Resting cerebral perfusion correlates with functional recovery in stroke patients

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Introduction: Restorative cell-based and pharmacological therapies show significant promise for improving functional outcome following stroke[1], but the current lack of robust biomarkers to monitor the effects of such interventions in humans limits their translation into patient care[2]. Recent research suggests that brain perfusion may represent a sensitive marker for vascular remodelling, with the potential to predict recovery [3-5]. The purpose of this study was to examine perfusion changes in recovering stroke patients, and to correlate these changes with functional outcome.

Methods: Six patients (age 53±10 y) with a non-lacunar ischemic stroke in the left middle cerebral artery territory resulting in motor impairment underwent MRI at 3 and 15 weeks after stroke onset (figure 1). Whole-brain resting perfusion was measured with a 3D pulsed continuous ASL sequence[6] using a 3.0 T GE TwinSpeed HDx MRI scanner. The motor function of the right arm was assessed with the Fugl-Meyer (FM) scale at both visits. Seven healthy controls (age 53±7 y) were also recruited. Perfusion images for all participants were normalised into standard space and smoothed with an 8 mm Gaussian smoothing kernel. Differences in perfusion between patients and controls were tested by fitting an analysis of covariance model at each intracerebral voxel, and correlations between perfusion and FM score was tested by fitting a multiple linear regression model to the perfusion values at each voxel[7-8] Age and gender were included as covariates for all analyses, and statistical comparisons were performed by permutation testing.

Results: At baseline, patients demonstrated a significantly lower perfusion in the left MCA territory and surrounding areas, with crossed cerebellar diaschisis (Figure 2). Between the 2 visits, resting perfusion in the patients significantly increased in the structurally intact contralesional sensorimotor area and the ipsilesional cerebellum, the anterior cingulate and cuneus (Figure 3). Higher perfusion in the ipsilesional thalamus, insula, medial temporal lobe, paracentral lobule and precuneus at baseline was associated with a higher FM score at 15 weeks (Figure 4). (Images are shown in radiological orientation.)

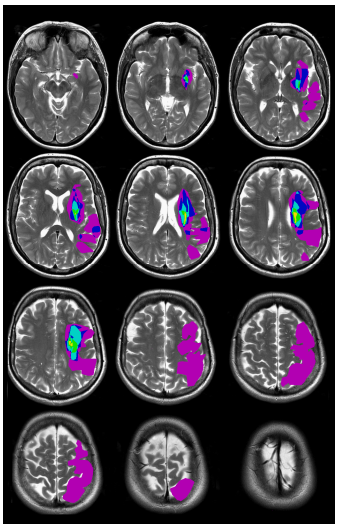

Figure 1. Lesion overlap maps for the 6 stroke patients, measured 15 weeks after stroke onset. (Images are shown in radiological orientation).

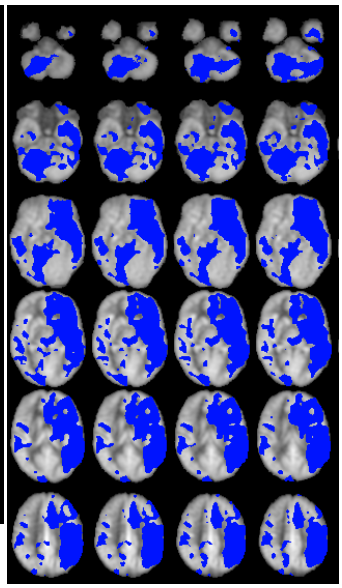

Figure 2 Significant clusters from the group comparison between patients and controls: patients show decreased perfusion in the left MCA territory and contralateral cerebellum (crossed-cerebellar diaschisis).

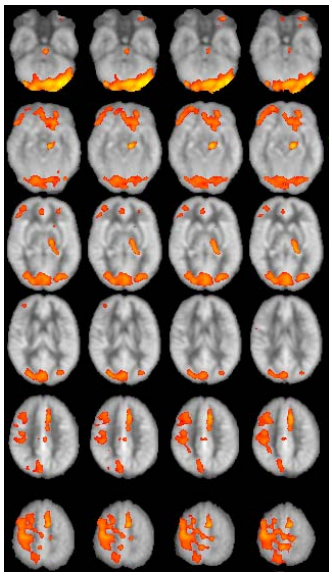

Figure 3 Significant clusters from the comparison between patients at 3 and 15 weeks after stroke onset. Red clusters denote regions where the perfusion increases between the baseline and follow-up scans.

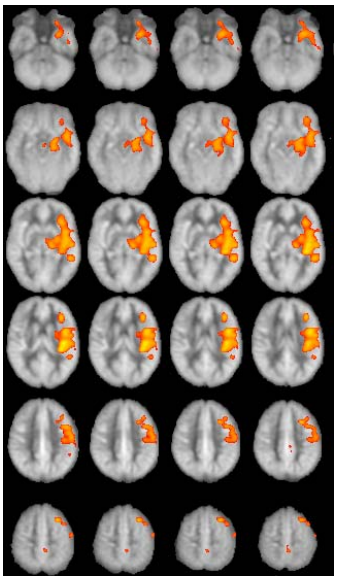

Figure 4. Correlations between perfusion and motor outcome: red clusters denote regions showing a positive correlation between baseline perfusion and FM score at 15 weeks.

Discussion: Resting perfusion measured with ASL provides an easily obtainable novel imaging biomarker for stroke recovery. The change in resting cerebral perfusion seen during stroke recovery may also have implications for the interpretation of fMRI findings.

References: [1]Zhang and Chopp, Lancet Neurol 8:491-500 (2009), [2]Hachinski et al., Stroke 41:1084-99 (2010), [3]Ding et al., J Cereb Blood Flow Metab 28:1440-8 (2008), [4]Lin et al., Stroke 33:2985-91(2002), [5]Honmou et al., Brain 134:1790-807 (2011), [6]Dai et al., Magn Reson Mod 60:1488-97 (2008), [7]Suckling & Bullmore, Human brain mapping 22, 193-205 (2004), [8]Chamberlain et al., Biol Psychiatry 65, 550-555 (2009)