Cerebral Blood Flow in Pediatric Multiple-Sclerosis Patients and Age-Matched Controls Using Phase-Contrast MRI

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Introduction: Vascular dysfunction is associated with various neurological disorders and has been proposed as a mechanism for multiple sclerosis (MS) [1]. Although arterial flow has been extensively studied in adults [2], venous flow/drainage remains less understood [3]. Further, relatively little data exists regarding pediatric cerebral blood flow. As part of an investigation of chronic cerebrospinal venous insufficiency (CCSVI) in children, we quantified cerebral blood flow in children with MS and in age-matched controls using phase-contrast (PC) MR.

Materials and Methods: Cerebral blood flow was quantified in 26 pediatric MS patients (mean age: 15.4 ± 3.6 years) and 26 age-matched controls (16.2 ± 2.5 years) using through-plane 2D PCMR on a 3T MRI scanner (3T TRIO, Siemens, Germany). Blood flows were measured in the left and right internal carotid arteries (ICA), vertebral arteries (VA), internal jugular veins (IJV), and epidural veins (EV) (see Fig. 1). Data were acquired at the level of C2-C3 using a slice perpendicular to the dominant orientation of the target vessels. Participants were imaged supine during free breathing to maintain resting cardiovascular physiology. Relevant imaging parameters were: spatial resolution 0.6x0.6 mm^2, TR 8.45 ms, temporal resolution 50.7 ms, velocity encodings 100 cm/s (ICA, VA, IJV scan) and 30 cm/s (EV scan), ECG gating, scan time ~2 minutes. Flow data were acquired at the beginning of each MRI examination and repeated at the end to test within-visit reproducibility (~60 minutes apart). Of the 26 MS patients, 18 returned for repeat scans to test between-visit reproducibility (~6 months apart).

For each vessel, total flow (L/min) was calculated using the analysis package Segment (v1.8, Medviso , Sweden) with background phase correction [4]. Reproducibility of repeated flow measurements was assessed by Pearson correlation coefficient and coefficient of variation (CoV). Between-group differences were evaluated on a per-vessel basis using Student's t test. The ratio of total measured venous flow to total measured arterial flow, (IJV+EV) / (ICA+VA), was calculated for each group to explore potential venous flow redistribution [3].

Results and Discussion: The mean ± SD flows measured in each vessel are provided in Table 1 (first-visit scans) and show no statistically significant differences between the MS and control subjects. Average ICA and IJV flow waveforms for the amalgamated groups are presented in Fig. 1, demonstrating symmetric ICA and right-side dominant IJV flows. The ratio of right IJV flow to total IJV flow was comparable to results in adults: MS = (64±26)%; controls = (57±26)% [3]. The ratio of total measured venous to arterial flow in the MS subjects was (83±19)% versus (90±12)% in controls (p=0.12), suggesting no gross flow redistribution. Across all vessels, the correlation coefficient of repeated flow measurements was 0.99 and 0.97 for the within-visit and between-visit measurements, respectively. The single-visit CoV was approximately 12% for arterial flows, 16% for IJV flow, and 22% for EV flow while the between-visit CoV was approximately 18% for arterial flows, 30% for IJV flow and 40% for EV flow. The higher venous CoVs reflects greater dependence on physiological conditions such as respiration and posture, as well as greater uncertainty in flow measurement in the smaller EVs.

Conclusion: No population difference in cerebral flow was detected in pediatric MS subjects relative to age-matched controls. This study establishes reference values for normal pediatric flow for future neurological studies. The inter-subject variability present in venous flow underscores the difficulty of attributing pathological significance to individual venous flows. However, arterial and venous flow measurements were highly reproducible within individuals.

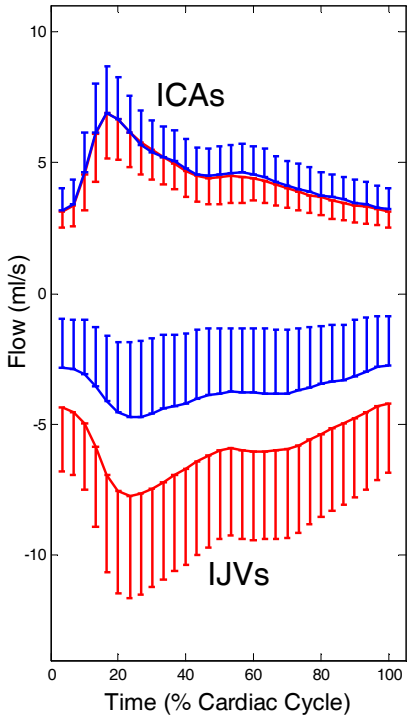

Figure 1: Average flow waveforms (±SD) across all MS and control subjects (N=52) for the right (red) and left (blue) ICA and IJV. Single-sided error bars used for clarity.

Table 1: Mean ± SD flows in pediatric MS patients (Ped MS) and controls (L/min).

	ICA		IJV		VA		EV	
	R	L	R	L	R	L	R	L
Ped MS	0.26±0.06	0.26±0.07	0.34±0.18	0.19±0.13	0.10±0.05	0.10±0.04	0.03±0.03	0.04±0.04
Controls	0.26±0.03	0.27±0.05	0.34±0.21	0.25±0.15	0.10±0.03	0.12±0.04	0.05±0.04	0.04±0.03
p-value	0.96	0.54	0.87	0.15	0.54	0.21	0.16	0.40

References: [1] Zamboni *J Neurol Neurosurg Psychiatry*, 80:392, 2009. [2] Spilt *JMRI*, 16:1, 2002. [3] Stoquart-ElSankari *J Cereb Blood Flow Metab*, 29:1208, 2009. [4] Heiberg *BMC Medical Imaging*, 10:1, 2010.