Arterial spin labelling characterization of cerebral perfusion during normal maturation from late childhood into adulthood: normal 'reference range' values

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Target audience Clinicians, physicists.

Purpose The transition from childhood, through adolescence and into adulthood, marks a period of structural and functional change in the normal development of the human brain. [1] We used non-invasive arterial spin labelling (ASL) MRI to investigate changes in cerebral haemodynamics during normal development between 8-32 years of age. Over this range, age-dependent mean and reference range values were calculated for: longitudinal relaxation time (T_1) and equilibrium longitudinal magnetization (M_0) (both needed for accurate perfusion quantification with ASL), cerebral blood flow (CBF), bolus arrival time (BAT), and bolus duration (T). These data should provide a useful tool for both optimizing ASL acquisitions made at a single inflow time (TI), and investigating age-matched haemodynamic abnormalities in patients.

Methods 27 healthy subjects (8-32 years, mean 19 years) were imaged using a 1.5 T Siemens Magnetom Avanto scanner. ASL data were acquired at 6 TIs (0.2-2.2s in 0.4s intervals), using a flow-sensitive alternating inversion recovery (FAIR) pulsed-ASL sequence, with 3D single shot GRASE data acquisition and background suppression.[2] A series of inversion recovery acquisitions (TI=0.2,0.6,1.4,2.4s) with identical readout to the ASL acquisition were also performed for quantification of T_1 and M_0. Prior to processing, the cortical grey matter (GM) in the ASL and T_1-mapping images was segmented into major vascular territories of the anterior, middle and posterior cerebral arteries (ACA, MCA and PCA respectively).[3] Within each subject, regional values of T_1 and M_0 were then calculated using the inversion recovery data. Following this, the mean ASL difference signal (dM) in each region was fit to a general kinetic model [4], to provide fitted values of BAT, CBF and T. Data from all subjects were used to calculate correlations with age and reference range regions [5], using a 95% confidence interval.

Results Cortical GM T_1 showed a highly significant negative correlation with age in all vascular territories ($p<0.001$). The same was true for M_0 in all regions in the male subjects, and the ACA and MCA territories in female subjects; however, in the latter, no significant correlation with age was seen in the PCA territory ($p=0.20$). The peak raw ASL signal (dM_{max}) demonstrated the same pattern. CBF was negatively correlated with age in all regions ($p<0.01$, see Fig 1). T showed a positive correlation with age in the ACA ($p<0.05$) and PCA territory ($p<0.001$), but no correlation in the MCA territory. No significant correlation between BAT and age was observed in any region.

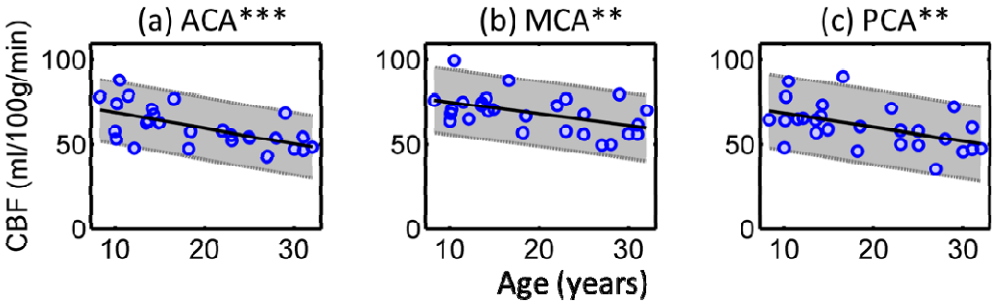

Figure 1 CBF vs age across all subjects, in the cortical GM territories of the anterior (a), middle (b), and posterior (c) cerebral arteries. Circles represent individual subjects, with the correlation shown as a solid line and the normal reference range in grey. ***p<0.001, **p<0.01.

Discussion The negative correlation between CBF and age throughout the GM illustrates the dynamic physiological changes which occur in normal development during this age range, and the importance of making age-matched comparisons when evaluating CBF in patients. The disparity between the development of M_0 and dM_{max} in males and females in the PCA territory over this age range may be driven by the known gender differences in the rate of cortical thinning that occur during adolescence, which varies by location throughout the brain.[6] The positive correlation between T and age (particularly evident in the PCA territory) suggest an increased rate of bolus dispersion with age in these regions, perhaps driven by a decrease in blood flow velocities, or increasing tortuosity of blood vessels with age.

Conclusion As the majority of clinical ASL studies are currently performed using a single TI, the data presented here should be of use when designing an optimized protocol for measuring CBF in children and young adults. Furthermore, the reference range values presented here should provide age-matched normal values in future clinical studies to investigate pathologies which lead to abnormal cerebral haemodynamics.

References 1 Gogtay N et al. *Proc Natl Acad Sci U S A* 2004; 101: 8174–9. 2 Günther M et al. *MRM* 2005; 54: 491–8. 3 Tatu L et al. *Neurology* 1998; 50: 1699–708. 4 Buxton RB et al. *MRM* 1998; 40: 383–96. 5 Royston P. *Stat Med* 1991; 10: 675–90. 6 Raznahan A et al. *Proc Natl Acad Sci* 2010; 107: 16988–93.