Longitudinal study of the corpus callosum thickness in developing monkeys

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Introduction: Corpus callosum (CC) is the largest fiber in the brain and connects the two hemispheres. The thickness of CC is of particular interest on the study of the agenesis of CC and it is found positive correlation exists between the CC thickness and intelligence [1]. Despite the vast literatures regarding its structure and function, the longitudinal changes of CC thickness from infancy to adolescence remains unclear [2, 3]. The non-human primate (NHP) models have been increasingly applied for studying neurodegenerative diseases and cognitive impairment relative disorders [4, 5]. This study is aimed to investigate the longitudinal changes of CC thickness in the rhesus monkeys from infancy to adolescence with the high resolution MRI images.

Methods: 4 young rhesus monkeys were scanned at the age of 6, 12, 18 and 24 months old respectively. 4 adult animals (6-11 years old) were scanned for comparison purpose. During MRI scanning, animals were anesthetized with 1-1.5% isoflurane mixed with air and immobilized with a head holder. Animal physiological parameters such as End-tidal CO_2, inhaled CO_2, O_2 saturation, blood pressure, heart rate, respiration rate, and body temperature were monitored continuously and regulated. MRI experiments were performed on a Siemens 3T Trio scanner (Siemens Medical System) using a phase-array knee coil (Invivo, Inc, FL).The T1-weighted images were acquired with MPRAGE sequence. MRI parameters were: TR / TE = 2500/3.48ms, FOV= 96 mm × 96 mm, voxel size was 0.5 × 0.5 ×0. 5mm^3, 6 averages. The CC was measured in the mid-saggital slice. CC was traced manually to quantify the area and perimeter of each region with the ImagJ software (Fig.1). The CC thickness was calculated with the formula: thickness = area*1/2 perimeter. One-way ANOVA and Pearson correlation analysis between the age and CC thickness were performed. SPSS 17.0 was used for statistical analysis. P-values less than 0.05 were considered statistically significant.

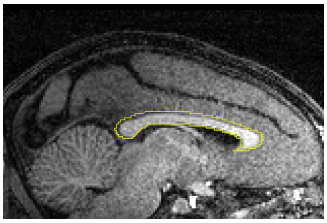

Fig. 1 MRI of a mid-sagittal section of an adult rhesus monkey brain. The perimeter of corpus callosum is marked (yellow line).

Results: The mean thickness of CC is increased significantly at 24 months old compared to 6 month group (Fig.2). The correlation between normalized thickness of the CC and age indicates that the CC thickness increase with age progressively from 6 month to 24 month (Fig.3). In comparison with the adult monkeys (108 month, 9 years old), the CC thickness at 24 month is thinner than but close to adult monkey.

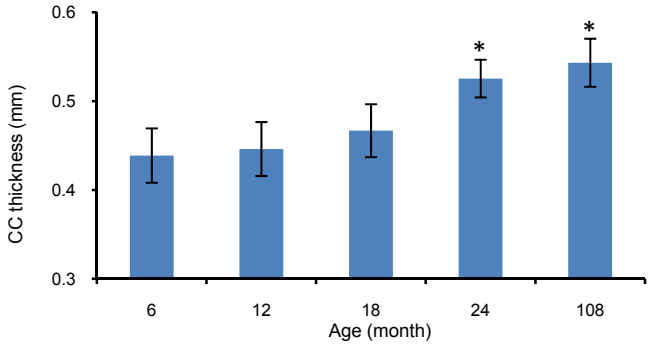

Fig. 2 Mean mid-sagittal thickness of the rhesus monkey corpus callosum at different age (mean±SD). *, p<0.05 compared to 6 month group.

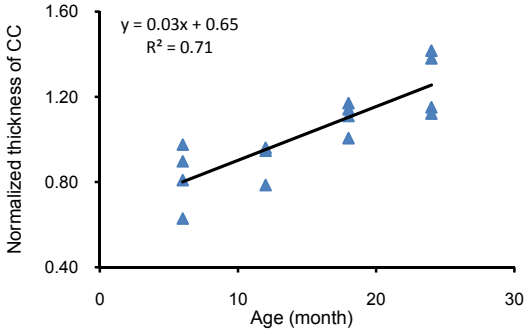

Fig. 3 A significant positive correlation of the mid-sagittal thickness of the rhesus monkey corpus callosum with age between 6 to 24 months.

Discussion: The evolution of corpus callosum (CC) was integral to the development of higher cognitive processes [9]. Significant positive correlations between callosal morphology and intelligence measures were observed in human subjects [8]. The CC was found significantly thinner in attention-deficit/hyperactivity disorder (ADHD) subjects in the anterior and, particularly, posterior callosal sections [10]. It was suggested that the CC thickness might be a marker to detect maturational delays or persist into adulthood. Therefore, the examinations of the CC thickness in the developing monkeys can improve our understanding of the development of higher cognitive processes in the NPH. This study found that the CC thickness demonstrated significant age-related elevation (R=0.84, P<0.001, Fig.3).Significant difference observed when 24 months old may indicate that 24th month might be a key time in the CC development. In comparison with adult monkeys, the CC thickness in 2 years-old monkeys is still thinner than 9 year-old adult monkey. It may suggest that CC is still in the development of maturation in this period [2-3]. Large sample size might improve the significance.

Conclusion: These preliminary data indicated that the CC thickness of the rhesus monkeys has age-dependent elevation from infancy to juvenile. There may exist fast developing period when 24 months old during the development of monkeys.

Reference: [1] Gazzaniga et al, Brain (2000); [2] Michael S. Franklin et al., Brain research (2008); [3] Peter J. Pierre et al., Brain research (2008); [4] Dudkin et al, NBP (2006); [5] Ratai EM et al, BMC Neurosci. (2009); [7] Hofer, S et al., Cereb Cortex (2008); [8] Luders, E.Neuroimage (2007); [9] Phillips, K. A et al, Neuroscience (2009); [10] Luders, E., Biol Psychiatry (2009)