Uncovering Hidden In Vivo Resonances Using Editing Based on Localized TOCSY

Malgorzata Marjanska,[1]* Pierre-Gilles Henry,[1] Patrick J. Bolan,[1] Brooks Vaughan,[2] Elizabeth R. Seaquist,[2] Rolf Gruetter,[1] Kâmil Uğurbil,[1] and Michael Garwood[1]

A novel single-shot spectral editing technique for in vivo proton NMR is proposed to recover resonances of low-concentration metabolites obscured by very strong resonances. With this new method, editing is performed by transferring transverse magnetization to *J*-coupled spins from selected coupling partners using a homonuclear Hartmann–Hahn polarization transfer with adiabatic pulses. The current implementation uses 1D-TOCSY with single-voxel localization based on LASER to recover the H1 proton of β-glucose at 4.63 ppm from under water and the lactate methyl resonances from beneath a strong lipid signal. The method can be extended to further spin systems where conventional editing methods are difficult to perform. Magn Reson Med 53:783–789, 2005. © 2005 Wiley-Liss, Inc.

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Low-concentration metabolites examined by in vivo proton NMR spectra are often obscured by very strong resonances. In the context of glucose metabolism studies, glucose signals are mostly covered by water and lactate by lipid resonances. One way to obtain information about such overlapped signals is to remove the strong resonance via spectral editing. A variety of different editing techniques have been developed (see (1) and (2), and references therein). Water suppression and spatial localization can be considered the simplest spectral editing technique. For example, such a technique was used to directly detect the glucose (H1 α-glucose) signal at 5.23 ppm in human brain at 4 T (3) with proton NMR. This accomplishment relied on excellent spatial localization and good shimming within the volume of localization (all first- and second-order shims were adjusted), as well as highly effective water suppression within this volume for the detection of the glucose resonance in close proximity to the water peak. However, in routine clinical settings using lower magnetic fields (1.5 T), the direct detection approach encounters difficulties because of the decreasing frequency difference between the H1 α-glucose and water resonance.

When the resonance overlap precludes direct detection approaches, more complex editing strategies can be employed. The majority of these strategies are based on utilizing the *J*-coupling as a means of discriminating between coupled and uncoupled spins. Difference editing is one class of such techniques that has been successfully used to observe lactate (4,5). Since difference editing needs two separate acquisitions to achieve complete spectral editing, it is vulnerable to subtraction artifacts arising from subject motion between scans and from hardware instabilities. An alternative approach to difference spectroscopy is multiple-quantum coherence filtering. This single-shot technique provides far greater elimination of intense singlets such as water than difference spectroscopy; it was used to detect the H1 β-glucose signal at 4.63 ppm (6), the glucose signals at 3.85 ppm, and lactate at 1.32 ppm (7) in rat brain. The recovery of the signal is not as good as in other techniques due to the limited inherent yield of multiple-quantum filter; only 40% of the β-glucose signal at 4.63 ppm (6), 45% of the glucose at 3.85 ppm, and 20% of the lactate methyl protons signals (7) was recovered in the study in the rat brain. Additionally, in many cases the phasing in the multiple-quantum filtered spectra is arbitrary since no singlet signals are allowed through the filter. There is a multiple-quantum technique that yields 100% of the signal intensity for A_3X spin systems, but this sequence heavily depends on a phase cycle to suppress undesired signals (8).

Recently a technique for recovering "underwater" metabolite resonances, such as H1 β-glucose and H1 β-galactose, was proposed for biologic samples (9). These metabolite resonances, which were eliminated by water suppression, were recovered through magnetization transfer using scalar or dipolar interactions while the water resonance remained suppressed. The use of total correlation spectroscopy (TOCSY) (10) ensured an in-phase magnetization transfer. The ratio of the peak areas for H1 protons of β-glucose (eliminated during water suppression) and α-glucose (unaffected by water suppression) in Ref. 9 was 1.4, which is close to the expected value of 1.5 for the two anomers. Approximately 93% of the H1 β-glucose signal was recovered. Therefore, this method in principle offers the potential for single-shot editing with close to 100% efficiency. In addition, the specificity of such editing can be improved by generating a coherence transfer from a narrowband region of the spectra within which the source spin resonates.

The aim of this study was to develop an editing method based on selective TOCSY in combination with spatial localization. A single-shot technique that connects 1D-TOCSY (11,12) with localization by adiabatic selective refocusing (LASER) (13) is applied toward detection of

[1]Center for Magnetic Resonance Research and Department of Radiology, University of Minnesota, Minneapolis, Minnesota, USA.

[2]Department of Medicine, University of Minnesota, Minneapolis, Minnesota, USA.

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*Correspondence to: Malgorzata Marjanska, Center for Magnetic Resonance Research, 2021 6th Street SE, Minneapolis, MN 55455, USA. E-mail: gosia@cmrr.umn.edu

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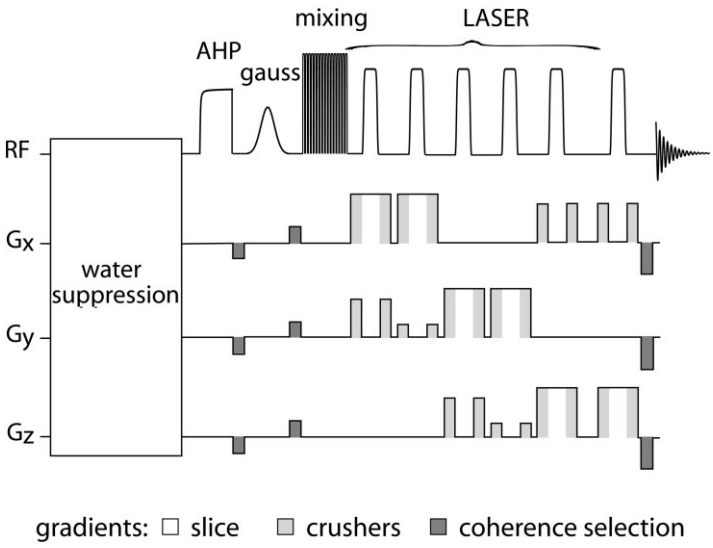

FIG. 1. 1D-TOCSY-LASER sequence with RF and gradient pulses schematically shown. The train of RF pulses labeled "mixing" is composed of adiabatic full-passage pulses and is used to transfer polarization to the target spin. Volume selection with LASER is preformed with another type of adiabatic full-passage pulse. Pulsed field gradients (G_x, G_y, G_z) are used for coherence selection (dark gray shading), for suppressing outer-volume signals (light gray shading), and for slice selection (white).

resonances of low-concentration in vivo compounds that are otherwise invisible. The considerably weaker signals of β-glucose under the water peak and lactate under the lipid resonance are experimentally detected using through-bond polarization transfer. These results show that the 1D-TOCSY-LASER technique can be utilized to detect a number of resonances that have *J*-coupled partners.

MATERIALS AND METHODS

Molecules

Glucose contains seven nonexchangeable protons and exists in the form of two anomers, α-glucose and β-glucose, with an equilibrium ratio of approximately 2:3. For both anomers, most nonexchangeable protons (H2–H6, designating hydrogens bonded to C2–C6, respectively) are strongly coupled and resonate in the range of 3.2–3.88 ppm. The H1 proton is weakly coupled to the H2 proton and appears as a doublet at 5.23 and 4.63 ppm for α- and β-glucose, respectively. The *J*-coupling between H1 and H2 is larger for β-glucose (7.95 Hz) than for α-glucose (3.75 Hz). All glucose resonances are affected by overlap from other contributions in spectra obtained from tissues: the H2–H6 glucose resonances are superimposed by signals from other metabolites; in addition, α-H1 and particularly β-H1 arise close to the water resonance and are easily affected by water suppression, especially at clinically relevant magnetic fields.

Lactate is an A_3X spin system with three methyl protons and one methine proton. The ^{1}H spectrum consists of a doublet at 1.32 ppm from the methyl group and a quartet at 4.11 ppm from the methine group. The *J*-coupling between the groups is 6.93 Hz. The spectral region from 1.0 to 1.5 ppm is frequently complicated in vivo by the presence of lipid resonances. The methine group, on the other hand, is typically not observed in vivo due to the low spectral representation and the close proximity to water.

Pulse Sequence

The new pulse sequence (Fig. 1) was designed for single-shot editing and localization using a combination of 1D-TOCSY (11,12) with LASER localization (13). Following a water suppression module, all resonances are excited using a nonselective numerically optimized adiabatic half-passage (AHP) pulse (14). A gaussian-shape 180° pulse is applied together with three coherence selective gradient pulses along a single axis to refocus resonances within the narrow bandwidth of the pulse. Note that other combinations of coherence selective gradients are possible. During the mixing period, transfer of magnetization through homonuclear *J*-coupling is preformed using a scheme reminiscent of selective TOCSY, which yields in-phase magnetization. Mixing is performed with a windowless train of adiabatic full-passage (AFP) pulses with initial pulse phases prescribed according to MLEV-16 (15). In the present implementation, the shapes of the amplitude- and frequency-modulated functions of these AFP pulses are based on hyperbolic tangent and tangent functions (tanh/tan), respectively (14,16), using empirically optimized pulse durations T_p and frequency sweep amplitudes *A*. The overall degree of spectral filtering of the unwanted coherences depends upon the selectivity of the gaussian pulse, the coherence selection gradients, and the length of the mixing time. The LASER sequence that follows the mixing period provides 3D localization whereby each dimension is selected with a pair of AFP pulses. The use of AFP pulses in LASER has advantages because such pulses tolerate RF field changes and the available peak RF power does not limit the pulse bandwidth, which should be large to minimize the displacement of the voxel for different chemical shifts. All pulses used in this work, with the exception of those used in water suppression and selective refocusing, are adiabatic. In the present implementation, the water suppression module consisted of variable pulse power and optimized relaxation delays (VAPOR) (17).

Phantom

The 1D-TOCSY-LASER editing scheme was initially tested and optimized for detection of the H1 glucose signals and

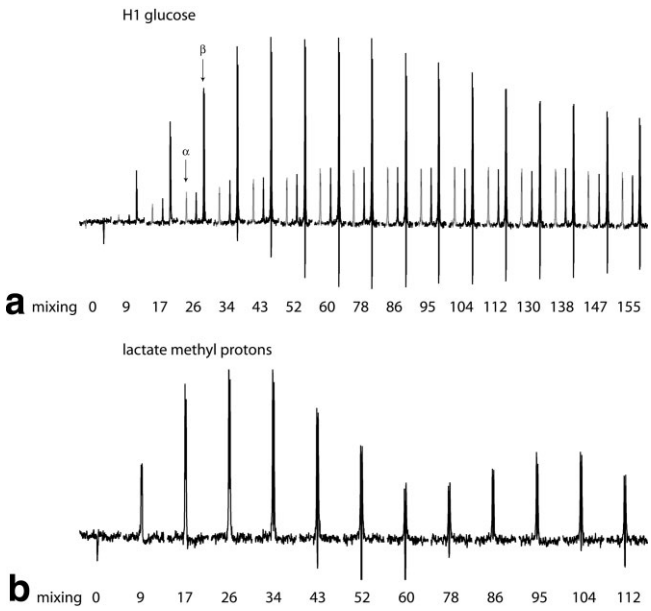

FIG. 2. (**a**) Series of ^{1}H 1D-TOCSY-LASER spectra optimized for detection of the H1 glucose peaks obtained at 9.4 T on an aqueous solution of D-glucose and lactate with mixing times arrayed from 0 to 155 ms. Only the region from 4.3 to 5.3 ppm is displayed. The right-most peak is H1 β-glucose, the left-most light-gray peak is H1 α-glucose, and the peak in the middle belongs to residual water. (**b**) Series of ^{1}H 1D-TOCSY-LASER spectra optimized for detection of the lactate $-CH_3$ signals obtained at 9.4 T on an aqueous solution of D-glucose and lactate with mixing times arrayed from 0 to 112 ms. Only the region at 1.32 ppm is displayed. Repetition time (TR) used = 3 s, number of excitations (N_{EX}) = 4, and 1-Hz line-broadening was used.

the lactate $-CH_3$ signals using an aqueous solution of D-glucose (200 mM) and lactate (37 mM). The transfer of magnetization between *J*-coupled partners depends on the strength of that coupling; hence, recovery of the signal depends on the length of the mixing time. The rate of magnetization transfer for the H1 glucose signals was measured using 17 experiments with mixing time arrayed from 0 to 155 ms in ~9-ms increments (Fig. 2a) and for the lactate methyl protons using 13 experiments with mixing time arrayed from 0 to 112 ms in ~9-ms increments (Fig. 2b).

Animals

All animal experiments were performed in accordance with the guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Care and Use Committee of the University of Minnesota. Following an overnight fast, male Sprague–Dawley rats (n = 7) were intubated and ventilated with a 70%:30% N_2O:O_2 mixture and 1.8% isoflurane. Body temperature was maintained at 37°C by warm water circulation. Both femoral veins and arteries were cannulated for glucose infusion and blood sampling. After completion of surgery, isoflurane was discontinued and replaced by i.v. α-chloralose (bolus 40 mg/kg, then infusion at 25.4 mg/kg/hr). Animals were placed in a homebuilt holder, and the head position was fixed using ear rods and a bite-bar. Blood gases and glycemia were measured every 15 min to ensure stable physiologic conditions. During the course of the experiment, the plasma glucose level was rapidly increased from ~5 to ~20 mM and maintained at this level for the duration of NMR measurement (18). In the post mortem studies, animals were euthanized inside the magnet.

Human Subjects

Normal volunteers (n = 4) were studied after giving informed consent according to procedures approved by the Institutional Review Board of the University of Minnesota Medical School. To prepare for the study, subjects had an i.v. catheter placed into one arm. Subjects were placed on a cushion to minimize acoustic noise and wore earplugs. Glucose infusions (i.v., 20% weight/volume) were administered at a rate of 400 cc/hr to raise and then maintain plasma glucose to approximately 12 mM after 60 min of infusion (19). The same rate of infusion was used during the entire experiment. The blood glucose level was measured immediately before and immediately after the NMR measurement using a OneTouch SureStep glucose monitor (Lifescan, Inc., Milpitas, CA). At completion of the study, the catheter was removed, and the subject was fed lunch and discharged.

In Vivo Spectroscopy

In vivo and post mortem animal spectra were acquired on a 9.4-T, 31-cm horizontal bore magnet (Magnex Scientific, Oxford, UK) interfaced with a Varian INOVA console (Varian, Palo Alto, CA). The magnet was equipped with a gradient insert capable of reaching 300 mT/m in 500 μs (Magnex Scientific, Oxford, UK). A quadrature 400-MHz ^{1}H surface RF coil was used to transmit and receive. Localizer T_2-weighted multislice rapid acquisition with relaxation enhancement images (TR = 5 s, TE = 60 ms, echo train length = 8, matrix = 256 × 128, slice thickness = 1 mm, 11 slices) were acquired to select a 6.0 × 3.7 × 6.0 mm volume of interest in the rat brain. Linewidths of 18 Hz for water were obtained after the adjustment of the first- and second-order shims using FAST(EST)MAP (20,21). In the 1D-TOCSY-LASER sequence, the AHP pulse duration length was 4 ms, and each AFP pulse in LASER was an offset-independent adiabatic pulse, HS8 (22), using T_p = 0.002 s and A = 6.25 kHz (bandwidth (FWHM) = 2A). For the detection of the H1 glucose signals, selective refocusing was performed with a 5-ms gaussian-shape pulse applied at the chemical shift of 3.43 ppm (the bandwidth was sufficiently broad to refocus H2 resonance of α-glucose at 3.23 ppm) to selectively refocus the source spin, the H2 proton, which is *J*-coupled to the glucose H1 spin. Coherence transfer was performed with a 60-ms-long train of tanh/tan pulses using T_p = 250 μs and A = 80 kHz. For the detection of the lactate methyl protons, selective refocusing was performed using a 5-ms gaussian-shape pulse applied at the chemical shift of the methine proton at 4.11 ppm, and the coherence transfer was performed with a 26-ms-long train of tanh/tan pulses (T_p = 250 μs, A = 80 kHz). The echo time was 39 ms for the LASER module. The echo time for the entire sequence, including

both refocusing and coherence transfer, was 109 ms for glucose editing and 74 ms for lactate editing. A repetition time of 3 s was used. All spectra were acquired in blocks of 64 scans with 4096 complex points and spectral width of 5 kHz.

In vivo human spectra were obtained on a 4-T, 90-cm horizontal bore magnet (Oxford Magnet Technology, Oxford, UK) interfaced with a Varian INOVA console (Varian, Palo Alto, CA). The magnet was equipped with a Sonata gradient coil (Siemens, Erlangen, Germany), which was capable of reaching 40 mT/m in 400 μs. A quadrature 169-MHz ^{1}H surface RF coil was used to transmit and receive. Gradient echo (TR = 0.15 s, TE = 17 ms, matrix = 256 × 128, slice thickness = 3 mm) images were acquired to select a 2.7 × 2.7 × 2.7 cm volume of interest in the visual cortex. Linewidths of 10 Hz for water were obtained after the adjustment of the first- and second-order shims using FAST(EST)MAP (20,21). In the 1D-TOCSY-LASER sequence, the AHP pulse duration was 4 ms, and each AFP pulse in LASER was a hyperbolic secant pulse, HS1 (13,23,24), using T_p = 0.004 s and A = 2.5 kHz. Selective refocusing for the detection of the H1 glucose signal was performed with a 15-ms gaussian-shape pulse applied at the chemical shift of 3.43 ppm, and the coherence transfer was performed with a 20.5-ms-long train of tanh/tan pulses (T_p = 1250 μs, A = 16 kHz). The echo time was 68 ms for the LASER module and 111 ms for the entire sequence including refocusing and coherence transfer. A repetition time of 4 s was chosen. Each free induction decay (FID) was acquired with 4096 complex points using a spectral width of 3 kHz. FIDs were stored separately in the memory and then frequency and phase corrected based on the Cr/PCr signal at 3.03 ppm prior to summation. Frequency corrections never exceeded 15 Hz.

RESULTS

In phantom experiments detecting glucose, the bandwidth of the gaussian pulse was set such that the signal from lactate (at 4.11 ppm) was not refocused. Maximum magnetization was obtained at the mixing times of 60 ms for β-glucose and 120 ms for α-glucose, which are in close agreement with theoretical predictions ($1/2J$ = 63 and 133 ms for β-glucose and α-glucose, respectively). Using a mixing time of 60 ms at 9.4 T, 73% of the signal for β-glucose and 45% of the signal for α-glucose was recovered compared to the signal obtained with only a LASER sequence using a corrected echo time. At 4 T, 22% of the signal for α-glucose was recovered using a mixing time of 20.5 ms.

For detection of the lactate methyl protons in phantom, the center of the selective gaussian pulse was placed at 4.11 ppm to refocus the methine proton. The bandwidth of that pulse was narrow to ensure that only a small amount of water was unavoidably refocused. The 91% magnetization transfer from the methine to methyl protons was obtained at a mixing time of 26 ms, which corresponds to 30% of the signal obtained from LASER sequence alone (this is due to the 1 to 3 spin ratio for the methine and methyl groups, respectively).

Glucose detection by 1D-TOCSY-LASER editing was evaluated in vivo in both rat and human brains. Figure 3a shows a time course of edited ^{1}H NMR spectra acquired during the glucose infusion study in the rat brain. The bottom spectrum was obtained directly after the beginning of the infusion. After the onset of glucose infusion, an intensity increase was observed at 4.63 ppm. This resonance was assigned to H1 β-glucose based on its increase in intensity, as well as on its chemical shift of 4.63 ppm,

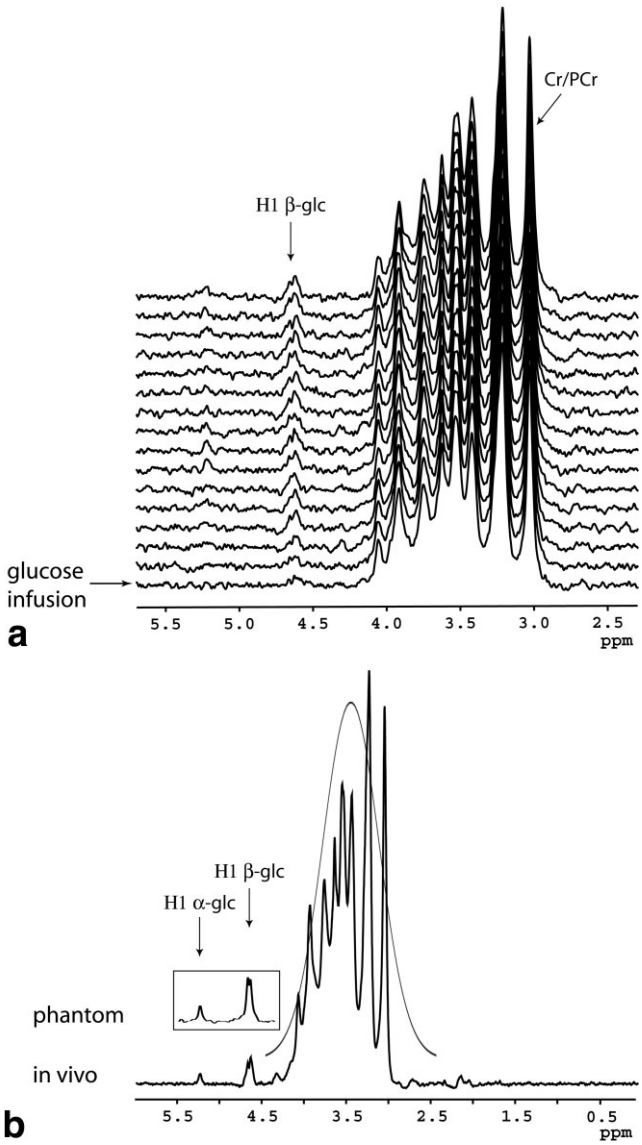

FIG. 3. (**a**) Series of in vivo ^{1}H NMR spectra obtained at 9.4 T on normal rat brain with 1D-TOCSY-LASER editing during glucose infusion. Each spectrum (baseline corrected, 5 Hz line-broadened) was acquired in approximately 3 min from 133 μL voxel. TR = 3 s N_{EX} = 64 for each spectrum, and mixing time = 60 ms. The concentration of plasma glucose was increased from 5.48 to 22.11 mM during the course of the experiment. (**b**) Sum of all the spectra shown in (a), 1024 scans. The profile of the selective gaussian-shape pulse is displayed using a light-gray line. The inset shows part of the spectrum around the H1 α-glucose and β-glucose resonances obtained with 1D-TOCSY-LASER editing of an aqueous D-glucose and lactate solution. The linewidths have been broadened to reflect the in vivo linewidths. glc, glucose; Cr/PCr, creatine/phosphocreatine.

observable splitting of 13 Hz due to *J*-coupling, and the constant phase and amplitude of the signal. The observed splitting of 13 Hz was consistent with the spectra obtained from aqueous D-glucose and lactate solution where linewidths were broadened to match the in vivo numbers. The observed splitting is larger than the *J*-coupling (7.95 Hz) due to the partly antiphase nature of the signal arising from adiabatic mixing and LASER localization. The intensity of the signal at 4.63 ppm corresponds to a concentration of 6.7 mM (quantified using the creatine signal assuming 8 mM creatine concentration), which is consistent with that expected for a plasma glucose level of 22 mM (25) and agrees with the expected intensity for H1 β-glucose based on the recovery of the signal observed on an aqueous mixture of D-glucose and lactate and this plasma glucose level. Assignment of the resonance at 4.63 ppm to glucose was further confirmed by its disappearance in post mortem studies (not shown).

Figure 3b shows the sum of all the spectra acquired during the time course. In this spectrum, the H1 resonances for both α-glucose and β-glucose were observed, since the *J*-coupled partners that are the source of polarization transfer for both anomers were within the bandwidth of the selective gaussian. The ratio of the H1 peak areas for β-glucose and α-glucose is not 3 to 2 as expected from the anomeric equilibrium ratio. This result is expected with the 60-ms mixing time used to obtain this edited spectrum, which was optimized for β-glucose detection. When the mixing time optimized for α-glucose detection (120 ms) was used, its signal was observed more clearly (not shown). The inset shows data obtained from the D-glucose and lactate aqueous solution using a 60-ms mixing time. The spectral appearance as well as the ratios of α-glucose to β-glucose signals observed in the phantom and in vivo are excellent agreement. The H1 resonances of β-glucose and α-glucose were observed consistently in all animals.

Figure 4 shows the ^{1}H LASER spectrum (Fig. 4a) and the 1D-TOCSY-LASER edited spectrum (Fig. 4b) obtained from visual cortex of a single human subject. These data are representative of the four subjects studied. These spectra were obtained during hyperglycemia (blood glucose concentration was 15.3 mM immediately after the NMR data were collected). In Fig. 4a, the H1 α-glucose resonance was observed at 5.23 ppm without any spectral editing. In Fig. 4b, the resonance of the H1 β-glucose at 4.63 ppm and the H1 α-glucose at 5.23 ppm were observed in the 1D-TOCSY-LASER edited spectrum. The observed splitting for the H1 β-glucose was 10 Hz, which was consistent with splitting observed in the phantom when lines were broadened to in vivo linewidths. The recovery of the H1 β-glucose signal is smaller than that observed in animal studies due to the shorter mixing time (20.5 ms). The length of the mixing time was constrained by the specific absorption rate (SAR) limits. The assignment of this signal to glucose was further reinforced by taking the difference of the TOCSY edited spectrum during infusion and that obtained prior to infusion. Comparison of the in vivo difference spectrum with the phantom spectrum indicated similar chemical shifts, amplitudes, and splitting (not shown). The recovery of the H1 α-glucose was smaller than the recovery of the H1 β-glucose, resulting in a different relative intensity due to the considerably shortened mixing time used compared to the optimal mixing time for the H1 α-glucose signal. The transfer to the H1 β-glucose is more efficient due to the higher value of the respective *J*-coupling.

The ability of the proposed novel editing method to elicit signal from other compounds was evaluated for lactate in rat brain. The localization was intentionally set so that ~40% of the localized voxel volume was outside the brain. Consequently, the resulting spectrum contained a

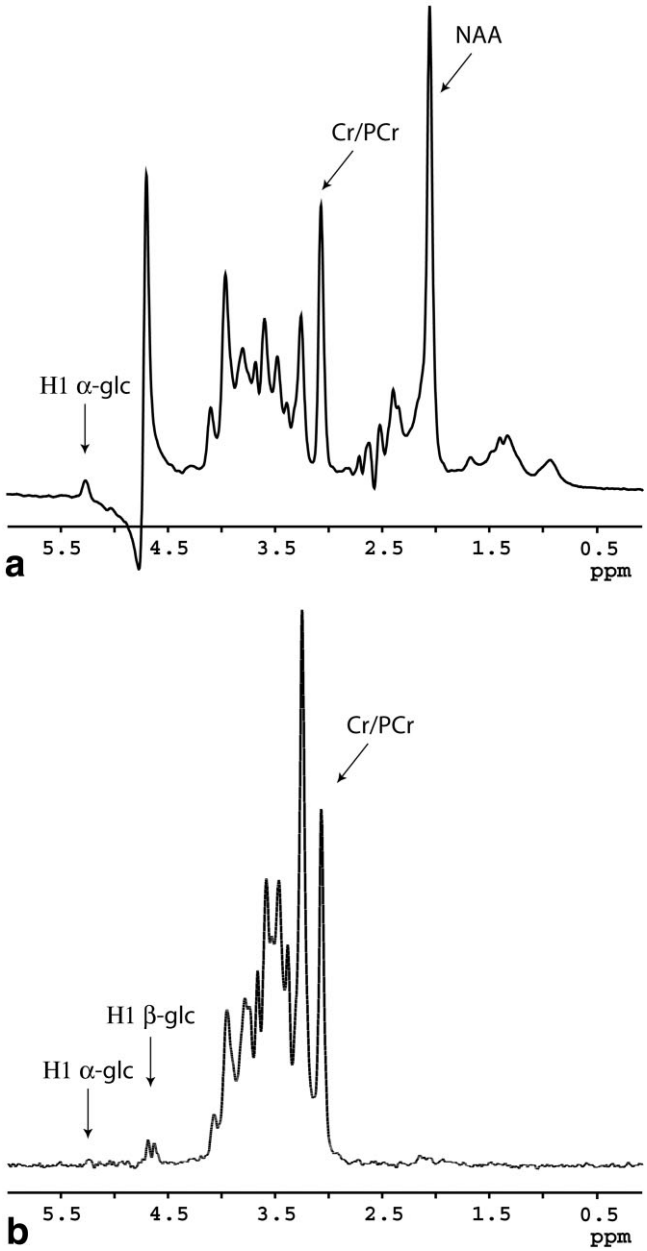

FIG. 4. (**a**) In vivo ^{1}H LASER spectrum obtained at 4 T from a 20-mL voxel in human visual cortex of a single normal control subject during glucose infusion (blood glucose concentration was 15.3 mM). TR = 4 s, N_{EX} = 128, 2-Hz line-broadening. (**b**) In vivo ^{1}H 1D-TOCSY-LASER spectrum obtained at 4 T directly following spectrum (a). TR = 4 s, N_{EX} = 512, mixing time = 20.5 ms, and 2-Hz line-broadening.

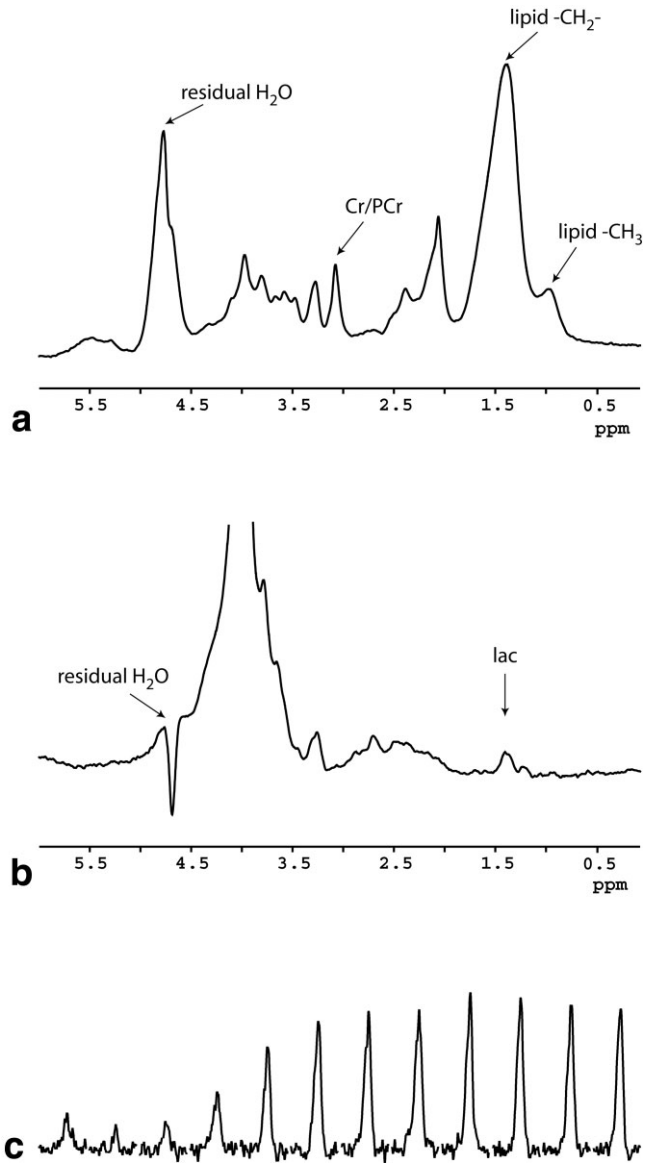

FIG. 5. (**a**) In vivo ^{1}H LASER spectrum obtained at 9.4 T on normal rat brain. The spectrum was obtained from a 250-μL voxel placed in such a way that 154 μL consisted of brain tissue and the rest of s.c. fat. TR = 3 s, N_{EX} = 4, and 10-Hz line-broadening. (**b**) In vivo ^{1}H spectrum obtained at 9.4 T from the same voxel as in (a) with editing. TR = 3 s, N_{EX} = 256, mixing time = 26 ms, and 10-Hz line-broadening. (**c**) Post mortem ^{1}H 1D-TOCSY-LASER spectra obtained at 9.4 T from the same voxel and using the same parameters as in (b). For each spectrum N_{EX} = 16, providing ~1 min time resolution. lac, lactic acid.

substantial amount of extraneous lipid signals from subcutaneous (s.c.) fat (Fig. 5a). The ^{1}H 1D-TOCSY-LASER edited spectrum obtained from this voxel exhibited excellent lipid suppression, and the lactate methyl protons were detected unambiguously (Fig. 5b). Assignment of the resonance at 1.32 ppm was confirmed by the growth of the resonance in post mortem study (Fig. 5c). The small amount of water contamination reflects the high spectral selectivity of the gaussian selective pulse.

DISCUSSION

This study showed that the homonuclear Hartmann–Hahn polarization transfer can be successfully combined with spatial localization in vivo to detect otherwise difficult to observe resonances. The favorable properties of the new single-shot technique, dubbed 1D-TOCSY-LASER, are demonstrated by showing the "clean" detection of the H1 β-glucose and the lactate methyl signal.

1D-TOCSY-LASER relies on the use of *J*-coupling for the editing and combines advantages of difference editing and multiple-quantum coherence filtering. All the information in this technique is obtained in single shot similar to multiple-quantum coherence filtering. Additionally, in the same way as *J*-difference spectroscopy, 1D-TOCSY-LASER offers the advantage of unambiguous determination of the frequency and phase in edited spectra from the simultaneously detected singlet resonances within the bandwidth of the selective gaussian pulse, such as creatine and phosphocreatine. The spectral quality is improved when the singlet resonances are exploited for frequency and phase correction of each acquisition. This is especially important in human studies when field and phase shifts due to patient motion can occur.

The signal of the H1 β-glucose that overlaps with that of water was detected in human and rat brain. The unequivocal detection of the H1 β-glucose signal was aided by excellent water suppression accomplished by a combination of VAPOR water suppression, a narrowband frequency-selective gaussian pulse, and coherence selective gradients.

The methyl resonance of lactate was observed in the rat brain under the mobile lipids resonances arising from s.c. fat. Lipids were intentionally introduced into the volume of interest to demonstrate the effectiveness of 1D-TOCSY-LASER in eliminating these intense overlapping resonances. The suppression of the lipids resonances was accomplished with the narrowband frequency-selective gaussian pulse and coherence selective gradients. The same excellent suppression of lipids should be possible in studies of fatty tissues and lipid-containing tumors. For the detection of the lactate methyl protons, the signal recovery at 9.4 T was similar to that previously obtained with multiple-quantum methods.

When high fields (>4 T) are available and the quality of spatial localization, shimming, and water suppression are excellent, the H1 α-glucose resonance can be detected without spectral editing. When these requirements are not fulfilled, however, the H1 β-glucose resonance can be observed using the single shot 1D-TOCSY-LASER technique. With 73% recovery, the H1 β-glucose signal at 9.4 T is as visible as the directly detected H1 α-glucose signal due to its higher concentration. The efficiency of the recovery of the signal of H1 β-glucose in human brain at 4 T decreases due to the shorter mixing time that had to be used because of the SAR limitations. The resulting nonoptimal efficiency (~40%) still compared well with multiple-quantum methods. The mixing time of 20.5 ms gave a SAR of 2.97 W/kg, conservatively estimated based on the type and length of RF pulses and the sensitive volume of the RF coil. This was the longest mixing time possible within the SAR limit of 3.2 W/kg in the brain. For the optimal mixing times for detection of β-glucose

(60 ms) and of α-glucose (120 ms), the SAR went up to 4.4 and 6.5 W/kg, respectively. At lower field strengths such as 1.5 or 3 T, this SAR limitation would be alleviated and optimal mixing times can be employed. At these lower field strengths, the 1D-TOCSY-LASER technique would in fact be of significant benefit since the α-glucose peak is not sufficiently resolved from water to be easily detectable in a nonedited spectrum. Instead, previous studies (e.g., (26,27)) conducted at such lower field strength have attempted to utilize the 3.4-ppm glucose resonance to monitor cerebral glucose content; however, this resonance appears in a very crowded region of the spectrum, and peaks observed in this region cannot be unequivocally ascribed to glucose.

CONCLUSIONS

In conclusion, using homonuclear Hartmann–Hahn (TOCSY) it is possible to perform localized single-shot editing of resonances that have been suppressed in the preparation phase of the sequence. This opens the perspective for a new class of editing methods that are fundamentally different from existing difference editing or multiple-quantum filtered methods.

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