Published in final edited form as:

Magn Reson Med. 2017 February ; 77(2): 490–497. doi:10.1002/mrm.26115.

3D MR spectroscopic imaging using adiabatic spin echo and hypergeometric dual-band suppression for metabolic mapping over the entire brain

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Abstract

Purpose—Large lipid and water signals in magnetic resonance spectroscopic imaging (MRSI) complicate brain metabolite quantification. Here we combined adiabatic hypergeometric dual-band (HGDB) lipid and water suppression with gradient offset independent adiabatic (GOIA) spin echo to improve 3D MRSI of the entire brain.

Methods—3D MRSI was acquired at 3T with 32-channel coil. HGDB pulses were used before excitation and during echo time. A brain slab was selected with GOIA-W(16,4) pulses, weighted phase encoded stack of spirals, and real-time motion/shim correction. HGDB alone or in combination with OVS and MEGA was compared to OVS only and no suppression.

Results—The combined HGDB pulses suppressed lipids to 2-3% of their full unsuppressed signal. The HGDB lipid suppression was on average 5 times better than OVS suppression. HGDB +MEGA provided 30% more suppression compared to a previously shown HGDB+OVS scheme. The number of voxels with good metabolic fits was significantly larger in the HGDB data (91-94%) compared to the OVS data (59-80%).

Conclusion—HGDB pulses provided efficient lipid and water suppression for full brain 3D MRSI. The HGDB suppression is superior to traditional OVS and it can be combined with adiabatic spin echo to provide a sequence that is robust to B_1 inhomogeneity.

Keywords

Magnetic resonance spectroscopy imaging (MRSI); Hypergeometric Dual Band (HGDB); Adiabatic spin echo (ASE); brain; lipid suppression; frequency selective radio frequency pulse

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[#]Presented in part at the 23rd ISMRM Meeting, Toronto, Canada, June 1-5, 2015

Introduction

In vivo magnetic resonance spectroscopic imaging (MRSI) has been used to investigate physiology and pathology of the human brain. MRSI provides detailed information about neuro-chemistry in correlation with its anatomical location. A large number of studies outlined the value of MRSI in neuro-psychiatric and neuro-oncological diseases (1). However, the clinical potential of MRSI is diminished by several technical limitations related to B_0 inhomogeneity, limited B_1 amplitude, low spatial resolution, artifacts caused by motion, field drift, and fat contamination (2). In particular, many clinical MRSI protocols operate with reduced brain coverage using volume selection such as PRESS (3), STEAM (4) or LASER (5) to avoid lipid contamination in brain spectra. These methods do not typically image cortical brain regions comprehensively if at all, which is suboptimal for studying many brain diseases. On the other hand, several lipid suppression/removal methods (6-12) have been proposed to extend brain coverage to cortical regions, but a robust and widely applicable solution is yet to be found.

Lipid signal originating from subcutaneous fat overlaps and dominates by 2-3 orders of magnitude the signal of brain metabolites and manifests at distance because of the broad point spread function (PSF) inherent in low resolution Fourier MRSI. Hence, minimizing contamination of lipid signal is necessary for quantification of brain metabolites. Existing lipid suppression methods include: 1) excitation based lipid suppression using outer volume suppression (OVS, (7)), inversion recovery (IR, (13)), frequency selective suppression (11,14,15); 2) k-space encoding to reduce lipid contamination based on optimizing PSF with high resolution (16), variable density (10), dual density sampling (17); 3) post-processing lipid removal using Hamming filtering, extrapolation of lipid signals (6), spectral-spatial sparsity and orthogonality (18), union of sub-spaces (19); and 4) hardware using dedicated lipid crusher coils (20).

In this work we introduced an efficient excitation based lipid suppression in a real-time 3D MRSI sequence (21,22) for whole brain metabolic imaging. We sought to eliminate the restrictions imposed by the LASER volume localization in our previous implementation of the real-time 3D MRSI. We employed frequency selective suppression using hypergeometric dual band pulses (HGDB, (15)), which have been shown to have sharp transition bands and pass-band that are well preserved in the presence of B_1 inhomogeneity. HGDB simultaneously suppress lipid signals (<2.0ppm) and the water signal (4.7ppm) while preserving metabolites within the 2.0ppm-4.0ppm spectral range. An adiabatic spin echo (ASE) was used for slice or slab selection as part of the current 3D MRSI sequence. To improve suppression factors, in contrast to using HGDB pulses in combination with OVS as previously shown (15), here we used HGDB pulses both in a pre-excitation block before ASE and also during ASE according to the MEGA suppression (12). Our motivation was to obtain a protocol that has robust performance within the limits of RF available on clinical scanners, and which is easier to setup, avoiding the lengthy positioning of OVS slabs when an automated procedure (23) is not available.

Methods

Hypergeometric dual-band pulses

HGDB pulses have been previously described for use with MRSI (15,24). Briefly, single band HG (HGSB) pulses are asymmetric adiabatic pulses that represent a generalized version of hyperbolic secant functions, derived from a class of complex analytical solutions of the Bloch equation (25,26). Their highly desirable property includes a sharp transition edge (20-30Hz) on one side of the frequency profile with low ripples and feasible pulse duration. Dual-band HG pulses can be obtained by adding two HGSB pulses shifted in frequency and time reversed to suppress water and lipid and resonances, respectively (15). The frequency and amplitude modulations of the HG pulses can be generated according to,

$$\omega_x = \Omega_0 \frac{\sqrt{z(1-z)}}{Az+B}, \quad \omega_y = 0, \quad \text{and} \quad \omega_z = \frac{Cz+D}{Az+B} \quad (1)$$

$$t = \ln \left(\frac{z^B}{(1-z)^{A+B}} \right), \quad z \in [\varepsilon, 1-\varepsilon], \quad t \in (-t_{\min} + t_{\max}), \quad T_p = t_{\max} + t_{\min}$$

where $(\omega_x, \omega_y, \omega_z)$ are the components of the B_1 vector, ε is the truncation factor that determines the pulse duration (T_p) and together with A, B, C, D parameters determine the transition band and the resulting frequency profile. In practice, numerical interpolation of the time axis needs to be done for equal time sampling intervals of the pulse shape. The separation between the N-acetyl aspartate (NAA) peak at 2.01ppm and the main lipid peak at 1.25ppm is 93Hz at 3T. In order to accommodate a safe margin (20-30Hz) for the NAA peak and the broadening of the lipid peak due to B_0 inhomogeneity a transition band much narrower than 93Hz needs to be accomplished. A transition band of 30Hz or smaller would fulfill this requirement. We searched for HGSB parameters (stepwise as described in (25)) and found $\varepsilon = 2.07 \cdot 10^{-6}$, $A=4.58$, $B=0.26$, $C=-6.5$, $D=9.5$, and $\Omega_0=12.24$ that would provide a pulse duration of 44ms and 25Hz transition band for both lipid and water. The maximum B_1 field for these pulses was 150Hz. Simulation and optimization of the pulse design were performed using both MATLAB (Mathworks, Inc., Natick, MA, USA) and GAMMA library (27).

HGDB pulse with FWHM pass-band of 345Hz (2.8ppm) and 296Hz (2.4ppm) at the flat top was obtained by shifting both HGSB pulses in opposite directions by half of the pass band from the center frequency, and having the fat pulse time reversed as described in (15). A margin of 0.2ppm was considered on each side at the top of the desired pass-band of 2.0-4.0ppm in order to accommodate B_0 frequency shifts. The real and imaginary components of single band pulses were separately added (complex sum) to obtain the dual band pulse (Eq. 2).

$$\begin{aligned} \text{HGSB}_{\text{Water}} &= \vec{\omega}_x e^{-2\pi(\vec{\omega}_z + \omega_{\text{freq.shift}})t}, \quad \text{HGSB}_{\text{Lipid}} = \vec{\omega}_x e^{2\pi(\vec{\omega}_x + \omega_{\text{freq.shift}})t} \\ \text{Re, Im(HGDB)} &= \text{Re, Im(HGSB}_{\text{Water}}) + \text{Re, Im(HGSB}_{\text{Lipid}}) \end{aligned} \quad (2)$$

The corresponding modulations of HGSB and HGDB pulses are shown in Supporting Figure 1.

The HGDB pulses were combined in a pre-saturation block composed of 5 pulses with variable flip angles and interspaced by gradient spoilers (10ms, 20mT/m) as shown in Figure 1A. The same HGDB flip angles proposed in (15) were used, providing a good choice also in our case as verified by measurements and simulations. The flip angle of the HGDB pulses used for MEGA suppression was set to 180°. In order to verify the frequency profile and suppression efficiency we performed Bloch simulations presented in Figure 1B and C.

To evaluate the performance of the proposed HGDB suppression scheme we performed six types of MRSI measurements and compared their results: a) no water and lipid suppression (noWFS), b) OVS lipid with WET (28) water suppression (OVS+WET), c) HGDB only suppression, d) HGDB combined with OVS (HGDB+OVS), e) HGDB combined with MEGA (HGDB+MEGA), and f) HGDB combined with MEGA and OVS (HGDB+MEGA+OVS). For HGDB only and HGDB+MEGA schemes 44ms HGDB pulses were used, while for HGDB+OVS and HGDB+MEGA+OVS schemes 30ms HGDB pulses were used to accommodate OVS within the 5 pulse HGDB presaturation block as proposed in Ref. (15).

Adiabatic spin echo

An axial brain slab was selected with an adiabatic spin echo. The ASE was obtained with an excitation hyperbolic secant adiabatic half passage (AHP) pulse (HS8 modulation; duration of 4ms; bandwidth of 5kHz; $B_{1,\text{max}}$ of 0.65kHz) and a pair of gradient offset independent adiabatic (GOIA) refocusing pulses (W16,4 modulation; duration 3.5ms; bandwidth 20kHz; $B_{1,\text{max}}$ of 0.82kHz) (29). The adiabatic localization provides sharp slab profile, minimal chemical shift displacement error, and insensitivity to B_1 field inhomogeneity.

3D MRSI acquisition

Weighted stack-of spirals was employed for 3D MRSI. Acceleration was obtained by simultaneously encoding (k_x, k_y, t) using constant-density spiral readout (30). Weighted phase encoding was implemented in z-direction to improve the PSF and signal to noise (21,31).

Real-time motion correction and shim update

Prospective real-time motion correction was performed during MRSI acquisition (21,22). RF pulses, spiral readout and shimming were updated each TR according to motion estimates and B_0 field maps provided by a double echo volumetric EPI navigator. Corrupted TR interleaves were reacquired to improve spectral quality.

MRSI of human subjects

Data were acquired with a 3T Magnetom TIM Trio scanner (Siemens Healthcare, Erlangen, Germany) running VB17A IDEA software. The system's standard 32-channel phased-array head coil was used for imaging. Prior to 3D MRSI structural anatomical images were acquired using 3D MEMPRAGE (TR/TE/TI=2530/1.64/1100 ms (32)). The brain slab imaged with 3D MRSI was shimmed with a GRE shimming technique (TR/TE1/TE2=749/2.48/5.21 ms). For all 3D MRSI scans TR/TE=1800/112ms, FOV=24×24×12cm, matrix 24×24×12 interpolated to 32×32×16, NA=8 weighted averages, and TA=11:10 min:s. An axial 50 mm thick slab was selected by ASE in the middle of the brain, which contained 6 consecutive MRSI slices. For MRSI acquisitions that used OVS eight fat suppression slabs were positioned around the brain. For all MRSI acquisitions the SAR was between 50-80% of the maximum SAR limit as monitored by the scanner.

Six healthy volunteers (four males, two females, age 28±6 years old) were scanned for in vivo validation. All experiments were performed under the IRB approved protocol and informed written consent was obtained before measurements.

Data processing and Statistical Analysis

The acquired MRSI data were exported from the MR system for further processing and analysis using MATLAB. The MR spectra were fitted using a Gaussian function to fit lipid resonances between 0.9–1.9ppm, and the metabolites resonances were fitted using a Voigt curve-fitting algorithm (33) with a confidence limit of $R^2 > 0.75$ for goodness of fit.

Metabolic maps were generated by calculating the area under curves of the fitted metabolites for NAA, creatine (Cre), and choline (Cho) signals. Lipid region of interests were defined to include all the voxels around the brain and the scalp for quantifying the lipid signal. Linear image interpolation was performed on both metabolic and lipid MRSI-derived maps to overlay the MRSI data on the anatomical MR images.

Statistical analyses were performed using GraphPad Prism (GraphPad Software, Inc. V4.03, CA, USA). Lipids concentrations were compared across the different suppression schemes using the non-parametric Mann-Whitney test with the threshold for statistical significance defined as $P < 0.05$.

Results

Figure 1B illustrates the simulated profile of the combined five HGDB pulses with different flip angles. Also, in Figure 1B the performance of HGDB pulses with respect to B_1 variation is demonstrated showing excellent flat top pass band, transition bands, and stop bands. For over two-fold variation in B_1 field amplitude there is no noticeable ripple of the flat top and stable stop bands around 2% for lipids and 4% for water. In Figure 1C the transition bands of HGDB pulses with 30ms and 44ms duration are compared. The 44ms pulse provided a narrower transition band of 25Hz compared to 43Hz transition of the 30ms pulse.

Results obtained with spectral fitting from several voxels of 3D MRSI acquired with different suppression schemes are presented in Figure 2. MR spectra from voxels located in the center of the brain, the occipital cortical gray matter as well as posterior scalp region that

typically have the largest lipid contamination were selected for display. The HGDB only and HGDB+OVS suppression schemes provided better lipid and water suppression compared with the conventional OVS+WET scheme. The HGDB+OVS had more lipid suppression compared to only HGDB due to inclusion of OVS. The HGDB+MEGA suppression scheme provided slightly better lipid suppression and considerable more water suppression compared to that of HGDB+OVS. Finally, combining OVS and HGDB+MEGA provides additional suppression in the lipid ring, however the benefits in the brain voxel spectra are minor compared to the HGDB+MEGA only scheme. HGDB+MEGA suppression completely eliminated the water signal over most part of the imaged brain, while large residual water signal is still observed with WET suppression and those suppression schemes that use HGDB pulses only as presaturation. Residual water with HGDB+MEGA was observed only in areas with worst B_0 inhomogeneity (frontal poles).

Lipid maps obtained with all six 3D MRSI acquisitions are compared in Figures 3A. In the case of no lipid suppression the ringing of lipid signal spreads throughout the 3D MRSI data set. In the case of OVS only suppression the efficiency of lipid suppression degrades from bottom slice to upper slice due to the challenge to cover well the head shape across all slices with a limited number of rectangular saturation bands while in the same time avoiding suppression in the cortical brain regions. The lipid suppression using HGDB only suppression was higher all around the head compared to OVS. HGDB+OVS improves lipid suppression compared to only HGDB, but on average is inferior to the HGDB+MEGA suppression. A closer look shows that HGDB+OVS has better performance in the posterior area, while HGDB+MEGA is superior in the lateral and anterior areas. The best suppression over the entire head is obtained when HGDB+MEGA suppression is combined with OVS saturation. The residual lipid signal at the occipital pole is reduced by HGDB+MEGA+OVS, but comparable suppression to HGDB+MEGA is obtained outside this region.

Quantification of the lipid suppression factors is provided in Figures 3i-j and Table 1. Lipid signal was fitted for all voxels within the lipid ring area around the brain. In Figure 3C voxel-wise ratios of lipid suppression to the no suppression data are compared, while in Figure 3D the lipid signal in each voxel is normalized to the mean lipid signal of the no suppression data (numerical values are given in Supporting Table 1). The median suppression factors are comparable for HGDB+MEGA and HGDB+MEGA+OVS, 3% and 2% ($P>0.05$) respectively, while both are significantly better ($P<0.05$) compared to the median suppression factor of 18% obtained with OVS. In addition, the 95% confidence intervals (CI) are much narrower for HGDB+MEGA and HGDB+MEGA+OVS compared to OVS+WET. This indicates a more robust and uniform lipid suppression around the head for HGDB versus OVS only suppression. Lipid suppression quantified for HGDB+OVS and HGDB schemes showed a significant improvement in lipid suppression factors up to 5% and 9% compared to noWFS, respectively ($P<0.05$). The HGDB only suppression scheme provided more than 2-fold better lipid suppression than OVS only scheme ($P=0.057$). HGDB+MEGA provided on average 30% more suppression compared to HGDB+OVS scheme. The best lipid suppression HGDB+MEGA+OVS provided on average 39% more suppression compared to the second best lipid suppression HGDB+MEGA.

Metabolic maps for the main metabolites NAA, Cho and Cre are compared in Figure 4. Voxels for which the goodness of fit is outside the acceptable limits ($R^2 \in [0.75, 1]$) are masked out. It can be noticed that the maps obtained with HGDB+MEGA+OVS and HGDB+MEGA are very similar, indicating that OVS has a small contribution to the quality of the spectral fits. By comparison, the data acquired without HGDB+MEGA suppression are markedly different, with a large number of missing voxels due to bad spectral fits. Quantitative estimation for the agreement among metabolic maps obtained with the metabolic maps is given by the root mean square error (RMSE) in Supporting Table 2. The method that provided the lowest residual lipid signal was considered as ground truth (HGDB+MEGA+OVS). Considering the case of NAA signal as being the most affected by lipid contamination, the lowest RMSE is obtained for HGDB+MEGA (16%), followed by HGDB+OVS (20%), HGDB (21%), OVS+WET (49%) and no suppression (83%). The number of voxels with acceptable goodness of fit for each method is also provided in Supporting Table 2. This result is reflected also by the percent number of “good” voxels which is the highest in the HGDB+MEGA+OVS (92%), comparable in HGDB+MEGA (91%), and followed by HGDB+OVS (83%), HGDB (75%), OVS+WET (60%) and noWFS (42%).

Discussion

Whole brain MRSI is highly desirable for imaging metabolism and neurochemistry of the brain. Key challenges for this goal remain robust lipid suppression/removal and correction of B_0 inhomogeneity. Many innovative approaches have been previously proposed to mitigate these problems (6-20,23,34-36). Our work here was focused on improving lipid suppression to extend brain coverage for a recently optimized real-time 3D MRSI method (21,22). The improvement included the incorporation of an advanced lipid suppression based on hypergeometric dual band pulses in the 3D MRSI pulse sequence. In addition to the previous demonstration of HGDB pulses (15), we showed that HGDB usage as part of MEGA editing provides robust suppression without the need of OVS. Using the HGDB+MEGA scheme we obtained similar or regionally better performance compared to HGDB+OVS scheme that was previously proposed (15). In our implementation HGDB pulses with narrower transition bands of 25Hz were designed, while the echo time was reduced to 112ms. We observed minimal differences in lipid suppression and metabolite RMSE between HGDB+MEGA and HGDB+MEGA+OVS schemes. In contrast, data obtained with commonly used OVS only suppression exhibit approximately 5-10 times more residual lipid contamination and a large variation in lipid suppression efficiency around the head. The large variation with OVS may be explained by the fact that OVS slabs are excited sequentially over a duration of 70-100ms, hence significant lipid signal recovery occurs for the first slab at the time when the last slab was suppressed, while for HGDB suppression all regions are simultaneously suppressed. The efficiency of lipid suppression had a large impact on the quality of spectral fits, resulting in 2-5 times larger metabolite RMSE and 30% less voxels with good fits for OVS alone compared to HGDB based suppression. Additionally, improved water suppression was noticed for HGDB compared to WET.

The advantage of using HGDB is related to their sharp transition bands, flat top pass-band and low ripple stop bands (25). HGDB pulses can tolerate large variations in B_1 amplitude and in combination with adiabatic spin echo are expected to perform well in conditions

where B_1 inhomogeneity is exacerbated such as high field MRI (≥ 3 T) and body imaging (prostate, breast, liver). Their low $B_{1,max}$ requirements (100-200Hz) allow to operate with low SAR and short repetition times for fast acquisition. The use of HGDB is user independent which does not require positioning of saturation bands as for OVS, making the protocol easier to perform for less experienced MR operators. On the other hand, OVS may not avoid suppressing some cortical regions due to head shape and may introduce additional variability due to OVS positioning in longitudinal MRSI studies. The proposed method may be easier to setup for clinical examinations since it does not require positioning of OVS bands.

HGDB present the same limitations as other frequency selective methods. Their performance is dependent on good B_0 homogeneity over the entire brain volume. In brain regions where upfield frequency shifts are larger than 30-60Hz some suppression of NAA may result, while for downfield frequency shifts there will be less efficient lipid suppression. HGDB pulses sacrifice metabolic information outside the pass band, such as methyl signals of lactate or alanine, though signals from other proton groups of these molecules will be inside the pass band. Conversely, HGDB pulses would not suppress lipid signals that are inside the pass-band. However, these lipid signals are much weaker compared to the 1.2ppm ($-\text{CH}_2$)_n and 0.9ppm - CH_3 lipid signals, and have a shorter T2 relaxation time. The combination of HGDB with OVS as demonstrated in (15) can provide suppression for lipid signals within 2-4ppm passband. Compared to IR, the HGDB suppression preserves the SNR of metabolites inside the pass band, while IR typically provides only 50-60% of the SNR but it is less sensitive to B_0 inhomogeneity.

Although HGDB pulses provided good suppression, residual lipid signal is still observed due to broad lipid resonances and B_0 inhomogeneity. The HGDB residual lipid signal of 2-3% is mostly accounted by the tail of the lipid signal between 1.5-1.9ppm, the suppression being complete at 1.2ppm ($-\text{CH}_2$)_n and 0.9ppm - CH_3 . By comparison, with OVS there is a significant residual lipid signal at 1.2ppm and 0.9 ppm. It is expected that improved performance of HGDB pulses may be obtained on scanners equipped with advanced shimming capabilities, such as higher spherical harmonics, shim arrays and better shimming algorithms (37-39). On the other hand, residual lipid signal can be removed with postprocessing methods (6,18,19,40). Combining acquisition and postprocessing methods may benefit either approach, since postprocessing methods have difficulties with the large dynamic range between lipid and metabolite signals, while acquisition methods can incur residual lipid signal.

In conclusion we demonstrated an optimized lipid suppression based on custom designed HGDB pulses in combination with adiabatic real-time 3D MRSI for whole brain metabolic imaging. Our imaging approach may be valuable for research and clinical applications in neuroscience.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding from National Cancer Institute, 1K22CA178269-01 (O.C.A.), MGH-MIT Strategic Initiative's Grand Challenge 3 on Neuroscience (O.C.A.), the Liaison Committee between the Central Norway Regional Health Authority, 46056808 (M.E.) and the Norwegian University of Science and Technology (M.E.). MR experiments were performed at Martinos Center for Biomedical Imaging, MGH, Harvard Medical School using scanners supported by the Center for Functional Neuroimaging Technologies, P41EB015896, a P41 Regional Resource supported by the National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Institutes of Health. This work also involved the use of instrumentation supported by the NIH Shared Instrumentation Grant Program and/or High-End Instrumentation Grant Program, grant S10RR021110.

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Figure 1.

Schematic depiction of the HGDB based pre-saturation block (5 pulses) and MEGA editing used with adiabatic spin echo sequence (A). Variable flip angles according to (15) were considered for the five HGDB pre-saturation pulses. For MEGA editing HGDB pulses with 180° flip angles were used. Simulated frequency profile showing the stop bands, transition bands and pass-band of the five HGDB pre-saturation pulses. B) Stable performance is noticed for change in $B_{1,max}$ from 80% to 200% of the nominal B_1 amplitude. C) Comparison of transition bands for HGDB pulses of 44 ms and 30 ms pulse duration (PD).

Figure 2.

MRSI spectra from voxels located in the center of the brain, occipital cortical gray matter and posterior lipid ring. MRSI was acquired with different water and lipid suppression schemes: a) no water and fat suppression (noWFS); b) conventional water WET and lipid OVS (WET+OVS); c) presaturation HGDB suppression (HGDB); d) presaturation HGDB pulses and OVS suppression (HGDB+OVS); e) HGDB and MEGA suppression (HGDB+MEGA); and f) HGDB, OVS and MEGA suppression (HGDB+MEGA+OVS). Superior lipid and water suppressions were achieved using combination of HGDB and MEGA (HGDB+MEGA), either alone or together with OVS (HGDB+MEGA+OVS), especially in the occipital areas that typically have the largest contamination with lipid signal. Data are left-right ordered from lowest to highest lipid suppression.

Figure 3.

Lipid maps from a healthy volunteer. In (A) axial T1-w MRI from six slices corresponding to the six MRSI slices. Lipid maps obtained with different MRSI water and lipid suppression schemes are shown in (A) HGDB+MEGA+OVS; HGDB+MEGA; HGDB+OVS; HGDB; OVS+WET; noWFS. The lipid maps were generated by integration of the area under the lipid signals between 0.2-1.9 ppm. Box plots (C and D) of the normalized lipid signal measured from all voxels within the region of interest most affected by lipid contamination (circular ROI depicted green on MRI in (B)). In (C) the lipid signal calculated for each MRSI acquisition was voxel-wise normalized to that of noWFS (values in Table 1). In (D) lipid signal in each voxel was normalized to the mean lipid value across all noWFS voxels (values in Supporting Table 1). Statistical significant difference was tested by Mann-Whitney t-test (* denotes $P < 0.05$). The area under the spectrum between 0.2-1.9 ppm was used to integrate lipid signal. Data are top-bottom ordered from highest to lowest lipid suppression.

Figure 4.

Structural (T1-w) and metabolic maps (NAA, Cho, Cr) from a healthy volunteer. T1-w MRI in a) shows six anatomical slices corresponding to metabolic maps. NAA, Cr, and Cho metabolic maps (from top to bottom) are shown for each of the MRSI data acquired with (b) HGDB+MEGA+OVS; (c) HGDB+MEGA; (d) HGDB+OVS; (e) HGDB; (f) OVS+WET; (g) noWFS suppressions. Voxels with goodness of fit outside the accepted range $R^2 \in [0.75, 1]$ were masked out. Data are top-bottom ordered from best to lowest quality metabolite fit.

Table 1**Lipid suppression efficiency**

Lipid signal was calculated for different suppression schemes and normalized voxel-wise to the no suppression case (first column). The different suppression schemes were also compared to each other. The columns and rows are ordered in the order of increased lipid suppression factors. Suppression factors are presented as median (%95 CI) over the entire lipid mask.

	noWFS	OVS+WET	HGDB [#]	HGDB+OVS [#]	HGDB+MEGA	HGDB+MEGA+OVS
noWFS	1	-	-	-	-	-
OVS+WET	0.177 (0.072-0.279) *	1	-	-	-	-
HGDB [#]	0.088(0.118-0.066) *	0.428(0.573+0.3 21)	1	-	-	-
HGDB+OVS [#]	0.053(0.106-0.021) *	0.257(0.516-0.108)	0.602(1.205-0.240)	1	-	-
HGDB+MEGA	0.032 (0.025-0.039) **	0.181 (0.113-0.246) *	0.423(0.770+0.27 1) *	0.703(1.279+0.4 45)	1	-
HGDB+MEGA+OVS	0.016 (0.013-0.019) **	0.093 (0.079-0.107) *	0.218(0.350+0.12 1) *	0.362(0.581+0.2 01)	0.614 (0.532-0.696)	1

* denotes $P < 0.05$,

** denotes $P < 0.01$.

[#] Results from 3 volunteers.