Age-Related Changes in Total Cerebral and Cardiac Blood Flow in Children and Adult Volunteers from 7 months to 60 years

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Introduction: Previous studies have shown that cerebral blood flow, cardiac output, and distribution of cardiac outflow to the head and body are age-dependent.[1, 2] However, the association of cerebral arterial inflow and cardiac outflow with age, particularly during early development in infants and children compared to adults, remain incompletely understood. Further, a systemic analysis of age-related changes of the fraction of cardiac outflow contributing to total cerebral flow across a wide range of ages has not been performed. 4D flow and 2D phase-contrast MRI (PC-MRI) have been shown to be reliable techniques for measuring cerebral and cardiac blood flow.[3, 4] The purpose of this study was to quantify both cerebral arterial inflow using 4D flow and cardiac outflow directed to the head and body (ascending and descending aorta) with 2D PC-MRI in a cohort of 40 normal subjects with ages ranging from 7 months to 60 years. Our goal was to systematically investigate the age dependence of changes in total cerebral arterial flow in relation to aortic flow in children and adult volunteers.

Methods: The study included twenty children with no history of cerebro- and cardio-vascular disease (n=20, 10 female, age=4.2±3.9 years, 0.6~13.2 years) and twenty healthy adult volunteers (n=20, 9 female, age=41.5±16.4 years, 19-60 years). 4D flow with volumetric coverage of the major intracranial vessels (Figure 1a: part I) and 2D PC-MRI with through-plane velocity encoding (Vz) at the level of the proximal ascending and descending aorta (Figure 1a: part II) were performed for all subjects in the same imaging session on clinical 1.5T and 3T MRI scanners (MAGNETOM Aera and Skyra, Siemens, Germany). Imaging parameters for intracranial 4D flow were as follows: TR/TE=5.2/2.8ms, flip angle=15º, velocity sensitivity=80-100cm/s, spatial resolution=1.2×1.2×1.5mm^3, temporal resolution=42ms, scan time=8-20 minutes. Imaging parameters for cardiac 2D PC-MRI were as follows: TR/TE=7.7/2.9ms, flip angle=30º, velocity sensitivity=150cm/s, spatial resolution=1.2×1.2×8mm^3, temporal resolution=28ms, scan time=12-22s. 4D flow and 2D PC-MRI data were pre-processed (i.e. noise masking, correction for velocity aliasing, eddy currents, and Maxwell terms) using a customized program (Matlab, MathWorks, MA, USA) as described previously.[5] Cerebral arterial inflow was calculated as cumulative blood flow in manually positioned 2D analysis planes (EnSight, CEI, NC, USA) at the left and right internal carotid arteries (ICA) and basilar artery (BA) (Figure 1a and Figure 1b). Blood flow in the ascending aorta (AAo) and descending aorta (DAo) was measured using commercial flow analysis tool (Argus, Siemens, Germany). The study was approved by the local institutional review board, and informed consent was obtained from all adults and children's parents. Adolescent assent was obtained for children 12-17 years of age.

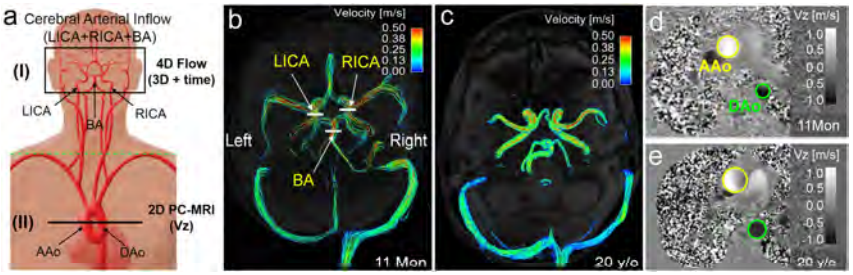

Figure. 1: 4D flow and 2D PC-MRI for the measurement of cerebral arterial inflow and aortic flow (a). 3D blood flow visualization of the intracranial vessels and aortic phase difference images for an 11-month-old child (b, d) and a 20-year-old adult (c, e). LICA=left internal carotid artery, RICA=right internal carotid artery, BA=basilar artery. Figure 1a was adapted from reference 6.[6]

Results: Intracranial 4D flow and aortic 2D PC-MRI data were successfully acquired for all 40 subjects. Figure 1 illustrates 3D blood flow visualization (time-integrated pathlines) of the intracranial vessels (Figure 1b and Figure 1c) and aortic 2D PC MRI images during peak systole (Figure 1d and Figure 1e) for an 11-month-old child and a 20-year-old adult, respectively. As shown in Figure 2a, quantification of total cerebral arterial inflow demonstrated a marked age related increase of flow by approximately three times for children at an early age up to 6 years (from 6.2 ml/cycle at 7 months to 25.1 ml/cycle at 6.1 years). Further increase in age maintained similar levels of cerebral arterial inflow up to ages of 25 years while ages > 40 years resulted in decreased cerebral inflow. Cerebral arterial inflow in young adults (age=22.9±2.9 years, 16.8±3.2ml/cycle) was significantly higher (P=0.001) compared to older adults (age=53.8±6.2 years, 11.4±2.8ml/cycle). On average, aortic flow (both AAo and DAo) increased as a function of age in children and young adults up to an age of 25 years (Figure 2b). Older adults (AAo: 59.4±16.3 ml/cycle; DAo: 40.1±11.7 ml/cycle) exhibited a trend towards decreased aortic flow compared to young adults (AAo: 73.9±16.7 ml/cycle; DAo: 50.3±11.9 ml/cycle) (Figure 2b), but the difference was not significant (AAo: P=0.059; DAo: P=0.084). The ratio between total cerebral arterial inflow and cardiac outflow (AAo flow) was significantly higher in children compared with adults (48.9±11.3% versus. 20.9±4.1%; P<0.001), indicating relatively high cerebral blood demand for brain development in children, particularly under the age of 10 years (Figure 2c). Correspondingly, DAo to AAo flow ratio was significantly lower in children compared to adults (39.9±12.8% versus 67.2±6.6%; P<0.001) indicating relatively higher systemic blood demand in adults (Figure 2d).

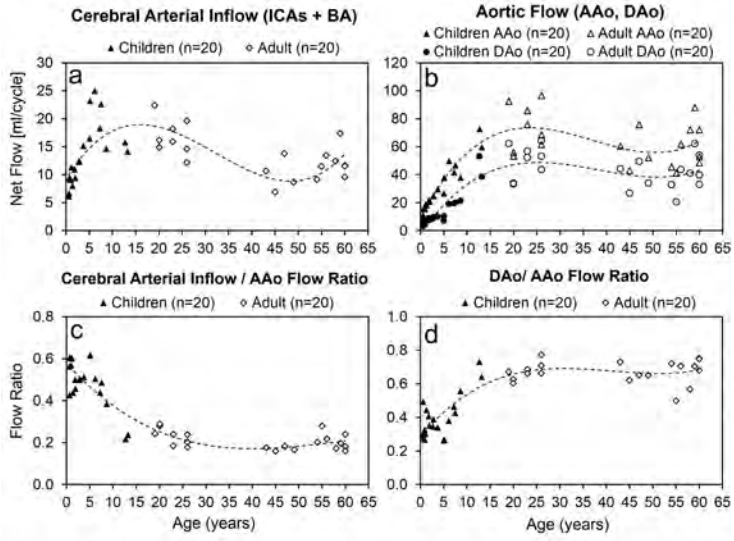

Figure. 2: Age-related changes of cerebral arterial inflow (a), aortic flow in the AAo and DAo (b), and cerebral arterial inflow to AAo flow ratio (c) and DAo to AAo flow ratio (d). The dashed lines show the overall trend of the age-related cerebral and aortic flow changes fitted by a third-order polynomial model.

Discussion: 4D flow and 2D PC-MRI were successfully employed to provide a systematic evaluation of total cerebral arterial inflow and aortic flow in children and adult volunteers over a large age range. Our findings demonstrated age-related changes in both cerebral and aortic blood flow as well as in the relationship between cerebral arterial inflow and AAo flow. The findings in this study indicate the importance of age-controlled control groups for the detection of abnormal intracranial and cardiac hemodynamics in cerebrovascular diseases. In this context, the results of this study can provide a benchmark of normal cerebral arterial inflow and aortic flow for future studies in patients with neurovascular disease (e.g. AVMs: cerebral arteriovenous malformations, VGAMs: vein of Galen aneurysmal malformations, ICAD: intracranial atherosclerotic disease, etc.). Further studies with larger cohorts more densely covering the spectrum of all ages are warranted for better understanding of the age-related cerebral and aortic blood flow changes.

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References: 1. Schoning M, et al, *J Cereb Blood Flow Metab* 1996; 16:827-833. 2. Brandfonbrener M, et al, *Circulation* 1995; 12:557-566. 3. Markl M, et al. *J Magn Reson Imaging* 2012; 36:1015-1036. 4. Stalder AF, et al, *Magn Reson Med* 2008; 60:1218-1231. 5. Bock J, et al. *ISMRM* 2007; 3138; 16:3050. 6. http://www.muschealth.com/aorta/your_aorta/