Regional differences in CVR developmental patterns in healthy children

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Introduction: Cerebrovascular reactivity (CVR) measures the capacity of brain blood vessels to dilate by assessing the change in cerebral blood flow (CBF) in response to a vasoactive stimulus. When combined with MRI, such hemodynamic parameters are valuable tools for the clinical assessment of cerebrovascular disease. However, very little is currently known about developmental changes of CVR. It is well documented that global CBF steadily declines from childhood to adulthood [1], while recent findings suggest that global CVR peaks around the late teens [2]. Regional changes in CVR with age, however, have not yet been explored. This information is important for refining our understanding of cerebral physiology in children as it may be complementary to the heterogeneous development of cortical regions [3]. The purpose of this study was to determine whether the developmental trajectories of CVR in children are region specific. We hypothesize that regional development of CVR will maintain the bi-phasic pattern described in [2], but that the rate of change will be regionally dependent.

Materials and Methods: Twenty-three healthy volunteers (10 males and 13 females) between 9 and 18 years old were imaged on a clinical 3T MRI scanner (MAGNETOM Tim Trio; Siemens Medical Solutions, Germany) using a 32-channel head coil. CVR data was acquired using blood-oxygen level-dependent (BOLD) imaging in combination with a computer-controlled gas sequencer (RespirAct™; Thornhill Research Inc., Toronto, Canada), which delivered programmed cycles of CO_2 at low (40 mmHg) and elevated (45 mmHg) concentrations to the subject via a rebreathing mask. The BOLD sequence parameters were: TR/TE = 2000/40ms, FOV = 220mm, matrix size = 64×64, slices = 25, slice thickness = 4.5mm, volumes = 240, time = 8min. CVR maps were computed by correlating the voxel-wise BOLD signal change to the measured end-tidal CO_2 waveform using FSL v4.1 (http://www.fmrib.ox.ac.uk/fsl/). Each voxel value was then normalized to the temporal mean BOLD signal to convert CVR into units of %ΔMR / mmHg(CO_2). The maps were projected into surface maps via the Constrained Laplacian Anatomical Segmentation using Proximities (CLASP) method and subsequently coregistered into the MNI-152 template through the CIVET pipeline [4]. Cortical measures were averaged in 7 cortical regions: cingulate (CN), frontal (FR), insula (IN), parietal (PA), parahippocampal (PH), occipital (OC), and temporal (TP) lobes. Mean regional CVR for each subject was computed and plotted against age and a piecewise linear curve fit was performed using MATLAB to compare developmental trajectory. In addition, the correlation between the initial slope of CVR change and the age at which CVR peaked was tested. Statistical significance was defined as a *p*-value < 0.05.

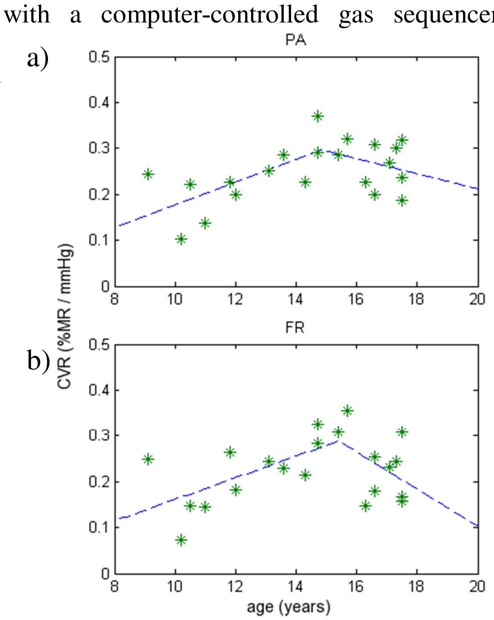

Figure 1. CVR measures versus age (*) and corresponding piecewise linear fit (--) in a) PA and b) FR regions.

Results: CVR in each cortical region exhibited different peaks ranging from age 14 to 16. Example trajectories are shown in Figure 1. Parameters computed from each curve fit is provided in Table 1, all of which are statistically significant ($p < 0.05$). There also appears to be an association between the slope of CVR change and age of peak CVR in each region ($r^2 = 0.571$, $p = 0.049$).

Discussion: This study shows that the development of CVR in children is not uniform across all cortical regions and peaks around the mid-teens. Additional CVR data with a wider age range is required to improve the model fit and the inclusion of CBF and high resolution structural measurements may provide insight into the relation between hemodynamic and cortical development patterns in the brain.

Region	Slope	Peak (age)	Corr Coeff (r)	*p*-value
CN	0.0279	14.9	0.6723	0.0166
FR	0.0235	15.4	0.7204	0.0082
IN	0.0255	15.4	0.7101	0.0143
PA	0.0248	14.8	0.7882	0.0014
PH	0.0140	15.7	0.6767	0.0453
OC	0.0265	14.7	0.6658	0.0253
TP	0.0225	15.4	0.6772	0.0221

Table 1. Best fit parameters for each cortical region showing different rates of CVR development and the ages when the slope changes.

References:
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