Differential parental control of neural morphology in the offspring

J. C. Wells[1], E. B. Isaacs[1], C. J. Edmonds[1], D. G. Gadian[1], A. Lucas[1]
[1]Institute of Child Health, University College London, London, United Kingdom

Introduction

During primate evolution, controlling mechanisms for maternal behaviour have shifted away from neuro-endocrine regulation towards intelligent strategies. This shift is predicted to benefit mothers, the primary providers of parental care, more than fathers. One mechanism by which this change has been achieved is genomic imprinting. We tested the hypothesis that encephalisation (a proxy for the parental brain genome) of mothers, but not fathers, is associated in the offspring brain with grey matter density in frontal lobe regions associated with intelligent functions.

Methods

Data were obtained from participants in a follow-up study of a randomised infant feeding trial following preterm birth. At birth, heights and head circumferences were obtained from parents (817 mothers, 655 fathers). The children were then followed up at regular time intervals into adolescence, when in a subsample brain scans were performed. Matching data for offspring brain MRI and parental anthropometry were available for 75 datasets (32M, 43F). The MRI studies were performed using a 1.5T Siemens Vision system, and included 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. The MPRAGE datasets were analysed using voxel-based morphometry (VBM; Wellcome Department of Imaging Neuroscience, Imstitute of Neurology, London), 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. Since brain development typically proceeds bilaterally, the scans were analysed using a conjunction analysis that searches explicitly for the presence of symmetrical bilateral effects (1).

As a proxy for parental brain genes, we used the encephalisation quotient (EQ), generated from data on head circumference and height to rank individuals in terms of relative brain volume, taking into account variability in body size (2). Head circumference itself has high heritability, and is highly correlated with brain volume. High heritabilities have also been reported from twin studies for brain volume, grey matter volume and white matter volume. These high heritabilities and the strong relationship between head circumference and brain volume justify the use of parental EQ in our analyses as a generic index of parental brain genes.

Results

EQ of both parents was significantly associated with EQ of the offspring ($p<0.001$ for maternal EQ and for paternal EQ). There was a highly significant positive correlation between maternal EQ and the child's grey matter density in the two frontal lobes (Talaraich x,y,z coordinates: ±36, 68, 4; $p<0.001$, after correction for multiple comparisons using the familywise error procedure). These coordinates fall within Brodmann's area 10 in the frontopolar prefrontal cortex, an area associated with the formulation of strategy and hypothesised to be important in food-sharing behaviour. We conducted an equivalent analysis for paternal EQ, but no voxels survived the cutoff for statistical significance of $p<0.05$ (corrected), and for the coordinates previously identified as significant in the maternal analysis, no voxels were significant for paternal EQ in uncorrected analyses. For each parent, the EQ of the other parent was then added to the model as a covariate. The results for maternal EQ remained highly significant (coordinates: ±34, 68, 3; $p<0.001$, corrected) following adjustment for paternal EQ (Figure 1), but paternal EQ remained unrelated to the outcome after adjusting for maternal EQ.

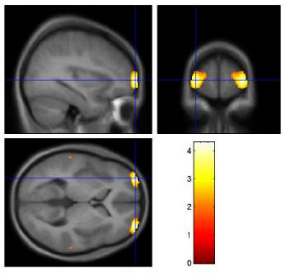

Fig. 1. Statistical parametric maps showing the regions where there was a significant positive correlation between maternal EQ and grey matter density in the offspring, adjusting for paternal EQ, generated using the bilateral conjunction analysis. The superimposition of Z-scores on the mean anatomical image is shown in colour for planes through the most significant frontal lobe voxels, marked by the cross-hairs. A threshold of $p<0.001$ (uncorrected) was chosen for display.

Conclusions

Our findings support the hypothesis that the maternal genome disproportionately controls development of frontal lobe regions, which may benefit maternal fitness through increased control of food allocation.

References

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