Characterisation of the Nature of Ischaemic Damage in Leukoaraiosis With Diffusion Tensor Imaging

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INTRODUCTION

Leukoaraiosis is the radiological term given to the rarefaction of white matter (WM) in periventricular regions seen on CT, which manifests as hyperintensity on T_2 weighted MR images. Clinical features are recurrent strokes and subcortical dementia. There is limited histological knowledge of the underlying pathology, particularly in the early stages of the disease, but post mortem studies usually reveal a reduction in myelin content, axonal loss and gliosis often accompanied by discrete lacunar infarction[1]. We hypothesised that this would result in reduced anisotropy and increased trace on diffusion tensor imaging and that the relationship between the trace and anisotropy may help to characterise the nature of the ischaemic change.

METHODS

We studied nine patients (mean age = 61.8 yrs, range: 44 to 74 yrs) presenting to a specialised cerebrovascular neurology clinic with recurrent strokes and leukoaraiosis demonstrated on CT or routine MR scans. Six had hypertension and six had evidence of mild cognitive impairment. In addition, we studied 11 age matched controls (mean age 66.3 yrs, range: 53 to 77 yrs). Diffusion tensor data were acquired using a diffusion-weighted spin-echo EPI sequence (TE = 130 ms; matrix = 256x128; max. b-value = 613.7s mm^{-2}, and trace and fractional anisotropy images computed in the manner previously reported[2]. Regions of interest (ROIs) were placed in the frontal and posterior WM adjacent to the horns of the lateral ventricles on the T_2-weighted image and mean trace and fractional anisotropy[3] (FA) values within these regions were recorded. We plotted trace against fractional anisotropy for all ROIs (controls and patients) and also included data from mature infarcts and a water phantom for comparison.

RESULTS

The tables below show mean and standard deviations of trace and FA measures in patients and controls, together with the p-value for the difference between patient and control groups in each ROI.

Mean and Standard Deviation of (Trace/3) Measurements

	R . Anterior	R. Posterior	L. Anterior	L. Posterior
Patient	1.118 (.330)	1.132 (.143)	1.133(.265)	1.165 (.300)
Control	0.749 (.110)	0.787 (.065)	0.822(.106)	0.823 (.069)
P-value	0.001	< 0.001	0.003	0.003

Mean and Standard Deviation of FA Measurements

	R. Anterior	R. Posterior	L. Anterior	L Posterior
Patient	0.525 (.105)	0.496 (.102)	0.548(.151)	0.507 (.137)
Control	0.778 (.093)	0.733 (.056)	0.745(.120)	0.702 (.056)
P-value	< 0.001	< 0.001	0.006	0.001

In patients with ischaemic leukoaraiosis, the fractional anisotropy is significantly lower and the trace significantly higher than in normal age-matched subjects. We found no significant difference between mean trace or FA values in anterior versus posterior or left versus right white matter regions in either patients or controls and therefore included all points in a plot of trace versus FA (Fig 1). This reveals a strong correlation between trace and anisotropy (r = -0.897). To our knowledge, this is the first time that a relationship between loss of anisotropy and increase in the trace has been demonstrated.

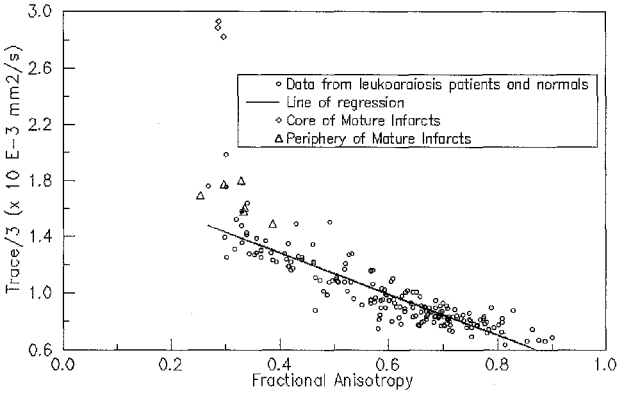

Figure 1 - Trace *vs* Fractional Anisotropy in all Subjects (see text)

The data are consistent with pathological findings of reduced myelin and axonal loss[1]. Data is also included from the core and periphery of mature infarcts and it is interesting to note their positions on the plot. In mature infarcts, the trace is substantially higher than in leukoariaosis (approaching that of free water at body temperature) when compared to regions of leukoaraiosis with the same fractional anisotropy. This is consistent with the proliferation of glial cells known to occur in leukoaraiosis[1] (i.e. the space due to axonal loss is filled by amorphous glial cells which hinder diffusion but without any preferred direction). This is further supported by measurements at the periphery of mature infarcts (presumably gliotic) which are comparable to those in leukoariosis (Figure 1).

The minimum observed fractional anisotropy is in the region of 0.3. We believe this reflects a systematic bias in our data due to noise[3]. This was confirmed by our measurements in a water phantom, where anisotropy is zero, but measured to be 0.3. However, this should not significantly affect either the patient and control comparisons or the observed relationship between trace and anisotropy, since the error in FA is common to all measurements.

CONCLUSIONS

Tissue exhibiting ischaemic leukoariaosis has a significantly higher rate of diffusion and lower anisotropy compared to healthy tissue. In this condition, we have shown that these two parameters are strongly correlated and suggest that this is consistent with the underlying tissue pathology. It would be informative to follow the progress of these patients over time to see whether their deterioration follows the pattern found here.

References:

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3. Pierpaoli C, Basser PJ *Magn. Reson. Med.* 36: 893,1996.

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