Hemispheric and gender differences in proton MRS control data

R. S. Briellmann[1], R. M. Wellard[1], G. S. Pell[1], G. D. Jackson[1,2]

[1]Brain Research Institute, Melbourne, Victoria, Australia, [2]Radiology and Medicine, The University of Melbourne, Melbourne, Victoria, Australia

Background: The human brain shows slight asymmetry in organization for both brain structure and function. There is also evidence for gender dependent differences in the organization of the brain. MRS can provide information on the metabolic function of the brain. Commonly assessed metabolites are: N-acetylasparatate (NAA) a neuron specific metabolite, creatine (Cr) an integral component of the energy cycle; the choline-containing metabolites (Cho) which relate to membrane turnover and are elevated in glial cells; myoinositol (mI), a putative marker of gliosis and an organic osmolyte; and glutamate, a neurotransmitters and its derivative glutamine (Glx). Previous MRS studies suggest hemispheric asymmetry of NAA, and an absence of gender effects. However, these studies were done on small populations.

Methods: We studied 81 healthy subjects (44 females, mean age 26 ± 12 years). The MRS was performed with a 3 tesla GE Horizon LX echo speed scanner (GE Healthcare, USA). Bilateral single voxel spectra (PRESS) were acquired from both temporal and frontal lobes. Acquisition parameters were: TR/TE 3000 /30 ms, 2048 data points, spectral width of 5000Hz, voxel dimensions 2x2x2 cm. Data were processed with the program LCModel (1) using the unsuppressed water peak as an internal reference. The following metabolites were assessed: NAA, Cho, Cr, mI and Glx, and hemispheric asymmetry indices were calculated. Statistical analysis was performed using ANOVA (with age included as a co-variate); a p-value below 0.05 was regarded as significant.

Gender and side interaction

		right hemisphere	left hemisphere	
temporal lobe				
NA	females	6.4 ±1.0	6.7 ±1.0	ns
	males	6.2 ±0.5	6.8 ±0.8	0.0003
Cho	females	1.6 ±0.3	1.7 ±0.3	ns
	males	1.6 ±0.2	1.7 ±0.3	ns
Cr	females	5.1 ±0.9	5.4 ±0.9	ns
	males	5.2 ±0.6	5.4 ±0.8	ns
Mi	females	4.0 ±1.1	4.3 ±1.1	ns
	males	4.2 ±0.7	4.3 ±1.0	ns
Gln+Glu	females	8.1 ±1.5	7.7 ±1.5	ns
	males	8.5 ±1.5	7.7 ±1.8	0.04
frontal lobe				
NA	females	7.0 ±0.7	7.5 ±0.9	0.02
	males	7.0 ±0.5	7.5 ±0.6	0.0001
Cho	females	1.5 ±0.2*	1.5 ±0.2	ns
	males	1.6 ±0.2	1.6 ±0.2	ns
Cr	females	5.1 ±0.5	5.3 ±0.6	ns
	males	5.1 ±0.4	5.5 ±0.4	0.0003
Mi	females	3.6 ±0.7	3.7 ±0.8	ns
	males	3.7 ±0.6	3.7 ±0.7	ns
Gln+Glu	females	8.8 ±1.4	9.1 ±1.5	ns
	males	9.1 ±1.4	9.4 ±1.6	ns

values expressed in Institutional units, representing approximately mmol
statistics: ANCOVA with age as co-variate
* right Cho males higher concentration than females (p=0.01)

Results: There was a marked asymmetry in NAA, present in both the temporal lobe (left 6.7 ± 0.9 mmol; right 6.3 ± 0.9, p=0.001) and the frontal lobe (left 7.5 ± 0.8 mmol; right 7.0 ± 0.6, p<0.0001). In the temporal lobe, there was also asymmetry in Glx (left 7.7 ±1.6 mmol; right 8.3 ±1.5 mmol, p=0.01), whereas in the frontal lobe there was asymmetry in Cr (left 5.4 ±0.5 mmol; right 5.1 ±0.4 mmol, p=0.0004). The other metabolites showed no side-to-side-difference.

Men had a higher left-hemispheric temporal lobe NAA, and a higher right-hemispheric Glx, whereas women showed no side-to-side asymmetry in any temporal lobe metabolite (table). Both men and women showed a higher left-hemispheric frontal lobe NAA, whereas only men showed a side-to-side difference in Cr. However, there was no gender difference in the asymmetry index of any metabolite. In the right frontal lobe, Cho was higher in men (1.6 ±0.2 mmol) than in women (1.5 ±0.2 mmol, p=0.01), the other metabolites showed no gender difference.

Discussion: This large study confirms the presence of marked side-to-side differences in NAA in both of the assessed regions. The higher NAA in the left hemisphere suggests an increased concentration of neurons in the left compared to the right hemisphere. This may be due to predominantly left-hemispheric specialization for higher cognitive functions in healthy subjects. Interestingly, Glx and Cr also showed asymmetry, which may suggest hemispheric differences in neurotransmitters and energy metabolism (associated with functional usage of these regions). The hemispheric asymmetry was particularly pronounced in men, consistent with earlier observations of a more asymmetric specialisation in men compared to women. Our results suggest that hemispheric side and gender should be taken into account when interpreting patient data.

References

1. Provencher SW. Estimation of metabolite concentrations from localized *in vivo* proton NMR spectra. In: Magn Reson Med, 1993: 672-679.