Association of Hippocampal Shape with Children's Cognitive Performance Analyzed Using Radial-Distance Mapping and Two Non-Rigid Registration Methods

Peter T Fwu[1], Elysia P Davis[2], Claudia Buss[2], Muqing Lin[1], Kevin Head[2], Curt A Sandman[2], and Min-Ying Su[1]

[1]Tu&Yuen Center for Functional Onco-Imaging, University of California, Irvine, CA, United States, [2]Women and Children's Health and Well-Being Project, Department of Psychiatry & Human Behavior, University of California, Irvine, CA, United States

Background and purpose:

The hippocampus is a brain structure prominently involved in learning and memory. Many studies have evaluated hippocampal changes during the course of normal and pathological aging, fewer studies have addressed its normal developmental trajectory in children. The human hippocampus is identifiable between 6-7 gestational weeks [1] and by birth the basic neuro-anatomical architecture of these regions is present [2-3]. Hippocampal development continues rapidly over the first two postnatal years [4-5], and becomes slower from childhood to young adulthood. We have collected an MRI dataset from a cohort of children 6-10 years old with a comprehensive cognitive evaluation at the time of imaging. In a previous study we have shown that the volume of the hippocampi in these children did not vary substantially with age, but the shape analysis was more sensitive to detect small subregional changes [6]. There are two major approaches for shape analysis: one by mapping the distance from the surface contour to the centerline of the hippocampus onto a 2-D grid map (termed "radial-distance mapping", or "RDM"), and the other by comparing the extent of transformation for each individual hippocampus to match to a standard template using non-rigid coregistration algorithms. In this study, we analyzed the association of hippocampal volume and shape with respect to their cognition performance in 4 different tasks.

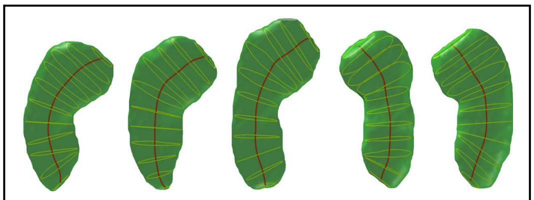

Fig.1: Example of 5 hippocampi showing various shapes. The centerline & cross-sections are used for normalization.

Methods:

The structural MRI scans were acquired from 103 children between the ages of 6-10 years (74 to 119 months old, mean: 7.3 ± 0.9 years), 50 males and 53 females. The hippocampus was manually outlined on the ICBM152 template using a protocol developed by the Montreal Neurologic Institute. Each hippocampus was further divided into the head, body, and tail segments manually by the operator to measure these sub-regional volumes. Shape analysis was performed using methods as previously reported in [6]. As shown in **Fig. 1**, there is a high heterogeneity, and they need to be normalized for shape analysis. The centerline of the hippocampus was first extracted using a level-set based algorithm, and the whole hippocampus was divided into 150 sections by uniformly segmenting each section perpendicular to the centerline. The radial distance at each surface grid point was measured. For registration-based methods, a template was generated using the average of all subjects. Two non-rigid registration algorithms using the surface grid point based RPM and volume-based Demons were applied to register each hippocampus to the template. Based on the deformation matrix, the radial distance difference (RDD) from the template at each surface point can be measured. RDD>0 means the subject has an expanded contour relative to the template, and RDD<0 means contracted contour compared to the template. Four tasks were used to evaluate the participants' cognitive capability, including sequential sequence, recognition, learning (immediate recall) and memory (delayed recall). Pearson's linear correlation analysis was used to evaluate the association between RDD value at each surface point and performance score as a continuous variable. Multiple comparisons were performed using the False Discovery Rate (FDR). We also performed separate analysis stratified by sex.

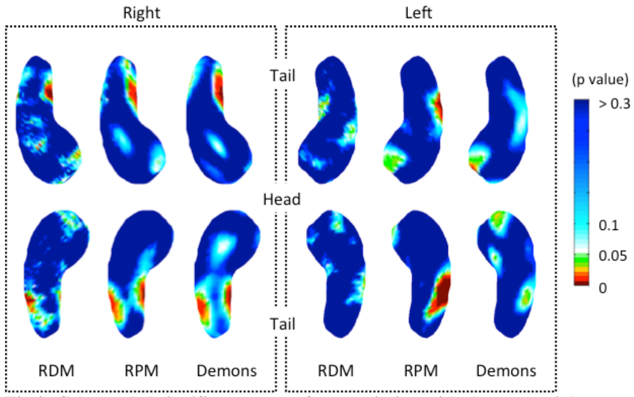

Fig.2: Color-coded significance maps for association with the sequential sequencing task scores analyzed using three methods. Green color represents the significant level at p < 0.05. The hippocampus was cut longitudinally and open to show top view and bottom view. The shape of the right tail segment was associated with this performance score, which survives FDR correction.

Results:

Fig. 2 shows the RDD significance map with respect to performance scores in the sequential sequence task using three different methods (RDM, surface-based RPM registration and volumetric registration using Demons). A region of interest (ROI) of 7.1 mm^2 was placed over the significant area, and the RDD value for each subject was extracted for further analysis, as shown in **Fig. 3**. Interestingly, no area was significantly associated with learning (immediate recall). None of the sub-field volumetric measurements was significantly correlated with test scores.

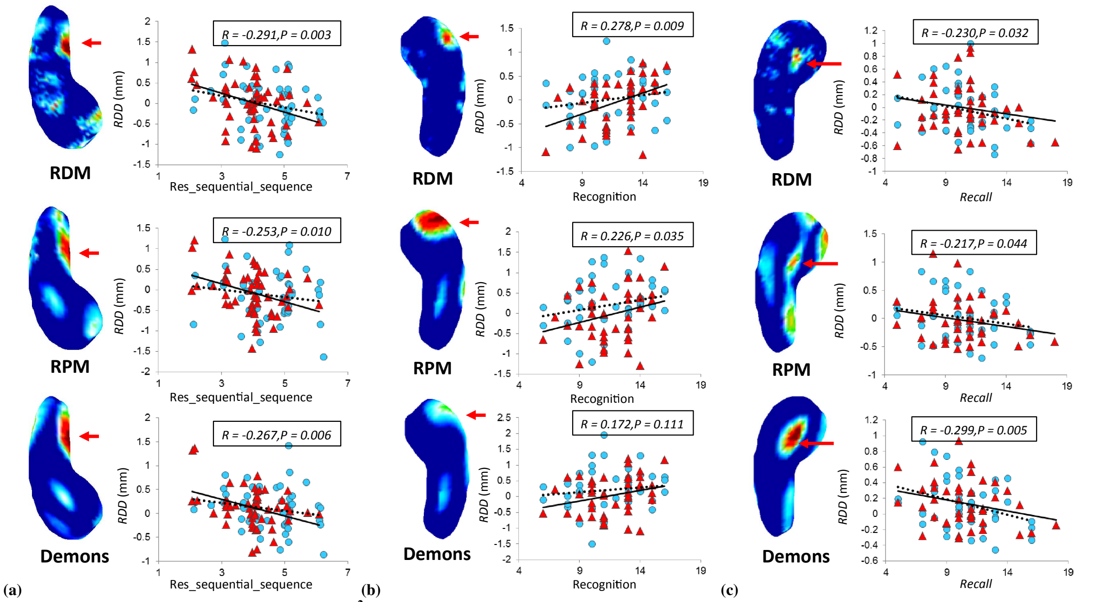

Fig.3: The ROI analysis by placing a 7.1 mm^2 area on the surface marked by arrows to correlate the hippocampal shape (a) with sequential sequence in the tail of right hippocampus; (b) with object recognition in the head of left hippocampus; (c) with memory (delayed recall) in the head/body of right hippocampus. There is no significant area associated with learning (immediate recall). Red triangle symbols represent girls, and blue circles represent boys. Results suggest that different areas in hippocampus are associated with different tasks.

Discussion:

The results suggest that different hippocampal regions are associated with different cognitive tasks. Techniques for super high spatial resolution imaging within hippocampus are being developed, and they may be used to evaluate the tissue layers that are associated with performance of different tasks. Hippocampal shape analysis may be further applied to detect early deviations from the normal developmental trajectory in young children for evaluating susceptibility for psychopathological disorders involving hippocampus.

References: [1] Humphrey. Trans Am Neurol Assoc 1964; 89:207-209. [2, 3] Arnold & Trojanowski. J Comp Neurol 1996; 367:274-292 and 367:293-307. [4] Utsunomiya et al. AJNR 1999; 20:717-723. [5] Knickmeyer et al. J Neurosci 2008; 28:12176-12182. [6] Lin et al. Int J Dev Neurosci. 2013; 31(7):473-481.