Surface deformation-based analysis of regional shape variations of hippocampus in children with FAS

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Introduction Fetal Alcohol Syndrome (FAS) – a condition caused by chronic maternal alcohol consumption during pregnancy is estimated to be the most common preventable cause of learning disability worldwide [1]. The effect of prenatal alcohol exposure on poorer infant growth is seen not only in children with full FAS but also in alcohol-exposed children who lack the characteristic facial dysmorphology [2-4]. Recent studies have reported very heavy alcohol use during pregnancy [5,6] and a high prevalence of FAS in the Cape Coloured community in the Western Cape Province of South Africa [7,8], with one of the highest incidences of FAS in the world. MRI studies of children and adults with Fetal Acohol Spectrum Disorder (FASD) have demonstrated disproportionately smaller cerebellum, parietal lobe, caudate nucleus, and corpus callosum [9]. Structural anomalies have also been documented in the perisylvian cortices of the parietal and temporal lobes. To date, shape analyses have only been performed of the corpus callosum [10]. We report initial results using shape analysis to analyse structural variations in the hippocampus.

Methods High-resolution structural MRI images were acquired of 12 children aged 9-12 years on a 3T Siemens Allegra Scanner (6 controls and 6 FAS/partial FAS). Hippocampi were manually delineated using MultiTracer software by an expert neuroanatomist (CW). The entire structure of the hippocampus was divided into three regions, namely head, body and tail. The head is the expanded anterior end. The tail lies posterior to the coronal section where the fornix crus are best defined. The body is the region in between. The segmented images were binarized to estimate three parameters: volume, major axis length and minor axis length. A point distribution model, which represents the mean geometry of a shape using landmark points, was used to capture the true geometry of the hippocampus. Approximately 2366 landmark points were used. Principal Component Analysis (PCA) was used to study correlations of movement between groups of landmark points among the control children who were used as the training set and to assess the geometric variations between the healthy and exposed subjects. Hotelling's T^2 statistics were computed using the sample covariance matrix to compare the mean shape values for control and exposed children.

Results and Discussion

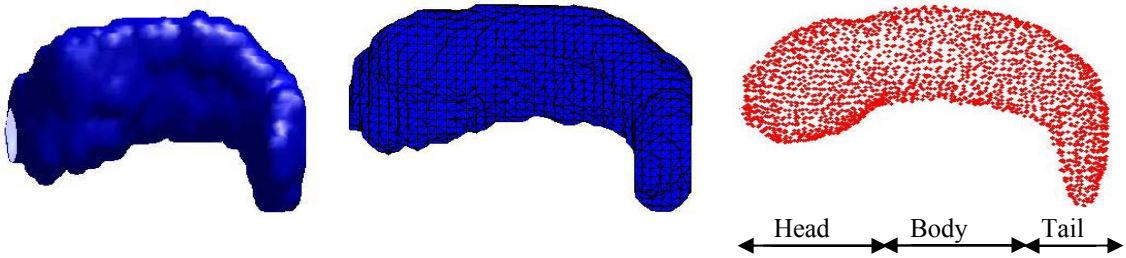

Figure 1 : (a) Reconstructed 3-D Model of left Hippocampus (b) Mesh model (c) Landmark points.

Figure 1 (a) shows the reconstructed three dimensional (3-D) model of the hippocampus of a single non-exposed control child; Figure 1(b), its corresponding mesh model; Figure 1(c), landmark points. Group means for the hippocampal regions are shown in Table 1. Only in the body region of the hippocampus do we see a reduction in the volume of exposed children compared to controls that tends towards significance (p<0.1, Student's t-test). The locations where there are significant shape differences between the control and exposed children are highlighted in blue in Figure 2 and are largely limited to the body region.

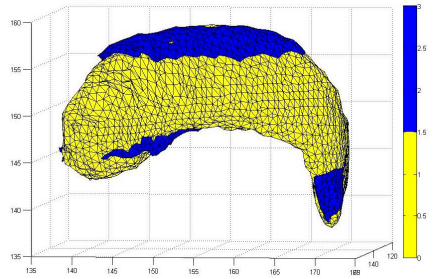

Figure 2: Regions of significant shape variations

Table 1: Mean Parameter Estimates for Hippocampus

Region of Interest	Head		Body		Tail	
Parameters	Control	FAS/Partial FAS	Control	FAS/Partial FAS	Control	FAS/Partial FAS
Volume (mm^3)	81.31	83.55	61.86	56.43*	87.57	87.96
Major axis length (mm)	12.09	12.62	11.94	11.60	16.52	16.10
Minor axis length (mm)	8.29	8.21	7.03	6.70	7.11	7.27

* ($p < 0.1$)

Conclusions In this work, shape analyses were used to study the effects of prenatal alcohol exposure on the hippocampus. Instead of using the whole hippocampal structure for shape analysis, it was divided in to head, body and tail regions. By contrast to the earlier findings by Archibald et al., (2001), who reported no significant reductions in hippocampal volume of exposed children, we find reductions in the body region of the hippocampus that tend towards significance, as well as shape variations in this region. These differences may become significant with a larger sample size. This method can be extended to other parts of the human brain, such as caudate nucleus and cerebellum, to gain a better understanding of regions most sensitive to prenatal alcohol exposure.

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