Journal of Magnetic Resonance **143,** 95–100 (2000)
doi:10.1006/jmre.1999.1958, available online at http://www.idealibrary.com on IDEAL®

Simultaneous Spectral Editing for γ-Aminobutyric Acid and Taurine Using Double Quantum Coherence Transfer

Hao Lei* and James Peeling*,†

*Department of Chemistry and †Department of Radiology, University of Manitoba, Winnipeg, Manitoba, Canada R3E 0W3

Received July 2, 1999; revised September 21, 1999

Conventional double quantum (DQ) editing techniques recover resonances of one metabolite at a time and are thus inefficient for monitoring metabolic changes involving several metabolites. A DQ coherence transfer double editing sequence using a dual-band DQ coherence read pulse is described here. The sequence permits simultaneous spectral editing for two metabolites with similar *J* coupling constants in a single scan. Simultaneous editing for taurine and γ-aminobutyric acid (GABA) is demonstrated using solution phantoms and rat brain tissue. Selectivity of the double editing sequence for the target metabolites is as good as that achieved using conventional DQ editing which selects each metabolite individually. With experimental parameters of the double editing sequence chosen to optimize GABA editing, the sensitivity for GABA detection is the same as that with GABA editing only, while the sensitivity for taurine detection is decreased slightly compared to that with taurine editing only.

Key Words: **double quantum filter; spectral editing; taurine; GABA; magnetic resonance spectroscopy.**

INTRODUCTION

Intense water and fat resonances and broad spectral lines due to tissue heterogeneity often complicate the observation of resonances of specific metabolites of interest in *in vivo* ^{1}H magnetic resonance (MR) spectroscopy. Spectral editing can be used to selectively observe resonances of a target metabolite (*1*). Such editing techniques generally allow the observation of only a single metabolite and are thus inefficient in situations where a number of metabolites are of interest.

Gradient selected double quantum (DQ) filtering techniques acquire edited spectra in a single shot and are thus less susceptible to motion artifacts and more suitable for *in vivo* applications than editing techniques requiring subtraction of sequentially obtained spectra (*2–4*). Acquisition of the DQ coherence transfer echo of lactate together with a spin echo (*5, 6*) or stimulated echo (*7*) of resonances of other metabolites has been described. An alternate approach to improved efficiency in data acquisition is to develop DQ filtering sequences that edit the resonances of a number of metabolites simultaneously. In this paper, a DQ filtering sequence for simultaneous editing for γ-aminobutyric acid (GABA) and taurine is described and its performance is demonstrated in phantoms and in rat brain tissue *in vitro.*

THEORY

A metabolite-editing DQ coherence transfer sequence is shown in Fig. 1 (*3*). To edit a particular metabolite, the frequency selectivity and the flip angle (θ) of the DQ read pulse as well as the duration of the DQ coherence creation period (2τ) are adjusted to optimize the sensitivity of detection of the target metabolite while eliminating spectral overlap (*8*). Usually t_1 is kept as short as possible to minimize signal loss through *J*-modulation (*3*), and τ_1 and τ_2 are usually set to $\tau - t_1$ and $\tau + t_1$, respectively, in order to refocus simultaneously the coherence transfer echo and B_0 inhomogeneity experienced by the DQ coherence during the t_1 period (*3*).

For *in vivo* DQ GABA editing, the γ-GABA resonance at 3.01 ppm is usually the target resonance (*4, 9–11*). The γ protons are weakly coupled to the β protons at 1.91 ppm by 7.3 Hz (*12*). Using a product operator formalism, an optimized DQ filtering sequence for *in vivo* GABA editing has been designed (*11*), with $2\tau = 1/4J = 34$ ms and a 90° frequency selective pulse which excites only the β-GABA resonance for the DQ coherence read pulse.

Taurine is a strongly coupled A_2B_2 spin system with chemical shifts 3.27 (N-CH_2) ppm and 3.43 ppm (S-CH_2) and J = 6.7 Hz (*12*). The signal intensity passing through a DQ filter for taurine is maximum at $2\tau = 37.5$ ms at 7 T (*13*), similar to the optimum value for GABA editing. As the two taurine methylene groups have similar chemical shift, in practice it is difficult to use a frequency-selective DQ read pulse to excite only one methylene group. A read pulse that converts the DQ coherence originating from both methylene groups into single quantum coherence can therefore be considered to be a "non-frequency-selective" read pulse. Then for taurine, the maximum edited signal intensity passing through the DQ filter occurs when $\theta = 60°$ when a DQ coherence selection gradient pair of the same polarity is used (*13*).

Since the optimum values of 2τ are similar for GABA and taurine, a dual-band DQ read pulse can be used to convert the

1090-7807/00 $35.00

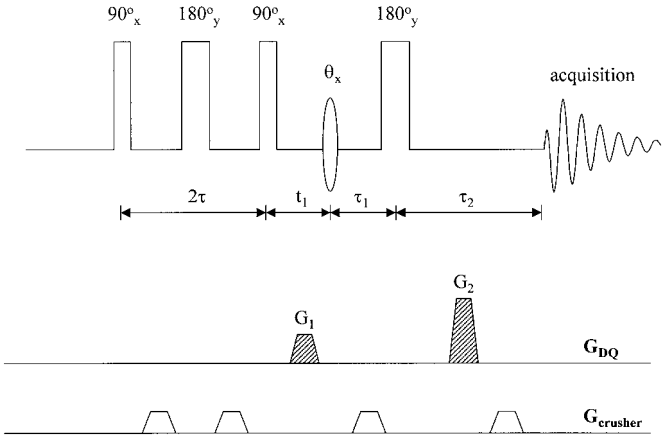

FIG. 1. A double quantum coherence transfer pulse sequence for spectral editing. G_1 and G_2 are 1-ms gradient pulses for selection of double coherence transfer pathways (G_{DQ}), with $G_2 = 2G_1 = 64$ mT/m; $\tau_1 = \tau - t_1$, and $\tau_2 = \tau + t_1$.

DQ coherence from both GABA and taurine into single quantum coherence. One wave form for such a dual-band pulse is

$$\mathrm{RF}(t) = A(t) \times \{W_{\mathrm{GABA}}[\exp[-i(\omega_{\mathrm{GABA}}t)] + W_{\mathrm{tau}}\exp[-i(\omega_{\mathrm{tau}}t + \Delta\phi)]\},$$

where $A(t)$ is the amplitude envelop function, W_{GABA} and W_{tau} are the amplitude weighting coefficients for GABA and taurine excitation bands, ω_{GABA} and ω_{tau} are the frequency offsets of the β-GABA and taurine resonances relative to the carrier frequency, and $\Delta\phi$ is the relative phase between the GABA and taurine excitation bands. For the 12-ms DQ read pulse used in this study, $A(t)$ is a single-lobe sinc function; $W_{\mathrm{GABA}} = 1.0$ and $W_{\mathrm{tau}} = 0.667$ so that the flip angle of the taurine excitation band is 60° when that of the GABA excitation band is 90°; the carrier frequency is on resonance for the γ protons of GABA, so that $\omega_{\mathrm{GABA}} = -332$ Hz and $\omega_{\mathrm{tau}} = 75$ Hz at 7 T; and $\Delta\phi$ is determined experimentally to give in-phase GABA and taurine signals. The real and imaginary wave forms of this pulse are shown in Fig. 2.

EXPERIMENTAL

All experiments were carried out on a Bruker Biospec/3 7 T/21 cm spectrometer equipped with actively shielded gradients. A homebuilt 3-cm-diameter saddle coil was used for both transmission and reception. The flip angles of all pulses were carefully calibrated (*14*), and all crusher gradients and coherence transfer pathway selection gradients were adjusted experimentally to a near magic-angle setting to maximize the efficiency of water suppression (*15*).

Experiments were performed using a 2.5-cm-diameter cylindrical phantom containing 15 mM creatine and 20 mM each of choline, GABA, and taurine in saline solution; a 1.2-cm-diameter vial containing homogenized rat brain tissue; and a 1.5-cm-diameter cylindrical phantom containing 20 mM each of GABA and taurine in deuterated water. Using the first two samples, spectra were acquired without editing and with editing for GABA, for taurine, and for GABA and taurine simultaneously. Nonedited spectra were acquired using a STEAM sequence (*16*), with a spectral bandwidth of 2500 Hz, 2k data points, 16 averages, TR = 2.0 s, TE = 20 ms, and TM = 30 ms. Edited spectra were acquired with the DQ filtering sequence shown in Fig. 1, with TR = 2.0 s, $t_1 = 7.5$ ms, a spectral bandwidth of 4000 Hz and 1k data points. For GABA editing, $2\tau = 34$ ms and the read pulse was a 12-ms single-lobe sinc pulse with the frequency on the β-GABA resonance and a 90° flip angle. For taurine editing, $2\tau = 37.5$ ms and the read pulse was a 12-ms single-lobe sinc pulse with the frequency on the taurine resonance at 3.27 ppm and a 60° flip angle. For simultaneous GABA and taurine editing, $2\tau = 34$ ms and the read pulse was a dual-band pulse with one frequency on the β-GABA resonance giving a flip angle of 90° (GABA band) and the other frequency on the taurine resonances at 3.27 ppm giving a flip angle of 60° (taurine band). Edited spectra were acquired using 16 and 256 averages for the phantom and rat brain tissue, respectively. Postacquisition spectral processing included zero-filling free induction decays (FIDs) to 4k data points and applying a 5-Hz exponential line-broadening prior to Fourier transformation.

Using the 1.5-cm-diameter phantom, the detection sensitivity of the double editing sequence was determined by comparing the peak areas of taurine and GABA signals recovered in

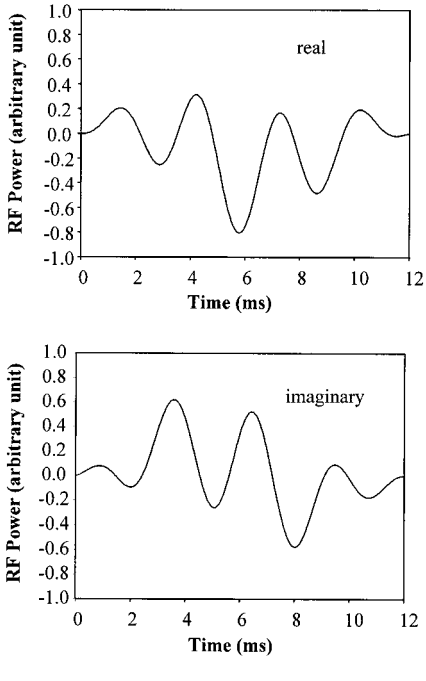

FIG. 2. Real and imaginary waveforms of the dual-band double quantum coherence read pulse for simultaneous GABA and taurine editing.

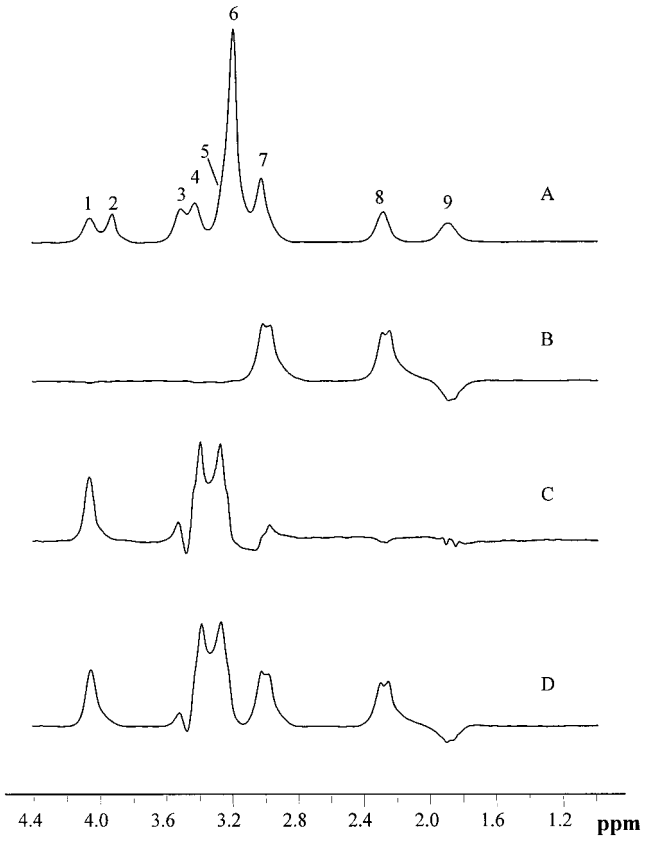

FIG. 3. Spectra acquired from the solution phantom without spectral editing (A) and with editing for GABA (B), taurine (C), or GABA and taurine together (D). The scaling factors for B, C, and D are twice that for A. Peak assignments: (1) choline (β-CH_2); (2) creatine, (CH_2); (3) choline, (α-CH_2); (4) taurine (S-CH_2); (5) taurine (N-CH_2); (6) choline (CH_3); (7) creatine (CH_3) + GABA (γ-CH_2); (8) GABA (α-CH_2); and (9) GABA (β-CH_2).

the simultaneous editing experiment to those recovered in a simple one-pulse experiment and to those recovered in single editing experiments. These experiment were done with TR = 12 s, a spectral bandwidth of 2500 Hz, 8k data points, and eight averages. The parameters for spectral editing in these experiments were as described above. The FIDs were zero-filled to 16k before Fourier transformation, but no line broadening was applied.

RESULTS

Figure 3 shows nonedited (A), GABA-edited (B), taurine-edited (C), and GABA- plus taurine-edited spectra (D) acquired from the solution phantom containing choline and creatine as well as GABA and taurine. In the nonedited spectrum (A), the γ-GABA resonance at 3.01 ppm is hidden beneath the creatine methyl singlet, the taurine resonance at 3.27 ppm is hidden beneath the choline methyl singlet, and the taurine resonance at 3.43 ppm overlaps that of the choline α-methylene protons. With GABA editing (B), the γ-GABA resonance is observed, along with the α- and distorted β-GABA resonances. The signals from creatine, choline, and taurine are suppressed completely. With taurine editing (C), the creatine and choline singlets are suppressed completely, and the γ-GABA resonance and the choline α-methylene resonance at 3.54 ppm are attenuated significantly, both with distorted phase. The choline β-methylene resonance at 4.06 ppm passes through the filter. With simultaneous GABA and taurine editing (D), both the γ-GABA resonances and the taurine resonances are recovered, with signal intensities indistinguishable from those in Figs. 3B and 3C. Using the phantom containing taurine and GABA solution only, editing for taurine or GABA individually gave peak areas 34.0 and 26.2%, respectively, of those obtained in the one-pulse experiment, while for simultaneous editing the corresponding peak areas were 26.8 and 26.4% of those obtained in the one-pulse experiment.

Figure 4 shows the nonedited (A), GABA-edited (B), taurine-edited (C), and GABA- plus taurine-edited spectra (D) acquired from rat brain tissue. Without spectral editing (A), the γ-GABA resonance and the taurine resonances are not resolved from the creatine and choline resonances. With spectral editing, the interfering creatine and choline resonances are suppressed along with the resonances of other metabolites, and the

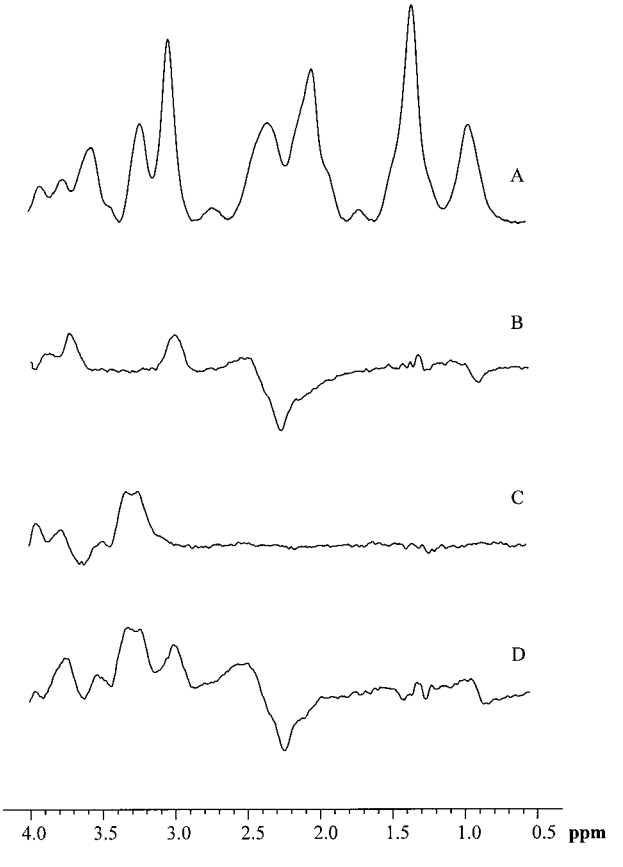

FIG. 4. Spectra acquired from rat brain tissue *in vitro* without spectral editing (A) and with editing for GABA (B), taurine (C), or GABA and taurine simultaneously (D). The scaling factor for A is twice that for B, C, and D.

γ-GABA resonances (B) and the taurine resonances (C) are observed unequivocally. With simultaneous GABA and taurine editing (D), both the γ-GABA resonances and the taurine resonances are recovered, with signal intensities indistinguishable from those in Figs. 4B and 4C. Distorted signals at about 2.3 ppm in Figs. 4B and 4D are probably GABA, *N*-acetyl aspartate, and glutamate signals that pass through the DQ filter (*9*). Signals with distorted phase between 3.5 and 4.0 ppm in Figs. 4C and 4D are residual signals from *myo*-inositol, creatine, and glucose that pass through the DQ filter (*13*).

DISCUSSION

The ability to obtain edited spectra from more than one metabolite in an *in vivo* ^{1}H NMR experiment may be useful in many situations, for example, when metabolically coupled compounds are of interest or when changes in more than a single observable metabolite are potential markers for disease staging or diagnosis. In addition, it is often convenient to obtain information about a metabolite whose concentration is unchanged and so can serve as an internal reference compound. In the present study the possibility of simultaneous DQ editing for more than one metabolite is demonstrated, using a DQ filtering sequence with a composite dual-band DQ coherence read pulse to edit for GABA and taurine together. GABA is an important inhibitory neurotransmitter in brain, and dysregulation of GABA metabolism has been implicated in the pathophysiology of disorders such as stroke, epilepsy, and schizophrenia (*17–23*). Taurine is a metabolic product of sulfur amino acid catabolism, whose role may include neurotransmission (*24*), osmoregulation (*25*), buffering of acidosis (*26, 27*), and neuroprotection during cerebral ischemia (*28*). *In vivo* observation of both GABA and taurine by conventional ^{1}H MR spectroscopy is hindered by severe spectral overlap of their resonances with those of a number of other metabolites such as creatine, choline, *myo*-inositol, and glucose (*12*). The sequence described here permits observation of GABA and taurine in a single experiment without interference from the resonances of these other metabolites.

When a DQ filtering sequence is used to observe a single metabolite, all experimental parameters can be adjusted to optimize the detection sensitivity and editing efficiency for that particular metabolite. However, compromise is necessary when two metabolites are edited simultaneously so that, theoretically, the detection sensitivity for both metabolites may be lower than when they are edited individually. In the present study, the detection sensitivity for GABA might be expected to be reduced due to the use of the dual-band DQ read pulse required for the double editing. Leakage of the taurine excitation band of the dual-band DQ read pulse into the γ-GABA resonance could decrease the detection sensitivity for GABA since the maximum detection sensitivity is obtained when the DQ read pulse excites only the β-GABA resonance (*11*). Some residual γ-GABA signal is observed in the taurine-edited spectrum (Fig. 3C), confirming the presence of such leakage. However, in this particular experiment, the effect of the leakage on the detection sensitivity for GABA is small, since the same GABA signal intensities were recovered in the single editing and double editing experiments. At lower field strength, when the frequency difference between the GABA γ-proton resonances and the taurine resonances becomes smaller, the decreases in detection sensitivity due to such leakage may become important. A possible solution for this would be to increase the length of the DQ read pulse to improve the frequency selectivity. However, using longer DQ read pulses could also decrease the detection sensitivity (*8*). Indeed, this may be the reason for the somewhat lower detection sensitivity for GABA determined in this study, compared to the theoretical value of 39.5% and the experimental value of 36% reported by Wilman and Allen (*11*).

Resonances from macromolecules (*29*) and glutathione (*30*) at about 3.0 ppm could potentially survive a DQ filter and contaminate the edited GABA signals observed in the rat brain sample in this study. However, such contamination is expected to be small. The macromolecule resonance should be suppressed by transverse relaxation during the relatively long echo time (68 ms) used in the present study. The β_a- and β_b-cysteinyl protons (2.9 ppm) in glutathione are coupled to each other and also to the α-cysteinyl proton (4.56 ppm) (*30*). Edited signals from the β-protons could be produced in this study only when the taurine band of the DQ read pulse extends into the neighborhood of 2.9 ppm. Any such leakage appears to be small in this study, as no signal was observed at 2.9 ppm.

In this study, the detection sensitivity for DQ taurine editing was 34%, agreeing well with an experimental value of 35% reported previously (*31*). In simultaneous editing for GABA and taurine, the experimental settings were adjusted to optimize the sensitivity for GABA detection, at the cost of reducing the detection sensitivity for taurine to about 27%. This loss in detection sensitivity for taurine can be attributed to two factors. First, since the carrier frequency in the simultaneous editing experiment was set on the γ-GABA resonance, off-resonance excitation and refocusing of the taurine resonances could compromise the efficiency of the coherence transfer, and thus the detection sensitivity for taurine (*3*). Because the frequency difference between the γ-GABA resonance and the taurine resonance is small (about 75 Hz) at the field strength (7 T) used in the present study, this effect should be small. However, caution must be exercised when two metabolites with a larger chemical shift difference are edited simultaneously. Second, the taurine detection sensitivity may be reduced by the use of $2\tau = 34$ ms, which is optimized for GABA editing (*11*), rather than 37.5 ms, which is optimum for taurine editing (*13*). Signals from *myo*-inositol and glucose could survive the DQ filter and potentially contaminate the edited taurine resonance observed in this study. However, it has been shown that contributions of *myo*-inositol and glucose to the edited taurine resonance are generally not significant (*13*).

The DQ coherences of taurine and GABA precess with different DQ frequencies during the evolution period (t_1). As a result, a phase difference between the taurine and GABA signals is introduced, which could affect the detection of both metabolites. To account for this, the relative phase between the GABA and the taurine excitation bands of the dual-band DQ read pulse can be adjusted experimentally until the final spectrum gives in-phase signals for both GABA and taurine.

The sequence described here can in principle be used to edit for any two metabolites for which the optimum values of 2τ are similar. The optimum 2τ value for a coupled spin system is determined mainly by the *J*-coupling constant(s) and the transverse relaxation time, and also on the chemical shift difference(s) and the field strength in the case of strong coupling. For many metabolites of common interest in ^{1}H MR spectroscopy, *J* is about 7 Hz (*12*) and the optimum 2τ values that have been reported lie around 40 ms. For example, the optimum 2τ values are 34–44 ms for lactate and alanine (*32–34*), 34 ms for GABA (*11*), 36 ms for glutamate at 3 T (*8*), 34 ms for glucose at 4.7 T (*35*), and 37.5 ms for taurine at 7.1 T (*13*). One problem that might prevent the generalization of this sequence for editing for any pair of metabolites is the off-resonance effects discussed above, and these effects must be considered in designing and optimizing a DQ filtering sequence for more than a single metabolite. Technically, the off-resonance effects can potentially be circumvented by using selective on-resonance double pulses (*36*) or resonance-offset-compensated adiabatic pulses (*37*) as the excitation/refocusing pulses. However, to fully understand how the off-resonance excitation/refocusing affects the outcome of a DQ editing experiment requires a rigorous theoretical treatment which has yet to be developed.

Since the proposed double editing sequence differs from conventional DQ sequences only in the DQ read pulse, it can be combined with spatial localization strategies previously developed for conventional DQ filtering, including PRESS (*8, 9, 38*), ISIS (*39*), and conventional or Hadamard encoded chemical shift imaging (*2, 4, 5, 33, 40*). However, when used with PRESS, caution must be exercised in setting the phase of the DQ read pulse relative to other pulses as well as the relative phase between the two excitation bands of the DQ pulse because of the loss of phase coherence through slice-selective excitation/refocusing (*9, 38*).

ACKNOWLEDGMENTS

This work was supported by a grant from the Research Partnership Program of the Natural Sciences and Engineering Research Council, the National Research Council of Canada, and Astra Pharma.

REFERENCES

1. P. S. Allen, R. B. Thompson, and A. H. Wilman, Metabolite-specific NMR spectroscopy *in vivo, NMR Biomed.* **10,** 435 (1997).
2. Q. He, D. C. Shungu, P. C. van Zijl, Z. M. Bhujwalla, and J. D. Glickson, Single-scan *in vivo* lactate editing with complete lipid and water suppression by selective multiple-quantum-coherence transfer (Sel-MQC) with application to tumors, *J. Magn. Reson. B.* **106,** 203 (1995).
3. J. E. van Dijk, A. F. Mehlkopf, and W. M. Bovee, Comparison of double and zero quantum NMR editing techniques for *in vivo* use, *NMR Biomed.* **5,** 75 (1992).
4. J. Shen, D. C. Shungu, and D. L. Rothman, *In vivo* chemical shift imaging of γ-aminobutyric acid in the human brain, *Magn. Reson. Med.* **41,** 35 (1999).
5. Q. He, Z. M. Bhujwalla, and J. D. Glickson, Proton detection of choline and lactate in EMT6 tumors by spin-echo-enhanced selective multiple-quantum-coherence transfer, *J. Magn. Reson. B.* **112,** 18 (1996).
6. A. H. Wilman, M. Astridge, R. E. Snyder, and P. S. Allen, Same-scan acquisition of both edited *J*-coupled multiplets and singlet resonances of uncoupled spins for proton MRS, *J. Magn. Reson. B.* **109,** 202 (1995).
7. H. Lei and J. Peeling, Simultaneous lactate editing and observation of other metabolites using a stimulated-echo enhanced double quantum filter, *J. Magn. Reson.* **137,** 215 (1999).
8. R. B. Thompson and P. S. Allen, A new multiple quantum filter design procedure for use on strongly coupled spin systems found in vivo: its application to glutamate, *Magn. Reson. Med.* **39,** 762 (1998).
9. J. R. Keltner, L. L. Wald, B. D. Frederick, and P. F. Renshaw, *In vivo* detection of GABA in human brain using a localized double-quantum filter technique, *Magn. Reson. Med.* **37,** 366 (1997).
10. A. H. Wilman and P. S. Allen, *In vivo* NMR detection strategies for gamma-aminobutyric acid, utilizing proton spectroscopy and coherence-pathway filtering with gradients, *J. Magn. Reson. B.* **101,** 165 (1993).
11. A. H. Wilman and P. S. Allen, Yield enhancement of a double-quantum filter sequence designed for the edited detection of GABA, *J. Magn. Reson. B.* **109,** 169 (1995).
12. K. L. Behar and T. Ogino, Assignment of resonance in the ^{1}H spectrum of rat brain by two-dimensional shift correlated and J-resolved NMR spectroscopy, *Magn. Reson. Med.* **17,** 285 (1991).
13. H. Lei and J. Peeling, A localized double quantum filter for *in vivo* detection of taurine, *Magn. Reson. Med.* **42,** 454 (1999).
14. W. H. Perman, M. A. Bernstein, and J. C. Sandstrom, A method for correctly setting the rf flip angle, *Magn. Reson. Med.* **9,** 16 (1989).
15. P. C. van Zijl, M. O. Johnson, S. Mori, and R. E. Hurd, Magic-angle-gradient double-quantum-filtered COSY, *J. Magn. Reson. A.* **113,** 265 (1995).
16. J. Frahm, K. D. Merboldt, and W. Hanicke, Localized proton spectroscopy using stimulated echoes, *J. Magn. Reson.* **72,** 502 (1987).
17. K. Gale, GABA and epilepsy: Basic concepts from preclinical research, *Epilepsia* **33**(S5), S3 (1992).
18. W. D. Lust, H. M. Assaf, A. J. Ricci, R. A. Ratcheson, and L. L. Sternau, A role for gamma-aminobutyric acid (GABA) in the evolution of delayed neuronal death following ischemia, *Metab. Brain Dis.* **3,** 287 (1988).
19. P. D. Lyden, GABA and neuroprotection, *Int. Rev. Neurobiol.* **40,** 233 (1997).
20. D. A. McCormick, GABA as an inhibitory neurotransmitter in human cerebral cortex, *J. Neurophysiol.* **62,** 1018 (1989).
21. F. M. Sherif and S. S. Ahmed, Basic aspects of GABA-transaminase in neuropsychiatric disorders, *Clin. Biochem.* **28,** 145 (1995).
22. D. P. van Kammen, F. Petty, M. E. Kelley, G. L. Kramer, E. J. Barry,

J. K. Yao, J. A. Gurklis, and J. L. Peters, GABA and brain abnormalities in schizophrenia, *Psychiatry Res.* **82,** 25 (1998).

23. H. F. Bradford, Glutamate, GABA and epilepsy, *Prog. Neurobiol.* **47,** 477 (1995).

24. R. J. Huxtable, Taurine in the central nervous system and the mammalian actions of taurine, *Prog. Neurobiol.* **32,** 471 (1989).

25. M. Puka, K. Sundell, J. W. Lazarewicz, and A. Lehmann, Species differences in cerebral taurine concentrations correlate with brain water content, *Brain Res.* **548,** 267 (1991).

26. T. Nakada, K. Hida, and I. L. Kwee, pH–lactate dissociation during anoxic insult: Taurine effect, *Neuroreport* **2,** 325 (1991).

27. T. Nakada, K. Hida, and I. L. Kwee, Brain pH and lactic acidosis: Quantitative analysis of taurine effect, *Neurosci. Res.* **15,** 115 (1992).

28. P. Saransaari and S. S. Oja, Mechanisms of ischemia-induced taurine release in mouse hippocampal slices, *Brain Res.* **807,** 118 (1998).

29. K. L. Behar and T. Ogino, Characterization of macromolecule resonances in the ^{1}H NMR spectrum of rat brain, *Magn. Reson. Med.* **30,** 38 (1993).

30. A. H. Trabesinger, O. M. Weber, C. O. Duc, and P. Boesiger, Detection of glutathione in the human brain in vivo by means of double quantum coherence filtering, *Magn. Reson. Med.* **42,** 283 (1999).

31. D. L. Hardy and T. J. Norwood, Spectral editing technique for the *in vitro* and *in vivo* detection of taurine, *J. Magn. Reson.* **133,** 70 (1998).

32. J. F. Shen and P. S. Allen, Reduced length for double-quantum filtering sequences, *J. Magn. Reson.* **92,** 398 (1991).

33. H. Lei and J. Peeling, Multiple-voxel double-quantum lactate edited spectroscopy using two dimensional longitudinal Hadamard encoding, *Magn. Reson. Med.* **42,** 19 (1999).

34. C. H. Sotak, D. M. Freeman, and R. E. Hurd, The unequivocal determination of *in vivo* lactic acid using two dimensional double-quantum coherence-transfer spectroscopy, *J. Magn. Reson.* **78,** 355 (1988).

35. J. R. Keltner, L. L. Wald, P. J. Ledden, Y. C. Chen, R. T. Matthews, E. H. Kuestermann, J. R. Baker, B. R. Rosen, and B. G. Jenkins, A localized double-quantum filter for the *in vivo* detection of brain glucose, *Magn. Reson. Med.* **39,** 651 (1998).

36. V. Blechta and J. Schraml, Selective on-resonance double pulses applied to an IS spin system, *J. Magn. Reson. A* **112,** 30 (1995).

37. M. Garwood, B. Nease, Y. Ke, R. A. de Graaf, and H. Merkle, Simultaneous compensation for B_1 inhomogeneity and resonance offsets by a multiple-quantum NMR sequence using adiabatic pulses, *J. Magn. Reson. A* **112,** 272 (1995).

38. L. Jouvensal, P. G. Carlier, and G. Bloch, Practical implementation of single-voxel double-quantum editing on a whole-body NMR spectrometer: Localized monitoring of lactate in the human leg during and after exercise, *Magn. Reson. Med.* **36,** 487 (1996).

39. M. A. Thomas, H. P. Hetherington, D. J. Meyerhoff, and D. B. Twieg, Localized double-quantum-filtered ^{1}H NMR spectroscopy, *J. Magn. Reson.* **93,** 485 (1991).

40. R. E. Hurd and D. M. Freeman, Metabolite specific proton magnetic resonance imaging, *Proc. Natl. Acad. Sci. USA* **86,** 4402 (1989).