Table S1: Demographics data of healthy controls, MCI and AD patients.

Entire DTI cohort			
	MCI Patients	***AD Patients***	***Controls***
N total	56	53	61
Gender F/M	25/31	33/20	22/39
Age (mean ± SD, range)	70.1 ± 8.0 50.1 – 84.6	74.1 ± 8.6 49.1 – 89.7	71.1 ± 8.3 51.1 – 86.2
CDR-sb* (mean ± SD, range)	1.4 ± 1.0 0 – 4.5	4.0 ± 2.1 1 – 11	0.1 ± 0.2 0 – 1
MMSE (mean ± SD, range)	27.9 ± 1.8 23** – 30	23.9 ± 2.7 18 – 29	29.9 ± 1.1 26 – 30
Tractography cohort			
		AD Patients	***Controls***
N total (all females)		15	15
Age (mean ± SD, range)		67.2 ± 8.5 49.1 – 78.4	67.1 ± 7.4 51.1 – 80.6
CDR-sb* (mean ± SD, range)		4.1 ± 1.8 1 – 7	0.1 ± 0.2 0 – 0.5
MMSE (mean ± SD, range)		23.7 ± 3.0 18 – 29	29.2 ± 1.2 26 – 30

*sb = sum of boxes
**One patient with MMSE=23 was confirmed MCI as activities of daily living (ADL) impairment did not warrant diagnosis of dementia

Table S2: Neuropsychological scores and CSF concentrations for healthy controls, MCI and AD patients. All values were significantly different (P<0.001) between each pair of groups except for the phonological verbal fluency which did not differ between healthy controls and MCI patients.

Neuropsychological test	**MCI Patients**	**AD Patients**	**Controls**
MMSE (mean ± SD)	27.9 ± 1.8	23.9 ± 2.7	29.9 ± 1.1
Categorical verbal fluency (animals)(mean ± SD)	19.7 ± 4.3	12.7 ± 5.5	23.4 ± 5.3
Phonological verbal fluency (S words)(mean ± SD)	12.5 ± 3.8	7.4 ± 4.5	12.8 ± 4.3
Boston naming test (mean ± SD)	13.6 ± 2.1	12.2 ± 1.3	14.5 ± 0.8
Trail making test (part A)* (mean ± SD)	50.9 ± 50.8	78.8 ± 21.1	38.0 ± 10.0
Trail making test (part B)** (mean ± SD)	143.5 ± 114.6	229.3 ± 54.6	92.4 ± 25.5
CSF concentrations* (pg/ml)**	**MCI Patients**	**AD Patients**	**Controls**
Tau (mean ± SD)	421.8 ± 242.6	705.5 ± 304.3	258.0±16.0
Phosphorylated tau (mean ± SD)	63.9 ± 26.1	97.9 ± 41.5	47.5 ± 17.6
β-amyloid (mean ± SD)	584.9 ± 264.9	413.8 ± 134.6	797.0 ± 266.1

*3 AD patients did not complete the test
**2 MCI patients and 22 AD patients did not complete the test
***Concentrations were collected for 26 controls

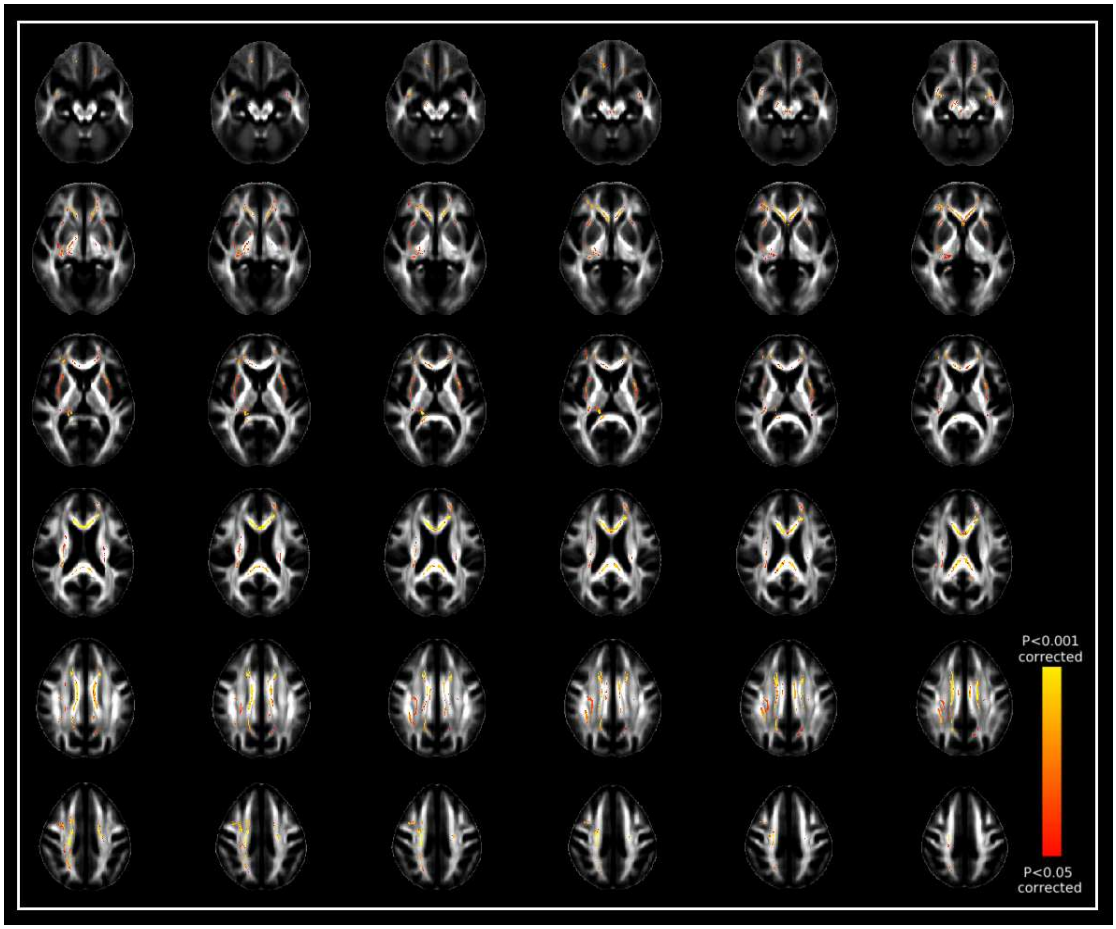

Figure S1: Significant FA differences across the three groups (*F*-test)

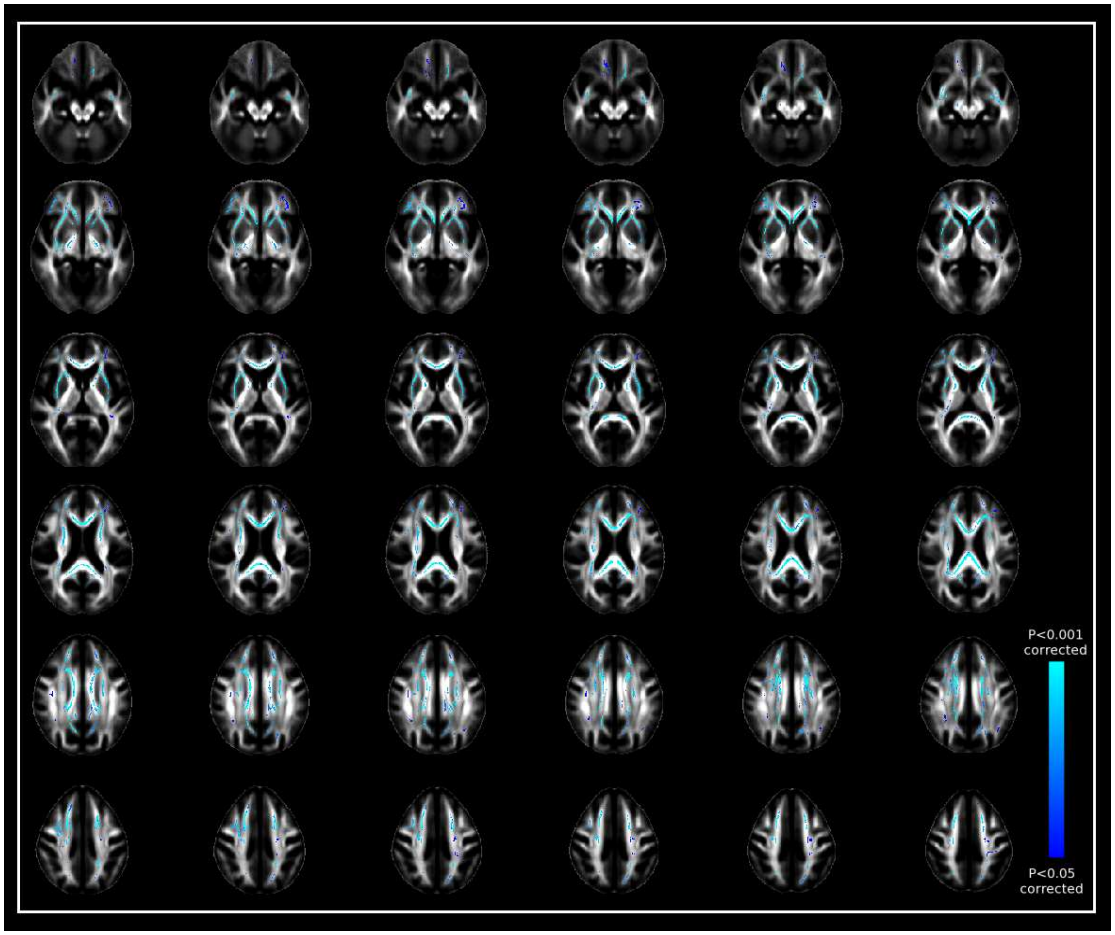

Figure S2: Significant MD differences across the three groups (*F*-test)

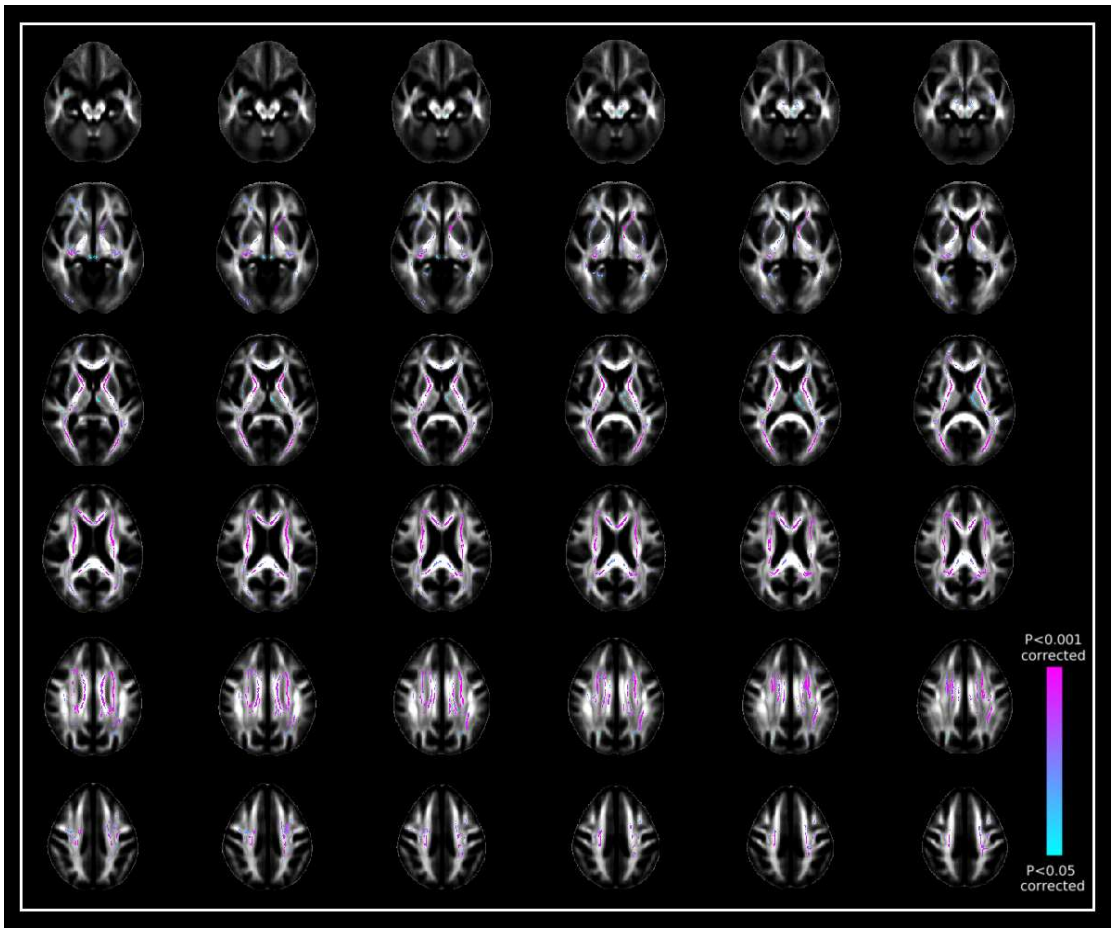

Figure S3: Significant MO differences across the three groups (*F*-test)

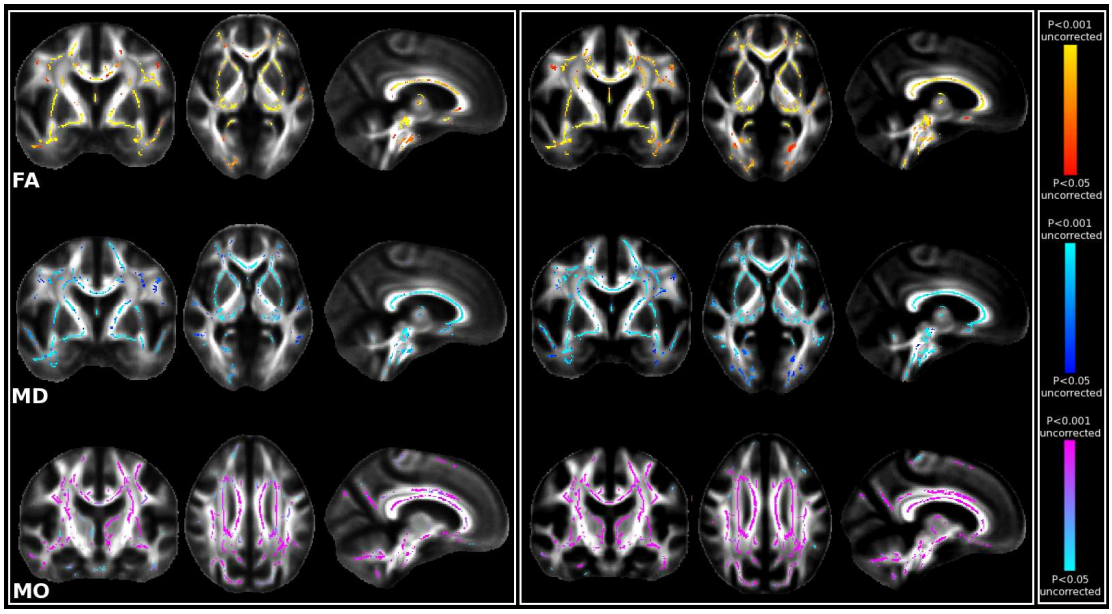

Figure S4: Results of the *F*-tests carried out across the three groups (CON, MCI, AD) on FA (first row), MD (second row) and MO (third row). *Left F*-tests performed with the age added as a nuisance covariate. *Right F*-tests performed without the age as a covariate. Despite a slight loss of statistical power due to the added covariate in the statistical model, the spatial pattern of the results is very similar between the two analyses.

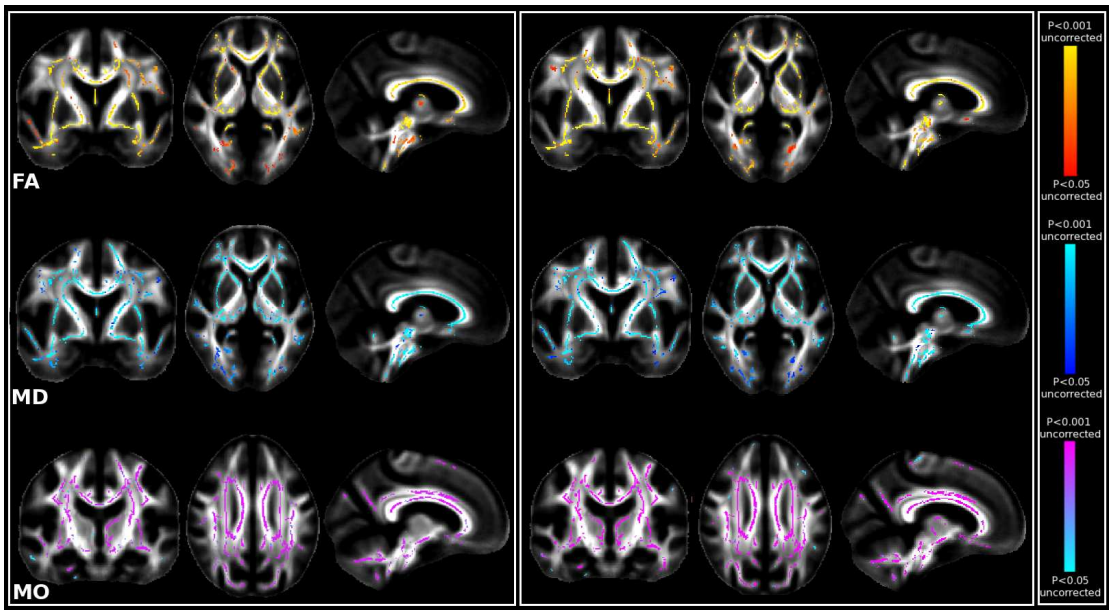

Figure S5: Results of the *F*-tests carried out across the three groups (CON, MCI, AD) on FA (first row), MD (second row) and MO (third row). *Left F*-tests performed excluding the 8 MCI patients who later converted to AD and dementia with Lewy bodies. *Right F*-tests performed on the entire cohort. Despite a slight loss of statistical power due to the loss of 8 subjects, the spatial pattern of the results is very similar between the two analyses.

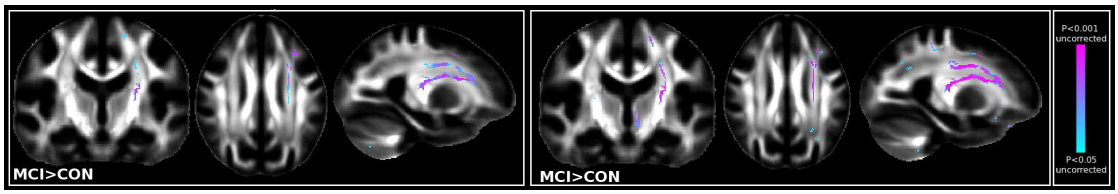

Figure S6: Results of the contrast showing an increase of MO in the MCI patients compared with healthy elderly. *Left* Results obtained excluding the 8 MCI patients who later converted to AD and dementia with Lewy bodies. *Right* Results obtained on the entire cohort. Again, the spatial pattern of the results is very similar between the two analyses.

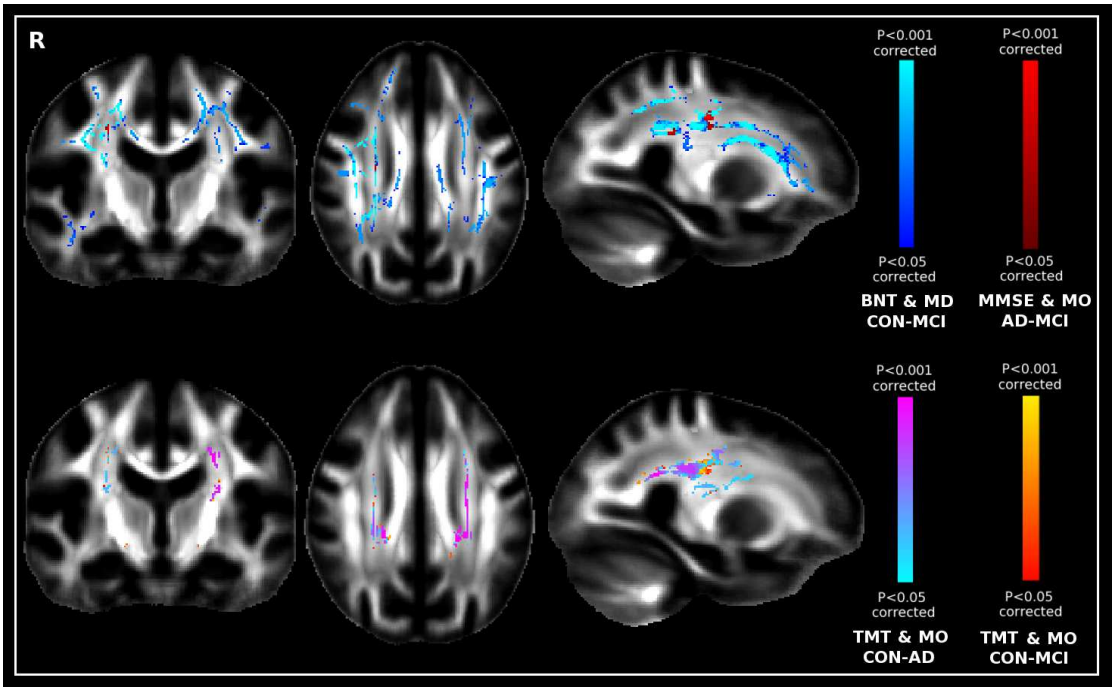

Figure S7: TBSS results showing significant differences across groups in correlations between neuropsychological scores and diffusion indices in the centrum semiovale (*Top*: Boston naming test and mean diffusivity, MMSE and mode of anisotropy; *Bottom*: Trail making test part A and mode of anisotropy, note that there is an almost perfect overlap between the contrast CON-AD and CON-MCI). More specifically, we found a significant negative correlation between MMSE and mode of anisotropy in MCI patients but not AD patients, a significant negative correlation between Boston naming test and mean diffusivity in MCI but not in control subjects, a significant positive correlation between Trail making test part A and mode of anisotropy in healthy controls but not in MCI or AD patients. BNT=Boston naming test; MD=Mean diffusivity; MO=Mode of anisotropy; TMT=Trail making test.

Criteria for Mild Cognitive Impairment (MCI)

According to the consensus conference in Stockholm in 2003 (Winblad et al., 2004), the following general criteria will apply for MCI:

1. Not normal, not demented (i.e., DSM-IV, ICD 10 criteria not met)
2. Cognitive decline
- Self and/or informant report and impairment on objective cognitive tasks
and/or
- Evidence of decline over time on objective cognitive tasks
3. Preserved basic activities of daily living / minimal impairment in complex instrumental functions

In our study, these criteria were implemented as follows:

1. MMSE $\geq$ 24/30.
2. Basic activities of daily living and complex instrumental functions are judged clinically and based on data from the NOSGER (no dimension > 10), IQCODE (< 4.0), and global CDR score ($\leq$ 0.5).
3. Difference in z-scores of $\geq$ 1 on two consecutive assessments separated by at least six months.
4. At least mild impairment in one or more of the following cognitive domains:
    a. Attention (divided, sustained, etc.)
    b. Memory (episodic, semantic, verbal, nonverbal, etc.)
    c. Language (naming, comprehension, repetition, etc.)
    d. Praxis (ideomotor, ideatoric, etc.)
    e. Gnosis (faces, objects, etc.)
    f. Executive functions (verbal + nonverbal fluency, set-shifting, errors, etc.)

Criteria for neuropsychologically-relevant cerebrovascular component of a neurodegenerative disease (modified from Erkinjuntti et al., 2000):

Part of the neuropsychological impairment probably due to a vascular cause judged by cognitive deficits suggestive for cerebrovascular disease
&
Presence or a history of neurologic signs as evidence for cerebrovascular disease such as hemiparesis, lower facial weakness, Babinski sign, sensory deficit, dysarthria, gait disorder, extrapyramidal signs consistent with brain lesion(s)
&
By brain imaging consistent with relevant cerebrovascular disease, but without signs of normal pressure hydrocephalus and specific causes of white matter lesions (e.g. multiple sclerosis, sarcoidosis, brain irradiation).