Age norms for diffusion tensor data - evaluation with TBSS

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Although it is known that FA increases throughout childhood and adolescents in many portions of the brain, reproducible quantitative normative age-related tensor data is not widely available in a clinically useful format. We propose to (i) present in tabular format the mean and lower limits of normal for FA in school aged children derived using TBSS and (ii) explore age effects on the axial and radial diffusivities in different white matter (WM) tracts.

Materials and methods: 34 normal children 6-18 years (16 males) right-handed, English speaking, FSIQ > 84 (WASI-III), no behavioral or emotional (CBCL T-score <70), language (CELF score >4), or academic problems were studied. Seven subjects were followed longitudinally over 1-3 years. MR imaging (3T): SS-EPI, 30 directions, 3 acquisitions, b=700, 2 mm^3 voxel, TR/TE 8240/74; no sedation. Analysis was done using TBSS (FMRIB Software Library, FMRIB Oxford, UK); the target image was a 9 year old. All subjects were nonlinearly registered to the target subject and affine transformed into MNI152 standard space. Voxel-by-voxel statistical analysis was performed to detect regional age-related changes in FA . Clusters of statistical significance were analyzed using a custom program written in IDL; FA and λ_l, λ_2, and λ_3 were averaged over 7 in-plane voxels contiguous with the local maxima on the FA skeleton. Linear regression was used to determine the age effects; change in FA per year was calculated over the 12 year age range studied. FA values within 2 S.D. of the mean are considered to be the lower limit of normal.

Results: The largest age effects on FA were in the occipital-temporal gyri and cingulum (cing) followed by the corticospinal tracts (CST), inferior frontal gyrus (IFG) right>left and external capsules; right=left. In these regions, FA increased 2-3.8% per year. There were minimal age effects on FA within the callosal genu and splenium. Age effects on λ_1 were highest in the left cingulum; 2% increase in λ_1/yr followed by the left inferior longitudinal (ILF) inferior fronto-occipital fasiculus (IFO) and superior longitudinal fasiculus (SLF). Increases or decreases of <0.1% in λ_1 were seen in the remainder of the tracts studied. The largest decreases in radial diffusivity were seen in the CST; -4.4-5% per yr followed by the left cingulum, uncinate, and occipito-temporal WM while the smaller decreases in radial diffusivity were seen in the left IFO and IFG.

Conclusions: Variable age effects on tensor metrics were seen across the brain in school-aged children using TBSS. Valid comparisons of FA and diffusivities between typically developing children and children with neuro developmental or psychiatric conditions probably require age-matched cohorts unless the affects of the disease are known to be large in comparison to the scale of age effects.

Table I. Examples of mean FA and lower limits of normal for age by location

	6 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs
Genu	0.87(0.81)	0.87(0.82)	0.88(0.82)	0.88(0.83)	0.89(0.83)	0.89(0.84)	0.90(0.84)
Mid body	0.65(0.55)	0.67(0.57)	0.69(0.59)	0.70(0.61)	0.72(0.63)	0.74(0.65)	0.76(0.66)
Splenium	0.87(0.77)	0.88(0.78)	0.89(0.79)	0.89(0.80)	0.90(0.81)	0.91(0.81)	0.92(0.82)
Rt ALIC	0.60(0.50)	0.62(0.52)	0.63(0.54)	0.65(0.56)	0.67(0.57)	0.69(0.59)	0.71(0.61)
Lt ALIC	0.54(0.45)	0.56(0.47)	0.58(0.49)	0.61(0.51)	0.63(0.53)	0.65(0.55)	0.67(0.57)
Rt PLIC	0.72(0.62)	0.73(0.64)	0.75(0.66)	0.77(0.68)	0.78(0.69)	0.80(0.71)	0.82(0.72)
Lt PLIC	0.67(0.59)	0.69(0.61)	0.71(0.63)	0.73(0.65)	0.75(0.67)	0.77(0.69)	0.79(0.70)
Rt CST	0.59(0.49)	0.63(0.53)	0.67(0.57)	0.70(0.60)	0.74(0.64)	0.78(0.67)	0.81(0.71)
Lt CST	0.67(0.57)	0.70(0.60)	0.73(0.63)	0.76(0.66)	0.78(0.68)	0.81(0.71)	0.84(0.73)
Rt unc	0.54(0.43)	0.56(0.46)	0.59(0.48)	0.61(0.51)	0.63(0.53)	0.66(0.55)	0.68(0.57)
Lt unc	0.44(0.34)	0.46(0.37)	0.48(0.39)	0.50(0.41)	0.52(0.43)	0.54(0.44)	0.56(0.46)
Rt ext cap	0.32(0.25)	0.34(0.27)	0.35(0.29)	0.37(0.30)	0.38(0.32)	0.40(0.33)	0.41(0.34)
Lt ext cap	0.36(0.26)	0.38(0.28)	0.40(0.29)	0.42(0.31)	0.43(0.33)	0.45(0.34)	0.47(0.36)
Rt ILF	0.51(0.39)	0.53(0.41)	0.55(0.43)	0.56(0.45)	0.58(0.47)	0.60(0.48)	0.62(0.50)
Lt ILF	0.52(0.41)	0.53(0.43)	0.55(0.45)	0.56(0.46)	0.58(0.47)	0.59(0.49)	0.61(0.50)
Lt SLF	0.47(0.37)	0.49(0.39)	0.50(0.41)	0.52(0.43)	0.54(0.45)	0.56(0.47)	0.58(0.48)
Rt SLF	0.47(0.39)	0.48(0.40)	0.49(0.42)	0.51(0.43)	0.52(0.44)	0.54(0.46)	0.55(0.47)
Rt IFO	0.62(0.46)	0.64(0.48)	0.66(0.50)	0.68(0.52)	0.69(0.53)	0.71(0.55)	0.73(0.56)
Lt IFO	0.61(0.48)	0.63(0.50)	0.64(0.51)	0.65(0.52)	0.66(0.53)	0.67(0.54)	0.68(0.55)
Rt IFG	0.35(0.25)	0.37(0.27)	0.39(0.29)	0.41(0.31)	0.43(0.33)	0.45(0.35)	0.47(0.36)
Lt IFG	0.30(0.19)	0.31(0.21)	0.33(0.22)	0.34(0.24)	0.36(0.25)	0.37(0.26)	0.39(0.27)
Lt cing	0.55(0.45)	0.58(0.49)	0.62(0.52)	0.65(0.56)	0.69(0.59)	0.72(0.62)	0.76(0.65)
Rt cing	0.49(0.37)	0.52(0.40)	0.55(0.43)	0.58(0.46)	0.60(0.49)	0.63(0.52)	0.66(0.54)
Rt oc tem	0.33(0.24)	0.36(0.27)	0.38(0.30)	0.41(0.32)	0.44(0.35)	0.47(0.38)	0.50(0.40)
Lt oc temp	0.35(0.21)	0.38(0.25)	0.42(0.28)	0.45(0.32)	0.49(0.35)	0.52(0.39)	0.56(0.42)