

Spinal cord 1H-MR spectroscopy in patients after brachial plexus root re-implantation

E. De Vita^{1,2}, C. Kachramanoglou¹, C. A. Wheeler-Kingshott³, D. L. Thomas¹, D. Choi¹, A. Thompson¹, and O. Ciccarelli¹

¹Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, London, United Kingdom, ²Lysholm Department of Radiology, National Hospital for Neurology and Neurosurgery, London, United Kingdom, ³Department of Neuroinflammation, UCL Institute of Neurology, London, United Kingdom

Introduction

Brachial plexus avulsion is a devastating injury that occurs most commonly in young adults after motorcycle accidents and leads to a disabling condition characterised by severe motor and sensory dysfunction and pain in the corresponding arm. A complete brachial plexus avulsion injury involves roots between C5 and T1. Re-implantation of avulsed spinal roots is an effective surgical technique¹ that leads to improved motor recovery. The spinal cord of treated patients appears normal on conventional spinal cord imaging, but this injury occurs at the junction of the nerve roots and the spinal cord, and secondary pathological changes occur in the spinal cord, including neuronal death². We aimed to assess whether ¹H-MR spectroscopy (MRS) of the upper cervical cord (i.e., above the site of injury) detects pathological changes in patients with brachial plexus root avulsion who have received re-implantation, when compared with healthy subjects. In patients, the relationship between metabolite concentrations and clinical disability was explored.

Methods

Nineteen healthy subjects and 10 patients treated with re-implantation of avulsed spinal roots were recruited. MR data were acquired on a Siemens 3T Tim Trio with the posterior part of an 8-channel Head coil, standard neck and upper-most spine coils. MRS was acquired with a single-voxel cardiac gated PRESS sequence (TE30ms, TR3s, 160 averages) with CHESS water suppression. A non water-suppressed spectrum (2 averages) was also acquired for eddy-current correction. The MRS voxel (mean volume 2.4ml, SD0.6ml) was placed along the main axis of the cord between C1 and C3 on T2-weighted sagittal images (Fig.1) with its prescription boundaries completely contained within the cord. Optimal shim currents were calculated off-line with in-house software based on: i) acquisition of field maps (2mm isotropic resolution, 1min. acquisition time); ii) minimisation of the magnetic field variation within the prescribed MRS voxel³. Data from two healthy controls and one patient were not used because of incorrect data acquisition. Spectral analysis was performed using LCModel 6.1⁴, and ratios of estimated metabolite concentrations calculated with respect to total Creatine concentration ([Cr]: Creatine plus Phosphocreatine) for N-acetyl-aspartate ([NAA]: NAA plus NAAG), total Choline ([Cho]: GPC plus Phosphocholine) and myo-Inositol ([Ins]). LCModel standard error estimates (%SD, Cramer-Rao lower bounds) were used to assess the confidence of the concentration estimates. Spectra for three controls and one patient with %SD of [Cr] >20% were excluded. Thus, the final MRS data came from 14 healthy controls (mean age: 36.1 yrs. (SD10.7), 13 men), and 8 patients (mean age: 35 yrs. (SD10.8), all men, time from injury 5.8 yrs. (SD 4.3)). [Ins]/[Cr] ratio was excluded from the analysis in three controls and one patient because of %SD of [Ins] >20%; additionally, [Naa]/[Cr] was excluded in three different controls and two patients because of %SD for [NAA] >20%. Differences in metabolite ratios between groups were estimated using the two-sample T test. Patient disability was assessed using neurological scales (DASH (disability for arm, shoulder and hand), VAS (visual analogue pain scale), EQ5D (health and quality of life), MRC muscle strength scale for the upper limb). Correlations between clinical scores and metabolite ratios were tested using the Pearson's correlation coefficient.

Results

The mean linewidth (LCModel estimate) over the 22 spectra analysed was 14 (SD3) Hz. Two typical post-processed spectra are shown in Fig. 1. Patients showed a greater [Ins]/[Cr] ratio than healthy controls (p=0.013)(Table 1). [NAA]/[Cr] and [Cho]/[Cr] did not significantly differ between groups (Table 1). In patients, there was a trend toward a significant correlation between a greater [Ins]/[Cr] and greater motor disability (or lower MRC score for the affected upper limb) (r -0.65, p=0.057). In addition, in patients, a lower [NAA]/[Cr] ratio correlated, although not significantly, with higher number of years from injury (r -0.71, p=0.056) and a lower [Cho]/[Cr] ratio correlated with greater motor disability (r 0.7, p=0.026).

Discussion

Our findings suggest that MRS of the upper cervical cord (above the site of injury) allows quantification of metabolites that provide insights into the underlying pathological processes in this unique group of patients. Patients showed a greater [Ins]/[Cr] ratio when compared with controls, which was associated, albeit weakly, with motor impairment in the upper limb. This suggests that reactive gliosis, including proliferation and astrocytic hypertrophy, may occur in the spinal cord above the site of injury, perhaps in response to the Wallerian degeneration of avulsed neuronal fibres. This process appears to be associated with greater motor disability. Although [NAA]/[Cr] and [Cho]/[Cr] ratios did not significantly differ between groups, they showed interesting associations with patient neurological status. In particular, axonal loss and dysfunction, as reflected by NAA, appeared to increase with time from injury, while inflammation with membrane turnover, as reflected by Cho, was lower in patients with greater motor impairment. Future work will increase the number of patients studied and will include also patients with brachial plexus avulsion who did not undergo re-implantation, in order to understand whether this technique is sensitive to microscopic changes specific to re-implantation. This information is important for the forthcoming clinical trials with stem cell transplantation in patients with brachial plexus avulsion injury¹.

Acknowledgments: Dr Evelyne Baeteau (Cyclotron Research Centre, Liège University, Belgium). This work is supported by the Department of Health's NIHR Biomedical Research Centres funding scheme. **References:** [1]Kachramanoglou C. *Br J Neurosurg.* 2010. [2]Scholz J. J. *Neurosci.* 2005. [3]Kim DH. *Magn Reson Med* 2002. [4]Provencher. *Magn Reson Med* 1993.

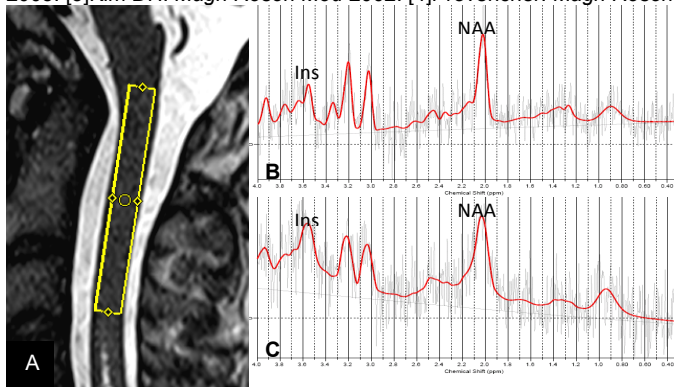


Table 1: Metabolite ratios in patients and controls

	Patients	Controls
NAA/Cr mean (SD)	1.21 (0.38)	1.19 (0.29)
Ins/Cr	1.86 (0.41)	1.31 (0.32)*
Cho/Cr	0.33 (0.11)	0.30 (0.08)

* Significantly different from patients p<0.013 (Two-sample T test)

Fig.1 (A): Location of the spectroscopic voxel between C1 and C3 on the T2-w sagittal image of one control. **(B):** Spectrum derived from voxel in (A) that shows reduced [Ins]/[Cr] ratio (1.37 (%SD 11)) in comparison with a spectrum obtained in a patient (2.11 (%SD 10)) **(C).**