Age-related changes of the human brain: Insights from double-wave vector imaging

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Double wave-vector (DWV) or d-PFG experiments with two diffusion weighting periods applied successively in a single acquisition offer access to microscopic tissue properties [1-4]. With a short mixing time τ_m between the two diffusion weightings, the experiment can be used to determine cell or compartment sizes [1, 4], for a long τ_m diffusion anisotropy present on a microscopic scale can be investigated [1]. For instance, even in a white matter (WM) region-of-interest (ROI) that appeared isotropic in a DTI experiment, i.e. has a fractional anisotropy (FA) equal to 0, anisotropic diffusion could be detected [5] demonstrating the additional information that DWV can provide compared to DTI. Recent studies showed that a measure of the microscopic diffusion anisotropy, the MA index, can be determined in the living human brain [6, 7], and normal values and their variation in a group of young (< 33 y), healthy volunteers have been reported [8]. In this study, DWV and DTI measurements were performed in a group of old (> 60 y), healthy volunteers. Their MA and FA values were determined and compared to those reported for young volunteers [8] in order to investigate age-related changes of the diffusion anisotropy.

Methods

Experiments were performed on a 3T whole-body MR system (TIM Trio, Siemens Healthcare) with a 32-channel head coil. 18 elderly, healthy volunteers (60 -79 y, 67.69 ± 4.65 y) were measured after their informed consent was obtained. The same acquisition protocol as for the young volunteers was used [8]. DWV measurements were performed with spin-echo echo-planar imaging using an isotropic resolution of 3.0 mm (TE/TR = 150 ms/6.5 s) in 35 slices (gap 0.5 mm). Each diffusion-weighting period had a *b* value of 500 s mm^{-2}, a diffusion time Δ of 25 ms, a mixing time τ_m of 45 ms, and a gradient pulse duration δ of 22 ms. 96 combinations of 18 directions of the diffusion weighting were applied [7]. With six images without diffusion weighting acquired in-between the total acquisition time was 11 min 10 s. Four DWV measurements, one standard DTI experiment (60 directions, TE/TR = 100 ms/4.8 s, isotropic resolution 3.0 mm), and a T1-weighted anatomical measurement (MPRAGE, voxel size 1x1x1mm^3) were performed for each volunteer (total session time ≈1h). Data processing steps included motion-correction, coregistration and DARTEL [9] normalization performed with SPM08. To allow for a reliable comparison of the age-related effects, both the DTI and DWV data of the 18 young, healthy subjects [8] together with the data of the current study were matched on a common template (cf. [9]).

Results and Discussion

In Fig. 2, cross sections of the normalized MA and FA maps averaged over all 18 old volunteers and the differences Δ (young-old, respectively) are shown. FA values vary significantly in WM depending on the actual fiber orientation distribution. In contrast, MA values appear more homogenous because they are independent of the actual fiber orientation. This has also been observed in the group of young subjects [8]. The FA difference image shows both, regions with positive and negative values, whereas the MA difference is dominated by positive values, i.e. the MA is generally larger for the younger volunteers. This finding can also be seen in the histogram plots of ΔMA and ΔFA for white matter voxels (Fig. 3): The FA difference is almost centered around 0 (mean +/- standard deviation: -0.012 +/- 0.053) but the MA difference shows a clear trend towards positive values (0.039 +/- 0.053), i.e. overall reduced MA values for the older group. FA and MA normal values together with their standard deviation in several ROIs are presented in Table 1. The FA values of the old group show much higher within-group variability, not only compared to the young group but also with respect to the MA of the old group. This could indicate that age-related changes of the fiber orientation distribution as reflected in the FA are more pronounced than changes of the tissue microstructure dominating the MA. Most WM ROIs show a decrease of the FA and MA in the older group. The effect strength for the FA age-related changes is in the order of magnitude as reported in longitudinal studies [10, 11]. However, the relative decay, in particular compared to the within-group variability, is generally more pronounced for the MA (splenium of corpus callosum, cerebral peduncle and forceps minor). In GM ROIs, both FA and MA values tend to be increased for the older subjects. But in the globus pallidus, the FA seems to be increased while the MA shows a slight decrease. This could indicate that the fiber density is reduced (MA) but the remaining fiber orientations are more coherent (FA), e.g. because only a fiber subpopulation is affected by aging.

In conclusion, DWV experiments may be able to provide information about the tissue microstructure that is complementary to that of DTI and, thus, could help to unravel the microstructural effects that are reflected by changes of the diffusion properties. Furthermore, because of the less pronounced within-group variability, it may provide a higher sensitivity to differences and changes of the tissue microstructure making it an interesting tool for neuroscience.

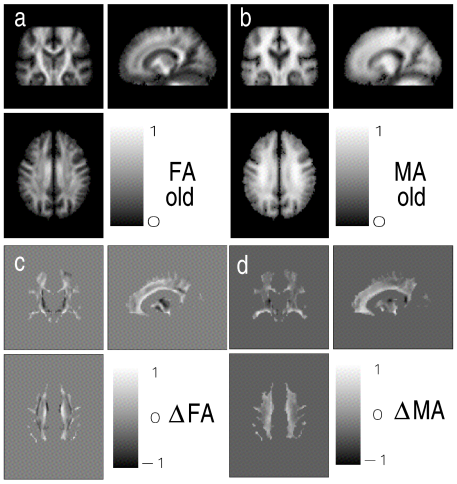

Fig. 2: Cross sections (cor, sag, tra) of the group-averaged FA (a) and MA (b) for 18 old, healthy volunteers and (c, d) their difference compared to a group of young volunteers (young-old). While FA shows significant variation within WM due to its dependency on the fiber orientation distribution, the MA appears more homogeneous. Only voxels with a WM content of > 50 % are shown in the difference images.

	PCI	SCC	CP	FM	CR	Put	PT	GP	SCV	MCP
Type	WM	WM	WM	WM	WM	GM	GM	GM	CER	CER
FA young [8]	0.627 ±0.048	0.778 ±0.04	0.736 ±0.071	0.462 ±0.046	0.478 ±0.06	0.100 ±0.008	0.274 ±0.033	0.225 ±0.029	0.192 ±0.017	0.643 ±0.055
FA old	0.544 ±0.112	0.771 ±0.155	0.575 ±0.169	0.378 ±0.064	0.481 ±0.083	0.272 ±0.144	0.396 ±0.047	0.295 ±0.078	0.159 ±0.040	0.583 ±0.106
MA young [8]	0.947 ±0.017	0.810 ±0.051	0.855 ±0.054	0.828 ±0.037	0.938 ±0.028	0.464 ±0.064	0.472 ±0.051	0.568 ±0.026	0.326 ±0.014	0.910 ±0.055
MA old	0.897 ±0.047	0.714 ±0.011	0.718 ±0.076	0.715 ±0.038	0.923 ±0.020	0.491 ±0.083	0.607 ±0.077	0.472 ±0.069	0.301 ±0.034	0.836 ±0.081

Tab. 1: Mean FA and MA values (± stdev) in ten (WM, GM and cerebellar) ROIs for young volunteers [8] in comparison with the old volunteers from this study (middle cerebellar peduncle right (MCP), pyramidal tract left (Pyr), superior cerebellar vermis (SCV), cerebral peduncle (CP), globus pallidus (GP), putamen (Put), posterior thalamus (PT), posterior limb of capsula interna (PCI), forceps minor (FM), splenium of corpus callosum (SCC), and corona radiate (CR)).

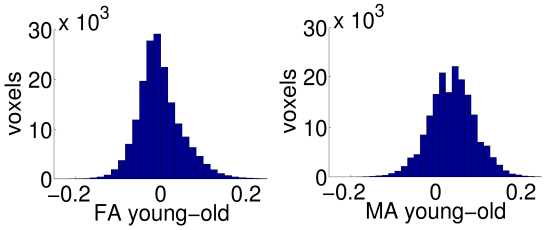

Fig. 3: Histogram plots of all voxels with a WM content of >50 % for the group-average FA (left) and MA (right) difference young-old.

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