DEVELOPMENTAL TRAJECTORIES OF GLOBAL OEF, CBF, CMRO2 USING SUSCEPTIBILITY-BASED OXIMETRY, PHASE CONTRAST MRI AND ASL

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TARGET AUDIENCE: Pediatrician, Developmental neuroscientist and psychologist, MRI scientist

PURPOSE: Global values of oxygen extraction fraction (OEF), cerebral blood flow (CBF) and cerebral metabolic rate of oxygen ($CMRO_2$) can serve as important surrogate markers for brain function. To date, however, scarce research has examined these parameters in typically developing children due to the invasive nature of existing techniques such as jugular venous oximetry and Positron Emission Tomography (PET). Recently, noninvasive and quantitative MRI methods for in vivo measurements of global OEF, CBF and $CMRO_2$ have been developed (1). The present study seeks to explore the developmental trajectories of OEF, CBF and $CMRO_2$ by applying these novel MRI methods in typically developing children and adolescents aged 7 to 17 years.

METHODS: MRI data was collected on 47 (23M/24F) participants 7-17 years of age on a Siemens 3T TIM Trio scanner. Phase-contrast (PC)-MRI (VENC = 80cm/sec; TE/TR=5.23/18ms; FOV=200x200mm^2; matrix=192x192; Slice Thickness=5mm) was acquired at the level of the mouth orifice (between C1 and C2 vertebrae) to quantify mean flow velocities in internal carotid and vertebral arteries. Total cerebral blood flow volume (CBFV) was calculated as the product of flow velocities and cross-sectional areas of the major arteries, and CBF by dividing CBFV with the brain volume estimated from T1 weighted structural MRI after skull striping in each individual subject. Susceptibility based MRI blood oximetry was acquired using a magnetic field mapping sequence (TE_1=5.18ms; TE_2=7.64ms; TR=100ms; FOV=200x200mm^2; matrix=192x192; Slice Thickness=5mm) applied at an axial plane perpendicular to the Superior Sagittal Sinus (SSS)(1). SvO2 (venous oxygen saturation fraction) was estimated by $SvO2 = 1 - (2|\Delta\phi| / [\gamma \Delta\chi_{do} B_0 (\cos^2\theta - 1/3) Hct])$ where $\Delta\phi$ is the phase difference between the venous blood in SSS and surrounding tissue, *Hct* is hematocrit, θ is the angle between vessel and *B*o, $\Delta\chi$do=4π·0.27 p.p.m. The arterial oxygen saturation fraction was assumed to be 98%. $CMRO_2$ was then calculated using quantified CBF and OEF, according to Fick's principle. Potential developmental changes of Hct across age were taken into account. All post-processing was done using MATLAB R2011a. Pearson correlation coefficients were calculated between all three parameters and age in male, female and the whole group of subjects. In addition, a pseudo-continuous ASL (pCASL) sequence with 2D EPI readout (TR/TE=4s/11ms, FOV=22cm, matrix=64x64, 24x5mm slices with 1mm gap, postlabeling delay=1.2s, labeling duration=1.5s) was applied to map regional CBF in the same developing cohort. Global CBF values estimated using PC-MRI and pCASL were correlated.

RESULTS: Global OEF estimated by MRI blood oximetry did not show significant variation with age (Fig. 1A). Global CBF estimated using PC MRI decreased with age (R = -0.61, p = 4.6E-6, Fig. 1B), which was also positively correlated with global CBF estimated using pCASL (R = 0.64, p = 1.4E-6, Fig. 1C). As a result, global $CMRO_2$ decreased with age (R = -0.52, p = 1.8E-4, Fig. 1D). The above developmental trends were similarly observed for male and female children.

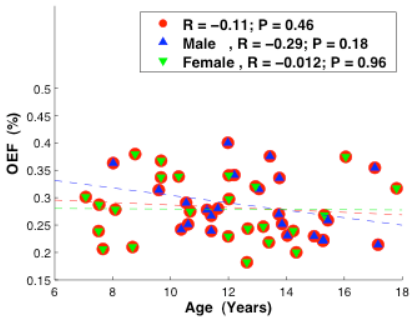

Fig. 1A

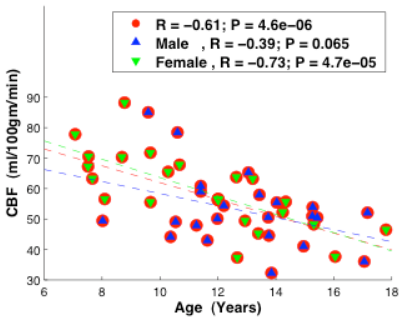

Fig. 1B

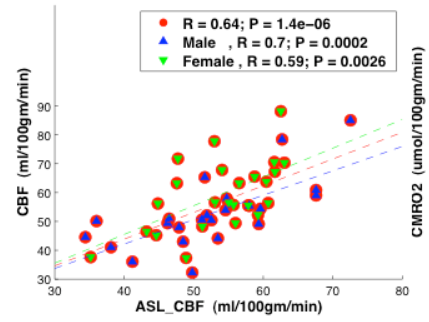

Fig. 1C

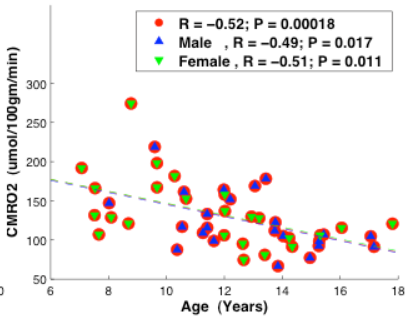

Fig. 1D

DISCUSSION: Past brain physiology and metabolism studies using nuclear medicine approaches have shown that CBF and CMR of glucose peak in toddlers (~5yr old) and then decrease with age in children and adolescents (2, 3). The observed developmental trajectories of CBF and $CMRO_2$ are in excellent agreement with existing literature. The strong correlation between global CBF estimated using PC MRI and pCASL adds further support to the validity of the proposed methods.

CONCLUSION: The present study applied PC MRI, blood oximetry and ASL to explore the developmental trajectories of global OEF, CBF and $CMRO_2$ in excellent agreement with literature. The noninvasive and quantitative nature of these novel MRI methods may open the door to measure developmental changes of brain function and metabolism across lifespan as well as in various neurodevelopmental disorders.

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