Serial MR spectroscopic imaging of NAA and Lactate levels after ischaemic stroke

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Introduction: Metabolic changes in tissue affected by acute ischaemic stroke comprise reduction in N acetyl aspartate (NAA) and presence of Lactate (Lac), which indicate loss of neuronal viability and a switch from oxidative metabolism to anaerobic glycolysis [1]. Following the levels of these metabolites over time might provide further information about tissue damage in ischaemic stroke. We performed MR spectroscopic imaging (MRSI) at 5 fixed time points in the same patients over 3 months using a novel tissue classification based in appearance of diffusion-weighted MR images (DWI).

Methods: Patients with ischaemic stroke underwent MRSI and diffusion tensor imaging at < 24 hours, 5 and 14 days and 1 and 3 months after onset. The MRSI volume of interest was centred on the slice showing the maximum extent of the stroke lesion on initial DWI. The MRS acquisition parameters were: TE/TR 145/1000 ms, FOV 320 mm, slice thickness 10 mm, acquisition matrix 24×24 (interpolated to 32×32), yielding 10 mm^3 voxels (*Figure 1a*). Automatic shimming and water suppression were applied. A 5-mm voxel size grid was superimposed on the same DWI slice. Each voxel was coded as 'definitely abnormal' (DAL), 'possibly abnormal' (PAL), 'ipsilateral normal' (INL) or 'contralateral normal' (CNL) on the DWI appearance (*Figure 1b*). This grid was superimposed over the MRSI grid and metabolites extracted from the DAL, PAL, INL and CNL areas. DWI at later time points were registered to the first time point and registration parameters used to find the MRSI voxels at later time points spatially equivalent to those in the initial scan. The concentrations of brain metabolites for each tissue type could therefore be followed over time. Using paired Student's t-tests we compared the area under the concentration-time curve (AUC) for each metabolite to examine differences in evolution in each tissue type.

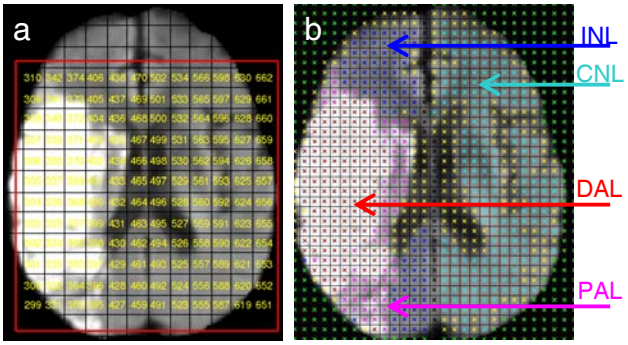

Figure1

Results: 51 patients with acute ischaemic stroke were recruited for the study, with 30 patients scanned up to 1 month and 21 patients up to 3 months after onset. *Figure 2* shows the temporal evolution of mean NAA and Lac levels in arbitrary units (a.u.) for each tissue type. NAA gradually fell up to 2 weeks in DAL, PAL and INL, with some recovery thereafter but still remained lower than CNL even at 3 months. AUC showed that NAA was significantly lower in DAL compared with PAL up to 1 month ($p=0.044$) but not up to 3 months ($p=0.23$) showing some recovery of DAL. NAA was significantly lower in DAL and PAL, compared with CNL, up to 3 months ($p<0.001$). Lac was high initially in DAL and PAL but then dropped sharply by 2 weeks with some Lac still present at 1 month. AUC showed that Lac was significantly higher in DAL and PAL compared with CNL up to 1 month, ($p=0.028$ and $p=0.020$). However, AUC did not show significant differences in Lac levels between DAL and PAL. Lac gradually fell to baseline levels by 3 months in DAL, but in PAL tissue lactate remained modestly elevated at 3 months.

Conclusion: This work shows that the degree of abnormality visible on initial DWI reflects the severity of underlying tissue damage since DAL tissue, i.e. that which appears 'whiter' on baseline DWI has significantly lower NAA compared with PAL tissue. The permanent neuronal loss as marked by NAA accumulates over the first 2 weeks and is still larger in DAL than PAL at 1 month; however, NAA levels in both tissue types are similar at 3 months. Lac probably represents the initial severity of ischaemic damage. Presence of some Lac at 1 and 3 months in PAL suggests ongoing oligaemia or tissue repair. More studies are required to determine whether later interventions might reduce tissue damage and improve outcome.

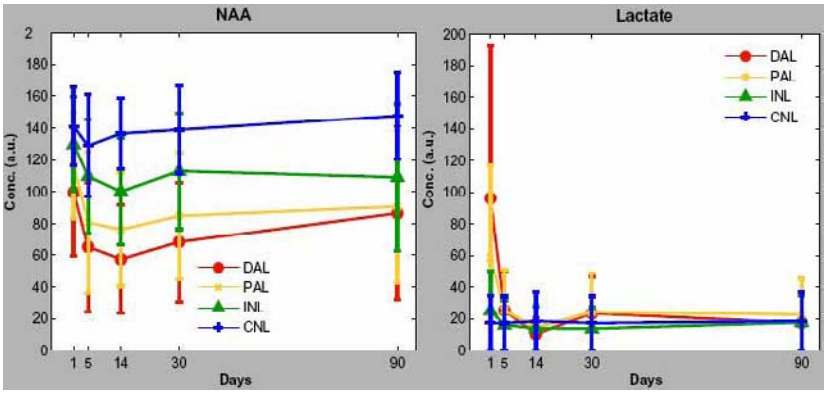

Figure2

[1] Parsons *et al.* Neurology 2000;55:498-506.