An ROI-based Assessment of Inter-session Variability of Fractional Anisotropy: Implications for Longitudinal Studies

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Introduction

Fractional anisotropy (FA) is an indicator of the integrity of white matter (WM) which changes during the progression of neurological diseases such as multiple sclerosis (MS)[1]. Since FA may act as a marker of disease severity and progression[2], in longitudinal studies precise assessments are important. It is necessary to determine whether FA measurements vary considerably on different days due to session-dependent variables such as field drift, different head orientation in the coil, and normal physiological changes. We hypothesized the variance introduced by imaging in different sessions is small compared to other independent variability sources (e.g. imaging noise). Methods to reduce intra-session variance, such as averaging multiple intra-session runs, would thus be sufficient to decrease variability between scans on different days. The results of our ROI-based experiment determine if session-dependent sources of variance are important when compared to other sources of variability. This information will be useful when designing longitudinal studies to monitor FA in individual patients.

Methods

Using a 3-T General Electric MR scanner (GE Healthcare, Waukesha, WI) with a standard quadrature head coil, four healthy volunteers were each scanned on 3 different days. In each session, a localizer scan, a high-resolution T1-weighted anatomical sequence, and a high-order shim preceded five diffusion tensor imaging (DTI) sequences (11-directions, b = 850 $s \cdot mm^{-1}$, TR / TE = 10000 / 72.8 ms, FOV = 24 cm, matrix size = 96 x 96, slice thickness = 4 mm, 32 slices, dual spin-echo EPI, 2.2 minute scan time). Geometric distortions inherent to diffusion-weighted EPI were corrected by using Functool 2 (native scanner post-processing software) to register diffusion weighted images to the T2-weighted volume within each DTI series. Functool 2 then generated the FA maps. Image registration of the T2 volumes to high-resolution anatomical volumes both within and across sessions was performed using FLIRT (FMRIB, Oxford University) and the same transforms were applied to the FA volumes. Stimulate (University of Minnesota) was then used to record FA in 26.6 mm^2 ROIs (~0.1mL volume) that were placed on the optic radiation, corticospinal tract, and the anterior and posterior corpus callosum (CC). For each participant and each ROI, FA was calculated for 1, 2, 3, 4 or 5 intra-session averages, and these averages were used to determine inter-session variability, calculated as the coefficient of variation (CV). After a linearization of the data, regression analyses separated general imaging variability from variability due only to imaging on different days, and these two values were compared. Finally, an ANOVA was performed in each ROI to determine if there was an effect of the number of intra-session averages on CV.

Results

Image registration was acceptable in all areas examined except the optic radiation, which was sometimes partially outside the ROIs, even between intra-session volumes. In other regions, regression analyses showed that imaging on different days is a relatively small source of variability compared to other independent sources of variability. In the anterior CC, the variance from intersession effects accounted for only 0.14% of the total variance, which was significantly lower than variance due to other effects (99.86%) (p = 0.038). Inter-session effects accounted for a small fraction of the total variance also in the posterior CC (6.34%) and the corticospinal tract (–2.09%, errorbars extend into the positive range) and both were nearly significant when compared to other variance due to other effects (p = 0.069 and p = 0.058 respectively)(see Figure, top). Similar results were not found in the optic radiation, but this is likely due to image registration errors between sessions.

As expected, CV in inter-session FA measurements decreased as runs averaged per session increased (See Figure, bottom). ANOVAs revealed a significant effect of number of runs averaged on CV in the anterior CC [$F(4,15) = 3.42$, p = 0.035] and posterior CC [$F(4,15) = 3.49$, p = 0.033]. Post-hoc Tukey multiple comparisons revealed that for both CC areas, 5 averaged intra-session runs had significantly lower CV than a single run (p=0.03 for both).

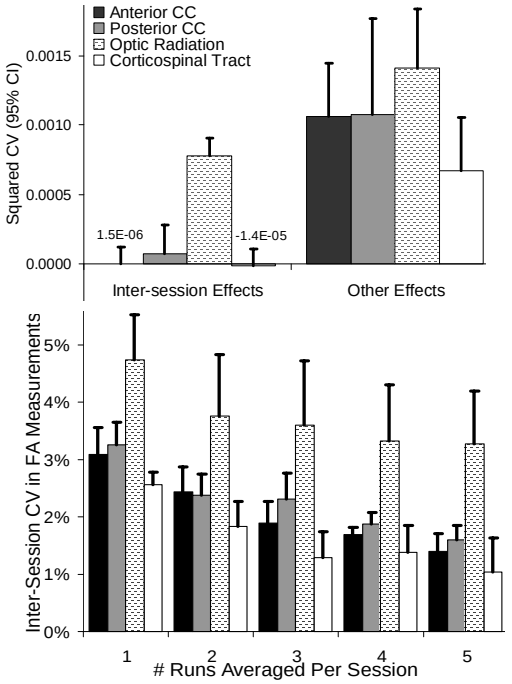

Figure: Top: In FA measurements, variance contributions from intersession sources are smaller than contributions from other sources such as noise. Bottom: Intersession coefficient of variation when measuring FA decreases as more intra-session runs are averaged. Error bars show the standard errors.

Conclusion

Our data show intersession effects on measurements of FA variation are considerably smaller than other effects such as noise. Thus, methods to reduce intra-session variability, such as averaging multiple runs, may be sufficient to reduce variability for longitudinal studies, so that small yet significant changes in FA can be detected.

References

1. Ge Y., *et al*. J Magn Reson Imaging. 2004; 20: 1-7.
2. Cassol E., *et al*. Mult cler. 2004; 10: 188-96.