Supplementary Information

Summary

This supplementary information contains additional results and information on the measurement models of the structural equation models reported in the main text. Supplementary table S1 reports the descriptive statistics for all cognitive tests, table S2 reports the full parameter estimates for the model in Figure 2B.

Supplementary results

As in our previous study[1], DT-MRI mean diffusivity (MD) showed high positive correlations among the twelve white matter tracts as well, similar to what was found for FA, T1 and MTR in the current study. This allowed for a general MD factor (g_{MD}) to be extracted that explained 38.22% of the variance. As might be expected, g_{MD} had a high negative correlation with g_{FA} ($r = -0.62$, $p < 0.001$), suggesting substantial overlap between these two indicators of white matter integrity. g_{MD} was also significantly associated with both g (ß = -0.13, p = 0.011) and g_{Speed} (ß = 0.17, p = 0.001), replicating the associations for g_{FA}. However, covarying g_{FA} markedly reduces these associations (ß = -0.49, p = 0.32 and ß = 0.48, p = 0.34, respectively), indicating substantial predictive redundancy. Including both g_{FA} and g_{MD} in the structural equation models (SEMs) would thus have introduced statistical collinearity problems while not adding complementary information on white matter integrity; MD and FA are, after all, defined from the same three diffusion tensor eigenvalues. Modelling was therefore restricted to g_{FA} in the SEMs.

Three different SEMs were tested, which are depicted in Figure 2A and B in the main text (model 2B was tested both with and without direct paths from g_{FA}, g_{T1}, and g_{MTR} to g). Not depicted in Figure 2 are the measurement models for the five latent factors (g_{FA}, g_{T1}, g_{MTR}, $g_{Speed,}$ and g), which were identical for all three models and can be derived from Table S2. g_{FA}, g_{T1}, and g_{MTR} were defined by the twelve tract-averaged values of their respective indices (FA, T1, or MTR), derived from the tractography analyses of the twelve major tracts studied in this sample. In addition, a number of correlated residual variances were specified, which can be found in Table S2. These were mostly neuroanatomically meaningful correlations between two corresponding bilateral tracts measured with the same white matter integrity tract indicator (e.g. tract-averaged FA for the left and right arcuate fasciculus) or between the three white matter integrity tract indicators measured in the same tract (e.g. FA, T1, and MTR in the left arcuate fasciculus). g_{Speed} was defined by simple reaction time, 4-choice reaction time and inspection time. g was defined by Symbol Search, Digit Symbol, Matrix Reasoning, Letter-Number Sequencing, Digit Span Backwards, and Block Design, with correlated residual variances between Digit Span Backwards and Letter-Number-Sequencing as well as between Block Design and Matrix Reasoning.

While all variables in the reported analyses were residualised for sex, this does not completely preclude sex differences in the reported associations. We therefore re-ran all SEMs in Figure 2 as multigroup analyses, which estimate separate path coefficients for men and women. These models fitted reasonably well (2A: $\chi^2(1548) = 2737.599$, CFI = 0.935, NNFI = 0.927, RMSEA = 0.060, SRMR = 0.070, AIC = 33011.4, BIC = 34053.8); 2B: $\chi^2(1800) = 3046.410$,CFI = 0.933,NNFI = 0.926, RMSEA = 0.057, SRMR = 0.054, AIC = 36246.3, BIC = 37337.2). Path coefficients from the three white matter tract integrity factors to g and g_{Speed} differed only little between the sexes (differences <= 0.06). Multigroup analyses that constraint these paths to be invariant between sexes yielded only slight increases in comparative fit indices (2A: AIC = 33032.6, BIC = 34054.8; 2B: AIC = 36275.7, BIC = 37342.3). When adding direct paths from the white matter tract integrity factors to g to model 2B the path coefficients were non-significant for men and women and the model fitted worse (AIC = 36381.5, BIC = 37448.1), which means the mediator effect of g_{Speed} held up for both sexes. Thus no noteworthy sex differences were found.

We relied on experimental reaction and inspection time tasks to assess cognitive information processing speed distinct from psychometric intelligence. However, two of the psychometric tests we used as indicators of g, WAIS-III Digit Symbol and Symbol Search, are often classified as tests of processing speed as well. To test for potential confounding we re-ran all models in Figure 2 excluding Digit Symbol and Symbol Search as indicators of g. These models also fitted reasonably well (2A: $\chi^2(755) = 1630.113$, CFI = 0.945, NNFI = 0.936, RMSEA = 0.058, SRMR = 0.055; 2B: $\chi^2(795) = 1780.445$, CFI = 0.944, NNFI = 0.936, RMSEA = 0.054, SRMR = 0.054, AIC = 34616.8, BIC = 35226.9). The path coefficient from g_{Speed} to g slightly decreased as a result of excluding the psychometric processing speed tasks from g (from -0.81 to -0.70), but the coefficients from the three WM tract integrity factors to g and g_{Speed} remained very similar (changes <= 0.03). When adding direct paths from the white matter tract integrity factors to g to model 2B the path coefficients were all still non-significant and the model fitted worse (AIC = 34620.2,BIC = 35242.4), thus the full mediation effect of g_{Speed} stayed intact.

In order to explore whether the observed g_{FA}, g_{T1}, and g_{MTR} associations are more related to lifelong-stable differences in intelligence or cognitive ageing, supplementary SEMs were ran that only differed from those in Figure 2 by having childhood IQ as an additional predictor of g. This was possible since our participants had sat the Moray House Test No. 12, a valid measure of full-scale IQ, at age 11 years as part of the Scottish Mental Survey of 1947[2]. When adding this variable from childhood, associations of g at age 72 years with the white matter tract integrity factors were independent of individual differences in early-life intelligence, thus reflecting cognitive change between age 11 and 72 years. The fit of the SEM in Figure 2A was slightly worse when age 11 IQ was added ($\chi^2(793)= 1857.294$, CFI=0.941, NNFI=0.933, RMSEA=0.057, SRMR=0.054, AIC=36764.412, BIC=37378.530). As in previous studies, IQ at age 11 was a strong predictor of g in old age (standardized path coefficient ß = 0.58), indicating substantial stability of intelligence over the life course[3]. With age 11 IQ in the model, g_{FA} and g_{T1} were still significant predictors of g (ßs = 0.13 and -

0.23, respectively), whereas the association with g_{MTR} fell below statistical significance (ß = 0.06). g_{MTR} showed a significant association with age 11 IQ (ß = 0.11), whereas g_{FA} and g_{T1} did not (ßs = 0.04 and -0.02, respectively). The changes in effect sizes compared to the model without age 11 IQ are weak and should thus be considered as preliminary; however, this pattern of results suggests that the individual differences in white matter tract integrity reflected by g_{FA} and g_{T1} are more linked to cognitive ageing, while those reflected by g_{MTR} are more linked to lifelong-stable differences in intelligence. Therefore, having the unusually valuable IQ score from age 11 enhances the present results by indicating that the three white matter integrity factors that contribute complementarily to cognitive ability at age 11 years might have different mechanisms of association, and have determinants from different periods in the life course. A very similar pattern of results emerged when age 11 IQ was added as a predictor of g to the SEM in Figure 2B (χ^2(921)= 2070.691, CFI=0.938, NNFI=0.930, RMSEA=0.055, SRMR=0.055, AIC=40015.279, BIC=40657.679), with the g_{MTR} effects very slightly attenuated but now just falling short of being a significant predictor of g_{Speed} (ß = -0.09), while g_{FA} and g_{T1} remained significantly associated with g_{Speed} (ßs = -0.20 and -0.30, respectively).

Table S1.

Descriptive statistics for the cognitive tests used in this study.

	Mean	S.D.	Minimum	Maximum
Mini Mental State Examination	28.84	1.29	24	30
WAIS-III Symbol Search	24.98	6.21	7	42
WAIS-III Digit Symbol	56.99	12.80	22	93
WAIS-III Matrix Reasoning	13.70	4.86	4	25
WAIS-III Letter-Number-Sequencing	10.86	2.99	2	20
WAIS-III Digit Span Backwards	7.95	2.34	2	14
WAIS-III Block Design	34.82	10.22	12	62
Simple reaction time (s)	0.27	0.05	0.18	0.52
4-choice reaction time (s)	0.64	0.08	0.45	0.89
Inspection time (correct responses)	112.58	10.68	77	137
Moray House Test IQ (age 11 years)	101.94	14.29	58.20	137.56

Table S2.

Parameter estimates for the full final structural equation model (Figure 2B), including the measurement models of the five latent factors g_{FA}, g_{T1}, g_{MTR}, g_{Speed}, and g.

	unstandardized estimate	S.E.	standardized estimate
g factor loadings:			
WAIS-III Symbol Search	1.00	0.00	0.74
WAIS-III Digit Symbol	1.11	0.07	0.84
WAIS-III Matrix Reasoning	0.64	0.07	0.49
WAIS-III Letter-Number-Sequencing	0.74	0.07	0.57
WAIS-III Digit Span Backwards	0.56	0.07	0.43
WAIS-III Block Design	0.75	0.07	0.56
g_{Speed} factor loadings:			
4-choice reaction time	1.00	0.00	0.77
Inspection time	-0.72	0.08	-0.54
Simple reaction time	0.64	0.07	0.50
g_{FA} factor loadings:			
Genu corpus callosum FA	1.00	0.00	0.62
Splenium corpus callosum FA	0.45	0.06	0.28
Left arcuate fasciculus FA	0.97	0.09	0.60
Right arcuate fasciculus FA	0.94	0.09	0.60
Left anterior thalamic radiation FA	0.92	0.09	0.58
Right anterior thalamic radiation FA	1.01	0.09	0.65
Left cingulum bundle FA	0.95	0.08	0.59
Right cingulum bundle FA	0.96	0.08	0.59
Left uncinate fasciculus FA	1.00	0.09	0.62
Right uncinate fasciculus FA	1.03	0.09	0.64
Left inferior longitudinal fasciculus FA	0.76	0.09	0.45
Right inferior longitudinal fasciculus FA	0.70	0.08	0.44
Common T1 factor loadings:			
Genu corpus callosum T1	1.00	0.00	0.82
Splenium corpus callosum T1	0.46	0.02	0.39
Left arcuate fasciculus T1	1.15	0.04	0.92
Right arcuate fasciculus T1	1.13	0.04	0.91
Left anterior thalamic radiation T1	0.89	0.03	0.75
Right anterior thalamic radiation T1	1.03	0.03	0.86
Left cingulum bundle T1	1.07	0.04	0.82
Right cingulum bundle T1	1.02	0.03	0.81
Left uncinate fasciculus T1	1.10	0.04	0.89
Right uncinate fasciculus T1	1.02	0.03	0.85
Left inferior longitudinal fasciculus T1	0.72	0.03	0.67
Right inferior longitudinal fasciculus T1	0.86	0.03	0.73

g_{MTR} factor loadings:			
Genu corpus callosum MTR	1.00	0.00	0.85
Splenium corpus callosum MTR	0.40	0.02	0.34
Left arcuate fasciculus MTR	1.08	0.05	0.87
Right arcuate fasciculus MTR	1.04	0.04	0.86
Left anterior thalamic radiation MTR	0.97	0.03	0.81
Right anterior thalamic radiation MTR	1.00	0.03	0.83
Left cingulum bundle MTR	1.15	0.03	0.93
Right cingulum bundle MTR	1.11	0.03	0.94
Left uncinate fasciculus MTR	1.06	0.04	0.86
Right uncinate fasciculus MTR	1.01	0.03	0.85
Left inferior longitudinal fasciculus MTR	0.80	0.03	0.70
Right inferior longitudinal fasciculus MTR	0.82	0.03	0.72
Latent predictors of g_{Speed}:			
Common FA factor	-0.23	0.08	-0.19
Common T1 factor	0.29	0.06	0.30
Common MTR factor	-0.11	0.05	-0.12
Latent predictors of g:			
Cognitive speed	-0.80	0.08	-0.81
Latent correlations between white matter integrity factors:			
Common FA - Common T1	-0.04	0.03	-0.08
Common FA - Common MTR	0.16	0.03	0.31
Common T1 - Common MTR	0.17	0.04	0.25
Correlated residuals:			
WAIS-III Digit Span Backwards with			
WAIS-III Letter-Number-Sequencing	0.28	0.04	0.28
WAIS-III Block Design with			
WAIS-III Matrix Reasoning	0.25	0.04	0.25
Right arcuate fasciculus FA with			
Left arcuate fasciculus FA	0.16	0.03	0.16
Right anterior thalamic radiation FA with			
Left anterior thalamic radiation FA	0.10	0.03	0.10
Right cingulum bundle FA with			
Left cingulum bundle FA	0.12	0.02	0.12
Right uncinate fasciculus FA with			
Left uncinate fasciculus FA	0.12	0.03	0.12
Right inferior longitudinal fasciculus FA with			
Left inferior longitudinal fasciculus FA	0.16	0.03	0.16
Right arcuate fasciculus T1 with			
Left arcuate fasciculus T1	0.03	0.01	0.03
Right arcuate fasciculus FA	-0.14	0.02	-0.14
Right uncinate fasciculus T1 with			

Left uncinate fasciculus T1	0.05	0.01	0.06
Right uncinate fasciculus FA	-0.18	0.02	-0.19
Right inferior longitudinal fasciculus T1 with			
Left inferior longitudinal fasciculus T1	0.02	0.01	0.03
Right inferior longitudinal fasciculus FA	-0.30	0.03	-0.33
Left arcuate fasciculus MTR with			
Genu corpus callosum MTR	-0.07	0.01	-0.06
Left arcuate fasciculus FA	0.11	0.02	0.11
Left arcuate fasciculus T1	-0.07	0.01	-0.07
Right arcuate fasciculus MTR with			
Genu corpus callosum MTR	-0.02	0.01	-0.02
Right arcuate fasciculus FA	0.10	0.02	0.10
Right arcuate fasciculus T1	-0.06	0.01	-0.06
Left anterior thalamic radiation MTR with			
Genu corpus callosum MTR	0.05	0.01	0.05
Left anterior thalamic radiation FA	0.21	0.03	0.21
Left anterior thalamic radiation T1	-0.25	0.02	-0.26
Right anterior thalamic radiation MTR with			
Genu corpus callosum MTR	0.07	0.01	0.07
Left arcuate fasciculus MTR	-0.06	0.01	-0.06
Right anterior thalamic radiation FA	0.18	0.02	0.18
Right anterior thalamic radiation T1	-0.14	0.02	-0.15
Left uncinate fasciculus MTR with			
Right arcuate fasciculus MTR	-0.12	0.01	-0.12
Left uncinate fasciculus FA	0.15	0.02	0.15
Left uncinate fasciculus T1	-0.09	0.01	-0.09
Right uncinate fasciculus MTR with			
Genu corpus callosum MTR	0.09	0.01	0.09
Left arcuate fasciculus MTR	-0.10	0.01	-0.09
Right anterior thalamic radiation MTR	0.08	0.01	0.08
Right uncinate fasciculus FA	0.16	0.02	0.16
Right uncinate fasciculus T1	-0.14	0.01	-0.15
Left inferior longitudinal fasciculus MTR with			
Left arcuate fasciculus MTR	0.11	0.01	0.11
Left inferior longitudinal fasciculus FA	0.22	0.03	0.22
Left inferior longitudinal fasciculus T1	-0.34	0.03	-0.41
Right inferior longitudinal fasciculus MTR with			
Right arcuate fasciculus MTR	0.11	0.01	0.11
Left uncinate fasciculus MTR	-0.07	0.01	-0.07
Right inferior longitudinal fasciculus FA	0.20	0.03	0.21
Right inferior longitudinal fasciculus T1	-0.33	0.03	-0.37
Genu corpus callosum T1 with			
Genu corpus callosum FA	-0.11	0.02	-0.12
Splenium corpus callosum T1 with			
Splenium corpus callosum FA	-0.59	0.05	-0.63
Left arcuate fasciculus T1 with			

Left arcuate fasciculus FA	-0.13	0.02	-0.13
Left anterior thalamic radiation T1 with			
Left anterior thalamic radiation FA	-0.23	0.03	-0.25
Right anterior thalamic radiation T1 with			
Right anterior thalamic radiation FA	-0.19	0.02	-0.20
Left cingulum bundle T1 with			
Left cingulum bundle FA	-0.32	0.03	-0.31
Right cingulum bundle T1 with			
Right cingulum bundle FA	-0.35	0.03	-0.34
Left uncinate fasciculus T1 with			
Left uncinate fasciculus FA	-0.14	0.02	-0.14
Left inferior longitudinal fasciculus T1 with			
Left inferior longitudinal fasciculus FA	-0.27	0.03	-0.30
Genu corpus callosum MTR with			
Genu corpus callosum FA	0.08	0.02	0.08
Genu corpus callosum T1	-0.18	0.02	-0.19
Splenium corpus callosum MTR with			
Splenium corpus callosum FA	0.61	0.05	0.63
Splenium corpus callosum T1	-0.76	0.05	-0.81
Left cingulum bundle MTR with			
Left cingulum bundle FA	0.18	0.02	0.17
Left cingulum bundle T1	-0.16	0.02	-0.15
Right cingulum bundle MTR with			
Right cingulum bundle FA	0.18	0.02	0.17
Right cingulum bundle T1	-0.17	0.02	-0.16

Notes: WAIS-III = Wechsler Adult Intelligence Scale III^{UK}, FA = fractional anisotropy, MTR = magnetization transfer ratio, T1 = longitudinal relaxation time.

References

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