The neural basis of declining IQ in preterm children

E. B. Isaacs[1], C. J. Edmonds[1], W. K. Chong[2], A. Lucas[1], D. G. Gadian[1]

[1]Institute of Child Health, University College London, London, United Kingdom, [2]Department of Radiology, Gt Ormond Street Hospital for Children NHS Trust, London, United Kingdom

Introduction Although IQ is thought to remain relatively stable in the normal population, a decline in IQ has been noted in children born preterm. However, it is not clear to what extent the inclusion of children with clear neurological damage has influenced these findings. This study examined IQ scores obtained in childhood and again in adolescence from a group of children born at 30 weeks gestation or less who had normal neurological examinations and no consistent abnormalities on visual inspection of MRI scans. Voxel-based morphometric analyses of 3D T1-weighted structural MRI datasets were carried out in adolescence to examine the neural basis of any IQ changes that were detected.

Methods Ninety-one children (49M; 42F) took part in the study. All children had been born at 30 weeks gestation or less (mean=29wks [range: 26-30]); mean birthweight=1178g [range: 663-1720g], mean number of days on ventilation=6 [range: 0-42]). They were first seen for IQ assessment in childhood (age 7.5-8yrs) when all were classified as neurologically normal, and then at adolescence (mean age 15y5m; range 12y5m to 19y4m). MRI was carried out only at adolescence; scans were available for 89 children but the first 12 of these were obtained on a scanner that was subsequently replaced and they were not used in the analyses. Three scans were discarded for technical reasons leaving a total of 74 scans available for analysis. These scans were acquired using a 1.5 Siemens Vision system. Investigations included: 1) 3D MPRAGE acquisition with TR 10ms; TE 4ms; TI, 200ms; flip angle, 12 degrees; matrix size, 256x256; field of view, 250mm, partition thickness, 1.25 mm; 128 sagittal partitions in the third dimension, and acquisition time, 8.3 min; and 2) coronal and axial turbo spin-echo T2-weighted scans. In addition to conventional neuroradiological assessment, the scans were also analysed using voxel-based morphometry (VBM; Wellcome Department of Imaging Neuroscience), which provides a means of detecting subtle abnormalities not seen on visual assessment. The images were spatially normalised, segmented, smoothed (12 mm FWHM) and then entered into statistical analyses. Because developmental abnormalities are frequently bilateral, the scans were normalised to a symmetrical template and analysed using a conjunction analysis that searches explicitly for the presence of symmetrical bilateral abnormalities (1). We report on regions that reached significance levels of $p<0.05$, corrected for multiple comparisons across the whole brain.

Results Mean IQ scores at both time points were within the average range of 90-109. However, paired t-tests revealed that both Verbal IQ (VIQ) and Performance IQ (PIQ) mean scores decreased significantly between the two time points, VIQ scores by approximately 8 points - from 105.7 to 97.8 - (VIQ $t(90)=6.33$, $p<0.001$), and PIQ scores by approximately 11 points - from 108.1 to 96.8 - (PIQ $t(90)=7.47$, $p<0.001$). The decline in mean IQ score could not be fully accounted for by the restandardisation of the Wechsler Intelligence Scales for Children that took place between the two assessments, nor by the use of short/long forms (short forms were used in the first assessment, long forms in the second).

Visual neuroradiological assessment of the MRI scans showed no consistent differences between those children who showed a large decline in IQ and those who did not. Bilateral VBM analyses showed a positive correlation between VIQ decline and white matter in a frontal lobe region (underlying the medial/superior frontal gyri [±20, 60, 2, $p=0.001$, corrected]; see Fig. 1). The analyses also showed a negative correlation between PIQ decline and grey matter density in the hippocampal region [±38, -21, -12, $p<0.03$], and a positive correlation between PIQ decline and grey matter density in the cerebellum [±46, -56, -32, $p=0.002$]. Subgroup analyses comparing Large Decline groups with Small Decline groups, as well as hippocampal volume measurements, were consistent with the correlation analyses.

Fig. 1. Statistical parametric maps showing the regions where there was a significant positive correlation between the VIQ decline and white matter density; *(a)* glass brain representation; *(b)* the superimposition of Z-scores on the mean anatomical image is shown for planes through the most significant frontal lobe voxels. Left is left in accordance with neurological convention. A threshold of $p<0.001$ (uncorrected) was chosen for display.

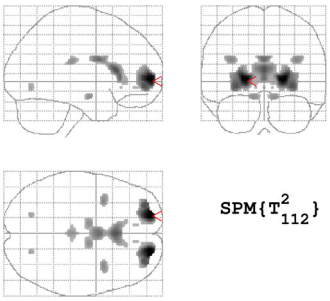

Fig 1a

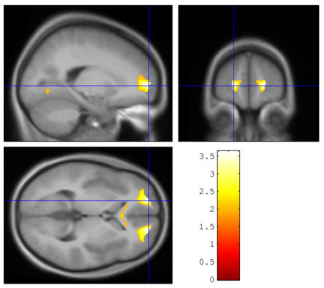

Fig 1b

Conclusions We conclude that preterm children are at risk of declining IQ over time even if they have not suffered obvious neurological damage. VBM analysis of structural MRI scans can identify the neural correlates of the declines in VIQ and PIQ that are seen in these children.

Reference (1) Salmond et al. Hum. Brain Mapp. 2000; 11:223-232.