

Supplementary

The appendix contains four tables concerning demographic and clinical characteristics of participants, all MR sequence parameters, and calculated diffusion tensor imaging (DTI)-based and generalized q-sampling imaging (GQI)-based metrics in the whole-brain fiber tracts and corpus callosum bundles using DSI studio. The list and content of supplemental materials related to our study are as follows:

- (I) The demographic and clinical characteristics of the subjects in this study are listed in *Table S1*.
- (II) The parameters of the sequences used for MR diffusion and complementary MR techniques are listed in *Table S2*.
- (III) DTI-based metrics of the groups (controls, asymptomatic, and symptomatic patients) are provided in *Table S3*.
- (IV) GQI-based metrics of the groups (controls, asymptomatic, and symptomatic patients) are provided in *Table S4*.

Table S1 Demographic and clinical characteristics of the subjects

| Controls, n=28 | | | | Asymptomatic (Cov+), n=25 | | | | Symptomatic (Cov+), n=41 | | | |
|----------------|-------------|-----------|----------------------|---------------------------|-------------|-----------|----------------------|--------------------------|-------------|-----------|----------------------|
| Subj. | Age (years) | Sex (F/M) | Hyperintense lesions | Subj. | Age (years) | Sex (F/M) | Hyperintense lesions | Subj. | Age (years) | Sex (F/M) | Hyperintense lesions |
| C1 | 18 | 0 | 0 | A1 | 19 | 0 | 0 | S1 | 18 | 0 | 0 |
| C2 | 22 | 1 | 0 | A2 | 25 | 1 | 0 | S2 | 24 | 0 | 0 |
| C3 | 23 | 1 | 0 | A3 | 29 | 1 | 0 | S3 | 25 | 0 | 0 |
| C4 | 24 | 0 | 0 | A4 | 30 | 0 | 0 | S4 | 27 | 0 | 0 |
| C5 | 26 | 0 | 0 | A5 | 34 | 1 | 0 | S5 | 28 | 1 | 0 |
| C6 | 28 | 1 | 0 | A6 | 39 | 1 | 0 | S6 | 29 | 0 | 4 |
| C7 | 30 | 1 | 0 | A7 | 37 | 0 | 0 | S7 | 30 | 0 | 2 |
| C8 | 30 | 1 | 0 | A8 | 39 | 1 | 15 | S8 | 30 | 0 | 0 |
| C9 | 32 | 1 | 0 | A9 | 36 | 0 | 0 | S9 | 30 | 0 | 0 |
| C10 | 36 | 0 | 0 | A10 | 42 | 0 | 0 | S10 | 33 | 0 | 1 |
| C11 | 37 | 1 | 0 | A11 | 42 | 1 | 0 | S11 | 34 | 1 | 11 |
| C12 | 38 | 0 | 0 | A12 | 43 | 0 | 27 | S12 | 35 | 1 | 1 |
| C13 | 39 | 1 | 0 | A13 | 46 | 1 | 0 | S13 | 36 | 1 | 0 |
| C14 | 41 | 0 | 0 | A14 | 46 | 0 | 0 | S14 | 41 | 1 | 21 |
| C15 | 42 | 1 | 0 | A15 | 47 | 0 | 0 | S15 | 43 | 0 | 11 |
| C16 | 44 | 0 | 0 | A16 | 47 | 0 | 7 | S16 | 44 | 0 | 9 |
| C17 | 45 | 0 | 0 | A17 | 48 | 1 | 6 | S17 | 44 | 0 | 9 |
| C18 | 45 | 1 | 0 | A18 | 49 | 0 | 0 | S18 | 45 | 0 | 8 |
| C19 | 45 | 1 | 0 | A19 | 51 | 1 | 16 | S19 | 45 | 0 | 57 |
| C20 | 46 | 0 | 0 | A20 | 51 | 0 | 11 | S20 | 45 | 1 | 27 |
| C21 | 47 | 0 | 0 | A21 | 53 | 0 | 25 | S21 | 46 | 0 | 2 |
| C22 | 48 | 1 | 0 | A22 | 54 | 0 | 62 | S22 | 47 | 0 | 0 |
| C23 | 49 | 0 | 18 | A23 | 62 | 1 | 10 | S23 | 47 | 0 | 0 |
| C24 | 54 | 1 | 0 | A24 | 60 | 0 | 0 | S24 | 48 | 0 | 7 |
| C25 | 55 | 1 | 11 | A25 | 66 | 1 | 6 | S25 | 48 | 1 | 11 |
| C26 | 57 | 0 | 37 | | | | | S26 | 48 | 0 | 0 |
| C27 | 58 | 1 | 0 | | | | | S27 | 49 | 0 | 4 |
| C28 | 66 | 0 | 40 | | | | | S28 | 49 | 0 | 17 |
| | | | | | | | | S29 | 50 | 0 | 3 |
| | | | | | | | | S30 | 51 | 1 | 2 |
| | | | | | | | | S31 | 52 | 0 | 11 |
| | | | | | | | | S32 | 53 | 0 | 15 |
| | | | | | | | | S33 | 54 | 1 | 2 |
| | | | | | | | | S34 | 55 | 0 | 29 |
| | | | | | | | | S35 | 56 | 0 | 4 |
| | | | | | | | | S36 | 57 | 0 | 85 |
| | | | | | | | | S37 | 58 | 0 | |
| | | | | | | | | S38 | 60 | 0 | 1 |
| | | | | | | | | S39 | 63 | 0 | 10 |
| | | | | | | | | S40 | 68 | 0 | 13 |
| | | | | | | | | S41 | 69 | 0 | 80 |

C, control subjects; A, asymptomatic patients; S, symptomatic patients; Sex, female (F=0), male (M=1); hyperintense lesions, number of lesions on FLAIR images; FLAIR, fluid-attenuated inversion recovery.

Table S2 The sequence parameters employed for MR diffusion and complementary MR techniques

| Parameters | ss-EPI DWI | ASL | FLAIR | SWI | MPRAGE | MRA |
|---------------------------------------|------------|-------|---------|---------|---------|---------|
| Repetition time (ms) | 4,900 | 4,300 | 6,000 | 28 | 2,000 | 19 |
| Echo time (ms) | 134 | 13.4 | 349 | 20 | 2.25 | 3.5 |
| Inversion time (ms) | NA | 800 | 1900 | NA | 900 | NA |
| b-values (s/mm ²) | 0–4,000 | NA | NA | NA | NA | NA |
| Slice thickness (mm) | 2 | 4 | 0.9 | 1 | 0.9 | 0.5 |
| Orientation | tra | tra | sag | tra | sag | tra |
| No. slices | 72 | 24 | 208 | 112 | 224 | 48 |
| Acquisition matrix (mm ²) | 96×120 | 60×64 | 206×224 | 286×384 | 256×256 | 241×256 |
| Bandwidth (Hz/Px) | 1,736 | 3,256 | 698 | 120 | 210 | 199 |
| PAT factor (GRAPPA, SMS) | 4 | 2 | 4 | 2 | 3 | 2 |
| Field of view (mm) | 240 | 220 | 208 | 220 | 230 | 180 |
| Labeling duration (ms) | NA | 1800 | NA | NA | NA | NA |
| Postlabeling duration | NA | 1800 | NA | NA | NA | NA |
| Total scan time (min) | 10:37 | 7:29 | 6:02 | 5:44 | 3:34 | 5:06 |

MR, magnetic resonance; ss-EPI DWI, single-shot echo-planar imaging diffusion-weighted imaging; ASL, arterial spin labeling; FLAIR, fluid attenuated inversion recovery; SWI, susceptibility-weighted imaging; MPRAGE, magnetization prepared rapid gradient echo single-shot echo-planar imaging sequence; MRA, magnetic resonance angiography; tra, transversal; sag, sagittal; PAT, parallel acquisition technique; GRAPPA, generalized autocalibrating partial parallel acquisition; SMS; simultaneous multislice imaging technique (acceleration mode); NA, not applicable.

Table S3 DTI-based metrics of the groups (controls, asymptomatic, and symptomatic patients)

| DTI-based metrics (mean ± SD) | F. minor | Body | Tapetum | F. major | WB |
|------------------------------------|-------------|-------------|-------------|-------------|-------------|
| Healthy controls, n=28 | | | | | |
| FA | 0.473±0.029 | 0.469±0.032 | 0.514±0.390 | 0.522±0.033 | 0.403±0.022 |
| MD | 0.794±0.042 | 0.799±0.05 | 1.080±0.229 | 0.873±0.059 | 0.933±0.053 |
| AD | 1.219±0.043 | 1.211±0.047 | 1.692±0.294 | 1.418±0.067 | 1.344±0.07 |
| RD | 0.581±0.047 | 0.593±0.057 | 0.774±0.199 | 0.601±0.062 | 0.727±0.049 |
| Asymptomatic patients (Cov+), n=25 | | | | | |
| FA | 0.458±0.034 | 0.467±0.028 | 0.504±0.047 | 0.500±0.030 | 0.392±0.027 |
| MD | 0.812±0.041 | 0.813±0.058 | 1.028±0.162 | 0.890±0.061 | 0.946±0.047 |
| AD | 1.227±0.053 | 1.229±0.071 | 1.605±0.199 | 1.415±0.085 | 1.348±0.071 |
| RD | 0.604±0.046 | 0.605±0.058 | 0.74±0.152 | 0.627±0.058 | 0.744±0.042 |
| Symptomatic patients (Cov+), n=41 | | | | | |
| FA | 0.453±0.026 | 0.459±0.027 | 0.511±0.040 | 0.506±0.038 | 0.394±0.018 |
| MD | 0.837±0.058 | 0.840±0.061 | 1.056±0.196 | 0.887±0.052 | 0.960±0.045 |
| AD | 1.257±0.061 | 1.256±0.066 | 1.653±0.250 | 1.416±0.077 | 1.372±0.053 |
| RD | 0.627±0.060 | 0.632±0.062 | 0.757±0.173 | 0.622±0.054 | 0.755±0.044 |

The results of calculated DTI-based metrics (FA, MD, AD, and RD) in the corpus callosum and WB fibers are presented as mean ± SD. MD, AD, and RD are expressed in units of $\text{mm}^2/\text{s} \times 10^{-3}$. DTI, diffusion tensor imaging; SD, standard deviation; F. minor, forceps minor; F. major, forceps major of the corpus callosum; WB, whole brain; FA, fractional anisotropy; MD, mean diffusivity; AD, axial diffusivity; RD, radial diffusivity.

Table S4 GQI-based metrics of the groups (controls, asymptomatic, and symptomatic patients)

| GQI-based metrics (mean ± SD) | F. minor | Body | Tapetum | F. major | WB |
|------------------------------------|-------------|-------------|-------------|-------------|-------------|
| Healthy controls, n=28 | | | | | |
| QA | 0.202±0.025 | 0.264±0.032 | 0.309±0.037 | 0.339±0.036 | 0.207±0.016 |
| ISO | 0.435±0.054 | 0.501±0.049 | 0.606±0.082 | 0.581±0.067 | 0.568±0.062 |
| RDI | 0.328±0.039 | 0.388±0.037 | 0.436±0.051 | 0.444±0.046 | 0.408±0.041 |
| Asymptomatic patients (Cov+), n=25 | | | | | |
| QA | 0.197±0.022 | 0.278±0.029 | 0.306±0.036 | 0.341±0.032 | 0.206±0.016 |
| ISO | 0.445±0.062 | 0.523±0.063 | 0.618±0.095 | 0.599±0.074 | 0.58±0.066 |
| RDI | 0.332±0.041 | 0.404±0.046 | 0.445±0.056 | 0.454±0.051 | 0.414±0.044 |
| Symptomatic patients (Cov+), n=41 | | | | | |
| QA | 0.187±0.028 | 0.258±0.042 | 0.304±0.044 | 0.327±0.045 | 0.194±0.019 |
| ISO | 0.436±0.070 | 0.508±0.075 | 0.614±0.112 | 0.581±0.072 | 0.557±0.069 |
| RDI | 0.323±0.047 | 0.390±0.054 | 0.440±0.063 | 0.443±0.052 | 0.398±0.046 |

The results of calculated GQI-based metrics (QA, ISO, and RDI) in the CC and WB fibers are listed with their SD. GQI, generalized q-sampling imaging; SD, standard deviations; F. minor, forceps minor; F. major, forceps major of the CC; WB, whole brain; QA, quantitative anisotropy; ISO, isotropy; RDI, restricted diffusion imaging; CC, corpus callosum.