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Axonal recovery after severe traumatic brain injury demonstrated in vivo by 1H MR spectroscopy

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Abstract Proton magnetic resonance spectroscopy (MRS) suggested almost complete axonal recovery 21 months after trauma in a patient with severe diffuse axonal injury. MRS while the patient was comatose showed evidence of severe diffuse axonal injury in occipitoparietal white matter, but occipital grey matter was relatively spared. At 21 months N-acetylaspartate was normal. At 33 months examination showed a Functional Independence Measure of 83 and a Rancho Los Amigos Scale of Cognitive Function of 7–8, a remarkable improvement considering all the initial findings, except those of MRS.

Keywords Diffuse axonal injury · Magnetic resonance spectroscopy · N-acetylaspartate

Introduction

Microscopic lesions in white matter characterise MRI of diffuse axonal injury (DAI) [1]. MR spectroscopy (MRS) of occipitoparietal white matter in DAI shows reduced N-acetylaspartate (NAA) and increased choline (Cho). Total creatine is rarely decreased and lactate rarely seen. Elevation of Cho is typically less pronounced in midoccipital grey matter [2]. Several studies have demonstrated the prognostic value of MRS after traumatic brain injury [3, 4, 5, 6, 7, 8, 9]. We report a patient with severe DAI who showed an almost full recovery (more than 50% increase of NAA) in white matter without resolution of focal pathology which could explain this increase. To our knowledge, such evidence of axonal recovery after DAI has not been reported previously.

Case report

A 28-year-old woman was hit by a car, and sustained a severe traumatic brain injury. EEG at 3 weeks showed reduced 6–7 Hz background frequency with low frequencies (2–3 Hz) frontocentrally. Single-photon emission computed tomography with 90mTC-HMPAO, without absolute quantification, showed diffuse cortical hypoperfusion. The patient was in coma, Glasgow coma scale 4–6, for 3 months. Over the following 100 days the first purposeful simple movement of the right leg was observed; there was severe spasticity of all limbs. By 21 months the patient had regained considerable communication skills, was able to walk with assistance and to eat. Outcome scores were Functional independence measure 60 and Rancho Los Amigos Scale of cognitive function 6. By 33 months the patient had improved further, received and read letters, she read short texts, wrote letters using a computer and communicated by telephone. Outcome scores were Functional independence measure 83 and Rancho Los Amigos Scale of cognitive function 7–8.

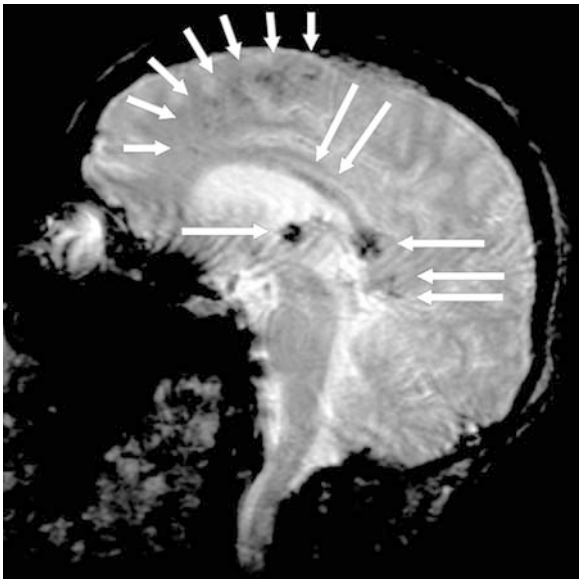

Fig. 1 MRI (on day 86) showing diffuse axonal injury: multiple areas of bleeding (*arrows*) in white matter including the corpus callosum

The patient had MRI and MRS 21 and 86 days and 21 and 33 months after injury, at 1.5 tesla. MRI included spin-echo T1- and T2- and gradient-echo T2*-weighted imaging. The supratentorial ventricles were manually outlined on the T2-weighted images, using standard window and level settings. The areas were calculated and the volume found by adding the areas from consecutive slices and multiplying by the slice thickness [10]. Two volumes of interest 25×25×20 mm^3 in occipitoparietal white matter and 21×27×20 mm^3 in midoccipital grey matter were examined using STEAM, TE 20, TM-interval 30, TR 1500 ms (third and fourth examinations 3000 ms), 128 averages (third and fourth examinations 86). Postprocessing of the spectra included eddy-current correction, zero filling, Gaussian apodisation (time constant 200 ms), fast Fourier transform, phase correction, and filtration of the residual water signal, but no other corrections of the baseline were employed. Quantitation was achieved using LCModel and the principle of reciprocity as in [11] with the addition of correcting for the effects of using a shorter TR. MRS from grey and white matter in 21 healthy adults aged 32 ± 8 years was used as a normal reference. Values within two SD of the average were taken as normal.

MRI and MRS on days 21 and 86 showed evidence of DAI: multiple microscopic haemorrhagic foci in white matter, including the corpus callosum (Fig. 1) and typical MRS abnormalities in white matter (Fig. 2) including, on day 86, a 42% (−6.4 SD)

►

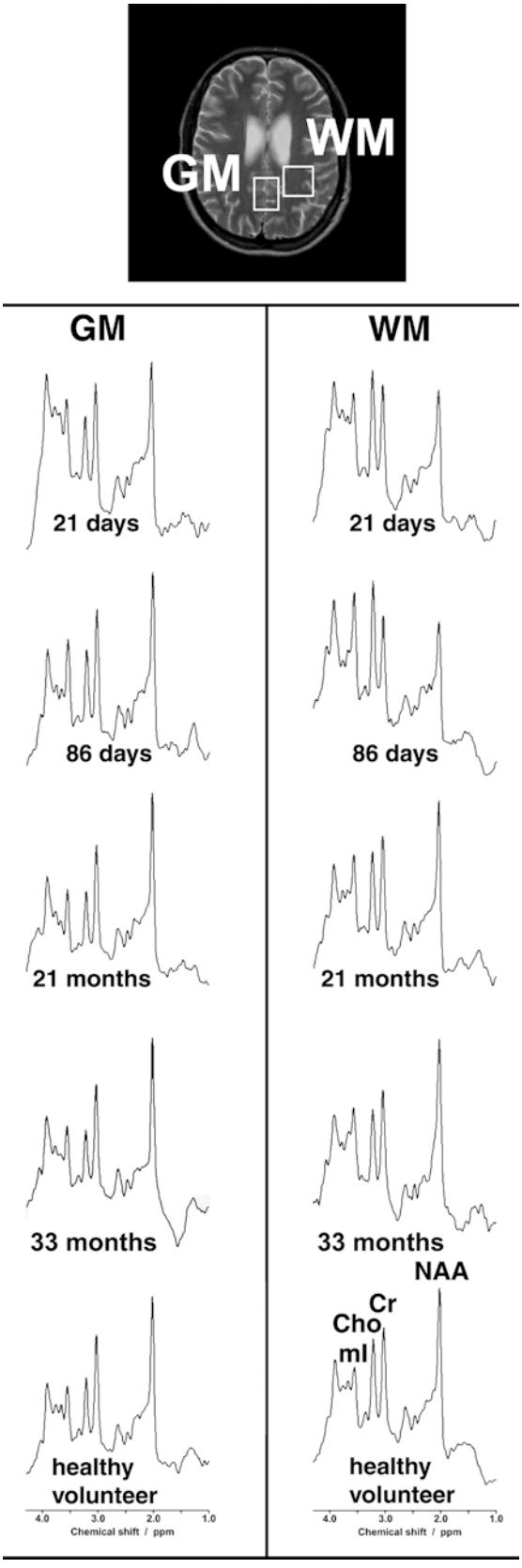

Fig. 2 Evidence of axonal recovery: MR spectra from occipitoparietal white matter (*WM*) and midoccipital grey matter (*GM*) in the patient 21 and 86 days and 21 and 33 months after the injury, and in a normal healthy adult. The voxel positions are shown on the localiser image at 21 months. MRS at 21 and 86 days post trauma was in agreement with MRI, showing evidence of diffuse axonal injury, with decreased N-acetylaspartate (*NAA*) and increased total choline (*Cho*). By 21 months NAA in white matter was normal, while myo-inositol (*mI*) was still slightly increased; at 33 months the spectra were similar. Total creatine (*Cr*) was normal on all studies

reduction in NAA and a 57% (+4.9 SD) increase in Cho. MRS in grey matter was near normal, the only abnormality being a 19% (−2.8 SD) reduction in NAA. At 21 months MRS was normal except for a 35% (+3.0 SD) increase in myo-inositol in white matter. The white matter concentration of the neuronal and axonal marker NAA had increased by 54% from its level on day 86, and was now within the normal range (11%, 1.7 SD below normal). MRS at 33 months was similar to that at 21 months, although NAA had risen further to 7% (1 SD) *above* the normal value. MRI was unchanged at 21 and 33 months except that at 33 months the ventricular volume showed a mild increase: normalised to day 21 the volume was 1.2 at 3 and 21 months and 1.3 on the last study.

Discussion

MRS on days 21 and 86, when the patient was still in coma, showed sparing of cortical grey matter, a positive prognostic sign. The optimistic prognosis was, however, counterbalanced by the severity of the white-matter abnormalities. This MRS mismatch between white and grey matter is not only rare; it provides a possible explanation of the patient's recovery mechanism. The axons of viable but damaged neurones in cortical grey matter have a capacity for regrowth into existing or only partially damaged myelin sheaths. NAA is synthesised in their cell bodies and transported slowly along the axons. The synthesis rate in neurones and axonal transport, rather than the rate of axonal regrowth, may, therefore, govern the rate of NAA reaccumulation in the white matter.

Late normalisation of MRS after severe traumatic brain injury is not in itself evidence of axonal recovery. Pseudonormalisation due to atrophy could in theory explain apparent recovery, but this is unlikely given our measurements of ventricular volume, indicating no further atrophy at 21 months compared with 86 days.

Recovery of NAA levels has been reported in focal lesions, mainly in white matter, e.g., herpes simplex encephalitis [12] and mitochondrial encephalopathy with lactic acidosis and stroke-like episodes [13]. If it is assumed that the MRS reflects global white-matter changes, axonal recovery could also be widespread. This assumption is supported by the fact that the white-matter regions appeared similar on MRI. Relatively good recovery after months in coma is seen occasionally, and global axonal recovery could be part of the explanation. MRS shows changes compatible with that, as in the third and fourth examinations of our patient; MRI did not show any evidence of recovery. It may also be the case that the near-normal MRS in grey matter predicted the awakening from coma, despite the evidence in white matter of severe axonal injury initially shown on both MRS and MRI.

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References

1. Evans SJJ, Gean AD (1999) Craniocerebral trauma. In: Stark DD, Bradley WG Jr (eds) Magnetic resonance imaging, 3rd edn. Mosby, St Louis, pp 1347–1360
2. Ross BD, Ernst T, Kreis R, et al (1998) 1H MRS in acute traumatic brain injury. JMRI 8: 829–840
3. Garnett MR, Blamire AM, Corkill RG, Cadoux-Hudson TAD, Rajagopalan B, Styles P (2000) Early proton magnetic resonance spectroscopy in normal-appearing brain correlates with outcome in patients following traumatic brain injury. Brain 123: 2046–2056
4. Ricci R, Barbarella G, Musi P, Boldrini P, Trevisan C, Basaglia N (1997) Localised proton MR spectroscopy of brain metabolism changes in vegetative patients. Neuroradiology 39: 313–319
5. Choe BY, Suh TS, Choi KH, Shinn KS, Park CK, Kang JK (1995) Neuronal dysfunction in patients with closed head injury evaluated by in vivo 1H magnetic resonance spectroscopy. Invest Radiol 30: 502–506
6. Friedman SD, Brooks WM, Jung RE, et al (1999) Quantitative proton MRS predicts outcome after traumatic brain injury. Neurology 22: 1384–1391
7. Brooks WM, Stidley CA, Petropoulos H, et al (2000) Metabolic and cognitive response to human traumatic brain injury: a quantitative proton magnetic resonance study. J Neurotrauma 17: 629–640
8. Sinson G, Bagley LJ, Cecil KM, et al (2001) Magnetization transfer imaging and proton MR spectroscopy in the evaluation of axonal injury: correlation with clinical outcome after traumatic brain injury. AJNR 22: 143–151
9. Cecil KM, Hills EC, Sandel ME, et al (1998) Proton magnetic resonance spectroscopy for detection of axonal injury in the splenium of the corpus callosum of brain-injured patients. J Neurosurg 88: 795–801
10. Christiansen P, Larsson HBW, Thomsen C, Wieslander SB, Henriksen O (1994) Age dependent white matter lesions and brain volume changes in healthy volunteers. Acta Radiol 35: 117–122
11. Michaelis T, Merboldt KD, Bruhn H, Hanicke W, Frahm J (1993) Absolute concentrations of metabolites in the adult human brain in vivo: quantification of localized proton MR spectra. Radiology 187: 219–227
12. Takanashi, J, Sugita, K, Ishii, M, Aoyagi, M, Niimi, H (1997) Longitudinal MR imaging and proton MR spectroscopy in herpes simplex encephalitis, J Neurol Sci 149: 99–102
13. Stefano, ND Matthews, PM, Arnold, DL(1995) Reversible decreases in N-acetylaspartate after acute brain injury, Magn Reson Med 34:721–727