Exogenous perfusion imaging in cortical developmental malformations

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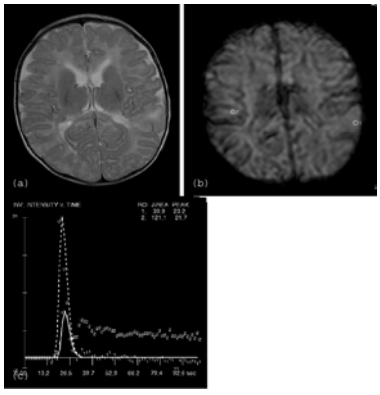
Introduction: Cortical developmental malformations are complex abnormalities that result from interruption of normal cellular proliferation, migration and organisation. Such malformations can be classified into four broad categories (1), those resulting from: (i) abnormal cellular proliferation or apoptosis (eg. cortical tubers in tuberous sclerosis complex (TSC)); (ii) abnormal migration (eg. heterotopia or pachygyria); (iii) late neuronal migration and cortical organisation (eg polymicrogyria and schizencephaly) and (iv) those otherwise not classified. This classification scheme suggests that cortical tubers develop at an earlier stage compared to polymicrogyria. We hypothesised that different timings associated with cortical malformation development lead to differences in parenchymal blood supply and hence different perfusion characteristics between cortical tubers and polymicrogyria. This study compared the perfusion characteristics of these two developmental abnormalities.

Methods: A total of 41 subjects participated, split into three groups: (i) thirteen patients with confirmed clinical diagnosis of TSC (mean age=11yrs, range=4 months-30yrs); (ii) 10 patients with polymicrogyria (mean age=6yrs, range=1-16yrs) and (iii) eighteen patients with developmental delay but with normal structural imaging who acted as surrogate disease controls (mean age=4yrs, range=9months-8yrs). All MR imaging and perfusion data were acquired at 1.5T (Infinion, Philips Medical Systems, Cleveland, Ohio). Standard imaging was performed (T2-weighted fast-spin-echo, FLAIR and T1-weighted, pre- and post- gadolinium-based contrast). Cerebral perfusion was assessed using an exogenous contrast-based method. A dynamic, single-shot, T2*-weighted EPI technique (TE=60ms; TR=1400ms) was used to obtain 100 time-points. Normal saline (10ml) was drawn into a 20ml syringe, followed by 0.1ml/kg of Gd-DTPA (Magnetvist, Schering AG, Berlin, Germany), such that the contrast lay at the lower end of the syringe. Contrast was injected intravenously by hand as a rapid bolus at the 10th dynamic, followed by a bolus injection of 10ml normal saline. Post-acquisition processing was performed via the manufacturer's software, as described previously (2). In summary, the signal time course from a prescribed region-of-interest (ROI) was inverted following baseline subtraction (pre-contrast steady-state signal) and a gamma-variate was fitted to the initial peak corresponding to the 1st-pass of the contrast bolus. Two outcome measures were used: first-moment mean transit time (TTfm) and regional cerebral blood volume (rCBV). Ratios of rCBV and differences in TTfm (right/left hemispheres for controls and lesion/contralateral region for localised abnormalities on imaging) were used for statistical comparisons. Hemispheric symmetry in TTfm and rCBV was assessed using the t-test. rCBV ratios and TTfm differences were compared across groups via analysis of variance.

Results:
Controls – No interhemispheric asymmetry was present in TTfm or rCBV (P>0.05).
Tubers - the rCBV ratio was significantly lower than in controls (P<0.01). No significant differences were found in relative transit times between tubers and controls (P>0.05). The size of the tubers on imaging did not correlate with rCBV ratio (Pearson correlation coef=0.11, P=0.43).
Polymicrogyria – No significant differences were found from the control group (P>0.05).

Discussion:
It must be noted that the methodology used in this study has certain limitations: (i) a normal control group could not be studied due to ethical considerations and (ii) the techniques employed can only be used to obtain measures on TTfm and rCBV relative to 'normal appearing' contralateral parenchyma and this assumption may not necessarily be valid (absolute perfusion measures are not forthcoming). Our initial supposition that there is reduced perfusion in cortical tubers compared to polymicrogyria has been validated in terms of rCBV ratio, on a group-basis. On histopathology, cortical tubers are known to have avascular features (3) and this may account for this study's findings.

1) 

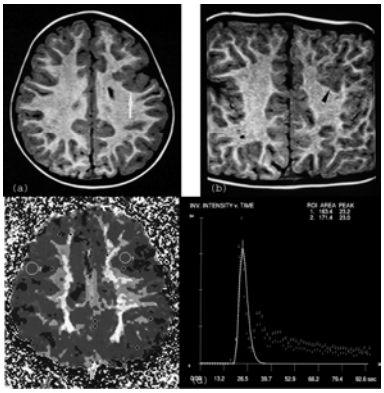
2) 

Figure 1, Axial T2-weigthed image depicting a left temporal lobe tuber, perfusion map and data showing lower lesion rCBV compared to contralateral parenchyma. Figure 2) Axial T2-weighted and curvilinear reconstructed T1-weighted images of a focal area of polymicrogyria with perfusion map and trace indicating equivalent perfusion characteristics in lesion and contralateral parenchyma.

References:
1. Barkovich AJ et al Classification system for malformations of cortical development. Neurology 2001; 57:2168-2178.
2. Wilkinson ID et al Short-term changes in cerebral microhemosynamics after carotid stenting. AJNR 2003; 24:1505-1507.
3. Nixon JR et al. Cerebral tuberous sclerosis: postmortem MRI and pathologic anatomy. Mayo Clin Proc 1989; 64:305-311.