Supplemental Material
Table S1. Characteristics of participants included in the analysis and the whole sample with cfPWV at visit 5.

| Characteristics                                      | Participants included in the study (n=1,484) | All visit 5 participants with inclusion criteria* (n=4,539) |
|------------------------------------------------------|---------------------------------------------|-------------------------------------------------------------|
| Age, year, mean ± SD                                 | 76.1±5.2                                    | 75.2±5.0                                                   |
| Sex, men, n (%)                                      | 597 (40.2)                                  | 1,832 (40.4)                                               |
| Race, African Americans, n (%)                       | 425 (28.6)                                  | 984 (21.7)                                                 |
| Center, n (%)                                        |                                             |                                                            |
| Forsyth, NC                                          | 352 (23.7)                                  | 943 (20.8)                                                 |
| Jackson, MS                                          | 403 (27.2)                                  | 925 (20.4)                                                 |
| Minneapolis, MN                                      | 327 (22.0)                                  | 1,388 (30.6)                                               |
| Washington, MD                                       | 402 (27.1)                                  | 1,283 (28.3)                                               |
| Education, high school or above, n (%)               |                                             |                                                            |
| Below high school                                    | 198 (13.2)                                  | 574 (12.7)                                                 |
| High school                                          | 612 (41.3)                                  | 1,911 (42.2)                                               |
| College or above                                     | 672 (45.3)                                  | 2,047 (45.2)                                               |
| Body mass index, kg/m², mean ± SD                    | 27.7±4.5                                    | 27.8±4.5                                                   |
| Ever smoking, n (%)                                  | 785 (55.1)                                  | 2,402 (55.6)                                               |
| Ever drinking, n (%)                                 | 1,119 (76.0)                                | 3,535 (78.8)                                               |
| Mean arterial pressure, mmHg, mean ± SD              | 87.8±11.4                                   | 87.5±11.3                                                  |
| Hypertension, n (%)                                  | 1,080 (73.4)                                | 3,239 (72.1)                                               |
| Use of antihypertensive drug, n (%)                  | 1,083 (73.0)                                | 3,262 (72.0)                                               |
| Diabetes, n (%)                                      | 392 (26.7)                                  | 1,135 (25.2)                                               |
| Heart rate, bpm, mean ± SD                           | 64.5±11.0                                   | 64.7±10.9                                                  |
| Carotid-femoral pulse wave velocity, m/s             | 11.8±3.3                                    | 11.6±3.1                                                   |
| Total physical activity, minutes/week, mean ± SD     | 180.9±176.6                                 | 192.5±187.6                                                |
| APOE, n (%)                                          |                                             |                                                            |
| APOE4 ≥1                                             | 1,003 (69.9)                                | 3,119 (71.4)                                               |
| APOE4 <1                                             | 431 (30.1)                                  | 1,247 (28.6)                                               |
| Cognitive status, n (%)                              |                                             |                                                            |
| Normal                                               | 937 (63.1)                                  | 3514 (77.7)                                                |
| Mild cognitive impairment                            | 481 (32.4)                                  | 872 (19.3)                                                 |
| Dementia                                             | 64 (4.3)                                    | 128 (2.8)                                                  |

*This applies to all inclusion criteria based on cfPWV
Table S2. Mean fractional anisotropy (FA) and mean diffusivity (MD) among included and excluded participants. ARIC study examination visit 5.

| Regions                  | FA                          | MD (10⁻⁴ mm²/s)               |
|--------------------------|-----------------------------|------------------------------|
|                          | Excluded (n=458)            | Included (n=1,484)           | Difference (SE) | Excluded (n=458) | Included (n=1,484) | Difference (SE) |
| Anterior corpus callosum | 0.407±0.06                  | 0.424±0.06                  | -0.017 (0.003) | 11.9±1.2         | 11.6±1.1          | 0.3 (0.06)       |
| Posterior corpus callosum| 0.559±0.07                  | 0.578±0.06                  | -0.019 (0.003) | 11.4±1.1         | 11.1±1.0          | 0.3 (0.06)       |
| Frontal lobe             | 0.271±0.02                  | 0.280±0.02                  | -0.009 (0.001) | 8.8±0.6          | 8.6±0.5           | 0.3 (0.03)       |
| Temporal lobe            | 0.275±0.02                  | 0.283±0.02                  | -0.008 (0.001) | 9.0±0.7          | 8.8±0.5           | 0.3 (0.03)       |
| Occipital lobe           | 0.223±0.03                  | 0.229±0.02                  | -0.007 (0.001) | 9.0±0.7          | 8.8±0.6           | 0.2 (0.03)       |
| Parietal lobe            | 0.290±0.03                  | 0.300±0.02                  | -0.010 (0.001) | 9.0±0.7          | 8.7±0.6           | 0.3 (0.03)       |
| Overall                  | 0.275±0.02                  | 0.284±0.02                  | -0.009 (0.001) | 9.0±0.6          | 8.7±0.5           | 0.3 (0.03)       |

T-test was conducted for FAs and MDs listed above. Bold indicates at p<0.05 from a t-test.
### Table S3. Correlations between FA and MD at different regions.

| Regions                  | Correlation | P value  |
|--------------------------|-------------|----------|
| Frontal lobe             | -0.75       | <0.0001  |
| Temporal lobe            | -0.63       | <0.0001  |
| Occipital lobe           | -0.68       | <0.0001  |
| Parietal lobe            | -0.67       | <0.0001  |
| Anterior corpus callosum | -0.50       | <0.0001  |
| Posterior corpus callosum| -0.66       | <0.0001  |
| Overall                  | -0.75       | <0.0001  |

ARIC study examination visit 5.
Table S4. Association of cfPWV and z-scores of FA. Mean differences estimated by multivariable linear regression by cognitive status.

| Regions                        | Cognitive status      | cfPWV (m/s) | Model 1 |          | Model 2 |          | Model 3 |          | Model 4 |          |          |          |
|--------------------------------|-----------------------|-------------|---------|----------|---------|----------|---------|----------|---------|----------|---------|----------|
|                                |                       | β (95% CI)  | P value | β (95% CI)| P value | β (95% CI)| P value | β (95% CI)| P value |
| Anterior corpus callosum       | Normal (n=937)        | -0.04       | 0.001   | -0.03    | 0.01    | -0.01    | 0.30    | -0.01    | 0.37    |
|                                | MCI/dementia (n=545)  | -0.03       | 0.02    | -0.02    | 0.08    | -0.03    | 0.06    | -0.03    | 0.07    |
| Posterior corpus callosum      | Normal (n=937)        | -0.02       | 0.04    | -0.01    | 0.19    | -0.02    | 0.13    | -0.01    | 0.22    |
|                                | MCI/dementia (n=545)  | -0.03       | 0.03    | -0.02    | 0.23    | -0.03    | 0.05    | -0.03    | 0.06    |
| Frontal lobe                   | Normal (n=937)        | -0.06       | <0.0001 | -0.03    | 0.002   | -0.03    | 0.01    | -0.02    | 0.05    |
|                                | MCI/dementia (n=545)  | -0.05       | <0.0001 | -0.03    | 0.01    | -0.03    | 0.05    | -0.02    | 0.05    |
| Temporal lobe                  | Normal (n=937)        | -0.03       | 0.09    | -0.02    | 0.09    | -0.04    | 0.003   | -0.03    | 0.002   |
|                                | MCI/dementia (n=545)  | -0.02       | 0.17    | -0.01    | 0.56    | -0.02    | 0.22    | -0.02    | 0.25    |
| Occipital lobe                 | Normal (n=936)        | -0.03       | 0.02    | -0.02    | 0.16    | -0.02    | 0.17    | -0.01    | 0.30    |
|                                | MCI/dementia (n=545)  | -0.03       | 0.04    | -0.03    | 0.02    | -0.03    | 0.04    | -0.03    | 0.05    |
| Parietal lobe                  | Normal (n=937)        | -0.04       | 0.003   | -0.01    | 0.24    | -0.03    | 0.02    | -0.01    | 0.15    |
|                                | MCI/dementia (n=545)  | -0.04       | 0.002   | -0.02    | 0.09    | -0.02    | 0.11    | -0.02    | 0.12    |
| Overall                        | Normal (n=936)        | -0.05       | <0.0001 | -0.03    | 0.01    | -0.03    | 0.003   | -0.02    | 0.03    |
|                                | MCI/dementia (n=545)  | -0.05       | 0.0003  | -0.03    | 0.02    | -0.03    | 0.04    | -0.03    | 0.04    |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of MDs between high and non-high cfPWV.

Model 1: Unadjusted.

Model 2: Adjusted for volume of white matter hyperintensities.

Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate

Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S6. Association of cfPWV and z-scores of FA (n=1484). Mean differences estimated by multivariable linear regression by WMH volumes.

| Regions                          | Cognitive status       | cfPWV (m/s) | Model 1 | P value | Model 2 | P value | Model 3 | P value | Model 4 | P value |
|----------------------------------|------------------------|-------------|---------|---------|---------|---------|---------|---------|---------|---------|
|                                 |                        | β (95% CI)  | β (95% CI) | β (95% CI) | β (95% CI) |
|                                 | High WMH volume (n=371)| -0.03 (-0.06, -0.003) | 0.03 | -0.03 (-0.06, 0.001) | 0.05 | -0.01 (-0.05, 0.02) | 0.40 | -0.01 (-0.05, 0.02) | 0.47 |
|                                 | Low WMH volume (n=371) | -0.03 (-0.06, 0.01) | 0.13 | -0.03 (-0.07, 0.01) | 0.13 | -0.03 (-0.07, 0.01) | 0.10 | -0.03 (-0.07, 0.01) | 0.09 |
| Posterior corpus callosum        | High WMH volume (n=371)| -0.03 (-0.06, -0.002) | 0.03 | -0.02 (-0.05, 0.01) | 0.13 | -0.01 (-0.04, 0.03) | 0.61 | -0.003 (-0.04, 0.03) | 0.88 |
|                                 | Low WMH volume (n=371) | -0.002 (-0.04, 0.03) | 0.91 | 0.00004 (-0.03, 0.03) | 0.99 | -0.03 (-0.07, 0.01) | 0.12 | -0.03 (-0.07, 0.01) | 0.15 |
| Frontal lobe                     | High WMH volume (n=371)| -0.07 (-0.10, -0.04) | <0.0001 | -0.05 (-0.07, -0.02) | 0.01 | -0.05 (-0.09, -0.02) | 0.001 | -0.04 (-0.07, -0.02) | 0.002 |
|                                 | Low WMH volume (n=371) | -0.02 (-0.06, 0.01) | 0.14 | -0.02 (-0.05, 0.01) | 0.27 | -0.02 (-0.06, 0.01) | 0.15 | -0.02 (-0.06, 0.01) | 0.17 |
| Temporal lobe                    | High WMH volume (n=371)| -0.05 (-0.08, -0.01) | 0.004 | -0.03 (-0.06, -0.002) | 0.04 | -0.05 (-0.08, -0.02) | 0.002 | -0.04 (-0.08, -0.01) | 0.01 |
|                                 | Low WMH volume (n=371) | -0.02 (-0.05, 0.02) | 0.35 | -0.02 (-0.05, 0.02) | 0.37 | -0.03 (-0.07, 0.005) | 0.09 | -0.03 (-0.07, 0.004) | 0.07 |
| Occipital lobe                   | High WMH volume (n=371)| -0.06 (-0.09, -0.03) | 0.0001 | -0.05 (-0.08, -0.02) | 0.001 | -0.05 (-0.08, -0.02) | 0.003 | -0.04 (-0.08, -0.01) | 0.01 |
|                                 | Low WMH volume (n=371) | 0.002 (-0.03, 0.04) | 0.90 | 0.0005 (-0.03, 0.04) | 0.80 | 0.003 (-0.04, 0.04) | 0.04 | 0.003 (-0.04, 0.04) | 0.90 |
| Parietal lobe                    | High WMH volume (n=371)| -0.06 (-0.09, -0.03) | 0.0003 | -0.03 (-0.06, -0.01) | 0.02 | -0.04 (-0.08, -0.01) | 0.01 | -0.03 (-0.06, -0.001) | 0.04 |
|                                 | Low WMH volume (n=371) | -0.01 (-0.04, 0.02) | 0.64 | -0.002 (-0.03, 0.03) | 0.89 | -0.01 (-0.04, 0.02) | 0.49 | -0.01 (-0.04, 0.02) | 0.54 |
| Overall                          | High WMH volume (n=371)| -0.07 (-0.10, -0.04) | <0.0001 | -0.05 (-0.07, -0.02) | 0.001 | -0.06 (-0.09, -0.02) | 0.001 | -0.04 (-0.07, -0.02) | 0.003 |
|                                 | Low WMH volume (n=371) | -0.02 (-0.05, 0.01) | 0.27 | -0.01 (-0.05, 0.02) | 0.42 | -0.02 (-0.06, 0.01) | 0.19 | -0.02 (-0.06, 0.01) | 0.21 |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of MDs between high and non-high cfPWV.

Model 1: Unadjusted.

Model 2: Adjusted for volume of white matter hyperintensities.

Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate

Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S8. Association of cfPWV and z-scores of FA (n=1484). Mean differences estimated by multivariable linear regression with further adjustment for FAs of other locations.

| Regions             | cfPWV (m/s) |                      |                      |                      |                      |
|---------------------|-------------|----------------------|----------------------|----------------------|----------------------|
|                     |             | Model 1 β (95% CI)   | P value             | Model 2 β (95% CI)   | P value             |
|                     |             | β                    |                      | β                    |                      |
|                     |             | -0.002 (-0.01, 0.01) | 0.70                 | -0.01 (-0.02, 0.01)  | 0.37                 |
| Anterior corpus callosum | -0.002 (-0.01, 0.01) | 0.70                 | -0.01 (-0.02, 0.01)  | 0.37                 | 0.004 (-0.01, 0.02)  | 0.58                 | 0.003 (-0.01, 0.02)  | 0.71                 |
| Posterior corpus callosum | -0.01 (-0.02, 0.01) | 0.43                 | -0.003 (-0.02, 0.01) | 0.68                 | -0.01 (-0.02, 0.01)  | 0.30                 | -0.01 (-0.02, 0.01)  | 0.35                 |
| Frontal lobe        | -0.02 (-0.03, -0.01) | <0.0001              | -0.01 (-0.02, -0.01) | 0.0003              | -0.01 (-0.02, 0.002) | 0.11                 | -0.01 (-0.01, 0.003) | 0.18                 |
| Temporal lobe       | 0.001 (-0.01, 0.01) | 0.88                 | -0.001 (-0.01, 0.01) | 0.84                 | -0.01 (-0.03, -0.003) | 0.02                 | -0.02 (-0.03, -0.003) | 0.01                 |
| Occipital lobe      | 0.004 (-0.01, 0.02) | 0.50                 | -0.002 (-0.01, 0.01) | 0.76                 | 0.003 (-0.01, 0.02)  | 0.68                 | 0.001 (-0.01, 0.01)  | 0.83                 |
| Parietal lobe       | 0.01 (-0.002, 0.01) | 0.15                 | 0.01 (0.002, 0.02)   | 0.01                 | 0.004 (-0.004, -0.01) | 0.31                 | 0.01 (-0.003, 0.01)  | 0.20                 |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of FAs between high and non-high cfPWV.

Model 1: Adjusted for FAs in other regions.
Model 2: Adjusted for volume of white matter hyperintensities.
Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate.
Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S7. Association of cfPWV and z-scores of MD (n=1484). Mean differences estimated by multivariable linear regression by cognitive status.

| Regions                  | Cognitive status       | cfPWV (m/s) |       |       |       |       |       |       |
|--------------------------|------------------------|-------------|-------|-------|-------|-------|-------|-------|
|                          |                        | Model 1 β (95% CI) | P value | Model 2 β (95% CI) | P value | Model 3 β (95% CI) | P value | Model 4 β (95% CI) | P value |
|                           |                        |              |       |              |        |              |        |              |        |
| Anterior corpus callosum | Normal (n=937)         | 0.04         | (0.02, 0.06) | 0.0003 | 0.03 | (0.01, 0.05) | 0.001 | 0.02 | (0.003, 0.04) | 0.02 | 0.02 | (0.004, 0.04) | 0.02 |
|                          | MCI/dementia (n=545)   | 0.05         | (0.01, 0.06) | 0.01  | 0.03 | (0.003, 0.05) | 0.03  | 0.03 | (-0.001, 0.05) | 0.06 | 0.02 | (-0.001, 0.05) | 0.06 |
| Posterior corpus callosum| Normal (n=937)         | 0.02         | (-0.004, 0.04) | 0.12  | 0.01 | (-0.01, 0.03) | 0.19  | 0.03 | (0.01, 0.05) | 0.01 | 0.02 | (0.005, 0.04) | 0.01 |
|                          | MCI/dementia (n=545)   | 0.02         | (-0.01, 0.04) | 0.15  | 0.01 | (-0.01, 0.04) | 0.23  | 0.02 | (-0.01, 0.04) | 0.18 | 0.02 | (-0.01, 0.04) | 0.20 |
| Frontal lobe             | Normal (n=937)         | 0.05         | (0.03, 0.07) | <0.0001 | 0.03 | (0.01, 0.05) | 0.001 | 0.03 | (0.01, 0.05) | 0.001 | 0.02 | (0.001, 0.04) | 0.005 |
|                          | MCI/dementia (n=545)   | 0.05         | (0.02, 0.07) | 0.0003 | 0.02 | (0.002, 0.05) | 0.03  | 0.03 | (-0.001, 0.05) | 0.02 | 0.02 | (0.0000, 0.04) | 0.05 |
| Temporal lobe            | Normal (n=937)         | 0.05         | (0.03, 0.07) | <0.0001 | 0.03 | (0.01, 0.05) | 0.002 | 0.03 | (0.02, 0.05) | <0.0001 | 0.03 | (0.01, 0.04) | 0.001 |
|                          | MCI/dementia (n=545)   | 0.03         | (0.002, 0.05) | 0.03  | 0.01 | (-0.01, 0.03) | 0.41  | 0.02 | (-0.01, 0.04) | 0.22 | 0.01 | (-0.01, 0.04) | 0.26 |
| Occipital lobe           | Normal (n=936)         | 0.04         | (0.02, 0.06) | <0.0001 | 0.03 | (0.01, 0.05) | 0.003 | 0.03 | (0.02, 0.04) | 0.03  | 0.02 | (-0.003, 0.03) | 0.09 |
|                          | MCI/dementia (n=545)   | 0.04         | (0.02, 0.07) | 0.002 | 0.03 | (0.002, 0.05) | 0.02  | 0.02 | (-0.01, 0.04) | 0.15 | 0.02 | (-0.01, 0.04) | 0.18 |
| Parietal lobe            | Normal (n=937)         | 0.04         | (0.02, 0.06) | 0.0001 | 0.02 | (-0.002, 0.04) | 0.08  | 0.03 | (0.01, 0.04) | 0.005 | 0.02 | (0.001, 0.03) | 0.04 |
|                          | MCI/dementia (n=545)   | 0.04         | (0.01, 0.06) | 0.01  | 0.01 | (-0.01, 0.04) | 0.23  | 0.02 | (-0.01, 0.05) | 0.12 | 0.02 | (-0.004, 0.04) | 0.12 |
| Overall                  | Normal (n=936)         | 0.05         | (0.03, 0.07) | <0.0001 | 0.03 | (0.01, 0.05) | 0.003 | 0.03 | (0.01, 0.05) | 0.001 | 0.02 | (0.01, 0.04) | 0.004 |
|                          | MCI/dementia (n=545)   | 0.04         | (-0.07, -0.02) | 0.0003 | 0.02 | (-0.001, 0.04) | 0.07  | 0.02 | (-0.002, 0.05) | 0.07 | 0.02 | (-0.001, 0.04) | 0.06 |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of MDs between high and non-high cfPWV. 
Model 1: Unadjusted.
Model 2: Adjusted for volume of white matter hyperintensities.
Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate
Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S8. Association of cfPWV and z-scores of MD. Mean differences estimated by multivariable linear regression by WMH volumes

| Regions                      | Cognitive status                  | cfPWV (m/s) | Model 1 | Model 2 | Model 3 | Model 4 | Model 4 |
|------------------------------|-----------------------------------|-------------|---------|---------|---------|---------|---------|
|                              |                                   | β (95% CI) | P value | β (95% CI) | P value | β (95% CI) | P value |
| Anterior corpus callosum     | High WMH volume (n=371)           | 0.03 (0.01, 0.06) | 0.02     | 0.03 (0.004, 0.06) | 0.03     | 0.02 (0.01, 0.05) | 0.14 |
|                              | Low WMH volume (n=371)            | 0.04 (-0.001, 0.07) | 0.05     | 0.03 (-0.01, 0.07) | 0.09     | 0.04 (0.01, 0.08) | 0.01 |
| Posterior corpus callosum    | High WMH volume (n=371)           | 0.02 (-0.01, 0.05) | 0.28     | 0.01 (-0.02, 0.04) | 0.49     | 0.001 (-0.03, 0.03) | 0.92 |
|                              | Low WMH volume (n=371)            | 0.001 (-0.03, 0.04) | 0.94     | 0.0001 (-0.04, 0.04) | 0.99     | 0.03 (0.001, 0.07) | 0.04 |
| Frontal lobe                 | High WMH volume (n=371)           | 0.06 (0.03, 0.09) | 0.0002   | 0.04 (0.01, 0.06) | 0.01     | 0.03 (0.01, 0.06) | 0.02 |
|                              | Low WMH volume (n=371)            | 0.02 (-0.01, 0.05) | 0.20     | 0.01 (-0.02, 0.04) | 0.01     | 0.02 (-0.01, 0.04) | 0.05 |
| Temporal lobe                | High WMH volume (n=371)           | 0.05 (0.02, 0.07) | 0.002    | 0.03 (0.004, 0.06) | 0.03     | 0.03 (0.0004, 0.06) | 0.05 |
|                              | Low WMH volume (n=371)            | 0.02 (-0.02, 0.05) | 0.37     | 0.005 (-0.03, 0.04) | 0.78     | 0.03 (0.001, 0.05) | 0.04 |
| Occipital lobe               | High WMH volume (n=371)           | 0.06 (0.03, 0.09) | <0.0001  | 0.05 (0.02, 0.08) | 0.001    | 0.03 (0.01, 0.06) | 0.02 |
|                              | Low WMH volume (n=371)            | 0.01 (-0.03, 0.04) | 0.72     | -0.003 (-0.04, 0.03) | 0.86     | 0.003 (-0.03, 0.03) | 0.87 |
| Parietal lobe                | High WMH volume (n=371)           | 0.05 (0.02, 0.08) | 0.002    | 0.03 (-0.001, 0.05) | 0.06     | 0.03 (-0.004, 0.06) | 0.08 |
|                              | Low WMH volume (n=371)            | 0.003 (-0.03, 0.03) | 0.85     | -0.005 (-0.04, 0.03) | 0.77     | 0.01 (-0.01, 0.04) | 0.35 |
| Overall                      | High WMH volume (n=371)           | 0.06 (0.03, 0.09) | 0.0002   | 0.04 (0.01, 0.06) | 0.01     | 0.03 (0.005, 0.06) | 0.02 |
|                              | Low WMH volume (n=371)            | 0.01 (-0.02, 0.05) | 0.42     | 0.004 (-0.03, 0.04) | 0.80     | 0.02 (-0.01, 0.04) | 0.19 |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of MDs between high and non-high cfPWV.

Model 1: Unadjusted.

Model 2: Adjusted for volume of white matter hyperintensities.

Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate.

Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S9. Association of cfPWV and MDs (n=1484). Mean differences estimated by multivariable linear regression with further adjustment for MDs of other locations

| Regions               | cfPWV (m/s)                                      |
|-----------------------|-------------------------------------------------|
|                       | Model 1 β (95% CI) | P value | Model 2 β (95% CI) | P value | Model 3 β (95% CI) | P value | Model 4 β (95% CI) | P value |
| Anterior corpus callosum | 0.01 (-0.002, 0.02) | 0.11    | 0.02 (0.004, 0.03) | 0.01    | 0.004 (-0.01, 0.02) | 0.53    | 0.01 (-0.01, 0.02) | 0.43    |
| Posterior corpus callosum | -0.01 (-0.02, 0.002) | 0.10    | -0.004 (-0.02, 0.01) | 0.48    | 0.01 (-0.005, 0.02) | 0.24    | 0.01 (-0.004, 0.02) | 0.21    |
| Frontal lobe           | 0.01 (0.01, 0.02) | <0.0001 | 0.01 (0.005, 0.02) | 0.001   | 0.01 (-0.001, 0.01) | 0.07    | 0.01 (-0.001, 0.01) | 0.10    |
| Temporal lobe          | 0.003 (-0.003, 0.01) | 0.34    | 0.003 (-0.003, 0.01) | 0.32    | 0.01 (-0.001, 0.01) | 0.10    | 0.01 (-0.001, 0.01) | 0.10    |
| Occipital lobe         | 0.01 (0.0003, 0.02) | 0.04    | 0.01 (0.004, 0.02) | 0.005   | -0.002 (-0.01, 0.01) | 0.60    | -0.002 (-0.01, 0.01) | 0.69    |
| Parietal lobe          | -0.01 (-0.01, -0.003) | 0.003   | -0.01 (-0.02, -0.01) | <0.0001 | -0.003 (-0.01, 0.002) | 0.25    | -0.004 (-0.01, 0.002) | 0.17    |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of MDs between high and non-high cfPWV.

Model 1: Adjusted for MDs in other regions.
Model 2: Adjusted for volume of white matter hyperintensities.
Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate
Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S10. Association of high cfPWV (upper 25th percentile) and z-scores of FA. Mean differences estimated by multivariable linear regression

| Regions                        | Elevated cfPWV (cfPWV≥13.65 m/s) | P value | Model 1 proxy | P value | Model 2 proxy | P value | Model 3 proxy | P value | Model 4 proxy | P value |
|--------------------------------|-----------------------------------|---------|---------------|---------|---------------|---------|---------------|---------|---------------|---------|
|                                | β (95% CI)                        |         | β (95% CI)    |         | β (95% CI)    |         | β (95% CI)    |         | β (95% CI)    |         |
| Anterior corpus callosum       | -0.35 (-0.55, -0.15)              | 0.001   | -0.30 (-0.50, -0.10) | 0.003   | -0.30 (-0.51, -0.09) | 0.01   | -0.28 (-0.49, 0.07) | 0.01   |
| Posterior corpus callosum      | -0.25 (-0.44, -0.07)              | 0.01    | -0.16 (-0.34, 0.02) | 0.08    | -0.20 (-0.39, -0.01) | 0.04    | -0.15 (-0.33, 0.03) | 0.11    |
| Frontal lobe                   | -0.45 (-0.65, -0.25)              | <0.0001 | -0.29 (-0.47, -0.11) | 0.002   | -0.39 (-0.59, -0.18) | 0.0002 | -0.30 (-0.49, -0.12) | 0.001    |
| Temporal lobe                  | -0.20 (-0.40, 0.01)               | 0.06    | -0.10 (-0.31, 0.10) | 0.31    | -0.34 (-0.55, -0.12) | 0.002   | -0.29 (-0.49, -0.08) | 0.01    |
| Occipital lobe                 | -0.29 (-0.50, -0.08)              | 0.01    | -0.23 (-0.44, -0.02) | 0.03    | -0.31 (-0.52, -0.09) | 0.01    | -0.28 (-0.50, -0.06) | 0.01    |
| Parietal lobe                  | -0.31 (-0.51, -0.11)              | 0.002   | -0.15 (-0.33, 0.04) | 0.12    | -0.32 (-0.53, -0.12) | 0.002   | -0.23 (-0.42, -0.05) | 0.01    |
| Overall                        | -0.40 (-0.61, -0.20)              | <0.0001 | -0.25 (-0.44, -0.06) | 0.01    | -0.40 (-0.61, -0.20) | 0.0001 | -0.32 (-0.51, -0.13) | 0.001    |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of FA between high and non-high cfPWV.

Model 1: Unadjusted.

Model 2: Adjusted for volume of white matter hyperintensities.

Model 3: Adjusted for age, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate

Model 4: Adjusted for factors included in Model 2 and Model 3.
Table S11. Association of high cfPWV (upper 25th percentile) and MDs. Mean differences estimated by multivariable linear regression.

| Regions                  | Model 1 β (95% CI) | P value | Model 2 β (95% CI) | P value | Model 3 β (95% CI) | P value | Model 4 β (95% CI) | P value |
|--------------------------|--------------------|---------|--------------------|---------|--------------------|---------|--------------------|---------|
| Anterior corpus callosum | 0.35 (0.15, 0.55)  | 0.001   | 0.30 (0.10, 0.50)  | 0.003   | 0.26 (0.08, 0.44)  | 0.004   | 0.25 (0.07, 0.43)  | 0.01    |
| Posterior corpus callosum| 0.21 (0.01, 0.41)  | 0.04    | 0.13 (-0.06, 0.33) | 0.18    | 0.22 (0.05, 0.39)  | 0.01    | 0.18 (0.02, 0.35)  | 0.03    |
| Frontal lobe             | 0.41 (0.21, 0.62)  | <0.0001 | 0.22 (0.04, 0.40)  | 0.02    | 0.27 (0.10, 0.45)  | 0.003   | 0.18 (0.02, 0.33)  | 0.02    |
| Temporal lobe            | 0.31 (0.10, 0.51)  | 0.003   | 0.16 (-0.03, 0.35) | 0.10    | 0.21 (0.04, 0.38)  | 0.01    | 0.15 (-0.01, 0.31) | 0.06    |
| Occipital lobe           | 0.33 (0.13, 0.53)  | 0.001   | 0.22 (0.03, 0.42)  | 0.02    | 0.19 (0.01, 0.36)  | 0.03    | 0.14 (-0.03, 0.31) | 0.10    |
| Parietal lobe            | 0.33 (0.13, 0.53)  | 0.001   | 0.15 (-0.03, 0.33) | 0.11    | 0.27 (0.10, 0.43)  | 0.002   | 0.18 (0.04, 0.32)  | 0.01    |
| Overall                  | 0.38 (0.18, 0.58)  | 0.0002  | 0.20 (0.02, 0.39)  | 0.03    | 0.27 (0.10, 0.43)  | 0.002   | 0.18 (0.04, 0.33)  | 0.01    |

Bold indicates statistical significance. β is the difference (unadjusted for Model 1, adjusted for Model 2 to Model 4) of MDs between high and non-high cfPWV.

Model 1: Unadjusted.

Model 2: Adjusted for volume of white matter hyperintensities.

Model 3: Adjusted for age, sex, race-center, education, APOE genotype, ever smoking, ever drinking, body mass index, mean arterial pressure, diabetes, physical activity (total minutes/week), LDL-C, heart rate

Model 4: Adjusted for factors included in Model 2 and Model 3.
Figure S1. Flowchart of participant selection.

1,942 participants with DTI information and sampling weights

273 excluded due to missing cfPWV

1,669 participants remain

57 excluded due to BMI≥40kg/m²

1,612 participants remain

46 excluded due to major arrhythmia

1,566 participants remain

13 excluded due to aortic revascularization surgery

1,553 participants remain

13 excluded due to aortic stenosis/aortic regurgitation

1,540 participants remain

12 excluded due to minor races/ethnicities, Blacks in Washington, Minneapolis and Whites in Jackson

1,528 participants remain

44 excluded due to history of stroke

1,484 participants remain
Figure S2. Scatter plot of correlation between cfPWV and white matter microstructural integrity in (A) overall (B) frontal lobe (C) temporal lobe (D) occipital lobe (E) parietal lobe (F) anterior corpus callosum (G) posterior corpus callosum.
PWV—occipital lobe FA correlation

PWV—occipital lobe MD correlation

(D)
PWV—anterior corpus callosum FA correlation

PWV—anterior corpus callosum MD correlation
