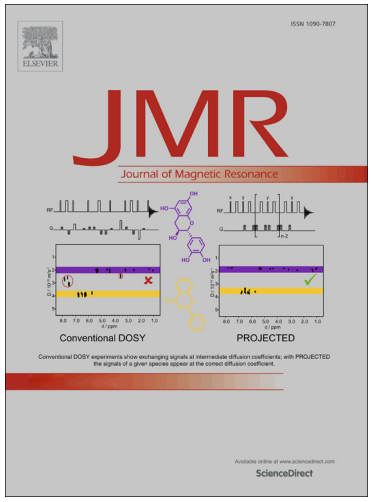
Accepted Manuscript



Reduction of variance in measurements of average metabolite concentration in anatomically-defined brain regions

Ryan J. Larsen, Michael Newman, Aki Nikolaidis

PII: S1090-7807(16)30166-5
DOI: http://dx.doi.org/10.1016/j.jmr.2016.09.005
Reference: YJMRE 5947

To appear in: *Journal of Magnetic Resonance*

Received Date: 4 April 2016
Revised Date: 9 September 2016
Accepted Date: 10 September 2016

Please cite this article as: R.J. Larsen, M. Newman, A. Nikolaidis, Reduction of variance in measurements of average metabolite concentration in anatomically-defined brain regions, *Journal of Magnetic Resonance* (2016), doi: http://dx.doi.org/10.1016/j.jmr.2016.09.005

Reduction of variance in measurements of average metabolite concentration in anatomically-defined brain regions

Ryan J. Larsen[1], Michael Newman[1], Aki Nikolaidis[1,*]

[1]Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign

[*]Current address: Center for the Developing Brain, Child Mind Institute

Abstract. Multiple methods have been proposed for using Magnetic Resonance Spectroscopy Imaging (MRSI) to measure representative metabolite concentrations of anatomically-defined brain regions. Generally these methods require spectral analysis, quantitation of the signal, and reconciliation with anatomical brain regions. However, to simplify processing pipelines, it is practical to only include those corrections that significantly improve data quality. Of particular importance for cross-sectional studies is knowledge about how much each correction lowers the inter-subject variance of the measurement, thereby increasing statistical power. Here we use a data set of 72 subjects to calculate the reduction in inter-subject variance produced by several corrections that are commonly used to process MRSI data. Our results demonstrate that significant reductions of variance can be achieved by performing water scaling, accounting for tissue type, and integrating MRSI data over anatomical regions rather than simply assigning MRSI voxels with anatomical region labels.

Keywords: ^{1}H-Magnetic Resonance Spectroscopy; absolute quantification; brain; tissue segmentation; partial volume

Introduction

Magnetic Resonance Spectroscopy (MRS) provides non-invasive measurements of brain health and metabolism. These measurements are not only sensitive to a wide range of disease states,[1] they are also sensitive to variance within healthy populations in intelligence,[2-5] cognitive function,[6,7] mood,[8] and personality.[9] However, these effects can be difficult to detect. For example, inconsistent results have been reported in correlations of intelligence with metabolite concentrations.[10] One possible reason for this is variation in analysis and quantification methods that are used.[10]

A variety of methods for quantitative analysis of MRS data have been proposed. Comprehensive processing schemes of MRS data typically include three basic steps: spectral analysis to calculate the signal amplitude of each metabolite, calibration of the metabolite amplitudes for accurate quantitation, and the merging of quantified data with anatomical information. Spectral analysis is typically performed using standard software packages, many of which employ prior knowledge in the form of metabolite basis functions.[11] Quantitation is performed by calibrating the signal to a known standard, which can be external or internal.[12] The use of water signal as an internal standard is well-established,[13] and has been shown to be the most reproducible method in inter-site comparisons.[14]

Data acquired using MRSI requires additional post-processing to integrate the quantified signal with available anatomical information. A frequency ramp can also be applied to shift the voxels relative to the anatomy, thereby centering the voxels on an anatomical region of interest.[15] Voxels can be assigned to anatomical brain regions, either by a trained rater[3] or by an automated approach.[16,17] Alternatively,