Effects of T_2 relaxation on ^{1}H MRS data: to correct or not to correct for?

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Introduction

Absolute metabolite concentrations are sometimes sought in ^{1}H MRS studies [1]. It has long been known that, in order to obtain true metabolite concentrations, correction for a multitude of factors needs to be performed. One of these factors is transverse relaxation, and most of the studies that afford the time to acquire multiple echo time (TE) data sets perform these T_2 corrections [2]. We present evidence that significant uncertainty is added to the measurement of an absolute metabolite concentration by the T_2 correction (in particular for data sets acquired with long TE's); a more "accurate" metabolite concentration is also accompanied by a larger measurement error, and the two effects can easily counterbalance each other. We also show that the separation between a group of Alzheimer disease (AD) patients and a group of age-matched normal controls (NC's) based on NAA and NAA/Cr decreases when T_2 correction is performed. Consequently, unless major T_2 changes are expected in a disease or longitudinal study, T_2 uncorrected metabolite concentrations may be better disease or disease progression markers.

Methods

Theory: The relationship between measured metabolite concentration c_m and absolute metabolite concentration c_a can be expressed as $c_m = c_a e^{-TE/T_2}$, and the relative error in c_a can be computed as $\sigma c_a / c_a = \sqrt{(\sigma c_m / c_m)^2 + TE^2 / T_2^2 (\sigma T_2 / T_2)^2}$. This relationship can be generalized for a J-resolved spectrum (PRESS-J) [3], a long effective TE method used for all data collection in this study.

For a PRESS-J acquisition similar to the one that we have used *in vivo* (described under the experimental section), it can be calculated that a 3.5% (measured) error in determining the NAA concentration (whose average T_2 was calculated to be 260ms), coupled to a 4% (measured) error in determining NAA T_2 values, will lead to an error in measuring the absolute NAA concentration of 4.8% (a 37% increase over the start value).

Experimental: Data was acquired on a 3T, whole body GE scanner. Four normal volunteers were scanned on four different days during the course of 6 months, three times each day, and spectra from a 8cc voxel in the posterior cingulate gyrus were acquired. A total of 128 spectra were collected, with TE varying from 35ms to 355ms in steps of 2.5ms (2 averages/ step). The spectra were then averaged together and quantified using LCModel.

36 early AD patients (medium age 71, average MMSE=25, average CDR=0.8) and 32 age-matched normal controls also underwent a scanning session, with a PRESS-J spectrum acquired from the same posterior cingulate gyrus region. For all the data sets acquired in this study, a mono-exponential fit was performed for the 128 singlet peak heights (NAA, Cr and Cho), and T_2 times extracted. These were then used to correct metabolite concentrations for transversal relaxation.

Results and discussion

Table 1 presents the average intra-volunteer, inter-day coefficients of variation (CV) for Cr, NAA and NAA/Cr, corrected and uncorrected for T_2 effects. Note the good qualitative agreement between the calculations presented under Theory and the increase in CV's following T_2 corrections. For the normal volunteers studied over a period of 6 months, 1 way ANOVA performed for each volunteer indicates that there are statistically significant changes in T_2 relaxation times between scanning days. The larger CV's in the absolute metabolite concentration, however, indicate that errors in measuring T_2, and not mean T_2 changes are the dominant mechanism for the errors in measuring absolute metabolite concentrations.

	Cr	NAA	NAA/Cr
Met conc. CV [%]	4.8	3.5	3.5
Abs. met. conc. CV [%]	5.8	4.3	5.0

Table 1: Coefficients of variation for met. concs. uncorrected (row1) and corrected (row 2) for T_2 relaxation.

In the case of the AD study, one way ANOVA indicates that there are significant INCREASES (as high as 8%) in the T_2 relaxation times of the AD patients as compared to NC's. These increases could mask further decreases in absolute metabolite concentration (such as NAA); consequently, better separation might be expected between AD and NC subjects when absolute metabolite concentrations are computed.

Figure 2, however, illustrates the contrary: here, ROC curves that distinguish the populations are presented for both corrected and uncorrected metabolite concentrations and concentration ratios. As can be observed from Figure 2a, no significant improvement is obtained in the separation between the 2 groups based on the NAA levels (the area under the NAA curve is 0.73±0.12, while the area under the absolute NAA concentration curve (absNAA) is 0.78±0.1). Moreover, a significantly worse separation between the 2 groups is obtained if the T_2 correction is performed (the area under the NAA/Cr curve is 0.78±0.11, while the area under the corrected curve absNAA/absCr is 0.64±0.13). These findings suggest that the additional error introduced in the absolute concentration measurements is detrimental to the sensitivity of the MRS technique in distinguishing AD patients from NC's.

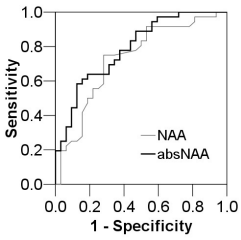

Figure2: ROC curves for *a) NAA and (absNAA) conc. b) NAA/Cr and absNAA/absCr*

Conclusions

We presented evidence showing that no significant improvements in ^{1}H MRS data quality are obtained when T_2 corrections are performed in a longitudinal, normal volunteer study, or in a cross-sectional AD/NC study. The errors in measuring T_2's are a significant factor in determining the precision of absolute concentration measurements, at least when a long TE sequence is used. Unless dramatic changes or differences are expected in a ^{1}H MRS longitudinal or cross-sectional study, it is suggested that metabolite concentrations that are not corrected for transverse relaxation might be a more sensitive marker of disease or disease progression.

References

1. Stengel et al, Magn Res Med **52**, 228 (2004); **2.** Isobe et al, Magn Res Imaging, **20**, 343 (2002); **3.** Hurd et al, Magn Res Med, **51**, 435 (2004);