Ageing and Fractional Anisotropy: Global and Regional Results

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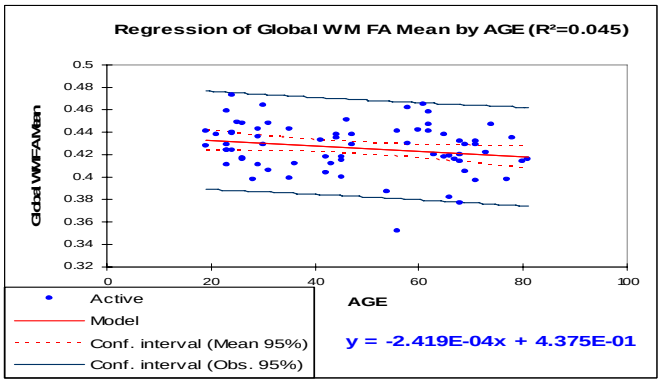
Introduction: In the recent years, diffusion-weighted MR methods such as DTI, DSI, and Q-ball have been frequently applied to improve diagnosis of neurological disorders that involve significant alterations of the white matter (WM). In particular, fractional anisotropy (FA) derived from DTI was measured in such diverse neurological disorders as traumatic brain injury (TBI), Alzheimer disease, Parkinson's disease, stroke, schizophrenia, and multiple sclerosis. The majority of the studies reported reduced FA value in the target groups compared to normal controls. We used a whole brain WM FA histogram approach to differentiate TBI patients from controls[1]. However, to use diffusion anisotropic imaging most effectively in neurologic disorders, we must account for age effects which may also decrease FA[2]. Because aging is associated with FA reduction[3], it is important to assess age effects on the FA histogram. In this work, we evaluate the effect of age on whole brain (global) WM FA and regional FA of the corpus callosum. The latter, a major WM structure connecting the cerebral hemispheres is a common site of axonal injury following TBI[4] . Given the increase in proportion of milder TBI and improvement of survival of TBI victims of all ages over the last few decades, accurate discrimination of TBI from normal controls requires a thorough description of age effects on WM structures. Furthermore, improved understanding of the effect of age on the FA histograms will also contribute to understanding of the effects of other neurological disorders on the WM.

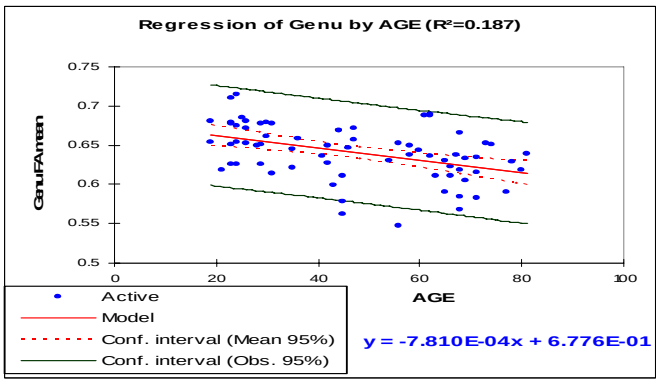
Materials and Methods: 70 healthy volunteers (age range 19-81 (Mean age = 47 years, SD= 19.22 years) were imaged with standard MRI sequences and DTI as a part of a multi-imaging protocol on a Siemens Sonata 1.5 T scanner. Single-shot spin-echo planar DTI was acquired in 6 directions with the following parameters FOV = 256*256, 128*128 matrix size, in-plane resolution of 2*2*4, 35 slices, TR/TE = 5800/97, b values of 0 and 1000 sec/mm^2, NEX = 10. The conventional sequences included high-resolution 3D FLASH T1, T2, Fluid Attenuation Inversion Recovery (FLAIR), Arterial Spin Labeling (ASL), Diffusion Weighted Imaging (DWI) and Susceptibility Weighted Imaging (SWI) sequence. Corresponding FA maps were generated using DTI studio (http://www.mri.kennedykrieger.org) software with an optimal background noise suppression threshold of 50 units.

Regions of interest (ROIs) were generated in a three-step procedure:

First, spatially normalized FA images were created. For that purpose, each FA map was spatially normalized to an FA template in SPM2 (http://www.fil.ion.ucl.ac.uk). The template was created from averaging 62 of the controls after normalization to the T1 template included in SPM2. To maximize spatial matching of white matter regions across subjects, normalization was strongly weighted by the white matter using the FA template. Second, we generated a White matter-only FA image. That image was created by segmentation (via SPM2) of each normalized FA image. A binary WM-only mask was created from each subject's normalized FA image using a thresholding function. Finally, ROIs were demarcated. That step was accomplished by applying a Boolean AND operator to the resulting WM masks with three corpus callosum ROIs. The latter were created from the FA template using anatomical landmarks to divide into anterior (genu), body and posterior (splenium) sections. CC-regional FA means and standard deviations (SD) for the 62 healthy subjects were obtained using Matlab scripts that were invoked using SPM2. Regional FA mean and SD were plotted vs. age (see below). The associations between FA and age for global WM, CC total, genu, body and splenium of CC regions were tested in linear regression models.

Results: All ROIs showed some decline in FA with age. However, the magnitude of the devline differed across the regions. The only significant age-related difference was observed in the genu of CC: correlation with age r = -.43, p < .001. This relationship is illustrated below and corresponds to a drop of .006 a.u per decade (0-0.014 a.u/year, 95% CI). The slopes were -7.8×10^{-4} a.u/year for genu, -1.9×10^{-4} a.u/year for the body and -2.8×10^{-4} a.u/year for the splenium. The slope for global WM was -2.4×10^{-4} a.u/year. In parallel with the decreases in FA with age we found an age-related increase in FA variance with age in all regions but the splenium. That increase was the greatest in the CC body: a slope of 9.4×10^{-5} a.u/year.





Discussion and conclusion: We found differential regional decline in FA with age. Although the trend was a small and insignificant in the total brain and posterior callosal regions, it was significant in the genu of the CC. In addition, we found a trend towards greater variance in FA with age suggesting a heterogeneous adverse effect of ageing on WM, which would, on average, cause a decrease in FA. Future work with this data set will examine the relative contributions of radial and axial diffusivity to the FA age effect. Future regional analysis will add to our understanding of the effect of age on WM FA which will then allow for more accurate assessment of TBI effects on global and regional FA as well as other disorders effecting WM.

References

References: [1]Global White Matter Analysis of Diffusion Tensor Images Is Predictive of Injury Severity in Traumatic Brain Injury (Benson et al 2007; Journal of Neurotrauma. Mar 2007, Vol. 24, No. 3: 446-459). [2]Correlation of white matter diffusivity and anisotropy with age during childhood and adolescence: A cross sectional DTI MRI study (Schmithorst,et al.2001; *Radiology* 2002;222:212-218). [3]Sullivan EV, Pfefferbaum A Diffusion tensor imaging and aging. Neurosci Biobehav Rev. 2006c;30:749-61. Epub 2006 Aug 1. [4]Levine B, Fujiwara E, O'Connor C, Richard N, Kovacevic N, Mandic M, Restagno A, Easdon C, Robertson IH, Graham SJ, Cheung G, Gao F, Schwartz ML, Black SE. In vivo characterization of traumatic brain injury neuropathology with structural and functional neuroimaging. J Neurotrauma. 2006 Oct;23(10):1396-411.