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Simultaneous editing of GABA and GSH with Hadamard-encoded MR spectroscopic imaging

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Abstract

Purpose: To evaluate the feasibility of simultaneous MR spectroscopic imaging (MRSI) of gamma-aminobutyric acid (GABA) and glutathione (GSH) in the human brain using Hadamard Encoding and Reconstruction of MEGA-Edited Spectroscopy (HERMES).

Methods: PRESS-localized MRSI was performed in GABA and GSH phantoms and in the human brain (n=3) using HERMES-editing and compared to conventional MEGA-editing of each metabolite. Multiplet patterns, signal intensities, and metabolite crosstalk were compared between methods. GABA+ and GSH levels were compared between methods for bias and variability. Linear regression of HERMES-MRSI GABA+/H₂O and GSH/H₂O versus gray matter fraction were performed to assess differences between gray matter (GM) and white matter (WM).

Results: Phantom HERMES-MRSI scans gave comparable GABA+ and GSH signals to MEGA-MRSI across the PRESS-localized volume. In vivo, HERMES-reconstructed GABA+ and GSH values had minimal measurement bias and variability relative to MEGA-MRSI. Inter-subject coefficients of variation (CV) from two regions within the PRESS-localized volume for HERMES and MEGA were ~6–12% for GABA+ and 6–19% for GSH. Inter-region CVs were 5 – 15% for GABA+ and 3 – 17% for GSH. GABA+/H₂O and GSH/H₂O ratios were ~1.8 times higher and ~1.9 times higher respectively in GM than in WM.

Conclusion: HERMES-MRSI of GABA+ and GSH was found to be practical in the human brain with minimal measurement bias and comparable variability to separate MEGA-edited acquisitions of each metabolite performed in double the scan time. HERMES-MRSI is a promising method for simultaneously mapping the distribution of multiple low concentration metabolites.

Introduction

In vivo proton (^1H) MR spectroscopy (MRS) can readily detect signals from a variety of molecules within the human brain, such as N-acetylaspartate, creatine, choline, myo-inositol and glutamate. However, relatively lower-concentration compounds such as gamma-aminobutyric acid (GABA) or glutathione (GSH) are difficult to quantify in conventional MRS at field strengths of 1.5 or 3T, because their resonances extensively overlap with the signals from the other, more abundant compounds. Therefore, for low-concentration compounds such as GABA+ and GSH, spectral editing techniques have been developed which selectively detect individual compounds, while suppressing overlapping signals from more concentrated compounds. A variety of editing methods have been proposed, including those based on multiple-quantum filtering (1–3) and J-difference editing (1, 2, 4).

Typically, spectral editing methods are designed to selectively detect a single compound, however recently it has been shown that it is possible to simultaneously edit multiple compounds using a Hadamard-encoded approach known as HERMES ('Hadamard Encoding and Reconstruction of MEGA-Edited Spectroscopy'). HERMES has been demonstrated for two (GSH and GABA, or N-acetyl aspartate (NAA) and N-acetyl aspartyl glutamate (NAAG) (5, 6)) or three metabolites (such as NAA, NAAG, and aspartate (Asp) (7)). In principle, depending on the size of the Hadamard encoding matrix, there is no upper limit on the number of metabolites (n) that can be simultaneously edited. Relative to separate MEGA acquisitions of n metabolites, HERMES offers scan-time savings of at least $1/n$ while maintaining signal-to-noise ratios (SNR) of the individually edited metabolites. Thus for a two metabolite acquisition, HERMES reduces the total scan time two-fold. HERMES can be thought of as performing two MEGA-PRESS scans simultaneously, and thus has the same SNR as the sequential acquisition of each metabolite separately.

Spectral editing methods are usually implemented in combination with single-voxel (SV) spatial localization, but have also sometimes been used in combination with MRSI (9–14).

This report describes the implementation of HERMES in combination with MRSI for simultaneous editing of GABA and GSH from multiple regions of interest. The feasibility of performing HERMES editing of GABA and GSH with a PRESS-localized spectroscopic imaging sequence was examined using both phantoms and in vivo experiments, and compared to results from conventional MEGA-encoded MRSI scans.

Methods

All experiments were performed on a Philips Achieva 3T scanner with a 32-channel head coil. The edited spectroscopic imaging sequence was based on the MEGA-PRESS pulse sequence with additional phase encoding gradients in two directions. A frequency-modulated 90° excitation pulse with a bandwidth of 4.3 kHz and a duration of 8.65 ms and amplitude-modulated 180° refocusing pulses with a bandwidth of 1.3 kHz and durations of 6.91 ms were used as described previously (14). TE_1 was 18 ms, TE_2 was 62 ms, and the editing pulses were 40 ms apart ($TE/2$). For both HERMES and MEGA-PRESS acquisitions, 20 ms sinc-Gaussian editing pulses with a bandwidth of 62 Hz were used.

Additional scan parameters common to all experiments were: TE = 80 ms (previously shown to be a reasonable compromise value that allows editing of both GABA and GSH (5)); TR = 1.5s; and elliptical k-space sampling. For all edited MRSI acquisitions, four excitations were averaged for each phase-encoding step: all four sub-acquisitions for HERMES or two edit-ONs and two edit-OFFs for MEGA. Prior to data acquisition, B₀ field homogeneity was optimized using a field-map-based 2nd-order shimming routine (15). In addition to the edited experiments, separate water-unsuppressed references were acquired for coil combination and phasing purposes. Water data were acquired with one average and with the same field-of-view and resolution as the edited MRSI scans.

Phantom Experiments

HERMES and MEGA MRSI experiments with PRESS localization were performed in three 1L phantoms: one containing 10 mM GABA and 10 mM GSH (pH 7.0), one containing 10 mM GABA only (pH 7.2), and one containing 10 mM GSH (pH 7.0) only. For the GABA MEGA-PRESS acquisition, the edit-ON pulse was applied at 1.9 ppm and the edit-OFF pulse at 7.5 ppm. In the GSH MEGA-PRESS acquisition, the edit-ON pulse was applied at 4.56 ppm and the edit-OFF pulse at 7.5 ppm. For the HERMES acquisition (5), the editing pulse frequencies were applied as described in reference (5).

Spectra were recorded from a 2-cm slice with a field of view of $10 \times 10 \text{ cm}^2$ and PRESS voxel dimensions of $5 \times 5 \text{ cm}^2$. Data were acquired with a 10×10 phase encoding matrix resulting in a nominal in-plane resolution of $1 \times 1 \text{ cm}^2$ and 2 cm^3 nominal voxel volume. MRSI data were subsequently interpolated to 20×20 . Water suppression was achieved using the 'VAPOR' sequence (16). In the HERMES acquisition, the ability to separate the signals of GABA and GSH ('crosstalk'), was quantified as previously described (6, 7) across all the voxels in the PRESS volume of interest.

In Vivo Experiments

Edited MRSI experiments were performed in 3 healthy adults (1 male; age 26 ± 0.6 years). A single 2-cm transverse slice placed immediately above the level of the lateral ventricles was recorded with a field of view of $18 \times 21 \text{ cm}^2$ (LR $\times$ AP) and a PRESS excitation volume of $8 \times 10 \text{ cm}^2$. The anterior edge of the PRESS excitation volume was placed just anterior to the genu of the corpus callosum (Figure 2a). The chemical shift displacement effect on the spins to which editing pulses are applied, relative to the detected 3 ppm spins, in the refocusing directions of the PRESS volume was 11% of the VOI dimension for GABA and 16% for GSH. Slice excitation was performed in the left-right direction while the first refocusing pulse was played out in the anterior-posterior direction and the second refocusing pulse was played out in the superior-inferior direction. Hypergeometric dual band (HGDB), a dual-band water and lipid suppression sequence, was used for simultaneous water and lipid suppression (17). Data were acquired with a 12×14 phase encoding matrix which resulted in a nominal in-plane resolution of $1.5 \times 1.5 \text{ cm}^2$ and nominal voxel size of 4.5 cm^3 . MRSI data were subsequently interpolated to 24×28 . Each scan had a total duration of 13 minutes.

GSH MEGA-PRESS acquisitions were performed with the same editing pulse frequency offsets as in the phantom experiments, but in the GABA+ MEGA-PRESS acquisition, the 'OFF' editing pulse was moved from 7.5 ppm to 0.7 ppm, so that the 'ON' and 'OFF' GABA+ editing pulses were symmetric about the 1.3 ppm lipid signal. This procedure has been previously found to reduce the amount of lipid contamination in the resulting GABA+ edited difference spectra (9). The HERMES sequence was also modified to include 0.7 ppm editing pulses in the GABA+ OFF sub-acquisitions (B and D) as shown in Figure 1. Spectra were also compared to HERMES and MEGA acquisitions with the OFF GABA+ editing pulse placed at 7.5 ppm. Note that the GABA editing pulses used for all experiments partially invert the 1.7 ppm macromolecule (MM) peak (18–20) and the 1.9 ppm homocarnosine peak (21, 22), so that the 3 ppm signal detected in the *in vivo* experiments contains components from MM and homocarnosine in addition to GABA, and is referred to as 'GABA+'.

T₁-weighted 3D MPRAGE scans with 1 mm isotropic resolution were also acquired to plan the PRESS MRSI scan volume of interest and used in data processing to estimate gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF) content of each voxel by segmenting these images using SPM12.

All MRSI scans were reconstructed using a 3DFFT, and multi-channel combination and phase-correction using data from the non-suppressed water acquisitions. Water was further filtered with an HLSVD algorithm (23). In the GABA+ and GSH spectra, the 3.0 ppm and 2.95 ppm peaks, respectively, were fitted with a single Gaussian model and a linear baseline to estimate GABA+ and GSH peak areas in voxels located at the center of the VOI (Supporting Information Figure S1) (24). GABA+ was fit from 2.75 ppm to 3.4 ppm while GSH was fit from 2.78 ppm to 3.15 ppm (Supporting Information Figure S2a; S2b shows examples of the HERMES sub-spectra). To compare the performance of HERMES to the individual-metabolite MEGA acquisitions, the ratio of GABA+ and GSH peak areas between HERMES and MEGA was calculated for each voxel. The closeness of this ratio to 1 (the value which would indicate no measurement bias in HERMES- compared to MEGA-encoded scans) was assessed for all subjects.

To estimate differences in GABA+ and GSH between GM and WM, the edited MRSI data (GABA+/H₂O and GSH/H₂O ratios) were examined for correlations with tissue composition (GM fraction). Tissue composition (GM fraction) for each nominal MRSI voxel within the PRESS-excited volume (without correction for point-spread function) was linearly regressed versus the GABA+/H₂O and GSH/H₂O ratios for all subjects, excluding voxels with a CSF percentage over 3%. The GM tissue fraction was calculated as $f_{GM}/f_{GM} + f_{WM}$ where f_{GM} is the GM volume fraction and f_{WM} is the WM volume fraction (to account for CSF).

To compare the reliability of HERMES and MEGA, the coefficient of variation (CV) of the water-normalized GABA+ and GSH peak areas across two 3 × 3 voxel regions in the left and right hemispheres (Area 1 and Area 2 respectively) within the PRESS volume of interest (Figure 2b) in each subject was calculated. These regions of interest are relatively homogeneous in tissue content and therefore reduce variance in the data due to different

tissue composition. CVs of the water-normalized GABA+ and GSH peak areas between subjects were also calculated in those two regions.

Results

Results from the HERMES and MEGA-encoded MRSI scans from the GABA and GSH phantom are shown in Figure 3a; arrays of 10×10 spectra are plotted over the PRESS excitation volume. The HERMES-encoded reconstructions of GABA and GSH are plotted in blue, while the separate MEGA-PRESS scans of each metabolite are plotted in red. It can be visually observed that there is a very high degree of concordance between the HERMES and MEGA-PRESS reconstructions, in terms of multiplet shape (the edited phantom GABA signal is a ‘pseudo-doublet’, whereas the GSH peak appears as a singlet due to line broadening), intensities, and signal-to-noise ratio (SNR). The multiplet patterns are also in very good agreement with those previously reported in edited single voxel acquisitions of GSH and GABA phantoms (5, 25) at the same echo time.

Results from the HERMES acquisitions performed in the phantoms containing either GSH or GABA only are shown in Figure 3b. It can be seen that the GABA and GSH signals are well separated with only a small amount of crosstalk across the VOI (median (interquartile range) 8.2% (6.7%) GSH crosstalk into the GABA combination in the GSH-only phantom, 11.7% (8.7%) GABA crosstalk into the GSH combination in the GABA-only phantom).

Representative HERMES and MEGA GABA+ and GSH spectra taken from a 13×10 voxel array in subject 2 are shown in Figure 4 and Figure 5 respectively. As in the phantom experiments, the GABA+ and GSH spectra are in good visual agreement between MEGA and HERMES acquisitions, although the GSH spectra are superimposed on somewhat different baselines, likely due to different levels of residual water signal.

Scattergrams overlaid on box plots of the GABA+ and GSH peak ratios (HERMES/MEGA) for all 3 subjects are shown in Figure 6. The HERMES/MEGA ratio is close to 1 in all subjects, demonstrating that HERMES and the individual MEGA-PRESS acquisitions give similar quantification of both GABA+ and GSH without any systematic bias (HERMES/MEGA GABA+ = 1.05 ± 0.1 , GSH = 1.06 ± 0.03 , over all subjects). Although both the median GABA+ and GSH peak area ratios are close to 1, the interquartile ranges are slightly larger for GSH, indicating that the GSH estimates have greater variability than those of GABA+.

The inter-regional GABA CV ranges were comparable between HERMES and MEGA at 6 – 15% and 5 – 13% respectively (Table 1). The inter-regional GSH CV ranges were also comparable between HERMES and MEGA at 3 – 15% and 5 – 17% for MEGA (Table 1). The average inter-subject GSH CVs were higher for HERMES than for MEGA at 14.8% and 7% respectively. However, both of these values are comparable to, or lower than, previously reported inter-subject CVs from single-voxel acquisitions of about 15 – 17% for GSH (26–28). The average inter-subject GABA+ CVs were comparable between HERMES and MEGA at 10.8% and 8.7% respectively and are consistent with previously reported inter-subject CVs from single-voxel acquisitions of 8–18% for GABA (24, 30–33). In addition,

the average water linewidths across all subjects was 8 Hz, which is comparable to that obtained with single-voxel acquisitions (31, 32) while the average NAA linewidth in the GABA-edited spectra across all subjects was 7 Hz.

Area 1 had more gray matter than Area 2 ($0.37 \pm 0.01\%$ for Area 2 versus $0.16 \pm 0.03\%$) with comparable levels of CSF ($0.05 \pm 0.02\%$ for Area 1 versus $0.02 \pm 0.01\%$ CSF for Area 2). As expected, Area 1 also had higher levels of GABA+/H₂O and GSH/H₂O of $9.94 \pm 0.94 \times 10^{-6}$ and $4.87 \pm 0.51 \times 10^{-6}$ respectively versus that of Area 2 which had GABA+/H₂O and GSH/H₂O levels of $9.52 \pm 1.07 \times 10^{-6}$ and $4.11 \pm 0.79 \times 10^{-6}$ respectively. This is consistent with previous literature reports which indicate higher GABA+ and GSH levels in gray matter (13, 32, 35–37).

Figure 7a shows the linear regression results for HERMES GABA+/H₂O versus GM tissue fraction in all three subjects. Regression analysis indicates 1.84 times greater GABA+/H₂O in pure GM compared to WM ($\text{GABA+}/\text{H}_2\text{O} = (8.1 \times \text{GM} + 9.6) \times 10^{-6}$, $p = 0.0002$ and $R = 0.32$). This GM/WM ratio is within the range of literature ratios reported previously: 2.18, 2.0, 1.74, and 1.52 (32, 35–37). The linear regression results for HERMES GSH/H₂O versus GM fraction is shown in Figure 7b. Regression analysis of the tissue dependence of GSH shows a correlation with 1.91 times greater GSH/H₂O in GM than in WM ($\text{GABA+}/\text{H}_2\text{O} = (4.9 \times \text{GM} + 5.4) \times 10^{-6}$, $p = 0.005$ and $R = 0.23$). This value is consistent with a previously reported value of 1.57 times greater GSH in GM than in WM (13).

Discussion

The data presented in this paper show that edited MRSI with HERMES encoding allows for the simultaneous mapping of GABA+ and GSH in the human brain at 3T. HERMES reduces the total measurement time relative to sequential measurements of each metabolite without any penalty in editing efficiency or signal-to-noise ratio (5, 6). In the current example, there was a two-fold scan time reduction from 26 to 13 minutes. HERMES experiments in phantoms demonstrated minimal crosstalk between the two metabolite reconstructions across the volume of interest. It is expected that HERMES-MRSI can be applied to other combinations of metabolites as well, as previously demonstrated using single-voxel localization, e.g. NAA and NAAG (6), or NAA, NAAG and aspartate (7).

Compared to editing methods based on single-voxel localization, edited MRSI (including HERMES-MRSI) presents a number of additional challenges; these include obtaining sufficient B₀ field homogeneity over the volume of interest, minimizing lipid contamination from peri-cranial fat, minimizing the effects of B₀ field drift over the duration of the scan, and minimizing subtraction artifacts due to head motion or other instabilities.

In the current study, excitation of peri-cranial lipids was largely avoided by using PRESS localization confined to the brain, and residual lipids were further suppressed in GABA+ edited scans by placing the ‘OFF’ editing pulse at 0.7 ppm, symmetric about the 1.3 ppm lipid resonance. A limitation of this approach, however, is that the addition of these editing pulses precludes symmetrical macromolecule suppression where additional editing pulses in the GABA+-OFF acquisitions at 1.5 ppm are typically needed (19, 20, 38). This

symmetrical suppression scheme enables the reduction of the macromolecule signal that can make up to 60% of the GABA+ signal (39). The HGDB dualband suppression pulse was also used to suppress the lipid signals at 1.3 ppm; however, this lipid suppression pulse also partially suppresses the NAA signal, leading to a reduced NAA peak at 2.0 ppm. In addition, the Glx signals at 3.75 ppm are reduced relative to conventional GABA-editing (40, 41) due to the more selective editing pulse of used: 20 ms vs. 14 ms for conventional GABA-editing (Supporting Information Figure S3a) (40, 41). In this study, a simple Gaussian model was used to fit both the GABA and GSH peaks. Although both metabolites have been shown to have more complicated multiplet patterns in both simulations and phantom experiments, these are less apparent here in vivo due to the shorter T_2 relaxation times and exponential line-broadening to improve the SNR. Because of this, it is unlikely that using different models will significantly alter the results presented here as shown previously for GABA (24).

In both phantom and in vivo experiments, the signal strengths vary across the VOI with the signals being stronger in the middle of the VOI and decreasing smoothly towards the edges. This reflects two effects: (1) the excitation profiles of the slice selective 180° pulses of the PRESS sequence (2) the filtering used in the reconstruction. It should be noted that reference signals (here, water) recorded with the same sequence will have the same sensitivity profile, so that ratios of GABA or GSH to water should not be affected.

Since the duration of the first spin echo is kept short, it is estimated that signal loss due to chemical shift displacement in the direction of the first refocusing pulse (anterior-posterior direction) is minimal, as previously shown for single-voxel simulations for GSH editing (25) and GABA editing (42). In the direction of the excitation pulse (left-right), chemical shift displacement was kept to a minimum with the use of high-bandwidth pulses with an estimated shift of 8.4 mm and 5.9 mm (approximately a half-voxel shift) between the coupled spins of GSH and GABA that are used for editing, respectively. Full effects from the chemical shift displacement effect are registered in the second refocusing direction: the slice direction (foot-head). Since the slice thickness is relatively small at 20 mm, chemical shift displacement effects were also small with an estimated shift of 3.2 mm and 2.3 mm between the edited and detected spins for GABA and GSH respectively (resulting in ~10% loss of edited signal). Although relatively small, these shifts have an effect on the SNR at the edge voxels of the VOI and were not considered for further analysis.

In this study, no specific efforts were made to monitor or correct for frequency drift or head motion; scans were performed in compliant healthy volunteers under stable conditions. B_0 field drift was largely avoided by not performing MRSI after other studies which involve gradient heating, known to be the most common cause of field drift (43, 44). Subject motion may be more of an issue in clinical and/or less-compliant subject populations who may move more (for instance pediatric subjects). Motion during MRSI scans result in artifacts such as line-broadening, reduced spatial resolution and concomitant increased lipid contamination (45). It has previously been shown that the robustness of edited MRSI scans to compensate for subject motion can be improved by including MR volume navigators for real-time motion and shim correction (45, 46). However, such an approach requires software for real-time updating of scan control parameters that is not currently widely available. It

should be noted that relative to MEGA-encoding, HERMES may have increased subject motion sensitivity since four sub-spectra are acquired, compared to two MEGA. In single-voxel-localized MEGA or HERMES, it is possible to use post-acquisition phase- and frequency-correction of individual transients in order to improve SNR and reduce subtraction artifacts (43, 47); note that because of the use of phase-encoding gradients, in MRSI there is no simple way to perform such a correction. The phase of the FID at each point of k-space is different (and unknown) due to the presence of the phase-encoding gradient. In addition, due to the presence of the editing pulses, phase-correction methods (for instance, those based on the spectral-registration routine) comparing the 4 Hadamard acquisitions will also typically fail (48); therefore there is currently no simple way to perform phase correction with this type of acquisition. This is a challenge which makes edited MRSI experiments (either with MEGA or HERMES-encoding) very sensitive to head motion, since subtraction artifacts on a small number of phase-encoding steps will propagate throughout the dataset once Fourier-transformed into the spatial domain.

Although edited MRSI acquisitions were performed in compliant healthy volunteers, it is likely that subtle movements during acquisition were present and are a source of the variance and outliers seen in the voxel-by-voxel metabolite area ratios between HERMES and MEGA. Another potential source of error is the reduced SNR in some of the transition voxels located near the edge of the PRESS box. This may result in compromised fitting of the metabolite peaks and consequently inaccurate metabolite ratios. This may be improved upon in the future with the use of improved localization techniques such as semi-LASER, which provides better slice profiles.

Linear regression analysis of the HERMES GABA+/H₂O peak areas showed ~1.84 times higher GABA+/H₂O in gray matter than in white matter, as similar to previous reports which indicate higher GABA+ concentrations in gray matter (32, 35–37). Although no consensus on the tissue-dependence of GSH exists in literature, linear regression analysis of the HERMES GSH/H₂O showed a correlation with ~1.91 times higher GSH/H₂O in gray matter than in white matter which is consistent with a previous literature report (13). This analysis did not account for the MRSI point-spread-function, so it is likely to underestimate the difference between tissue types. For both 3 × 3 voxel areas, the inter-region GABA+ and GSH CVs were comparable between HERMES- and MEGA- encoded MRSI indicating that both methods were equally reliable in editing GABA+ and GSH within a similar anatomical location. Between subjects, HERMES- and MEGA-encoded MRSI sequences edited GABA+ equally reliably. However, the average inter-subject CV for the HERMES GSH measurement is ~7% higher than that of the MEGA measurement of GSH. This is possibly due to the more difficult curve-fitting of the HERMES GSH spectra due to the complicated baseline near the 2.95 ppm GSH resonance.

Recently (49) it has been shown that simultaneous measurement of glutamate, glutamine, GABA, and glutathione is possible at 7T using by spectral editing without subtraction in combination with single voxel localization. Such methods in the future may also be possible in combination with MRSI in order to map the distributions of these compounds.

The GABA+ signal observed in MEGA-PRESS in the human brain at 3T is known to contain contributions from GABA, homocarnosine and macromolecules. It is possible that other, unknown, compounds might also contribute some intensity. The results present in supporting figure S3 show that the amplitude of GABA+ to be very similar between MEGA-PRESS and HERMES encoding. In the current experiments in vivo, the effects of field drift and eddy currents may have caused the effective editing pulse frequency to have shifted upfield slightly from its intended position at 1.9 ppm, which also would result in reduced co-editing of Glx (50).

In summary, HERMES-encoded MRSI was shown to be feasible for simultaneous editing of GABA+ and GSH using a PRESS-localized sequence at 3T. Scan time was reduced by a factor of 2 compared to sequential MEGA-encoded MRSI scans, but without any reduction in SNR or increase in measurement variability. HERMES-encoded MRSI is a practical method for mapping the distribution of multiple, low-concentration brain metabolites.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure1.

Frequencies and inversion envelope of the editing pulses for HERMES editing of GABA+ and GSH in vivo with symmetrical lipid suppression lobes applied in GABA-OFF scans. These lobes (indicated in red) are placed at 0.7 ppm in sub-acquisitions B and D so as to be symmetrical about the 1.3 ppm lipid resonance relative to the 1.9 ppm GABA 'ON' editing pulse.

Figure2.

(a) PRESS excitation volume placements of in vivo HERMES and MEGA experiments overlaid on triplanar T₁-weighted images. (b) Two 3 × 3 voxel areas overlaid on an axial T₁-weighted image from which inter-region and inter-subject CVs were calculated.

Figure3.

GABA and GSH multiplets from HERMES phantom experiments. (a) The first row shows the results from the combined GABA-GSH phantom. HERMES and MEGA-PRESS have equivalent GABA and GSH signal intensities and multiplets across the entire volume of interest. (b) In the GABA-only and GSH-only phantoms (second row) GSH and GABA are segregated into their respective reconstructions with minimal metabolite crossover across the volume of interest.

Figure4. PRESS excitation volume overlaid on an axial T_1 -weighted image (top). Representative MEGA- and HERMES-encoded GABA+ spectra plotted from 2.2 to 4 ppm across the entire volume of interest shown top from subject 2. The MEGA- and HERMES-encoded GABA+ spectra are in good agreement between methods.

Figure 5. PRESS excitation volume overlaid on an axial T₁-weighted image (top). Representative MEGA- and HERMES-encoded GSH spectra plotted from 2.2 to 4 ppm across the entire volume of interest shown top from subject 2. The MEGA- and HERMES-encoded GSH spectra are in good agreement between methods.

Figure6.

Scattergrams plotted on top of box plots of the voxel-by-voxel GSH and GABA+ peak area ratios (HERMES/MEGA) for each subject. The number of voxels included for each subject ranged from 85 to 88 voxels and were located at the center of the VOI (excluding voxels at the edges). Median ratio values for both GABA+ and GSH were close to one, indicating that HERMES and MEGA give comparable results.

Figure7.

(a) Linear regression of HERMES MRSI GABA+/H₂O ratios versus gray matter fraction for all three subjects. GABA+/H₂O was estimated to be 1.84 times higher in gray matter than in white matter ($p = 0.0002$). (b) Linear regression of HERMES MRSI GSH/H₂O ratios versus gray matter fraction showing a correlation with 1.91 times greater GSH/ H₂O in gray matter than in white matter ($p = 0.005$).

Table 1

Coefficients of variation of the GABA+ and GSH peak areas across the voxels in each subject for both HERMES and MEGA-PRESS acquisitions. The average coefficients of variation are also listed and are equivalent between methods for GABA+ and are close for GSH.

Inter-regional CVs						
GABA+						
	Area 1		Area 2			
Subject	HERMES	MEGA	HERMES	MEGA		
1	5.8%	9.3%	6.2%	8.2%		
2	5.9%	5.2%	14.8%	5.4%		
3	7.0%	13.2%	10.2%	8.3%		
Average	6.2%	9.2%	10.4%	7.3%		
GSH						
	Area 1		Area 2			
Subject	HERMES	MEGA	HERMES	MEGA		
1	7.1%	5.5%	3.5%	8.0%		
2	15.2%	16.9%	7.0%	5.0%		
3	10.0%	9.8%	12.5%	8.6%		
Average	10.8%	10.7%	7.7%	7.2%		
Inter-subject CVs						
	Area 1		Area 2			
Subject	HERMES	MEGA	HERMES	MEGA	Average HERMES (both areas)	Average MEGA (both areas)
GABA+	9.5%	5.9%	12.0%	11.4%	10.8%	8.7%
GSH	10.5%	5.6%	19.2%	8.4%	14.8%	7.0%