Developmental trajectories of cerebrovascular reactivity in healthy children

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Introduction: The capacity for cerebral blood vessels to dilate plays a critical role in the autoregulation of cerebral blood flow (CBF), which is responsible for maintaining a consistent supply of oxygen and nutrients to the brain. Non-invasive imaging strategies have been developed to assess vessel distensibility by measuring the relative changes in CBF in response to the administration of a vasoactive stimulus. The resulting measure is expressed as cerebrovascular reactivity (CVR) and has become a valuable tool in the clinical assessment of cerebrovascular disease.[1,2] However, little is currently known about CVR during the years of critical growth from childhood through adolescence. We know from previous studies that CBF peaks in the first decade of life and gradually declines until it reaches adulthood values.[3,4] From a mechanistic point of view, CVR should theoretically be lower during childhood as cerebral blood vessels are already dilating at baseline to accommodate the increased blood flow. CVR data throughout normal childhood is currently not available, but such data could aid in the interpretation of CVR studies in children with cerebrovascular disease. The purpose of this study was to measure CVR changes at different ages and compare them to changes in CBF in healthy children. We hypothesized that CVR will continuously increase with age and that these changes are inversely correlated to CBF.

Materials and Methods: Sixteen healthy volunteers (7 males and 9 females) between 9 and 18 years old with no history of respiratory, cardiovascular or cerebrovascular disease were imaged on a clinical 3T MRI scanner (MAGNETOM Tim Trio; Siemens Medical Solutions, Erlangen, Germany) using a 32-channel head coil. Changes in CBF were assessed with blood-oxygen level-dependent (BOLD) imaging in combination with a computer-controlled gas sequencer (RespirAct^{TM}; 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 as follows: TR/TE = 2000/40ms, FOV = 220mm, matrix size = 64×64, slices = 25, slice thickness = 4.5mm, volumes = 240, time = 8min. Baseline CBF was measured using a pulsed arterial spin labeling (ASL) sequence: PICORE Q2TIPS, TR/TE = 2500/13 ms, TI1 = 700 ms, TI2 = 1800 ms, FA = 90°, FOV = 220 mm, matrix = 64×64, slices = 13, thickness = 4.5 mm. CVR maps were computed offline using FSL v4.1 (http://www.fmrib.ox.ac.uk/fsl/) by correlating the voxel-wise BOLD signal change to the measured end-tidal CO_2 waveform. Each voxel value was then normalized to the temporal mean BOLD signal to convert CVR into units of %ΔMR / mmHg(CO_2). Baseline CBF maps were computed from the ASL data using the vendor processing pipeline, which follows the standard pulsed ASL quantification model.[5] Each CVR and CBF map was averaged based on tissue segmentation of grey matter (GM) and white matter (WM). Pearson correlation analysis was performed on the resulting data.

Results: The measured CBF and CVR values in each subject are plotted with respect to age in Figure 1. A gradual reduction of CBF with age was observed for both GM and WM with respective correlation coefficients r^2 = -0.375 and r^2 = -0.531. The change in mean GM and WM CVR exhibited an opposite pattern as CVR linearly increases with age and peaks at around the late teenage years. However, the relation does not hold after age 17 as the CVR values declined drastically. The correlation for a linear fit was r^2 = 0.660 and r^2 = 0.600 for GM and WM, respectively, for data points up to age 17.

Discussion: Our study shows a linear upward trend in the evolution of CVR with age in healthy subjects. As CBF declines with age, cerebral vessels no longer need to dilate at baseline to maintain constant blood pressure and, hence, have greater capacity to expand. The eventual peak and decline in CVR, however, indicate that other factors beside CBF may be influencing CVR in the late teen years. Additional data needs to be collected to further substantiate this finding as well as extend the age range for a more comprehensive understanding of how CVR is affected.

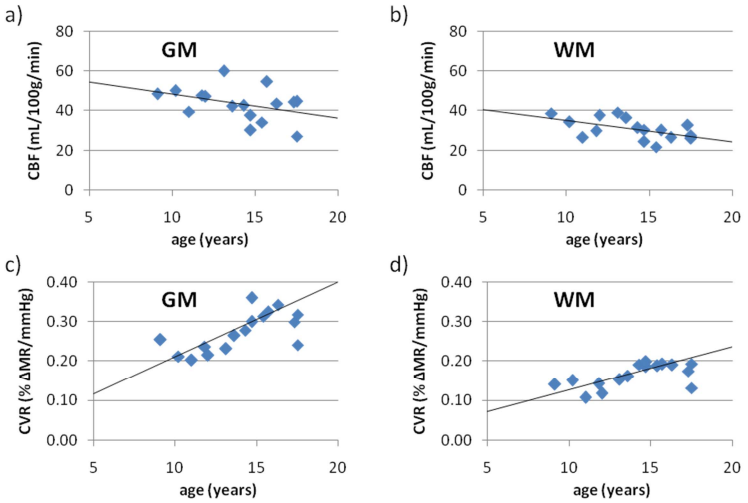

Figure 1. Mean CBF in (a) GM and (b) WM, and mean CVR in (c) GM and (d) WM plotted with age. Trend lines for CVR only accounted for data points below 17 years.

References:

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