Analysis of brain volume in a 19 year-old extremely-preterm born cohort

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Synopsis

This abstract presents an analysis of brain tissue volume in a cohort of 69 extremely preterm born young adults and 50 term-born controls at 19 years of age.

Introduction

The consequences of extremely preterm birth are a global health concern. Rates of prematurity are increasing throughout the world and long-term sequelae range from physical impairments such as cerebral palsy or blindness to social and executive function impairments such as autism. In the UK, studies have shown that although survival rates at the lowest gestations are increasing, rates of disability remain unchanged [1]. The long-term impact of these deficits on adolescence is currently poorly understood and the adolescent brain phenotype of extreme prematurity is currently unknown. Our work comprises a study of 69 extremely preterm born 19 year olds and 50 of their age-matched peers, social-economically matched at 6 years of age. Neuroimaging carried out on this cohort will enable us to establish the long-term effects of extreme prematurity on the appearance and structure of the brain. This work investigates how brain tissue volumes differ in this extremely preterm born group of young adults.

Methods

Imaging data were acquired for a cohort of 119 adolescents at 19 years of age. Data for 69 extremely preterm adolescents (F/M=41/28, mean birth gestation=25.0±0.8wks) and 50 (F/M=30/20) term-born socio-economically matched peers were acquired on a 3T Phillips Achieva. We acquired 3D T1-weighted MPRAGE (TR/TE=6.93/3.14ms) volumes at 1mm isotropic resolution to obtain a tissue segmentation and region labels using the Geodesic Information Flows framework [2]. This method produces a state-of-the-art segmentation and regional labeling by voxel-wise voting between several propagated atlases guided by the local image similarity. Region labels in this routine are specifically defined for the cerebellum (combining both grey and white matter components). We investigate how these pure tissue volumes vary between preterm status and by gender and correlate our results with information on height and weight.

Results

Figure 1 shows an example segmentation of an extremely preterm born adolescent with tissue volumes labeled. Figure 2 shows tissue volume results grouped by EP/term status and by gender. Grey and white matter absolute volumes are both significantly reduced in the EP relative to the term groups. White matter volume is between 22.4-59.5cm3 (95%ci) lower in preterm females (371cm3±39.2cm3) than term females (412cm3±37.5cm3); white matter volume is between 40.0-47.8cm3 lower in preterm males (399cm3±46.4cm3) than their term-born counterparts (464cm3±36.7cm3) and white matter volume is also significantly lower in term-born females than term-born males (-29.8cm3 to -73.3cm3 95%ci). Grey matter volume is between 13.0-56.2cm3 (95%ci) lower in preterm females (565cm3±42.9cm3) than term females (600cm3±47.6cm3); grey matter volume is between 33.6-96.7cm3 lower in preterm males (610cm3±62.7cm3) than their term-born counterparts (675cm3±37.1cm3) and grey matter volume is also significantly lower in term-born females than term-born males (-49.1cm3 to -100cm3 95%ci). We also investigate the GM to WM ratio (Figure 2f). The GM/WM ratio is significantly higher (0.03-0.11, p=0.001) in preterm females (1.52±0.09) than in term females (1.45±0.07). Similarly this ratio is also higher (0.02-0.13,p=0.006) in preterm males (1.53±0.09) than in term males (1.46±0.08). Differences between preterm males and preterm females (p=0.86) and between term males and term females (p=0.97) are not significant, suggesting that this feature may be representative feature of the preterm brain summarising differences in an underlying white matter layout independent of brain size. Comparable analysis for cerebellum size suggests a similar significant relationship in volume between groups. In addition to investigating the GM/WM ratio, normalisation by brain volume (including ventricular CSF) illustrates how grey, white and cerebellar volume are influenced by total brain volume. Differences between grey matter distributions for each group are reduced such that the results no longer reach significance, suggesting that the grey matter proportion is not detectably altered. Differences between normalised cerebellum volumes also do not reach significance. Differences between normalised white matter volumes do remain significant, suggesting that it is the white matter component that is affected most strongly by extremely preterm birth. Carrying out a correction for subject height does not remove the significant correlations described above, suggesting a non-linear relationship between height and brain size.

Conclusion

The analysis in this work has allowed a characterisation of the adolescent preterm brain to be made. The results suggest that the white matter component of the preterm brain is more significantly reduced than the cortical grey and cerebellar volumes. Analysis by both age and gender has allowed us to separate effects due to natural variability in head size from those due to extreme prematurity. Across groups, the most variable results are seen in the EP male group, perhaps suggesting a more variable response to extremely preterm birth. This might be borne out by future studies of neurocognitive function [4]. Our future work will investigate how the observation of a relative white matter reduction reveals itself on microstructural imaging and how these features manifest in neuropsychological examinations.

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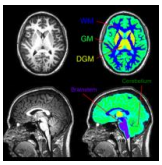
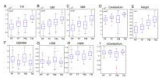
Figures



Multi-class brain tissue volume estimation.



Volumetric results for total intracranial volume, grey and white matter, cerebellum, normalise results against TIV, height and weight.