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Spatial Hadamard encoding of J-edited spectroscopy using slice-selective editing pulses

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Abstract

A new approach for simultaneous dual-voxel J-difference spectral editing is described, that uses spatially selective spectral-editing pulses and Hadamard encoding. The theoretical framework for Spatial Hadamard Editing and Reconstruction for Parallel Acquisition (SHERPA) was developed, applying gradient pulses during the frequency selective editing pulses. Spectral simulations were performed for either one (GABA) or two molecules (glutathione and lactate) simultaneously detected in two voxels. The method was tested in a two-compartment GABA phantom, and finally applied to the left and right hemispheres of ten normal control subjects, scanned at 3 Tesla. SHERPA was successfully implemented at 3T and gave results in close agreement with conventional MEGA-PRESS scans in both the phantom and in vivo experiments. Simulations for GABA editing for (3 cm)³ voxels in the left and right hemispheres suggest that both editing efficiency losses and contamination between voxels are ~2%. Compared to conventional single-voxel single-metabolite J-difference editing, two or four-fold acceleration is possible without significant loss of SNR using the SHERPA method. Unlike some other dual-voxel methods, the method can be used with single-channel receiver coils, and there is no SNR loss due to unfavorable receive-coil geometry factors.

Graphical abstract

Keywords

spectral editing; dual-voxel; GABA; glutathione; lactate

Introduction

Single-voxel (SV) magnetic resonance spectroscopy (MRS) of the human brain is commonly used for both clinical and research studies. It is often desirable to measure spectra from multiple brain regions, but sequential collection of SV data quickly becomes time-prohibitive, and is also inefficient, in that only a fraction of the total scan time is used to collect signal from any one region. Consequently, strategies for the simultaneous acquisition of MRS data in multiple locations have been developed, most notably MR spectroscopic imaging (MRSI) using phase-encoding and other techniques (1,2). While MRSI can offer full brain coverage and relatively high spatial resolution (3), it does also place increased demand on scanner stability, difficulties in simultaneously optimizing field homogeneity over all regions, and is usually considered more artifact prone than SV-MRS, particularly with regard to head motion.

Therefore there has been interest in the development of techniques that simultaneously excite a limited number of voxels, and use a variety of methods to reconstruct the spectra from individual regions (4–6). These methods can be viewed as hybrid methods that have some of the advantages of both SV-MRS (i.e. good quality, less artifact-prone, easy to process and display) and MRSI (all voxels acquired simultaneously). The limitations of SV-MRS and MRSI are particularly relevant for the detection of low-concentration metabolites that require spectral editing in order to be reliably detected, such as γ -aminobutyric acid (GABA), lactate (Lac), and glutathione (GSH) (7–9). Because low-concentration molecules are being observed, acquisition times are usually long, and edited MRSI remains very challenging (10, 11), emphasizing the need for simultaneous, multi-voxel edited methods.

In this article, a new approach for simultaneous multi-voxel detection using J-difference editing is described. The method, dubbed ‘Spatial Hadamard Editing and Reconstruction for Parallel Acquisition’ (SHERPA), allows for J-difference editing to be performed simultaneously in multiple voxels by the use of dual- or multi-slice RF pulses, and the application of a field gradient during the editing pulses to encode location-dependent

editing. The editing pulses are applied according to a spatial Hadamard editing scheme, allowing difference-edited spectra from the two or more voxels to be separately reconstructed.

Theory

It has recently been shown that a Hadamard-encoded editing scheme allows the simultaneous acquisition of two or more metabolites in the edited spectrum of a single brain region (13). In a similar manner, SHERPA also uses a Hadamard encoding scheme, but in the case of SHERPA the purpose is to simultaneously acquire edited signals from two voxels.

The method is initially illustrated for the case of one metabolite. The first step is to replace the slice-selective excitation pulse of the MEGA-PRESS sequence (12) with a dual-band excitation pulse, exciting two voxels simultaneously (as shown in Figure 1a). The editing pulses are then applied during a field gradient, which allows independent control of the editing pulse frequencies in the two locations (as shown in Figure 1b). Four experiments are performed with the editing pulses either on-resonance (ON) or off-resonance (OFF) with respect to the editing target: (ON_{vox1}, ON_{vox2}); (ON_{vox1}, OFF_{vox2}); (OFF_{vox1}, ON_{vox2}); and (OFF_{vox1}, OFF_{vox2}), denoted Experiments A-D in Figure 1b. Experiments A and D, (ON_{vox1}, ON_{vox2}) and (OFF_{vox1}, OFF_{vox2}), require the same editing frequency in both voxels, and thus have the editing gradient set to zero. Experiments B and C, (ON_{vox1}, OFF_{vox2}) and (OFF_{vox1}, ON_{vox2}), require different editing pulse frequencies in the two voxels, and thus have the editing gradient on with opposite polarity in each. The predicted outcome of these four experiments is schematically illustrated in Figure 1 for the example of GABA editing, with editing pulses applied at 1.9 ppm in ON scans (ω_{ON} , at some other frequency off-resonance in the OFF scans (ω_{OFF}) and $TE \sim 1/2J$ (68 msec).

Combining the experiments (A+B-C-D) gives the J-difference-edited spectrum for Voxel 1, with signal from Voxel 2 suppressed. The combination (A-B+C-D) gives the J-difference-edited spectrum for Voxel 2, with signal from Voxel 1 suppressed. The function of the editing gradient G_E is to ensure that the editing pulse is experienced at the ON frequency in one voxel while at the OFF frequency in the other. Assuming the positions of the two voxels are x_1 and x_2 respectively, the strength of the slice-selective gradient is therefore given by:

$$G_E = (\omega_{\text{ON}} - \omega_{\text{OFF}}) / \gamma (x_1 - x_2)$$

Assuming that the gradient field is zero at $x = 0$, the frequency at which the editing pulse should be applied for experiment B is given by:

$$\omega = \omega_{\text{ON}} + \gamma G_E x_1$$

and for Experiment C:

$$\omega = \omega_{\text{OFF}} - \gamma G_E x_1.$$

Note that the orientation of the editing gradient is the same as that of the gradient used for slice-selective excitation. Often in spectral editing, the choice of the OFF editing pulse frequency can be relatively arbitrary. In the case of the SHERPA experiment, the OFF pulse frequency directly influences the editing gradient strength, and should be carefully considered; too small a difference between ON and OFF results in a weak gradient and difficulty in separating the 2 voxels, while the choice of a large difference may result in suboptimal editing within each voxel.

Finally, SHERPA also offers the possibility of editing two molecules (double editing, as in the 'DEW' experiment (14)) by placing the 'OFF' editing pulse at the target editing frequency of a second molecule. DEW-SHERPA allows two molecules to be simultaneously edited from two different voxel locations.

Methods

Simulations

SHERPA spectral simulations were performed for GABA, lactate (Lac) and glutathione (GSH). Density-matrix simulations were performed for a B_0 field strength of 3T using 'FID-A', a MATLAB-based software package (15), with GABA chemical shifts and coupling constants taken from reference (16), and those for GSH and Lac taken from reference (17). Simulations were spatially resolved in the excitation direction to include the effects of the editing pulse field gradient across the voxel. For the simulations and experiments, single-lobed sinc-Gaussian editing pulses (7) and conventional amplitude-modulated slice-selective refocusing pulses were used (18, 19). To determine the frequency variation of the editing pulse across the voxels in Experiments B and C, Bloch simulations were performed for the editing pulses in the GABA SHERPA and DEW SHERPA experiments examined in this study and the frequency offset at each voxel-edge was calculated. These same Bloch simulations were also performed for GABA SHERPA with a smaller distance (5 cm) between the two voxels, using two different editing pulse gradient strengths (0.041 mT/m and 0.054 mT/m). Density-matrix simulations were also performed.

Spatially Resolved GABA-edited SHERPA Simulations

GABA-edited SHERPA was simulated for two voxels of 30 mm thickness and 66 mm spacing (center-to-center). Ideal dualband slice-selective excitation was assumed, i.e. that the GABA spins are fully excited within the voxel slice width and not excited outside. A one-dimensional array of 16 spectra at a spatial resolution of 1.875 mm was calculated for each voxel. The pulse sequence shown in Figure 1A was simulated with echo time of 80 ms and 14-ms editing pulses with a 90 Hz bandwidth, applied at 1.9 ppm for ON and 1.0 ppm for OFF acquisitions. Experiments A and D were simulated with the editing gradient set to zero. In Experiment B (ON_{vox1} , OFF_{vox2}) the gradient strength was set to 0.041 mT/m, so that the editing pulse was close-to-resonance for 1.9-ppm GABA spins in Voxel 1, and off-resonance in Voxel 2, as described above. For Experiment C (OFF_{vox1} , ON_{vox2}), the gradient was applied with opposite polarity. The editing pulse in Experiment D (OFF_{vox1} , OFF_{vox2}) was applied at 1.0 ppm.

The Hadamard combinations ($A + B - C - D$) and ($A - B + C - D$) were calculated for all spatial locations. Spectra from locations within each voxel were then added together. The imperfection in separation of signals from the two voxels was quantified by calculating the signal from Voxel 1 that appears in the Voxel 2 Hadamard combination (expressed as a percentage of the signal from Voxel 1 that appears in the Voxel 1 Hadamard combination). This quantity is referred to as ‘crosstalk’ in this paper. The SHERPA efficiency for each voxel was also calculated by dividing the simulated SHERPA signal by the signal simulated from an equivalent MEGA-PRESS experiment.

Spatially Resolved Simulations of GSH- and Lac-edited DEW-SHERPA

To demonstrate the feasibility of SHERPA for editing two metabolites at a time, the double-editing With (DEW) method (14) was adapted to simultaneously edit GSH and Lac for both voxels. Spatially resolved spectral simulations were performed in a similar manner to above, but with 9 spectra per voxel, a TE of 140 ms and 30 ms editing pulses with a bandwidth of 40 Hz, which had sufficient selectivity to ensure separation between the ON GSH (4.56 ppm) and the ON Lac (4.1 ppm) editing pulses. Experiment A was simulated with no editing gradients and editing pulses applied at 4.56 ppm. Thus for GSH, this serves as the (ON_{vox1} , ON_{vox2}) experiment, while for Lac, this is the (OFF_{vox1} , OFF_{vox2}). Conversely Experiment D was simulated with no editing gradients and editing pulses applied at 4.1 ppm, to serve as (OFF_{vox1} , OFF_{vox2}) for GSH and (ON_{vox1} , ON_{vox2}) for Lac. Experiment B was simulated with a 0.021 mT/m editing gradient, so that the editing pulse is on-resonance at 4.56 ppm in Voxel 1 and at 4.1 ppm in Voxel 2, to serve as (ON_{vox1} , OFF_{vox2}) for GSH and (OFF_{vox1} , ON_{vox2}) for Lac. Similarly, Experiment C was simulated with a -0.021 mT/m editing gradient, so that the editing pulse is on-resonance at 4.1 ppm in Voxel 1 and at 4.56 ppm in Voxel 2, to serve as (OFF_{vox1} , ON_{vox2}) for GSH and (ON_{vox1} , OFF_{vox2}) for Lac.

As with GABA-edited SHERPA above, Hadamard combinations of the experiments were calculated, and crosstalk and SHERPA efficiency quantified for both GSH and Lac. Co-editing of different compounds (aspartate (Asp)), creatine (Cr), GABA, N-acetyl aspartate (NAA), N-acetyl aspartyl glutamate (NAAG), glycerophosphocholine (GPC), phosphocholine (PC), glucose (Glc) and ascorbate (Asc) was also simulated in the DEW-SHERPA experiments assuming equimolar concentrations and with chemical shifts and coupling constants taken from reference 17 (for all metabolites except GABA).

Phantom SHERPA experiments

All experiments were performed on a Philips Achieva 3T scanner using a 32-channel phased-array head coil for receive and a body coil for transmit ($B_1 = 13.5 \mu T$). To demonstrate the capability of SHERPA to accurately distinguish concentration differences between the two voxels, SHERPA experiments were performed in a 1L agarose gel phantom (pH 7.2) with different concentrations of GABA in the top half (10 mM) and bottom half (16 mM) of the phantom. Acquisition parameters were the same as the simulations described above, with the following additional parameters: chemical-shift-selective water suppression; two outer-volume suppression bands to saturate signal in the phantom cap and base; TR 2 s; $2.7 \times 2.7 \times 2.7 \text{ cm}^3$ voxels; and 64 signal averages (i.e. 16 averages for each sub-experiment A-D). Spectra were line-broadened using a 5-Hz exponential filter and Hadamard-

reconstructed to give difference-edited spectra for both voxels. SHERPA experiments were acquired with (dualband) excitation of both voxels which were calculated by summing two individual single band excitation RF pulses (20) and reducing the B_1 amplitude and lengthening the duration of the pulse to maintain the correct flip angle (as described in reference 3). For comparison, SHERPA experiments with only Voxel 1 or voxel 2 excited, were also acquired using conventional single-band slice-selective excitation pulses (20). For comparison, two MEGA-PRESS acquisitions for each voxel excited separately were also collected. In these MEGA-PRESS acquisitions, 14 ms sinc-Gaussian editing pulses with a bandwidth of 90 Hz were placed at 1.9 ppm in the ON case and at 7 ppm in the OFF case.

One challenge with SHERPA is how to acquire matched non-water-suppressed data for each voxel for quantification, or other, purposes (such as phased-array coil combination). The approach taken here was to use the saturating effect of MEGA pulses applied on-resonance (i.e. when the editing pulses is applied at the water frequency, the water signal is effectively dephased (12)), repeating the SHERPA sequence with editing pulses applied to the water resonance in a Hadamard fashion. This allows for the separation of water signals from each voxel. Thus, the same four-part pulse sequence was performed with 10 ms editing pulses with a bandwidth of 122 Hz applied at 4.68 ppm and 5.25 ppm (and no water suppression). These SHERPA water signals were compared to the unsuppressed water scans from each voxel obtained during the MEGA-PRESS acquisition.

In vivo experiments

SHERPA GABA editing was performed in 10 healthy adults (3 female, 7 male; age 25 ± 3 years) in $3 \times 3 \times 3$ cm³ voxels located symmetrically in the left and right frontoparietal lobes (as shown in Figure 2a). DEW-SHERPA experiments for Lac and GSH were also performed in one healthy subject (1 male, age 22) in $3.6 \times 3.6 \times 3.6$ cm³ voxels centered on the same locations (Figure 2b). An outer-volume suppression pulse was applied to the scalp adjacent to voxel 1 (right hemisphere) to suppress lipid signal from the scalp. Water suppression was achieved using the VAPOR sequence (21), and shimming performed up to second order. Non-water-suppressed SHERPA scans were also acquired with 16 averages, in order to obtain water references for both the SHERPA and DEW-SHERPA experiments. GABA MEGA-PRESS acquisitions of each voxel separately were also taken in another subject (1 male, age 28) for comparison to the SHERPA data.

Acquisition parameters were the same as for the phantom GABA experiments, except 320 averages were acquired. DEW-SHERPA editing of GSH and Lac was performed as in the simulations, with 512 averages; and TR 2s.

Prospective frequency correction for B_0 field drift during the scan was performed for DEW-SHERPA editing based on the water frequency of interleaved water-unsuppressed scans from the localized voxels that were acquired every 32 averages (22).

Reconstruction Software and Data Analysis

Prior to SHERPA reconstruction, individual transients of the GABA SHERPA experiment were phase-and-frequency corrected based on the residual water frequency (23). To reconstruct the spectra from each voxel, in-house software was used to combine the signals

from the different channels. The spectra from each coil were first separated into the two voxels using the Hadamard combinations, as described above. Then, data from each coil were phased by the first point of the FID of the unsuppressed water signal from each voxel, and then combined. This separation into the voxel-specific spectra before coil combination addresses coil-dependent phase differences between signals from the two voxels. After combining the data from the different channels, the data were zero-filled and the GABA peak at 3.0 ppm was fit using a Gaussian lineshape model. The resulting GABA peak area and the area of the water reference peak were then used to estimate GABA concentrations (in institutional units, 'i.u.') using the Gannet program (24). The SHERPA water reference area was multiplied by a factor of two to account for the water signal being saturated in two of the four Hadamard experiments. To compare the spectra from the SHERPA acquisitions to the MEGA-PRESS acquisitions from the same voxels, the signal-to-noise ratio was calculated for each spectrum by finding the maximum value of the fitted GABA peak and dividing by twice the standard deviation of the noise.

Results

Bloch simulations of the frequency variation of the editing pulse across the voxel in the GABA SHERPA experiments shown in Figure 3a indicate a slight frequency variation (± 0.2 ppm) of the editing pulse across the voxel. Spatially resolved simulations of GABA-edited SHERPA, shown in Figure 3b, demonstrate that spatially dependent manipulation of the coupling evolution occurs as intended. GABA sub-spectra for each spatial location across the two voxels, and the voxel-sum spectra show the expected modulations, with positive outer lobes in ON spectra and negative outer lobes in OFF spectra. It can be seen that in Experiments B and C, the peak heights of the sub-spectra vary within the 'ON' voxel as the editing frequency shifts slightly from 1.9 ppm along the applied gradient. Hadamard combinations of the sub-experiments, shown in Figure 3c and 3d, demonstrate good separation of the GABA signal from each voxel. The SHERPA efficiency within each voxel was 97.8% (of that of MEGA-PRESS) and the crosstalk was 2.2%.

GABA-edited SHERPA spectra from the phantom are shown in Figure 4a. Good agreement can be seen between the SHERPA reconstructions with either dual-voxel or single-voxel excitations, and in comparison to conventional single-voxel MEGA-PRESS spectra from each voxel. In addition, there is minimal crosstalk between the two voxels, as demonstrated in the SHERPA reconstructions of data collected when only one voxel is excited at a time. The ratio (voxel 1/voxel 2) of estimated GABA concentrations was found to be 1.61:1 for SHERPA, which agreed well with the ratio 1.68:1 for SHERPA reconstructions of single voxel excitation data, and also ratio of 1.67:1 found for the MEGA-PRESS data. All these concentration ratios are close to the actual concentration ratio of 1.6:1. Figure 4b shows the reconstructed water spectra from the corresponding SHERPA and MEGA-PRESS acquisitions, which are again consistent between the different experiments.

Figure 5a shows GABA-edited brain spectra from both voxels of all ten subjects. Prior to plotting, spectra were normalized to the water signal. As expected, the GABA peak at 3.0 ppm is comparable between the two voxels for each subject, and also between subjects. This is verified in the GABA concentrations, which are also comparable between the voxels and

are calculated as 3.25 ± 0.44 I.U. for voxel 1 and 3.05 ± 0.54 I.U. for voxel 2. Figure 5b shows that the GABA-edited SHERPA spectra are very similar to those from a standard MEGA-PRESS acquisition of the two voxels acquired separately. This is reflected in their respective signal-noise-ratios of 13 and 12 for voxel 1 and voxel 2 respectively with SHERPA and 10 and 12 respectively with MEGA-PRESS.

Bloch simulations of the editing pulses used in the DEW-SHERPA experiment show a small frequency variation of the editing pulse across the voxel (± 0.13 ppm) as illustrated in Figure 6a. Spatially-resolved DEW-SHERPA simulations demonstrate feasibility to simultaneously detect GSH and Lac in both voxels with minimal crosstalk between the voxels (Figure 6b and 6c). Figure 6d shows that Asp, Cr, NAA, NAAG, GPC, PCh, and Glc are co-edited in the GSH-Lac-edited spectra, but no overlap with the resonances of interest (GSH at 2.95 ppm and Lac at 1.32 ppm) is observed. Figure 7 shows the results of a DEW SHERPA experiment performed in the brain of one subject (normalized by the water signal prior to plotting) where the GSH peak at 2.95 ppm and the lactate and co-editing macromolecule peaks at ~ 1.32 ppm can be seen.

When the voxels are placed closer together in the GABA SHERPA experiment (Figure 8), keeping the editing pulses gradients at 0.041 mT/m results in a higher editing efficiency and a smaller percent crosstalk (96.8% and 3.3% respectively) than increasing the editing pulse gradients to 0.054 mT/m (93.7% and 6.7% respectively).

Discussion

In this article, it is demonstrated that spectral editing of two different brain regions can be performed simultaneously using spatially dependent spectral editing pulses in SHERPA. For the examples given here, detecting either GABA, or GSH and Lac simultaneously, there is little crosstalk between the two voxels and minimal loss of signal compared to conventional MEGA-PRESS scans. SHERPA should also be applicable to any other J-coupled molecules that can be edited with MEGA-PRESS (such as NAAG and 2-hydroxyglutarate (13, 25), for instance) and can be applied to other combinations of brain regions.

One issue that has to be carefully considered with SHERPA is minimization of inhomogeneous editing within-voxel. In deciding the appropriate strength of editing gradients (intrinsically linked to the editing-off frequency and the distance between the voxels), a compromise must be met between achieving full inversion across the ON voxel and no inversion in the OFF voxel. Failing on either count will result in incomplete separation of signal from the two voxels, while incomplete within-voxel inversion also results in a loss of editing efficiency. For the implementations shown here, the loss in editing efficiency and crosstalk are both small ($\sim 2\%$ for both). This becomes more difficult to achieve when the voxels become closer together, and stronger editing gradients may be needed. However, depending on the voxel separation and the spin system, a weaker editing gradient strength may still result in high editing efficiency and low crosstalk, as seen for GABA here. For DEW-SHERPA, the frequency difference between the two edited metabolites fixes the editing gradient strength. A larger frequency difference requires a

stronger editing gradient, which leads to a greater frequency variation within each voxel, which may lead to a lower overall editing efficiency of both metabolites.

An advantage of the SHERPA method over parallel-reconstruction methods such as PRIAM (4) is that SHERPA can be performed on a single-channel receive coil and is not reliant upon phased-array coil geometry. However, SHERPA can be performed with phased-array receive coils, providing care is taken in reconstructing the spectra from each voxel after acquisition. The relative phase of the MR signal in each coil of the phased-array differs between the two voxels. Therefore, the Hadamard transform of the FIDs from each coil was taken before coil combination, so as to separate the signal from each voxel for each coil, before combining the channels using a phase-sensitive average across all coils.

The demonstration of GSH and Lac editing with the DEW method (originally proposed for GSH and ascorbate (14), but adapted for GSH and Lac) shows the capability of SHERPA to simultaneously edit two metabolites from two voxels, a four-fold acceleration compared to sequential MEGA-PRESS acquisitions. This dual editing with SHERPA (DEW-SHERPA) is possible for spin systems where both the spins targeted by the editing pulses and the observed spins of each molecule are sufficiently resolved from another. This presentation of DEW-SHERPA is preliminary, and intended as a demonstration of principle, rather than a mature technology. In order to convert simultaneous detection of GSH and Lac into simultaneous quantification, further refinements of the acquisition parameters will be required, in addition to more refined post-processing and frequency-domain modeling using simulated basis functions. In theory, SHERPA can also be adapted to edit more than one metabolite where the spectra from the observed spins overlap, by integrating it with a HERMES editing scheme (13).

One challenge when acquiring edited data from two voxels simultaneously is the need to shim both voxels at once. In the data presented, this was achieved by performing a projection-based shim of a cuboid including both voxels. This approach was adopted pragmatically, but may not result in optimal shimming of the voxels, and more advanced shimming methods that only consider the tissue within the two voxels would be expected to perform better (4). There was some evidence of a frequency shift between some pairs of voxels, which, if large enough, would result in imperfect editing and separation of signals, so dual-voxel shimming should include a further constraint to not only maximize homogeneity but also to minimize differences in the center frequency (Ω_0) between the two voxels.

One area that has received much attention recently in edited MRS, is the robustness of measurements in the presence of B_0 field instability (22, 26). Although it is possible to achieve little crosstalk between the two SHERPA voxels, this is unlikely to hold in the presence of significant frequency drift. In this case, the editing pulse of one voxel may start to impinge on the other voxel resulting in a loss of separation, in addition to the usual issues of subtraction artifacts (22, 26) and losses of editing efficiency. These issues can be reduced by applying prospective field-frequency correction during the acquisition (22).

When extending this method to clinical applications, it is likely that SHERPA will have greater motion sensitivity than MEGA-PRESS, since four sub-spectra are now needed instead of two. This would affect the quality of both spatial localization and editing, similar to MEGA-SPECIAL, which also acquires four subspectra for localization and editing (27).

In conclusion, the SHERPA method has been developed to acquire J-difference-edited spectra from multiple voxels simultaneously, using spatially dependent editing pulses. SHERPA was demonstrated to detect either one metabolite (GABA) or two metabolites (GSH and Lac) per experiment, providing two- and four-fold acceleration, respectively, over sequential MEGA-PRESS measurements.

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Abbreviations

Asc	ascorbate
Asp	aspartate
Cr	creatine
DEW	Double Editing With
GABA	gamma-aminobutyric acid
Glc	glucose
GPC	glycerophosphocholine
GSH	glutathione
HERMES	Hadamard Encoding and Reconstruction of MEGA-Edited Spectroscopy
Lac	lactate
MEGA-PRESS	MEscher and Garwood-Point RESolved Spectroscopy
NAA	N-acetyl aspartate
NAAG	N-acetyl aspartyl glutamate
PC	phosphocholine
PRIAM	Parallel Reconstruction In Accelerated Multivoxel MR spectroscopy
SHERPA	Spatial Hadamard Editing and Reconstruction for Parallel Acquisition
SV	single-voxel

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Figure 1.

SHERPA schematic. (a) Pulse sequence based on MEGA-PRESS with dualband excitation pulses and field gradients applied during the editing pulses. The editing pulses and their associated field gradients are highlighted in orange. (b) Spatially dependent editing pulses can be applied to separate the difference spectra of two voxels (shown as Vox 1 and Vox 2 bottom left). The gray shading denotes the dualband slice-selective range of Voxel 1 and Voxel 2. SHERPA consists of four sub-experiments A-D. The editing encoding (ON/OFF) is spatially dependent in experiments B and C through the introduction of a gradient G . ω_{ON} and ω_{OFF} correspond to the 'on' and 'off' editing pulse frequencies respectively. The right hand column shows spectral simulations of the expected spectra for each experiment, in this case for editing of the GABA molecule.

Figure 2. Voxel placements of in vivo SHERPA experiments overlaid on a T_1 -weighted axial image (left) and coronal image (right). The voxels are placed symmetrically about the midline in the left (green) and right (purple) frontoparietal lobes. (a) 3 cm $\times$ 3 cm $\times$ 3 cm GABA-edited SHERPA and (b) 3.6 cm $\times$ 3.6 cm $\times$ 3.6 cm lactate and glutathione DEW SHERPA.

Figure 3.

Spatially resolved simulations of SHERPA GABA-editing. (a) Editing pulse profile overlaid on the two excited voxels. The effective editing offset is marked for the voxel centers and edges. (b) The four sub-experiments A-D were simulated for a 1-D spatial arrays within Voxel 1 and Voxel 2. Only the 3-ppm GABA signal is shown. The voxel-average spectrum is also shown in each case to the right of the 1D array. (c) Hadamard combinations of the four experiments shown in (b). (d) Voxel average spectra corresponding to (c) demonstrate minimal crosstalk between the two voxels.

Figure 4.

SHERPA and MEGA-PRESS spectra in a two compartment phantom containing GABA in a ratio of 1.6:1.0 (voxel 1: voxel 2). (a) GABA-edited spectra from Voxel 1 (left) and Voxel 2 (right) are shown, acquired with SHERPA (dual and single-voxel excitations) and MEGA-PRESS (single-voxel excitations). There is good qualitative and quantitative agreement in both voxels between the SHERPA and MEGA-PRESS GABA spectra. (b) SHERPA and MEGA-PRESS spectra of the unsuppressed water signal are also consistent between methods.

Figure 5.

(a) Comparison of the in vivo GABA-edited SHERPA spectra between two equally sized voxels placed symmetrically about the midline in all 10 subjects. The edited spectra are consistent between subjects and between voxels of the same subject, demonstrating equal editing efficiency in both voxels as well as good repeatability of the experiment between subjects. Spectra are colored by location, as shown in Figure 2a with voxel 1 located left of subjects' midline and voxel 2 located right of the subjects' midline. (b) In vivo comparison between GABA-edited SHERPA and MEGA-PRESS acquisitions for one subject. The GABA-edited spectra at 3.0 ppm are consistent, demonstrating that the editing efficiency

and quality of the SHERPA experiments is comparable to that of two conventional MEGA-PRESS editing experiments of twice the total duration.

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Figure 6.

Spatially resolved simulations of DEW-SHERPA editing of GSH and Lac. (a) Editing pulse profile overlaid on the two excited voxels. The effective editing offset is marked for the voxel centers and edges. (b) The four sub-experiments A-D were simulated for 1-D spatial arrays within Voxels 1 and 2. The 2.95-ppm GSH signal (left) and the 1.3 ppm Lac signal (right) are shown for each experiment. The voxel-average spectrum is also shown in each case, demonstrating inverted signals in OFF experiments and positive signal in ON experiments. (c) Hadamard combinations of the four experiments show minimal crosstalk between the voxels, and positive GSH and negative Lac signals as expected. (d) Simulations of metabolites that may potentially co-edited in the DEW-SHERPA experiment, plotted between 4 ppm and 0 ppm. The GSH (2.95 ppm) and Lac (1.32 ppm) resonances are resolved from other co-edited signals. Abbreviations: Asp aspartate; Cr creatine; NAA N-acetylaspartate; NAAG N-acetylaspartylglutamate; GPC glycerophosphocholine; PCh phosphorylcholine; Glc D-glucose; Asc ascorbate.

Figure 7.

In vivo DEW SHERPA-editing of GSH and Lac in one subject. GSH-edited and Lac-edited spectra were acquired in two locations simultaneously, demonstrating the feasibility of fourfold editing acceleration with DEW-SHERPA. In addition to GSH and lactate, signals also co-edit from aspartyl resonances and macromolecules (MM).

Figure 8.

Further SHERPA implementations. Reducing the voxel spacing from 66 mm to 50 mm, it is possible either to scale up the editing gradient to 0.054 mT/m, sacrificing signal within the voxel (upper) or to maintain the same gradient strength and accept partial editing in the OFF voxel (lower). The latter option gives more signal in the intended voxel and, unexpectedly, less crosstalk signal.