Regional Metabolite Concentrations in Young Adult Brain Measured by ^{1}H MRS at 3T

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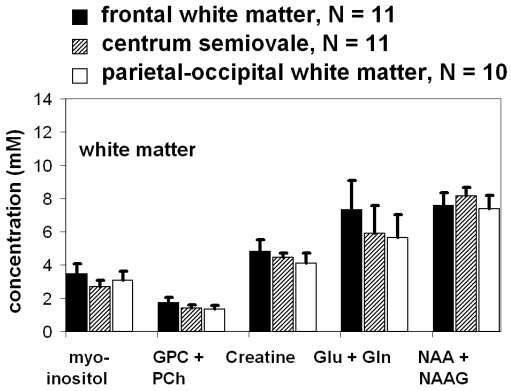
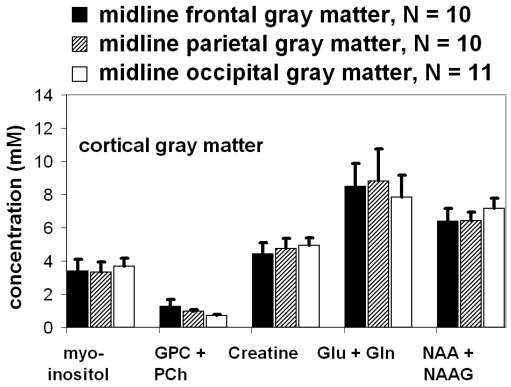
Introduction. MRS and MRSI are becoming increasingly useful in the diagnosis of a variety of diseases. Although in some cases the spectra are grossly abnormal, the question frequently arises as to whether subtle abnormalities are present. In such cases, it is useful to have reference values for normal metabolite concentrations. Normative studies performed to date have demonstrated that metabolite concentrations vary with the age of the subject, vary between locations in the brain, and vary between gray matter and white matter. Ideally, reference values would come from the same anatomical location, from normal subjects of a similar age, collected with the same technique and parameters at the same field strength. Normative studies have been reported for 1.5T (1), 2T (2,3), and 4T (4). Higher field strengths are expected to improve signal-to-noise and resolution, as when 3T is compared to 1.5T (5). Most previous studies have used a relatively limited number of subjects, and in aggregate, they have not covered all possible ages of subjects and have not covered all areas of the brain. We are attempting to complete part of the picture by conducting a study to establish normative values for young adults at 3T.

Methods. *Subjects.* 35 normal young adults (20 M, 15 F; age range 20-41, mean 31.4 years) were studied. Because metabolite concentrations have been shown to vary with age (3,6,7), we recruited subjects from a limited age range over which metabolite concentrations were not expected to vary due to age. *MRI and MRS.* Scanning was performed on a 3T Philips Intera scanner. Sagittal and axial T1 weighted images were acquired as localizers. Single voxel spectroscopy was performed on voxels graphically prescribed from the T1 weighted images (PRESS localization; CHESS water suppression; TE=35ms; TR=2000ms; 128 NEX). An unsuppressed water spectrum (TR=5000ms, TE=35ms, 4 NEX) was also acquired for each voxel. A total of 93 voxels were collected from 9 anatomical locations, with 9-11 voxels per location, and no repetitions of the same location in the same subject. All locations were on the left side or midline. Most voxels were approximately 20 x 20 x 20 mm in size (range 5.7 – 8.8 cm^3, mean 7.9 cm^3), although the dimensions were adjusted to match the size and shape of the targeted anatomical area. In order to correct for CSF included within the voxels, we acquired a heavily T2-weighted image with location and slice thickness corresponding to the location of each spectroscopic voxel (FSE; ETL=8; TE=500ms; TR=3000ms). A phantom containing water was placed beside the head and included in the field of view. *Processing*. We estimated metabolite concentrations using an automated fitting routine, LCModel (8). Referencing to the unsuppressed water peak allowed absolute quantitation of metabolite levels. The levels were then corrected for CSF partial volume according to the method in reference 9.

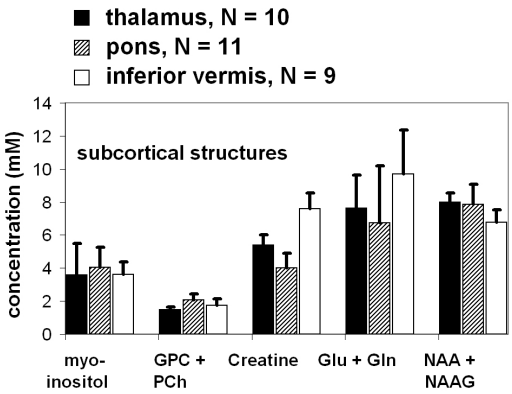


Results. Absolute concentrations, in mM, were calculated for myoinositol, glycerophosphocholine + phosphocholine, creatine, NAA+NAAG, and Glu+Gln. Concentrations of each metabolite at each location, as mean and standard deviation, are plotted in the figures. The highest [NAA+NAAG] was 8.2 mM in the centrum semiovale, and the lowest was 6.4 mM in the midline frontal gray matter. The highest [GPC+PCh] was 2.1 mM in the pons, and the lowest was 0.7 mM in the midline occipital gray matter. Creatine varied from 4.1 mM (parietal-occipital white matter) to 7.6 mM (inferior vermis). Myoinositol varied from 2.7 mM (centrum semiovale) to 4.0 mM (pons). Glu+Gln varied from 5.7 (parietal-occipital white matter) to 9.7 mM (inferior vermis).



Discussion. The results generally agree with those reported by others (2), including the location of the highest [NAA+NAAG] in the centrum semiovale, lowest [NAA+NAAG] in the midline frontal gray matter, lowest [GPC+PCh] in the midline occipital gray matter, highest [creatine] in the inferior vermis, lowest [creatine] in the parietal-occipital white matter, lowest [myoinositol] in the centrum semiovale, and lowest [Glu+Gln] in the parietal-occipital white matter. Our values are consistently about 20-25% lower than those reported by reference 2; several factors may account for the systematic difference, including localization method (PRESS vs STEAM), T1 relaxation effects (TR 2000 ms vs 6000 ms), and correction for inclusion of CSF (done in the current study but not in the referenced study).

In general, the various white matter regions differ more from gray matter regions than from each other, and the pons and inferior cerebellar vermis differ from both gray and white matter regions. Variance between subjects was high in pons, midline frontal gray matter, and inferior vermis; these are the three regions nearest to bone/air/tissue interfaces and are most difficult to shim. Variance was also high for Glu+Gln, a complex peak that normally has low SNR.



The establishment of normative values will aid diagnosis in clinical situations where no appropriate reference voxel can be obtained from the patient being studied. Further studies will need to be done to cover other anatomical areas, as well as pediatric and geriatric age groups, to account for metabolite changes during normal maturation and ageing. 3T has advantages for future clinical use, including increased spectral resolution, particularly for coupled spin systems, which should improve quantitation in all regions and improve delineation of subtle metabolite abnormalities. Increased susceptibility artifacts at 3T are a potential disadvantage.

References.

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