White matter volume and anisotropy in very low birth weight preterm born children: association with cognitive outcome

P-L. Khong[1], D. Qiu[1], A. Yung[2], G. Poon[2], C. Leung[3], S. Chua[4], G. McAlonan[4], B. Lam[2]

[1]Diagnostic Radiology, The University of Hong Kong, Hong Kong, Hong Kong, Hong Kong, [2]Paediatric and Adolescent Medicine, The University of Hong Kong, Hong Kong, Hong Kong, Hong Kong, [3]The Duchess of Kent Children's Hospital, Hong Kong, Hong Kong, Hong Kong, [4]Psychiatry, The University of Hong Kong, Hong Kong, Hong Kong, Hong Kong

Introduction:

Low birth weight premature infants are at risk of brain injury, especially to the white matter. These complications result from either the inability to repair the lesions acquired around birth, or disruption of the normal maturation process. It has been shown in normal and disease populations that white matter parameters are associated with cognitive function (1-3). We hypothesize that mean white matter volume and anisotropy are reduced in children who were born very low birth weight (<1500 grams) preterm (<37 weeks gestation) compared to healthy age-matched children born at term (≥37 weeks gestation, >2500grams) and that these parameters of white matter damage correlate with cognitive outcome.

Methods:

Twenty-five children (14 males, 11 females) aged between 8.8 years to 11.5 years (mean age=10.14 years, sd=0.76 years) who were born very low birth weight preterm and 13 age-matched healthy term control subjects (9 males, 4 females, mean age=10.11 years, sd=1.18 years) were recruited for MR imaging studies. Children requiring sedation for MR imaging and those with congenital brain malformations and cerebral palsy were excluded. Pre-term children underwent cognitive assessment using the Wechsler Intelligence Scale for Children to obtain the full scale intelligence quotient (FSIQ) within 9 months of MR imaging. The following MR imaging sequences were performed using a 1.5T imager with a standard head coil; axial fast spin-echo T2-weighted images (TR=4000ms, TE=100ms, slice thickness=5mm with 1.5mm gap, field of view=23cm, acquisition matrix=320 x 224), coronal fluid-attenuation inversion recovery images (TR=9000ms, TE=140ms, TI=2250ms, slice thickness=5mm with 1.5mm gap, field of view=23cm), 3D T1-weighted gradient-echo images (TR=12ms, TE=4ms, flip angle=15º, field of view =23cm, slice thickness=1.5mm with no gap of the whole brain), DTI in 25 gradient encoding directions using single-shot echo-planar imaging (TR=10000ms, TE=100ms, acquisition matrix=128 x 128, field of view =28cm, slice thickness of 5mm with 1.5mm gap, b factor=1200s/mm^2). Mean white matter (WM) volume and mean WM fractional anisotropy (FA) were computed for each subject by SPM2 (Wellcome Dept of Imaging Neuroscience, Institute of Neurology, UK) and the differences between the two groups were compared using the student's t-test. Spearman's correlation, followed by multiple regression analyses, was performed to determine the association between WM volume, FA and gender, birth weight (BW), gestational age (GA) and FSIQ in the preterm group.

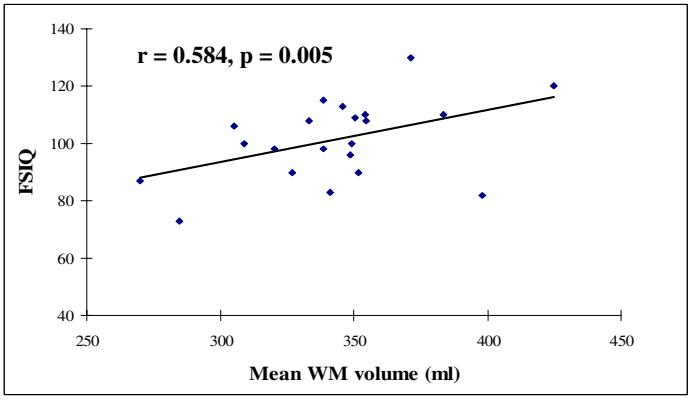
Results:

There were no significant differences in gender and age between the pre-term and term control groups. BW and GA of the preterm group was 1141.6grams +/- 213.9 grams (mean +/- sd) and 29.4 weeks +/- 3.1 weeks (mean +/- sd) respectively. Except for three subjects who had mild ventriculomegaly and periventricular leukomalacia, conventional MR imaging was normal. WM volume and FA were significantly lower in the preterm group compared to the control group (Table below, p=0.014 and p<0.001 respectively). Of the 25 preterm children, 21 returned for IQ tests. FSIQ score was 106 +/- 12.8 (mean +/- sd). Using Spearman's univariate analysis, significant correlations were found between FSIQ and WM volume (scatterplot below, r=0.584, p=0.005), BW (r=0.485, p=0.026) and GA (r=0.474, p=0.030), but not FA. Significant correlations were also found between gender and FA (r=0.592, p=0.002), GA and BW (r=0.757, p<0.001). Multiple regression analysis found only WM volume to be an independent variable significantly affecting FSIQ after adjusting for GA, BW and gender (r^2=0.420, p=0.011).

	Pre-term (*n=25*) Mean (sd)	**Term controls (*n=13*) Mean (sd)**
Age (yrs)	10.14 (0.76)	10.11 (1.18)
Mean WM* volume (mls)	341.8 (32.9)	368.9 (25.8)
Mean WM FA*	0.346 (0.014)	0.364 (0.012)

Table of demographic data of preterm children and term controls

*** indicates p < 0.05**



Scatterplot of FSIQ vs mean white matter volume of preterm children (*n=21*)

Conclusion:

Both mean WM volume and anisotropy remain reduced in preterm born children at late childhood. Only mean WM volume correlated with long-term cognitive outcome, suggesting that mean WM volume is reliable in predicting long-term cognitive outcome in preterm born children whilst mean FA of the whole brain white matter is not.

References:

1) Peterson BS et al, Pediatrics 2003;111:939-48, 2) Schmithorst VJ et al, Hum Brain Mapp 2005; 26:139-47, 3) Haier RJ et al, NeuroImage 2004; 23: 425-33.