

Age and Gender Effects on Whole Brain Cerebral Blood Flow in Adolescents

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Introduction: Both gender and age have long been assumed to have effects on brain function. Measurements in cerebral blood flow (CBF) with radioactive imaging techniques (SPECT and PET) have been employed to understand the neural basis of gender and age differences in brain function. However, findings have been extremely controversial (1-3), which could be due to limitations of imaging techniques (spatial/temporal resolutions and partial volume effect) and relatively small sample sizes. In addition, the effects of gender and age on CBF have not well explored in adolescents. To increase our knowledge in this area, MRI techniques (with higher spatial and temporal resolution) were employed to measure global CBF with 267 adolescents.

Material and Methods: Adolescents aged 12 to 15 years (N = 267, 130 male and 137 female) participated in the study. Informed written consent was obtained from each volunteer. **fMRI imaging acquisition:** Experiments were performed on a 3T Siemens Trio MRI scanner (Siemens, Erlangen, Germany). A pulsed arterial spin labeling (PASL) sequence was used to measure resting CBF (4). Field-of-view (FOV) = 24 cm, matrix = 64 x 64, TR/TE = 2440/19 ms, TI₁/TI₂ = 700/1000 ms, 13 slices and repetitions = 100. The equilibrium brain tissue magnetization (M₀) was measured using similar parameters as described above but TR/TI₁/TI₂ = 8000/5000/6000 ms and repetition = 4. **Data analysis:** Quantitative CBF was determined using MATLAB 7 (Math Works, Natick, MA), as follows. Raw ASL images (ΔM) were obtained by subtracting the labeled and unlabeled images. The voxel-by-voxel CBF mapping was then computed by the following equation (4): $CBF(mL/100g/min) = \frac{\lambda \Delta M}{2\alpha M_0 T_{I_1} \exp(-T_{I_2}/T_{1a})}$ Where λ = 0.9 is the blood/tissue water partition coefficient, T_{1a} = 1.6s is the longitudinal relaxation time of blood at 3T, α = 0.95 is the inversion efficiency.

Results and Discussion: Global CBF as a function of age is demonstrated in Figure A. It shows that CBF is decreased with age. Significant difference in CBF was observed between 12 and 15 years of age (p < 0.01). No significant main effects of gender were found in the study (Figure B, NS) consistent with what has been previously reported (3). For the interaction between gender and age, it shows a significant negative correlation between age and CBF for females (r = -0.32, p < 0.0005) but not males (r = -0.1, p = 0.1) (Figures C and D). The result is consistent with at least one previous report showing a greater rate of CBF decline with age among females (5). Nonetheless, the low r values showed in Figures C and D also indicate that there are marginal decreases in CBF during the early adolescent developmental period. In summary, our data demonstrated that global CBF in teenagers was age-dependent not gender-dependent. Although dramatic difference between female and male CBF has been previously observed (1,2,5), this was not true in the present study. To our knowledge, this is the first study to quantify global CBF using MRI for a large sample of adolescents. The results provide better understanding of brain functions for adolescent across age and gender. Compared to PET, MRI strategies enable non-invasive, non-radioactive, better image quality (higher spatial and temporal resolution) and cost-effective CBF measurements. MRI CBF measurement will further facilitate longitudinal studies of brain function and development for adolescents.

References: (1) Rodriguez et al., (1988) JCBFM 8:783-789; (2) Gur et al., (1982) Science 217:654-661; (3) Matsuda et al., (1984) Stroke 15:336-342; (4) Wang et al., (2003) MRM 49:796-802 ; (5) Gur et al, (1990) Schizophrenia Bulletin 16:247-254.

