A Post-processing Method to Accurately Quantify N-acetylaspartate in Short Echo Time *In Vivo* ^{1}H Spectra

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A method, which has been shown to minimize the complexity in the quantification of *in vivo* cerebral metabolites in short echo time (TE) ^{1}H spectra, is to incorporate a priori knowledge in the fitting (e.g., the LCModel). The purpose of this study is to introduce a post-processing method, which does not require *a priori* knowledge, to quantify the singlets in short TE *in vivo* ^{1}H spectra. Using this time-domain fitting method results in lower N-acetylaspartate (NAA) and higher glycerolphosphocholine plus phosphorylcholine (GPC+PC) levels and an overall reduction in the coefficient of variations, compared to the LCModel.

Introduction:

Independent of field strength, reliable and accurate quantification of *in vivo* cerebral metabolites in short echo time (TE) ^{1}H spectra, including the N-acetylaspartate (NAA), phosphocreatine plus creatine (PCr+Cr) and glycerolphosphocholine plus phosphorylcholine (GPC+PC) singlets, is complicated by complex overlapping multiplets (e.g., from glutamate, glutamine and γ-aminobutyric acid) and by overlapping peaks from macromolecules. An approach to alleviate the complexity is to incorporate *a priori* knowledge of multiplet structures, which dramatically improves the precision and accuracy of the quantification (1,2,3). The purpose of this study is to introduce a post-processing method, which does not require *a priori* knowledge, to quantify the singlets in short TE *in vivo* ^{1}H spectra and to compare results to that of using the LCModel (2).

Subjects and Method:

The proposed method is based on quantifying the three dominate singlets, NAA, PCr+Cr and GPC+PC, in the time domain where the appropriate number of data points at the beginning of the free induction decay (FID) are omitted in order to minimize the contribution of the lesser amplitudes of multiplets and of macromolecules.

In vivo short TE ^{1}H spectroscopy data was collected on 19 healthy, normal control subjects (8 males and 11 females, mean age 25±4 years). A quadrature volume head coil was used to acquire single voxel ^{1}H spectroscopy data on a GE LX 1.5 T whole body MR imager. Based on sagittal and coronal scout images, a $2x2x2cm^3$ voxel was localized in the left dorsolateral prefronatl cortex using the STEAM sequence. The experimental parameters include: TR=6sec, TE=20ms, TM=13.7ms, 2,048 data points, 2.0KHz spectral bandwidth, 96 water suppressed averages and 4 water unsuppressed averages.

The post-processing and quantification steps were 100% automated. The unsuppressed water spectra was used to correct for any Eddy current effects. No apodization was applied and any residual water signal was removed by using the operator independent SVD-based method. Five Gaussian damped sinusoids (NAA at 2.01ppm, PCr+Cr at 3.02, 3.93ppm, GPC+PC at 3.21ppm and myo-inositol at 3.54ppm) were used to model the *in vivo* data in the time domain using the Marquardt algorithm. Each FID was modeled multiple times by omitting 8 to 96 data points (in steps of 4) at the beginning of the FID [i.e., having the results of using 23 different delay times (DT's) ranging from 3.5 up to 47ms]. The resulting metabolite levels were compared to quantifying the pre-processed data using the LCModel (2), which incorperated the *a priori* knowledge of 15 metabolites plus a macromolecule/lipid lineshape. The fitting window ranged from 4.2ppm to 1.0ppm. The unsuppressed water signal along with the appropriate correction factors (3) were applied to both set of results in order to have comparable absolute quantification values.

Results and Discussion:

The mean NAA level and FWHM (±SD) are plotted as function of DT in Figure 1. As one would expect, by increasing the number of omitted data points the influence of signal arising from the multiplets/macromolecules diminishes (i.e., the NAA peak is quantifying NAA plus the overlapping signals). This initial NAA overestimation in level and FWHM diminishes as the DT increases and reaches a plateau as the contribution of the overlapping signals of lesser amplitudes becomes negligible (approximately between DT=29ms and 37ms). In theory, if a resonance is composed of a single damped sinusoid, the amplitude and FWHM results should be the same for all DT's (i.e., independent of what DT is used). Therefore, reaching this plateau infers the influence of the overlapping resonances is negligible and the resulting amplitude arises from a single specie. A similar behavior of initial overestimation followed by a plateau is observed with PCr+Cr and GPC+PC.

By choosing the DT=37ms (Figure 1), which lies within the plateau region for all three metabolites, the quantified NAA, PCr+Cr and GPC+PC levels are 8.2±0.6, 5.8±0.4 and 1.1±0.2 mmol/kg wet weight. The LCModel results of these three metabolites are 9.6±1.4 (Figure 1), 6.3±1.1 and 0.7±0.3 mmol/kg wet weight, respectively. Assuming the proposed method provides results of amplitudes of single species and using a paired t-test, the LCMdel significantly overestimated NAA by 18% ($p<0.0001$) and significantly underestimated GPC+PC by 34% ($p=0.0001$). The coefficient of variations were also were at least half of that using the LCModel for NAA and PCr+Cr.

Conclusion:

A method is introduced to accurately and reliably quantify the singlets in short TE *in vivo* ^{1}H spectra without the use of a priori knowledge. The key is to omit sufficient number of data point at the beginning of the FID until the contribution of the overlapping signals is negligible.

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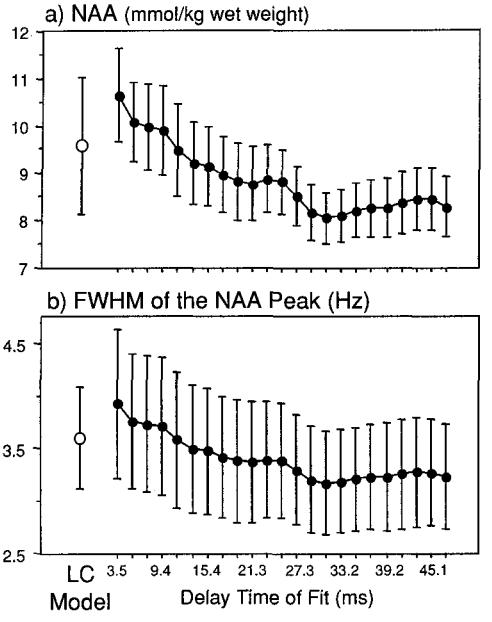

Figure 1: The mean (±SD) a) NAA levels and b) FWHM of the NAA peak are plotted as a function of DT (i.e., the number of omitted data points at the beginning of the FID).