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Diffusion tensor imaging of normal brain development from infancy to early childhood

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Introduction

MRI plays an important role in the diagnosing pathologies in pediatric brain. Diffusion tensor image (DTI) is sensitive to differentiate white and gray matter and facilitate evaluation for maturation of white matter. It is important to understand the development of white matter, such as myelination, in early development of the brain in children with developmental delay. DTI has been used in various studies on developmental brain diseases, yet the normal reference values according to age are not clearly established. This study aims to provide the fraction anisotropy (FA) value of DTI in normal pediatric brain according to age from infancy to early childhood.

Methods

Children from 6 to 60 months of age were recruited. Children with any history of perinatal adverse events were excluded. Based on the screening developmental assessments including gross motor function measure (GMFM), Bayley scales of infant development-II (BSID-II, for those aged < 3) and Wechsler preschool and primary scale of intelligence (WIPPSI, for those aged ≥ 3), any children with possible developmental delay were excluded. MRI Images of all subjects were acquired on a 3-Tesla MRI Scanner (Signa HDxt; GE Medical systems, Milwaukee, WI). Voxel-wise statistical analysis of the diffusion weighted images was performed using the Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL version 4.1). Atlas-based regions of interest were automatically created using Johns Hopkins University White-Matter Tractography Atlas (Kegang Hua, Neuroimage, 2008). FA values according to different ages were analyzed through non-linear regression analysis and Pearson's correlation test.

Results

Twenty-one participants were recruited after screening developmental assessments. Clinical history and results of developmental evaluation are described in Table 1. Each participant was confirmed to be in a normal range of development in aspect of both cognitive and motor functions. FA value rapidly increased in strong correlations to the age until first 24 months in white matter fibers such as anterior thalamic radiation, projection

to hippocampus, corticospinal tract, inferior longitudinal fasciculus, superior longitudinal fasciculus, inferior fronto-orbital fasciculus and corpus callosum (R>0.7 and p<0.05 for all the above listed fibers). However, the increase in FA value was subtle after 24 months (-0.1<R<0.35 and p>0.05 for all the above listed fibers).

Conclusion

This study provides the reference range of FA value in children with normal motor and cognitive function aged between 6 and 60 months. For most of white matter tracts, FA value rapidly increased according to age until the first 24 months, whereas the changes in FA value kept plateau after 24 months. These reference values could be later used to compare FA values of children with various disease spectrums

Table 1. Demographics of normal subjects

Characteristics	Total (n=21)	6-24 months (n=8)	24-60 months (n=13)
Sex (male / female), *n*	12/9	3/5	6/7
Age, months	31.7 ±17.8	13.0±4.9	43.2±11.8
Gestational age, weeks	38.7 ±1.3	39.1±1.6	38.5±1.1
Mode of delivery (NSVD/C-sec/Unknown), *n*	9/10/2	3/4/1	6/6/1
Birth weight, kg	3.05 ±0.3	3.15±0.3	3.0±0.3
BSID-II PDI score	105.1±9.6*	99.6±10.4*	102.5* (95, 109)
BSID-II MDI score	100.4±10.0*	106±8.3*	102.5* (92, 114.5)
WPPSI score			
Total IQ	99.8±8.8§		99.8±8.8§
Performance IQ	97.9±12.8§		97.9±12.8§
Verbal IQ	101.7±10.0§		101.7±10.0§

Values are shown as mean± standard deviation. BSID-II was used for the subjects under three years old (n=12) and WIPPSI was used for over three years old (n=9). *Number of children who underwent BSID-II was 12, 8, and 4 among the total population, children aged 6-24 months, and children aged 24-60 months, respectively. §Number of children who underwent WPPSI was 9 among the total population and only for children aged 24-60 months. Abbreviations: NSVD, normal spontaneous vaginal delivery; C-sec, caesarean section; BSID, bayley scales of infant development; GMFCS, gross motor function classification system; PDI, psychomotor Developmental Index; MDI, mental Developmental Index; WPPSI, wechsler Preschool and Primary Scale of Intelligence; IQ, intelligence quotient
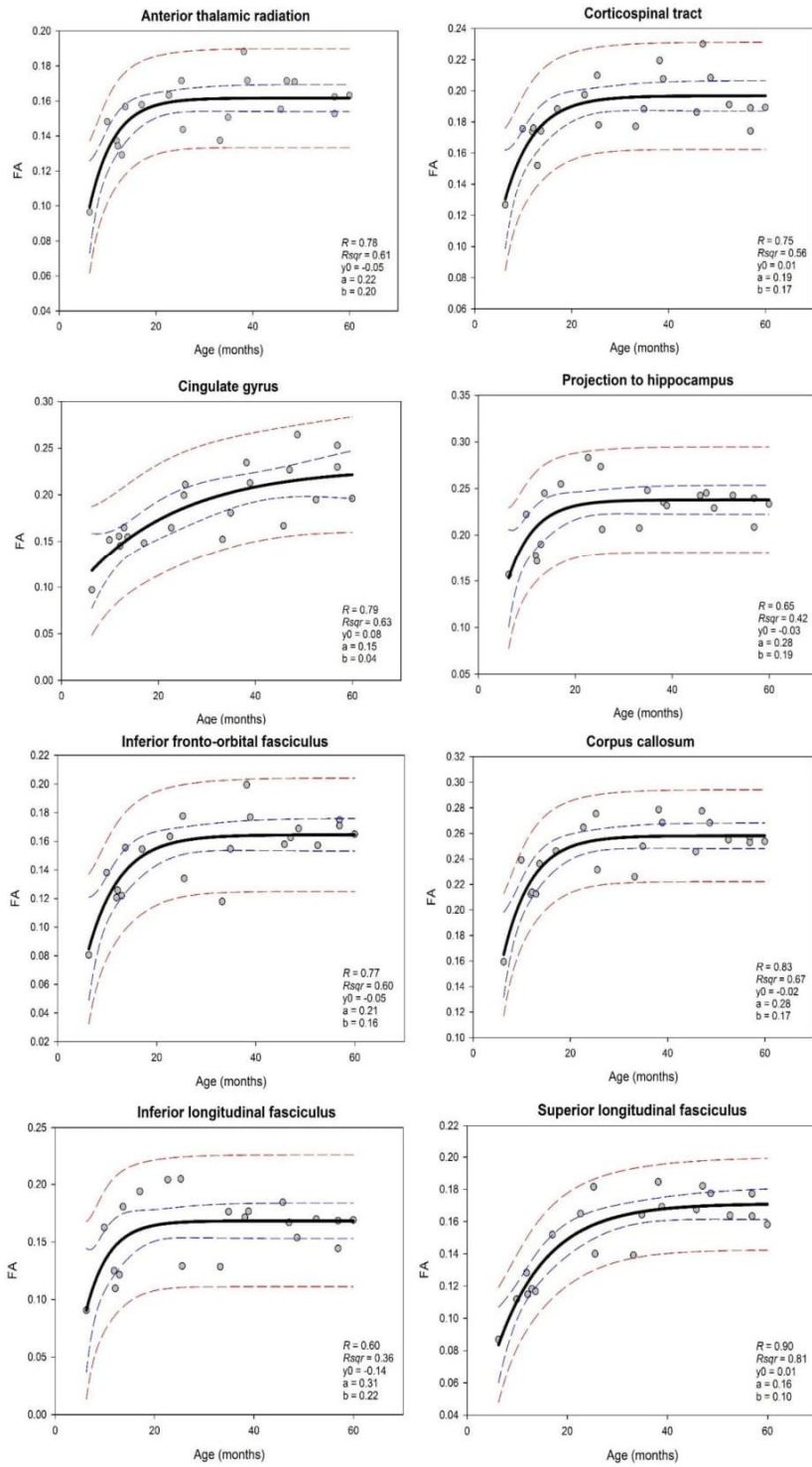
Changes of FA value according to aging in white matter tracts (anterior thalamic radiation, projection to hippocampus, corticospinal tract, cingulate gyrus, inferior longitudinal fasciculus, superior longitudinal fasciculus, inferior fronto-orbital fasciculus and corpus callosum) were fitted to exponential curve [equation; $FA = y_0 + a*(1-\exp(-b*x))$, $R>0.6$, $p<0.05$]. All the parameters and coefficients were described in each graph; 95% confidence index was depicted as blue dash and 95% prediction index was depicted as red dash Abbreviation; FA, Fractional anisotropy

Figure. 1 FA value of each white matter tract in normal subjects