Quantification of Short-TE Metabolite Signals in Human Brain Using QUEST and a Simulated Basis Set

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Introduction

Recently, the implementation of short-TE spectroscopy at 3T has shown that glutamate (Glu), gamma amino butyric acid (GABA), and glutamine (Gln) in the brain can be reliably measured with standard single-voxel ^{1}H-MRS PRESS, without resorting to editing schemes [1]. However, despite the greatly improved spectral quality due to the reduction of *J*-coupling effects and reduced T_2 decay for the metabolites, short-TE spectra introduce specific problems in quantification due to strongly overlapping metabolite resonances and the presence of macromolecules and lipids. In this study, *in vivo* quantification of short-TE metabolite signals from the basal ganglia (voxel size, 2×3×2 cm^3) at 3T was carried out with the QUEST method [2] using a simulated metabolite basis set. To assess the performance of QUEST, a Monte Carlo study was performed using a simulated ^{1}H-MRS spectrum. The Cramer-Rao lower bounds (CRLB) for metabolite quantification were calculated, which is an estimate of the uncertainty in the peak amplitude determined by QUEST.

Methods

Twelve metabolite signals used in QUEST were quantum-mechanically simulated in NMR-SCOPE [3] (Figure 1A). The spin Hamiltonian parameters (number of spins, chemical shifts, J-couplings) were obtained from Govindaraju *et al.* [4]. Monte Carlo simulation was carried out to test the performance of the spectral quantification method using a simulated ^{1}H-MRS spectrum (Figure 1A, top). The performance of the spectral fitting was evaluated by comparing the means with the true values, as well as the standard deviations (SDs) with the CRLB.

In vivo ^{1}H signals of 10 healthy human subjects (24 - 57 years old) were measured from the left and right basal ganglia at 3T (Siemens Trio TIM System with a 12-channel receive-only array head coil) and quantified with QUEST using a simulated basis set. Single-voxel ^{1}H-MRS was performed using a conventional PRESS sequence with TR/TE= 2500/30 ms and 96 acquisitions for averaging. For absolute quantification, the amplitudes of the metabolites estimated by QUEST were converted to concentrations (mM) using water as an internal standard. The metabolite signals were also corrected for T1 and T2 effects according to the average of values reported in the literature [1]

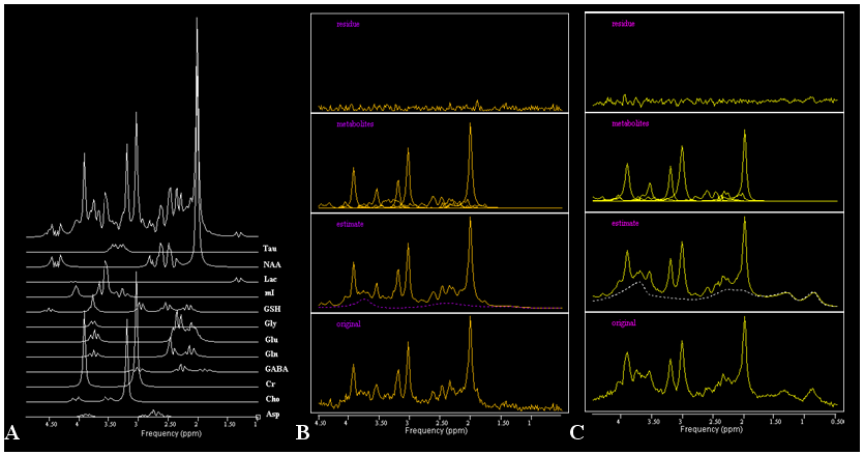

Figure 1. (A) Simulated basis set at 3T in NMR-SCOPE using a PRESS sequence with TE = 30 ms and a simulated MRS spectrum (top), (B) Example of spectral fitting in the Monte Carlo study using the simulated basis set, and (C) Spectral fitting of in vivo short-TE ^{1}H-MRS data measured on the basal ganglia

Results

In the Monte Carlo study, each signal was weighted according to the published *in vivo* concentration values for normal adult brain [4]. The noise level in this study (Figure 1B, bottom) was chosen to yield a SNR of 65:1 for Cr, similar to the SNR measured from *in vivo* basal ganglia (Figure 1C, bottom). The results of the simulation study show that the estimated mean values are very close to the true values and the SDs approximate the CRLBs (Table 1). The CRLBs for QUEST spectral fits were less than 5% for all metabolite signals. *In vivo* results of QUEST quantification using the simulated metabolite basis set are shown in Table 2. An example of spectral fitting is given in Figure 1C. The measured metabolite concentrations gave estimated mean values very close to the reported values for human brain in the literature [4].

Table 1. Results (Mean/SD) of a Monte Carlo study on a simulated MRS spectrum

Metabolites	NAA	Cr	Cho	Ins	Glu	Gln	GABA
True Amp(a.u)	191	128	13.3	26.0	52.4	29.1	8.1
Estimate	191	127	13.2	25.4	55.0	26.8	8.09
SD	2.2	2.6	0.4	1.9	3.8	2.1	0.5
CRLB (Amp)	2.1	1.6	0.49	1.0	3.3	2.2	0.5

Table 2. In vivo metabolite concentrations (Mean/SD) in basal ganglia (n = 10, left and right)

	Concentration (mM, Left)		Concentration (mM, Right)		L-R diff
Metabolite	Mean ± SD	CRLB(%)	Mean ± SD	CRLB(%)	P value
NAA	8.1 ± 0.6	2.6 (1.6 - 4.4)	7.4 ± 0.7	3.0 (1.5 - 4.9)	0.029
Cr	11.9 ± 2.1	2.3 (1.7 – 3.2)	11.7 ± 1.9	2.1 (1.4 - 2.9)	0.719
Cho	2.2 ± 0.5	5.3 (2.8 – 9.0)	2.3 ± 0.4	5.5 (2.3 – 10)	0.785
Ins	4.3 ± 3.2	15 (4.8 - 29)	3.4 ± 2.2	16 (6.2 - 27)	0.494
Glu	11.4 ± 1.8	10.6 (8.1 – 14.9)	10.9 ± 2.5	11.3 (5.9 – 23)	0.605
Gln	2.1 ± 0.9	58 (34 – 84)	2.2 ± 1.6	65 (32 – 100)	0.899
GABA	1.3 ± 0.3	33 (26 – 46)	1.0 ± 0.4	36 (22 – 63)	0.133
Glx	13.8 ± 2.8	16 (10 – 22)	12.5 ± 2.2	14 (6 – 32)	0.309

Discussion

Due to strong signal overlap, quantification of metabolites from *in vivo* short-TE ^{1}H-MRS spectra requires *a priori* knowledge based on metabolite basis sets. Recently, Cudalbu *et al.* [5] and Tkac *et al.* [6] reported that a simulated basis set can be used in place of a measured basis set. They also showed that the *in vivo* concentration estimates obtained with the two basis sets were similar. In the present study, simulations of the basis sets were used for QUEST quantification. Our results suggested that six metabolites (i.e., NAA, Ins, Cr, Cho, Glu, and Glx) can be reliably quantified in human basal ganglia (voxel size, 2×3×2 cm^3) at short TE using 3T. However, it was not possible to quantify other metabolites such as GABA (CRLB = 33%) and Gln (CRLB = 58%).

References [1]. Mullins *et al.*, MRM 60: 964-969 (2008). [2]. Ratiney *et al.*, NMR Biomed 18: 1-13 (2005). [3]. Graveron-Demilly *et al.* JMR 101:233-239 (1993). [4]. Govindaraju *et al.*, NMR Biomed 13:129-153 (2000). [5]. Cudalbu *et al.*, NMR Biomed 21: 627-636 (2008). [6]. Tkac *et al.*, ISMRM 16 (2008).

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