

Age-related decrease in NAA concentration and NAA/creatine ratio revealed by single voxel ^1H -MRS and compartmentation analysis in fifty subjects

J.C.W. Brooks, N. Roberts, G.J. Kemp†, M.A. Gosney‡, V. Spark, M. Lye‡ and G.H. Whitehouse

Magnetic Resonance and Image Analysis Research Centre (MARIARC), †Department of Musculoskeletal Science, ‡Department of Geriatric Medicine, University of Liverpool, Liverpool, L69 3BX, UK

Introduction

The extent to which age-related brain atrophy is due to neuronal loss has been widely debated. A recent study (1) using proper stereological methods, found a global decline of 10% in neocortical neuron number from the age of 20 to 90 years. In vivo studies of age-related changes in the size of neuronal populations, and analysis of regional and sex-specific differences, are possible via measurement of the concentration of the neuronal marker N-acetylaspartate (NAA) using ^1H -MRS (2). We have applied quantitative single voxel ^1H -MRS, incorporating correction for metabolite T_2 relaxation times and compartmentation analysis to correct for the amounts of brain water and CSF in the voxel, to measure NAA concentration in 10 male subjects for each decade between the age of 20 and 70 years. The voxel was prescribed in frontal lobe grey matter, the volume of which is reported to be preferentially reduced with age in MRI studies (3, 4).

Subjects and Methods

Subjects were recruited from the local community and screened for possible neurological disease. All subjects gave written consent to participate in the study, which had local Ethics Committee approval. Examinations were performed on a 1.5 T SIGNA whole body imaging system (General Electric, Milwaukee, USA) using the standard quadrature headcoil. Images suitable for prescription of the voxel and estimation of voxel grey and white matter fractions using SPM (5) were obtained using a 3D fast IR prepared GRASS sequence ($TE/\text{flip}/TI = 3.5 \text{ ms}/30^\circ/450 \text{ ms}$, 1.6 mm slice thickness, 124 contiguous slices, $FOV = 20 \text{ cm}$). Water suppressed ^1H spectra were acquired using the STEAM sequence from 8 cm^3 voxels, placed over the interhemispheric cleft of the frontal lobes, and analysed using time domain fitting routines in MRUI software. Acquisition of spectra at five TE values (30, 72, 144, 216, 288 msec) and constant relaxation decay ($RD=TR-TE/2-TM=2971.3 \text{ msec}$) allowed correction for T_2 relaxation. Compartmentation analysis was performed using both spectroscopy and imaging based approaches, as described in (6) and (7), respectively. Using results from both compartmentation techniques, two sets of absolute concentrations were determined for N-acetylaspartate (NAA) and creatine/phosphocreatine (Cr) in units of millimoles per litre of brain water.

Results

The fraction of CSF estimated by compartmentation analysis increased significantly with age ($p<0.001$). The grey matter fraction of the voxel, with mean value 85% (SD 5%), did not depend on age ($p=0.62$). The Figure shows the concentrations of NAA and Cr and the ratio of NAA to Cr as a function of age (data are the average of values acquired using the two compartmentation techniques). The results of regression analysis of NAA, Cr and the ratio NAA:Cr are presented in the Table. Significant decreases in both NAA concentration ($p<0.01$) and NAA:Cr ($p<0.001$) were observed with age (see Figure).

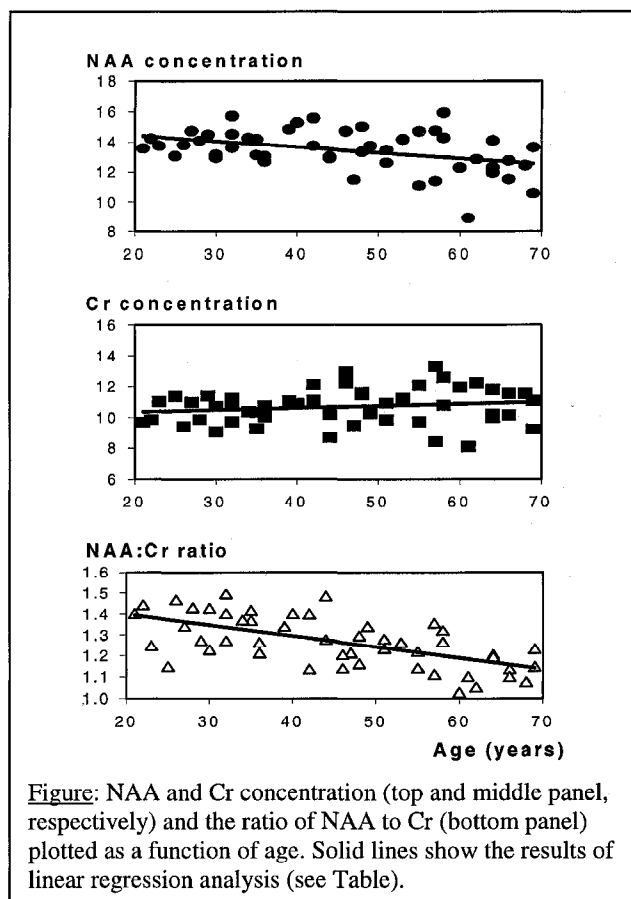


Figure: NAA and Cr concentration (top and middle panel, respectively) and the ratio of NAA to Cr (bottom panel) plotted as a function of age. Solid lines show the results of linear regression analysis (see Table).

	[NAA]	[Cr]	[NAA]/[Cr]
IMAGING	-0.44 (0.002)	0.14 (0.35)	-0.63 (<0.001)
SPECTRO	-0.35 (0.013)	0.18 (0.20)	-0.63 (<0.001)

Table: Results of regression analysis against age, expressed as correlation coefficient (p-value).

Discussion

We have shown a significant decrease in NAA concentration in frontal lobe grey matter with age, and this is probably the result of an age-related decrease in neuronal number (1). This decrease in NAA concentration was not found in a previous, smaller, mixed-sex ^1H -MRS study over a similar age range (8). However, both this (8) and another report (9) were consistent with the present study in finding an age-related decrease in NAA:Cr, which was attributed to increasing Cr concentration with age, a tendency which was not significant in our study.

References

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