Water Loading: A Perturbation Model of Metabolic Activity in ^{1}H-MRS

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Introduction

The internal reference used in ^{1}H-MRS quantitation can greatly influence the sensitivity and hence utility of spectroscopy. In this study, we examined water loading as a metabolic perturbation model for comparing the detection sensitivity of the three internal referencing techniques: creatine (ratio), water peak (total water), and absolute quantitation (tissue water).

Background

Oral water load produces systemic alterations in tissue osmolality, including brain tissue. The effect of a water load on metabolite concentrations for mild shifts in osmolality depends on the quantitation method employed. Under mild hypo-osmolality, the total water brain water volume is unchanged as the CSF space, ventricles and sulci, gives way to the expanding brain tissue. Thus, internal referencing methods that utilize only the tissue water signal may be very sensitive to even mild shifts in osmolality. In contrast, because the total water volume is relatively unchanged, methods that utilize the total water signal will be insensitive to these shifts. It is difficult to predict the effect of mild hypo-osmolality with creatine (Cr) based quantitation methods. The net effect will depend on the osmolytic capacity of Cr relative to that of the other metabolites.

Methods and Materials

^{1}H-MRS experiments were performed on thirteen healthy young adults after a 12-hr overnight preoperative fast (NOP) at the General Clinical Research Center. Each participant underwent three 'H-MRS experiments: the first immediately prior to a 3-hour oral water load period (pre-load); the second at the end of the 3-hour oral water load (drinking rate: 20ml of water per kg of body mass per hr) (water-load), and the third, 3 hours post completion of the water load and after consumption of a meal (post-load). Blood samples for serum sodium and osmolality measurements were taken every 20 minutes throughout the experiment to monitor participant status. As a control study, on a day of their choosing, each participant repeated the three 'H-MRS exams under non-fasting, normo-osmolar conditions. All studies were performed on 1.5-T Magnetom Vision whole-body MRI system (Siemens Medical Systems, Iselin, NJ) using a Siemens standard 27-cm circularly polarized proton head coil. All voxels-of-interest were 6cm^3 volumes localized in the temporal-parietal region along the Sylvian fissure. Each spectroscopy experiment included a water-suppressed spectrum (TE/TM/TR=20/10/4000 ms, NEX=64, 1250-Hz SW, 2048 complex points), an 8-averaged water reference, and a logarithmically sampled 16-point T_2 data set (TM/TR = 10-ms/12-s) for compartmental analysis. The data was quantified with LCModel using the water reference data. Each T_2 data set was fit with a biexponential model analyzed with Sigma Plot 6.0 (SPSS Science, Chicago, IL). To calculate the concentration values relative to tissue water, the water peak reference was corrected for T_2 relaxation and CSF signal contributions.

Results and Discussion

For data analysis, we only focused on the changes that occurred between the pre-load and the water-load states since only these two states were specifically controlled for osmolality status by restricting the consumption of liquids and solids and by controlling the amount and rate of water consumed. Because each participant acted as his or her own control, all statistical analyzes employed a paired t-test for comparing the pre-load and water-load states. For additional comparisons, the 1st and 2nd experiments of the control studies were also analyzed; however none of those comparisons were significantly different. The increase in the cerebral tissue water signal (~ 6%) due to water loading is easily observable in the normalized water signals (Fig 1). The maximum signal consistently occurs for the water-load period, whereas the maximum tissue water signal occurs randomly for the three time points of the control studies. The total water signal did not change (Fig 2) throughout the experiment, a indication that there is a 1:-1 stoichiometry between the change in tissue water and the change in the CSF water. The molality concentration measurements (tissue water) for the water-load states show a proportionate decrease when compared to the pre-load concentrations (Fig 3 & 4). In comparison, concentrations calculated as ratios or relative to the total water peak did not exhibit any significant changes. In order to assess the overall spectral changes, the metabolite concentrations (minus NAA) were compared as a single cluster in a meta-analysis, irrespective of metabolite type. Because NAA consistently had Cramer-Rao Lower Bounds (CRLBs) on the levels of 6% or less (on the order of the increase in the tissue water), NAA was deemed to have the stability to be analyzed separate from the other metabolites. As before, only the concentrations referenced with the tissue water showed a significant change with water loading (Figs 3 & 4). The use of ratios and the total water peak are common quantitation techniques; however, as this study shows, these techniques have reduced sensitivity to water-dependent metabolic activity. Given that inflammation is a common immunologic response in many pathologies, tissue water referencing would appear to provide the optimum sensitivity to metabolic disturbances.

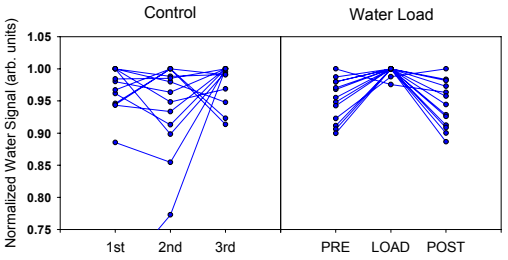


Figure 1

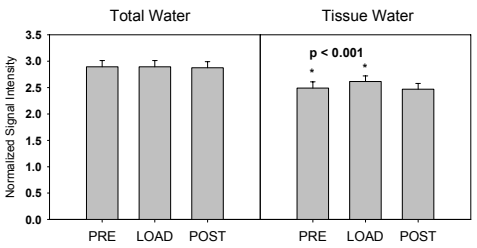
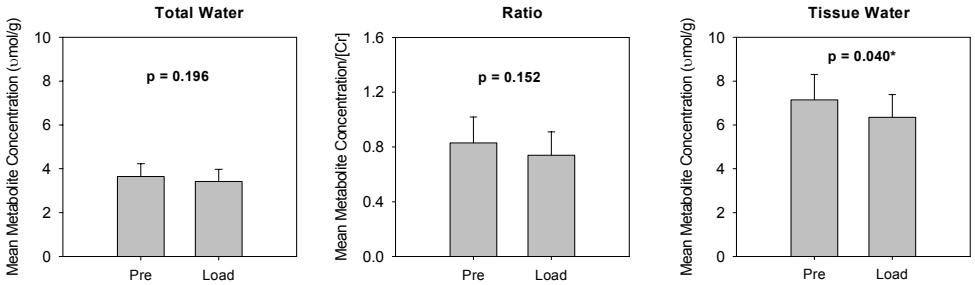


Figure 2

Figure 3



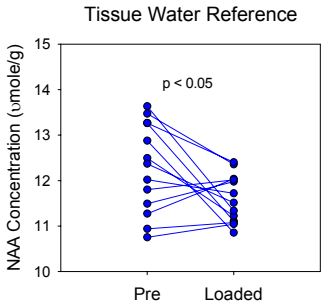


Figure 4