Longitudinal hippocampal shape changes between term-equivalent and 7 years in very preterm and full-term children

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Background: The hippocampus is an important brain structure known to be involved in learning and memory functioning. The hippocampus is vulnerable in infants born very preterm (VPT: <30 weeks' gestational age), where volume reductions have been observed [1]. The normal developmental trajectory for the hippocampus is to become inverted and infolded during early development [2], which we have previously shown to be disrupted in VPT infants compared with their term-born peers [3]. No previous study has mapped the early developmental trajectory of regional hippocampal changes between term and 7 years. The aim of this study was to investigate changes in hippocampal shape longitudinally between term-equivalent and 7 years of age in both full-term (FT) and VPT children, and to determine whether the developmental trajectory differs between groups.

Methods: At term-equivalent, T2 and proton density (PD) weighted images were acquired on a 1.5 T GE scanner (1.7 mm coronal; TR 4000 ms; TE 60 / 160 ms; flip angle 90°; FOV 180 × 135 mm2; matrix 256 × 224). Hippocampi were manually delineated on combined T2 and PD image volumes. At 7 years of age, the same subjects were scanned with a 3 T Siemens Trio scanner, and hippocampi were manually segmented on the T1 weighted image (TR, 1900 ms; TE, 2.27 ms; matrix, 256 x 256; FOV, 210 x 210 mm; 0.8 mm^3 isotropic voxels). 24 FT and 119 VPT children had successful hippocampal segmentations at both time-points. The spherical harmonics-point distribution model (SPHARM-PDM) shape analysis pipeline was applied to the binary hippocampal masks at both time-points, including enforcement of spherical topology, generation of smoothed PDM shape representations of the segmentation boundaries, and registration to enforce correspondence. 7 year hippocampal meshes were registered to the term meshes by Procrustes alignment, which included a scaling component to account for the size difference in hippocampi between time-points. Statistical comparisons between time-points were carried out for both the FT and VPT groups separately. Difference vectors were computed between the time-points, which were subsequently used to calculate group-wise differences. All analyses were Bonferroni corrected for multiple comparisons.

Results: Both the FT and VPT groups exhibited significant hippocampal shape change between infancy and 7 years. There were several areas of expansion from infancy to 7 years into the inner medial border of the hippocampus, and a corresponding contraction along the lateral border (Fig 1a). All zones of major expansion and contraction were statistically significant (Fig 1b).The overlay of the 7 year hippocampus onto the infant hippocampus further demonstrated hippocampal infolding between time-points (Fig 1c). A portion of the left hippocampal head, body and tail as well as a region on the right hippocampal tail underwent statistically significantly different development from 0 to 7 years in VPT compared with FT children (Fig 1d).

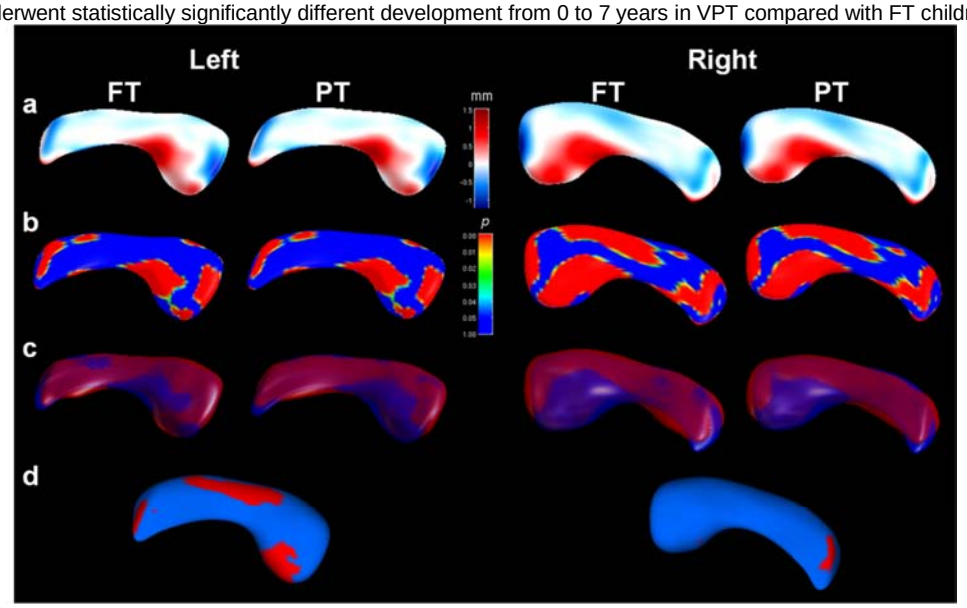

Figure 1. Shape differences between infancy and 7 years for full-term (FT) and very preterm (VPT) children. (a) Displacement map with areas of expansion (red) and contraction (blue), overlaid on mean of all hippocampi. (b) Statistical p-value map of significant regions of shape difference between time-points, after Bonferroni correction. (c) Mean overlay of 7 year (blue) and infant (red) hippocampi. (d) Statistical p-value map for areas of longitudinal shape change that significantly differed between FT and VPT children, after Bonferroni correction.

Discussion & Conclusions: Results indicate that both FT and VPT infants' hippocampi undergo further infolding or 'curling up' between infancy and 7 years. Furthermore, the developmental trajectory of the hippocampus between infancy and 7 years in VPT children differs from that of FT children, particularly for the left side. It is uncertain whether this difference reflects disruption to development or developmental 'catch up' for the VPT hippocampus. This is the first study to examine morphological differences in hippocampal development longitudinally in early childhood, hence contributing to our understanding of early hippocampal development. Further research is underway to determine if there is functional significance for these findings.

References:

1. Thompson, D.K., et al., Ann Neurol, 2008. 63(5): 642-651.
2. Okada, Y., et al., Neuroreport, 2003. 14:1405-1409.
3. Thompson, D.K., et al., ISMRM, 2011. Abstract no. 1508.