

RESULTS

The first aim of this study was to investigate the frame-by-frame variations in the phase of the FID and the frequency and amplitude of the residual water signal in water-suppressed acquisitions in the living brain and in a motionless phantom. The extent of these frame-by-frame variations may be used to estimate the end effects of motion on the averaged/summed spectrum. A typical example of a frame-by-frame acquisition at the centrum semiovale is shown in Fig. 1a,b. The SD of the phase variation in this example was 4.8°, the SD of the frequency variation was 0.80 Hz, and the SD of the amplitude variations was 0.052 of the mean amplitude. The frame-by-frame phase, frequency, and amplitude variations in vivo as well as in a motionless phantom are summarized in Table 1. These variations were similar in the centrum semiovale, the cerebellum, and the occipital cortex. The SD of phase variations in all the in vivo examinations was $3.9 \pm 0.5°$ (n = 15 examinations), smaller than the phase variation in the motionless phantom. The SD of the frequency variations in vivo (0.83 ± 0.32 Hz, n = 15) was very small but in the motionless phantom in water-suppressed acquisitions these variations were smaller. The SD of the amplitude variations in vivo was 0.028 ± 0.013 of the mean amplitude, n = 15, similar to that of a motionless phantom in water-suppressed acquisitions (Table 1).

The second aim of this study was to determine whether the in vivo phase, frequency, and amplitude variations lead to lower spectral quality. To this end, spectra that were processed with global and individual processing schemes were compared (see Materials and Methods). The outcome of these two different postprocessing schemes is shown in Fig. 1b,c, in a frame-by-frame mode (focusing on the water signal). It appears that as a result of the individual processing scheme, the frames show a more reproducible pattern than with the global processing scheme. However, in the summed spectrum the brain metabolite signals appear similar and not predominantly affected by the individual processing scheme (Fig. 1d,e). The intensity and the linewidth of the creatine (Cr) signal were compared in globally and individually processed spectra and the results are summarized in Table 1. In all of the examinations, the line width and intensity of the Cr signal was not significantly different in the spectra processed with the two processing schemes. We conclude that the effects of phase and frequency variations on the results of these brain MRS studies are negligible.

DISCUSSION

In this work we have shown that physiological motion is not likely to significantly affect the results of PRESS ^{1}H-

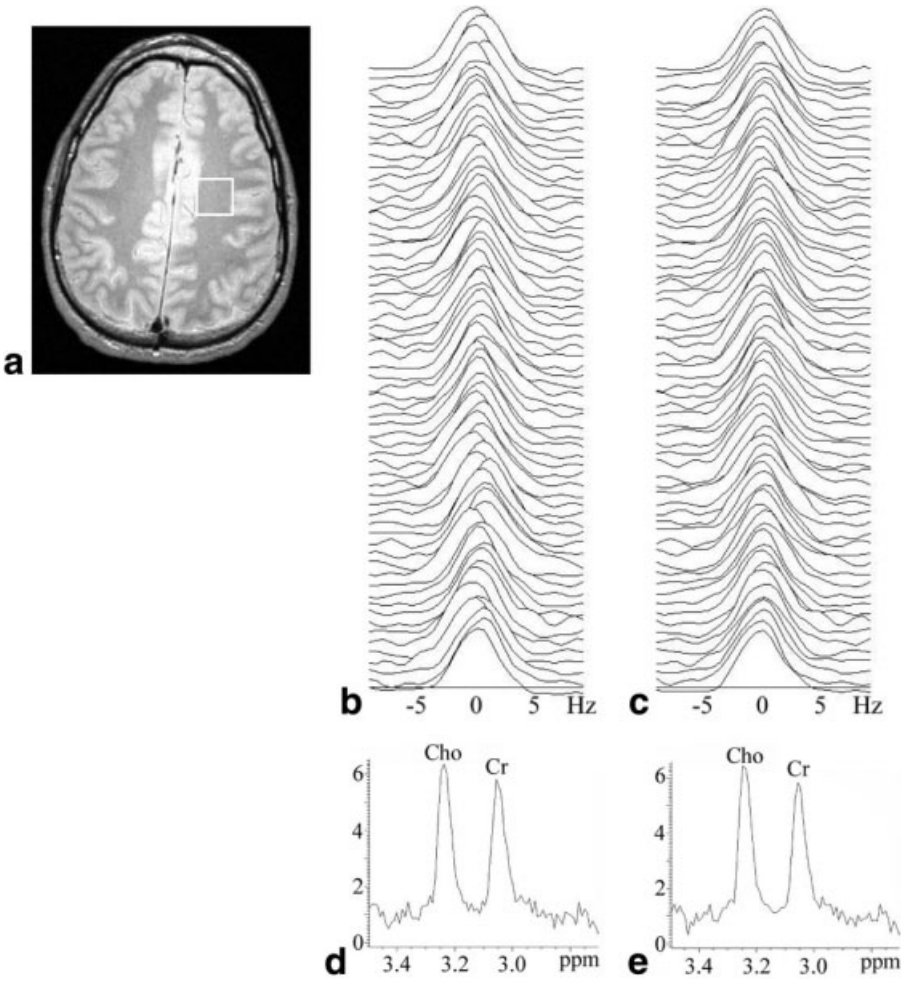

FIG. 1. Frame-by-frame ^{1}H-MRS in the centrum semiovale. **a:** Anatomical image at the level of the centrum semiovale acquired with a low flip angle RARE sequence (17), the location of the MRS voxel is indicated by in the white square. **b:** The water signal of the ^{1}H-MRS acquired in a frame-by-frame mode processed with global processing. 64 frames (2.1 min) are shown. **c:** The same spectra that are shown in **b**, processed with an individual frame-by-frame phase correction and frequency registration. **d,e:** The chemical shift region of the choline (Cho) and creatine (Cr) signals in the summed spectrum of globally processed frames (the same spectra shown in **b**) and individually processed frames (the same spectra shown in **c**), respectively.

MRS of the brain at 3 T. The finding that the phase variations in a motionless phantom were smaller but of the order of the variations that were observed in vivo suggests that these variations could originate from the inherently low amplitude of the FID in water-suppressed acquisitions. Indeed, we have shown that the SD of frame-by-frame phase variations is dependent on the amplitude of the FID and the noise of the measurement (unpubl. results). This correlation explains the higher SD values that were obtained in vivo compared to a motionless phantom, as the latter were acquired with a higher residual water signal (and higher FID amplitude). These results suggest that phase variations could originate from low SNR, and not necessarily reflect motion of the sample. It was previously suggested that the major component of motion-related signal loss in cardiac gated MRS of the brain is due to linear motion, which leads to frame-by-frame phase variations (19). In the same study (at 1.5 T) it was found that these phase variations corresponded to the noise level, as confirmed in our laboratory (unpubl. results). Since the summation of the frame-by-frame individually corrected spectra was not significantly different than that of the globally processed spectra, we conclude that the phase, frequency, and amplitude variations in the brain PRESS ^{1}H-MRS studies are negligible.

However, the phase detection/correction algorithm was based on the amplitude of the FID, on the one hand, and was shown to be correlated to the magnitude of the amplitude of the FID on the other (unpubl. results). Therefore, we cannot exclude the possibility that imperfections in this method could obscure differences in phase variations between the in vivo and the in vitro studies. Nevertheless, zero-order phase correction algorithms that are based on the phase of the first data point, similar to the algorithm used here, were previously used to determine the phase variations of ^{1}H-MRS of the brain at 1.5 T (9,10).

The above discussion suggests that physiological motion may produce phase variations that are below the threshold of detection set by the SNR of our studies. Previously, it was demonstrated that it is possible to detect the frequency of paced breathing using a Fourier analysis of the time course of the brain water signal acquired with PRESS ^{1}H-MRS at 3 T (20). However, in the same study it was impossible to detect any frequency of correlated motion using the Fourier analysis of the time course of the brain water signal acquired during normal (nonpaced) breathing. In the current study, the subjects were instructed to breath normally. Indeed, no specific time-correlated frequency was found to be contributing to the phase modulation of the spectra, even in spectra that were acquired with the high end of the SNR of the residual water signal.

Phase variations, if found, would suggest that physiological motion during the duration of the pulsed field gradients leads to phase dispersion of the signal. The find-

Table 1
Frame-by-Frame Phase, Frequency, and Amplitude Variations of PRESS ^{1}H-MRS of the Brain and Their Effect on the Summed Spectrum

	Water signal			Creatine signal	
	SD of phase variation (degree)	SD of frequency variation (Hz)	SD of amplitude variation[a]	Absolute intensity difference (%)[b]	Width (Hz)
Centrum semiovale (n = 5)	3.8 ± 0.7	0.79 ± 0.27	0.026 ± 0.017	6.2 ± 2.5	7.3 ± 1.2
Cerebellum (n = 5)	3.9 ± 0.5	1.10 ± 0.20	0.028 ± 0.008	6.0 ± 4.6	8.5 ± 2.6
Occipital cortex (n = 5)	4.1 ± 0.3	0.64 ± 0.33	0.031 ± 0.014	1.9 ± 1.7	7.7 ± 1.0
Motionless phantom (n = 3)	2.1 ± 0.5	0.074 ± 0.020	0.037 ± 0.023	ND	2.3 ± 0.2

SD, standard deviation. The results are reported as mean ± standard deviation. n, number of examinations.
[a]Standard deviation of the frame-by-frame FID amplitude variation divided by the mean of the amplitude.
[b]Percent absolute difference in signal intensity between globally processed spectra and individually processed spectra (see Materials and Methods).
Signal width, (full width at half height) was determined on globally processed spectra. ND not determined.

ing that phase variations in vivo were of the order of the phase variations in a motionless phantom suggests either: 1) that the level of motion-induced phase variations was small and was not fully detected under the SNR conditions of water-suppressed acquisitions; or 2) that most of the phase dispersion due to physiological motion during the pulsed field gradients had been refocused by the even number of refocusing pulses applied in the PRESS sequence.

Frequency variations, if found in vivo, would suggest that physiological motion leads to sampling of varying locations of varying B_0 distribution and homogeneity. The finding that the frequency variations in vivo were on the order of 1 Hz suggests that such a variation of B_0 is not predominant in ^{1}H-MRS of the human brain at 3 T.

Amplitude variations in vivo could indicate varying B_1 homogeneity across anatomical scales on the order of physiological motion in the brain (up to 2 mm). Since the current study was performed with a volume coil, this would be unlikely. Indeed, the amplitude variations found in the living human brain were very small and similar to amplitude variations in a motionless phantom.

In conclusion, the current study suggests that physiological motion does not affect the end results of brain PRESS ^{1}H-MRS at 3 T and therefore is not a major cause of signal loss. This finding implies that cardiac gating and breath pacing/gating are not routinely required for brain PRESS ^{1}H-MRS at 3 T.

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