

Biochemical markers of intelligence: a proton MR spectroscopy study of normal human brain

Rex E. Jung^{1,2}, William M. Brooks^{1,3*}, Ronald A. Yeo², Stephen J. Chiulli⁵, David C. Weers^{1,2} and Wilmer L. Sibbitt Jr^{1,4}

¹Clinical and Magnetic Resonance Research Center, University of New Mexico Health Sciences Center, 1201 Yale Boulevard North-East, Albuquerque, NM 87131, USA

Departments of ²Psychology, ³Neurosciences and ⁴Rheumatology, University of New Mexico, Albuquerque, NM 87131, USA

⁵St Joseph's Rehabilitation Hospital, Albuquerque, NM 87131, USA

Proton magnetic resonance spectroscopy (¹H-MRS) offers a unique non-invasive approach to measurement of N-acetylaspartate (NAA) and choline (Cho), putative markers of neuronal and glial integrity. Previous studies revealed that these neurochemicals predict cognitive impairment in diseased subjects, although little is known about their relationship to cognitive functioning in healthy people. We measured the concentrations of NAA and Cho in the left occipitoparietal white matter of 26 healthy adults and compared them with intellectual performance assessed by the Wechsler Adult Intelligence Scale-3. We found that NAA ($b = 0.6$, $p < 0.01$) and Cho ($b = -0.42$, $p < 0.01$) were independently associated with the Full-Scale Intelligence Quotient. Together, these metabolites accounted for a large proportion of the variance in intelligence ($r^2 = 0.45$). Possible mechanisms underlying these correlations, such as mitochondrial function and myelin turnover, are discussed. ¹H-MRS is a sensitive new tool to assess the neuronal underpinnings of cognitive function non-invasively.

Keywords: intelligence; proton magnetic resonance spectroscopy; choline; N-acetylaspartate

1. INTRODUCTION

Despite much controversy regarding its nature and determinants, the construct of intelligence figures prominently in both psychology and society. The psychological study of intelligence has yielded a hierarchical model with a broad overarching general intellectual factor (g), and underlying specific abilities (Anderson 1992). Further attempts have been made to reduce the bases of human intelligence into 'cognitive correlates' hypothesized to be fundamental underpinnings of intellectual reasoning (Vernon 1987). Individual variation in intelligence predicts school and occupational attainment better than any other single attribute (Ceci & Williams 1997). Genetic and environmental differences contribute to individual variation in intelligence, in approximately equal measures (Tambis *et al.* 1986). As the fields of psychological assessment and neuroimaging have developed there have been many attempts to specify exactly which components of brain variation are associated with individual differences in intelligence (Matarazzo 1992). The recognition of this important, but poorly understood, brain-intelligence link has resulted in the introduction of increasingly sensitive and diverse methods to study brain structure, electrical activity and metabolism in relation to specific intellectual abilities (Deary & Caryl 1997).

Head circumference studies have yielded only small correlations with intelligence quotient (IQ) (Wickett *et al.*

1994; Gould 1981), and direct brain measurement with magnetic resonance imaging (MRI) has shown that full-scale IQ generally correlates with brain volumes. Across two recent studies with substantial sample sizes, brain volume accounted for 16% (Reiss *et al.* 1996) and 4% (Andreasen *et al.* 1993) of the variance in IQ scores. Thus, while the 'quantity' of brain tissue may account for a certain fraction of the variance, other factors including cellular integrity, 'quality' of the neuronal circuitry, dendritic arbour, number of synapses and metabolic efficiency probably account for the remaining variance in intelligence (Andreasen *et al.* 1993).

Magnetic resonance spectroscopy (MRS) allows for analysis of brain chemistry *in vivo*. Rae *et al.* (1996) reported a strong correlation ($r = 0.52$) between IQ and brain pH, as determined from ³¹P-MRS in normal subjects, although a study of the temporal lobe in epileptic patients failed to replicate this finding (Anderson *et al.* 1998). Proton MRS (¹H-MRS) detects signals from neurometabolites including N-acetylaspartate (NAA) and creatine (Cre)- and choline (Cho)-containing compounds. Reduced NAA is commonly associated with neuronal injury or death (Ross *et al.* 1994), impaired cognition (Brooks *et al.* 1999a; Friedman *et al.* 1998) and poor functional outcome (Friedman *et al.* 1999). The Cre peak represents the sum of intracellular Cre and phosphocreatine. The Cho peak reflects the sum of all visible Cho moieties—predominantly glycerophosphocholine and phosphocholine—(Barker *et al.* 1994) and is commonly elevated in a stroke and multiple sclerosis due to membrane

*Author for correspondence (brooks@lizard.unm.edu).

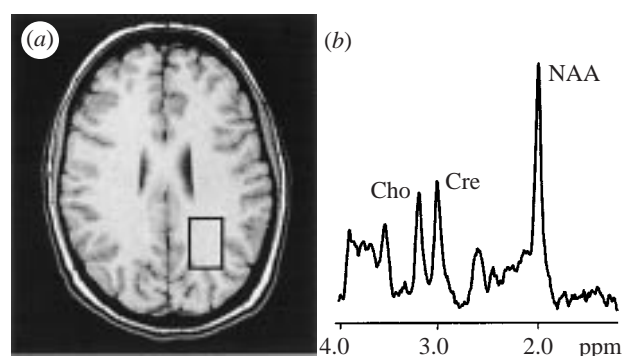


Figure 1. (a) MRI and (b) MRS. Voxel location within the left occipitoparietal white matter and resulting spectra from one experimental participant. ppm, parts per million.

breakdown, inflammation and/or demyelination (Ross *et al.* 1994).

While ^1H -MRS provides measures of neuronal injury and/or viability in overt disease, the functional correlates of neurometabolites measured by ^1H -MRS in a healthy brain have rarely been studied. Nonetheless, an emerging body of MRS literature links neurometabolic abnormalities to cognitive dysfunction in such diseases as HIV encephalopathy (Lopez-Villegas *et al.* 1997), adrenoleucodystrophy (Rajanayagam *et al.* 1997), hepatic encephalopathy (Huda *et al.* 1998; Haseler *et al.* 1998), traumatic brain injury (Friedman *et al.* 1998, 1999; Ross *et al.* 1998) and neuropsychiatric systemic lupus erythematosus (Brooks *et al.* 1999a). We hypothesized that, just as in disease, neurometabolic status contributes to variation in brain function in normal individuals. Hence, ^1H -MRS measures of neurometabolic concentrations should be associated with intellectual functioning in the normal human brain.

2. METHODS

(a) Subjects

Twenty-seven participants (17 female, 10 male) were recruited from the local college community. Informed consent was obtained from all participants prior to study under a protocol approved by the Institutional Review Board. Participants were screened to exclude obvious organic or medical diseases that might introduce bias into the study: prior traumatic brain injury, disorders of attention, learning disability, neurological disease, psychiatric diagnosis and use of psychoactive medications. One participant did not meet the experimental criteria listed above (psychiatric diagnosis treated with psychoactive medication) and was removed, leaving a final sample of 26.

(b) MRI and MRS

All MR acquisitions were carried out on a 1.5 T clinical MR scanner using standard software (GE Medical Systems, Waukesha, WI, USA). Imaging included sagittal T_1 - and axial T_1 - and T_2 -weighted series. A stimulated echo acquisition mode (STEAM) pulse sequence, including water suppression, was employed to sample one (12.6 cm^3) voxel location (echo time (TE) = 30 ms, recycle time (TR) = 2000 ms, 128 averages) within left occipitoparietal white matter. Specific voxel locations were prescribed from a T_1 -weighted axial imaging series, and were localized to maximize white matter and minimize grey matter contributions (figure 1).

Table 1. Demographic, intellectual and spectroscopic data from the sample

	mean	s.d.	minimum	maximum
age	22.0	4.6	17	35
VIQ	110.8	13.0	88	137
PIQ	109.5	9.2	94	127
FSIQ	111	11.4	91	135
Cho (mM)	1.64	0.18	1.32	2.02
Cre (mM)	6.79	0.44	5.92	7.77
NAA (mM)	12.38	0.53	11.39	13.29

(c) Spectroscopic analysis

Spectroscopic data were transferred to a Sun UltraSparstation (Sun Microsystems, CA, USA) for analysis using Magnetic Resonance User Interface (MRUI) (Katholieke Universiteit, Leuven, Belgium). Residual water resonances were removed using time-domain Hankel Lanczos singular value decomposition filtering. Following water filtering, time-domain fitting of Gaussian line shapes to NAA, Cre and Cho was carried out by variable projection to measure the areas corresponding to NAA, Cre and Cho. The area from the water peak was determined independently from the unsuppressed water scan using singular value decomposition. Data were quantified by employing the internal water signal as a concentration reference standard and correcting for metabolite and water T_1 and T_2 effects during echo and recycle times using literature values (Barker *et al.* 1993).

(d) Intellectual measurement

On a second occasion (within a week of scanning), intellectual examination was undertaken with the Wechsler Adult Intelligence Scale—3rd edn (WAIS-3), a reliable, valid and standardized test. Three subtests were not administered (comprehension, object assembly and picture arrangement). Prorated summary scores were generated for verbal IQ (VIQ) and performance IQ (PIQ), from which the Full-Scale Intelligence Quotient (FSIQ) was calculated. Each intelligence quotient (VIQ, PIQ, FSIQ) has a mean of 100 and a standard deviation of 15 (Wechsler 1997).

(e) Data analysis

Linear regression models were used to assess potential predictors of intelligence (FSIQ, VIQ, PIQ), the dependent variables. Independent variables were neurochemical concentrations of NAA, Cre and Cho. Pearson correlation coefficients were used to assess the relationships between individual intellectual subtest scores and neurochemical concentrations. Statistical analysis was conducted in SPSS for Macintosh (SPSS Inc. 1995).

3. RESULTS

As expected in a college-age cohort, the mean scores on the WAIS-3 were above average and variance was slightly reduced compared with normal national values (Wechsler 1997). The gender distribution of this sample reflected the undergraduate distribution of introductory psychology classes. Table 1 summarizes the demographic, neurochemical and intellectual performance of the participants.

High-quality spectra were acquired from all participants. Figure 1 shows a representative example of the

Table 2. Statistically significant results from three step-wise regressions of IQ scores on MRS metabolites

IQ score	r^2 for model	metabolite	beta	p
FSIQ	0.45	NAA	0.60	0.009
		Cho	-0.42	0.008
VIQ	0.23	NAA	0.44	0.013
PIQ	0.44	NAA	0.54	0.003
		Cho	-0.49	0.005

Table 3. Pearson correlation coefficients (and significance for probability levels) for WAIS-3 subtests and MRS metabolites

WAIS-3 subtest	Cho	Cre	NAA
FSIQ	-0.32	0.24	0.52**
PIQ	-0.40*	0.14	0.45*
picture completion	-0.11	0.36	-0.12
digit symbol-coding	-0.09	0.08	0.43*
block design	-0.30	0.02	0.41*
matrix reasoning	-0.39*	-0.13	0.13
symbol search	0.11	0.26	0.35
VIQ	-0.24	0.27	0.48*
vocabulary	-0.19	0.44*	0.32
similarities	-0.19	0.37	0.18
arithmetic	-0.36	-0.05	0.36
digit span	-0.08	-0.17	0.38
information	-0.39*	0.31	0.29
letter-number sequencing	-0.40*	-0.01	-0.02

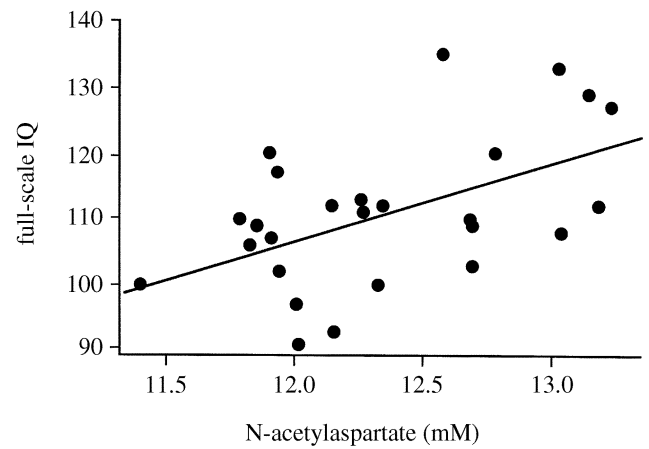
* $p < 0.05$; ** $p < 0.01$.

spectral quality. Mean metabolic concentrations of this cohort were consistent with literature values (Brooks *et al.* 1999b).

Spectroscopic measures of Cho and NAA were independently associated with IQ scores and accounted for a large proportion of the variance ($r^2 = 0.23-0.45$). In each analysis, NAA was selected to be entered in the first step of the regression and was significant for all intellectual indices. Cho was then added to NAA in the second step, and was significant for FSIQ and PIQ (table 2). Cre was not significantly associated with any measure of IQ. Neither age nor gender was associated with metabolic measures (all $p > 0.4$). Note that NAA concentrations were positively correlated with IQ and subtest scores, while Cho concentrations were negatively correlated with IQ and individual subtests (table 3). A scatter plot of the independent relationship between NAA and FSIQ is presented in figure 2.

4. DISCUSSION

This research establishes the relationship between individual neurometabolic concentrations and intellectual function in the normal human brain. The relationship appears to be rather general, as both verbal and visuo-spatial intellectual skills were related to metabolite concentrations. The finding of independent relationships between NAA and Cho with IQ scores suggests that two independent factors influence intelligence in normal

Figure 2. Scatter plot showing the correlation ($r = 0.52$) between FSIQ and NAA.

brain. However, the specific roles that NAA and Cho play in neuronal status in normal individuals have yet to be determined. In disease states, decreased NAA and elevated Cho are related to poorer function and outcome, possibly indicative of neuronal damage and/or inflammation (Ross *et al.* 1994; Davie *et al.* 1995). However, we cannot conclude that decreased NAA and elevated Cho reflect the same pathological processes in this normal population. Rather, these observations may reflect natural variation in density and proportion of neurons and glial cells, each of which has distinct neurometabolic patterns (Urenjak *et al.* 1993).

NAA is associated with lower IQ in such disorders as mental retardation (Hashimoto *et al.* 1995), temporal lobe epilepsy (Gadian *et al.* 1996) and Williams syndrome (Rae *et al.* 1998a). Our current results extend these findings by showing that lower NAA is related to reduced performance in a sample consisting exclusively of normal subjects. Although reduced NAA may indicate neuronal death or injury, increasing evidence suggests that mitochondrial dysfunction may also cause decreases in this neurometabolite (Fu *et al.* 1998; Bates *et al.* 1996). Specifically, inhibition of the mitochondrial respiratory chain has been demonstrated to lead to decreased NAA production, reflecting potentially reversible metabolic derangement as opposed to neuronal death *per se* (Bates *et al.* 1996). In the context of normal brain functioning, this finding raises the possibility that variability in mitochondrial function might contribute to the functional capacity of the brain in total.

We also observed a negative correlation between Cho and IQ in our normal cohort. During disease, elevated Cho is associated with membrane breakdown and inflammation (Davie *et al.* 1995), two processes that are likely to impair cognitive functioning (Brooks *et al.* 1999a; Friedman *et al.* 1998, 1999). However, other studies show increased Cho in the cerebellum associated with better intellectual functioning in Duchenne muscular dystrophy (Rae *et al.* 1998b) and recently abstinent alcoholics (Martin *et al.* 1995), although some concerns regarding the comparability of these studies and the present results remain. For example, Cho is known to vary with changes in cell density and type (Miller *et al.* 1996). Indeed, Rae *et al.* (1998b) reported increased Cho in the cerebellum but not the frontal lobes. Second, the significance of changes

in Cho following alcohol abuse and then abstinence is unclear. On the other hand, since myelin is under-continuous repair even in normal subjects, higher concentrations of Cho compounds might indicate more active myelin turnover, resulting in less efficient white matter functioning. Alternatively, elevated Cho could reflect a greater contribution from glial than from neuronal elements (Urenjak *et al.* 1993), reflecting natural variation in neuronal–glial composition associated with intelligence.

Unlike other functional neuroimaging studies, this protocol did not employ an activation paradigm, but rather explored the neurometabolic substrate of human brain function, that is neurometabolites intrinsic to neurons and their supporting cells. Thus, the ¹H-MRS technique explored the basic relationship of neurometabolite concentrations (i.e. brain tissue composition and status) to intellectual function, rather than brain anatomy or other metabolic indices such as blood flow, or oxygen or glucose uptake. The finding that intracellular neurometabolites at rest are related to cognitive ability suggests a neuronal contribution to intelligence in normal subjects. Moreover, this metabolite–cognition link observed in healthy participants implies that at least some of the association observed between neurometabolites and cognition in disease states may be related to pre-morbid neurometabolic factors.

Anatomical perspectives on cognition have emphasized the importance of white matter interconnections in multiple neuronal networks (Mesulam 1990). Accordingly, our measurements of neurochemistry were made in occipitoparietal white matter. We also selected this brain location because it provides consistent high-quality spectra, and metabolites in this location correlate with function in diseased cohorts (Brooks *et al.* 1999a; Friedman *et al.* 1998, 1999). The main association pathways sampled by our experimental paradigm included axonal fibres from the posterior aspects of the superior and inferior longitudinal, occipitofrontal and arcuate fasciculi, as well as the splenium of the corpus callosum. As this voxel location sampled numerous association pathways connecting many brain regions, metabolic concentrations in this voxel may widely influence cognitive processing. However, the relationship between neurometabolite concentrations in this voxel and concentrations in other regions of the brain important to intellectual functioning (e.g. frontal lobes) remains to be determined.

Several factors currently limit the generalization of these results. First, this is a relatively young and healthy cohort of college-age subjects. Thus, the applicability of these findings to other populations (i.e. the elderly or diseased populations) may be limited. Second, we do not know if the metabolite–IQ relationships associated with this brain location will be observed with other locations throughout the brain, although findings from the cerebellum show some promise. Third, the relationship of these metabolites to other elements of cognitive ability not limited to overall intellectual functioning remains to be elucidated.

The central finding of associations between intelligence and biochemical markers of neuronal functioning in normal subjects demonstrates that ¹H-MRS may prove to be a highly valuable tool within the cognitive neuro-

sciences. Although much has been learned about brain function by ‘fine-grained’ analysis of cognitive skill, the current results demonstrate that, for at least some questions, a broader perspective on cognitive functioning can illuminate brain–behaviour relationships. Future research using ¹H-MRS will be necessary to determine (i) the specific role of neurometabolite concentrations in health, (ii) the differential contribution of neurometabolites to cognitive functioning across the life span, and (iii) the regional importance of neurometabolism to cognitive functioning.

This work was supported by a grant (NS 35708) to Dr Sibbitt from the National Institutes of Health. The MRUI software package which is funded by the European Community project TMR/Networks ERB-FMRX-CT970160 was provided by Aad van den Boogaart, Katholieke Universiteit, Leuven, Belgium. Peter Barker kindly provided software for spectroscopic quantification. We thank Blaine Hart for screening the localizing issues.

REFERENCES

- Anderson, M. 1992 *Intelligence and development: a cognitive theory*. Oxford: Blackwell.
- Anderson, B., Elgavish, G. A., Chu, W., Simor, T., Martin, R. C., Hugg, J. W. & Kuzniecky, R. I. 1998 Temporal lobe pH and IQ: no consistent correlation. *Intelligence* **26**, 75–79.
- Andreasen, N. C., Flaum, M., Swayze, V. D., O’Leary, D. S., Alliger, R., Cohen, G., Ehrhardt, J. & Yuh, W. T. 1993 Intelligence and brain structure in normal individuals. *Am. J. Psychiatry* **150**, 130–134.
- Barker, P. B., Soher, B. J., Blackband, S. J., Chatham, J. C., Mathews, V. P. & Bryan, R. N. 1993 Quantitation of proton NMR spectra of the human brain using tissue water as an internal concentrations standard. *NMR Biomed.* **6**, 89–94.
- Barker, P. B., Breiter, S. N., Soher, B. J., Chatham, J. C., Forder, J. R., Samphilipo, M. A., Magee, C. A. & Anderson, J. H. 1994 Quantitative proton spectroscopy of canine brain: *in vivo* and *in vitro* correlations. *Magn. Reson. Med.* **32**, 157–163.
- Bates, T. E., Strangward, M., Keelan, J., Davey, G. P., Munro, P. M. & Clark, J. B. 1996 Inhibition of N-acetylaspartate production: implications for ¹H-MRS studies *in vivo*. *NeuroReport* **7**, 1397–1400.
- Brooks, W. M., Jung, R. E., Ford, C. C., Greinel, E. J. & Sibbitt Jr, W. L. 1999a Relationship between neurometabolite derangement and neurocognitive dysfunction in systemic lupus erythematosus. *J. Rheumatol.* **26**, 81–85.
- Brooks, W. M., Friedman, S. D. & Stidley, C. A. 1999b Reproducibility of ¹H-MRS *in vivo*. *Magn. Reson. Med.* **41**, 193–197.
- Ceci, S. J. & Williams, W. M. 1997 Schooling, intelligence, and income. *Am. Psychol.* **52**, 1051–1058.
- Davie, C. A., Feinstein, A., Kartounis, L. D., Barker, G. J., McHugh, N. J., Walport, M. J., Ron, M. A., Moseley, I. F., McDonald, W. I. & Miller, D. H. 1995 Proton magnetic resonance spectroscopy of systemic lupus erythematosus involving the central nervous system. *J. Neurology* **242**, 522–528.
- Deary, I. J. & Caryl, P. G. 1997 Neuroscience and human intelligence differences. *Trends Neurosci.* **20**, 365–371.
- Friedman, S. D., Brooks, W. M., Jung, R. E., Hart, B. L. & Yeo, R. A. 1998 Proton MR spectroscopic findings correspond to neuropsychological function in traumatic brain injury. *Am. J. Neuroradiol.* **19**, 1879–1885.
- Friedman, S. D., Brooks, W. M., Jung, R. E., Chiulli, S. J., Sloan, J. H., Montoya, B. T., Hart, B. L. & Yeo, R. A. 1999 Quantitative ¹H-MRS predicts outcome following traumatic brain injury. *Neurology* **52**, 1384–1391.

- Fu, W., Luo, H., Parthasarathy, S. & Mattson, M. P. 1998 Catecholamines potentiate amyloid beta-peptide neurotoxicity: involvement of oxidative stress, mitochondrial dysfunction, and perturbed calcium homeostasis. *Neurobiol. Dis.* **5**, 229–243.
- Gadian, D. G., Isaacs, E. B., Cross, J. H., Connelly, A., Jackson, G. D., King, M. D., Neville, B. G. & Vargha-Khadem, F. 1996 Lateralisation of brain function in childhood revealed by magnetic resonance spectroscopy. *Neurology* **46**, 974–977.
- Gould, S. J. 1981 *The mismeasure of man*. New York: W. W. Norton.
- Haseler, L. J., Sibbitt Jr, W. L., Mojtahedzadeh, H. N., Reddy, S., Agarwal, V. P. & McCarthy, D. M. 1998 Proton MR spectroscopic measurement of neurometabolites in hepatic encephalopathy during oral lactulose therapy. *Am. J. Neuroradiol.* **19**, 1681–1686.
- Hashimoto, T., Tayama, M., Miyazaki, M., Yoneda, Y., Yoshimoto, T., Harada, M., Miyoshi, H., Tanouchi, M. & Kuroda, Y. 1995 Reduced N-acetylaspartate in the brain observed in *in vivo* proton magnetic resonance spectroscopy in patients with mental retardation. *Pediatr. Neurol.* **13**, 205–208.
- Huda, A., Guze, B. H., Thomas, A., Bugbee, M., Fairbanks, L., Strouse, T. & Fawzy, F. I. 1998 Clinical correlation of neuropsychological tests with ¹H magnetic resonance spectroscopy in hepatic encephalopathy. *Psychosom. Med.* **60**, 550–556.
- Lopez-Villegas, D., Lenkinski, R. E. & Frank, I. 1997 Biochemical changes in the frontal lobe of HIV-infected individuals detected by magnetic resonance spectroscopy. *Proc. Natl Acad. Sci. USA* **94**, 9854–9859.
- Martin, P. R., Gibbs, S. J., Nimmerrichter, A. A., Riddle, W. R., Welch, L. W. & Willcott, M. R. 1995 Brain proton magnetic resonance spectroscopy studies in recently abstinent alcoholics. *Alcohol Clin. Exp. Res.* **19**, 1078–1082.
- Matarazzo, J. D. 1992 Psychological testing and assessment in the 21st century. *Am. Psychol.* **47**, 1007–1018.
- Mesulam, M. M. 1990 Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Ann. Neurol.* **28**, 597–613.
- Miller, B. L., Chang, L., Booth, R., Ernst, T., Cornford, M., Nikas, D., McBride, D. & Jenden, D. J. 1996 *In vivo* ¹H-MRS choline: correlation with *in vitro* chemistry/histology. *Life Sci.* **58**, 1929–1935.
- Rae, C., Scott, R. B., Thompson, C. H., Kemp, G. J., Dumughn, I., Styles, P., Tracey, I. & Radda, G. K. 1996 Is pH a biochemical marker of IQ? *Proc. R. Soc. Lond. B* **263**, 1061–1064.
- Rae, C., Karmiloff-Smith, A., Lee, M. A., Dixon, R. M., Grant, J., Blamire, A. M., Thompson, C. H., Styles, P. & Radda, G. K. 1998a Brain biochemistry in Williams syndrome. Evidence for a cerebellar role in cognition? *Neurology* **51**, 33–40.
- Rae, C., Scott, R. B., Thompson, C. H., Dixon, R. M., Dumughn, I., Kemp, G. J., Male, A., Pike, M., Styles, P. & Radda, G. K. 1998b Brain biochemistry in Duchenne muscular dystrophy: a ¹H magnetic resonance and neuropsychological study. *J. Neurol. Sci.* **162**, 148–157.
- Rajanayagam, V., Balthazor, M., Shapiro, E. G., Krivit, W., Lockman, L. & Stillman, A. E. 1997 Proton MR spectroscopy and neuropsychological testing in adrenoleukodystrophy. *Am. J. Neuroradiol.* **18**, 1909–1914.
- Reiss, A. L., Abrams, M. T., Singer, H. S., Ross, J. L. & Denckla, M. B. 1996 Brain development and IQ in children: A volumetric imaging study. *Brain* **119**, 1763–1774.
- Ross, B. & Michaelis, T. 1994 Clinical applications of magnetic resonance spectroscopy. *Magn. Reson. Q.* **10**, 191–247.
- Ross, B. D. (and 15 others) 1998 ¹H MRS in acute traumatic brain injury. *J. Magn. Reson. Imaging* **8**, 829–840.
- Tambs, K., Sundet, J. M. & Magnus, P. 1986 Genetic and environmental contributions to the covariation between the Wechsler Adult Intelligence Scale (WAIS) subtests: a study of twins. *Behav. Genet.* **16**, 475–491.
- Urenjak, J., Williams, S. R., Gadian, D. G. & Noble, M. 1993 Proton nuclear magnetic resonance spectroscopy unambiguously identifies different neural cell types. *J. Neurosci.* **13**, 981–989.
- Vernon, P. A. (ed.) 1987 *Speed of information processing and intelligence*, pp. 177–200. Norwood, NJ: Ablex.
- Wechsler, D. 1997 *Wechsler adult intelligence scale—third edition: administration and scoring manual*. San Antonio: The Psychological Corporation and Harcourt Brace.
- Wickett, J. C., Vernon, P. A. & Lee, D. H. 1994 *In vivo* brain size, head perimeter, and intelligence in a sample of healthy adult females. *Personal Individ. Diff.* **16**, 831–838.

