PNAS

Supporting Information for

Evidence of association between higher cardiorespiratory fitness and higher cerebral myelination in aging.

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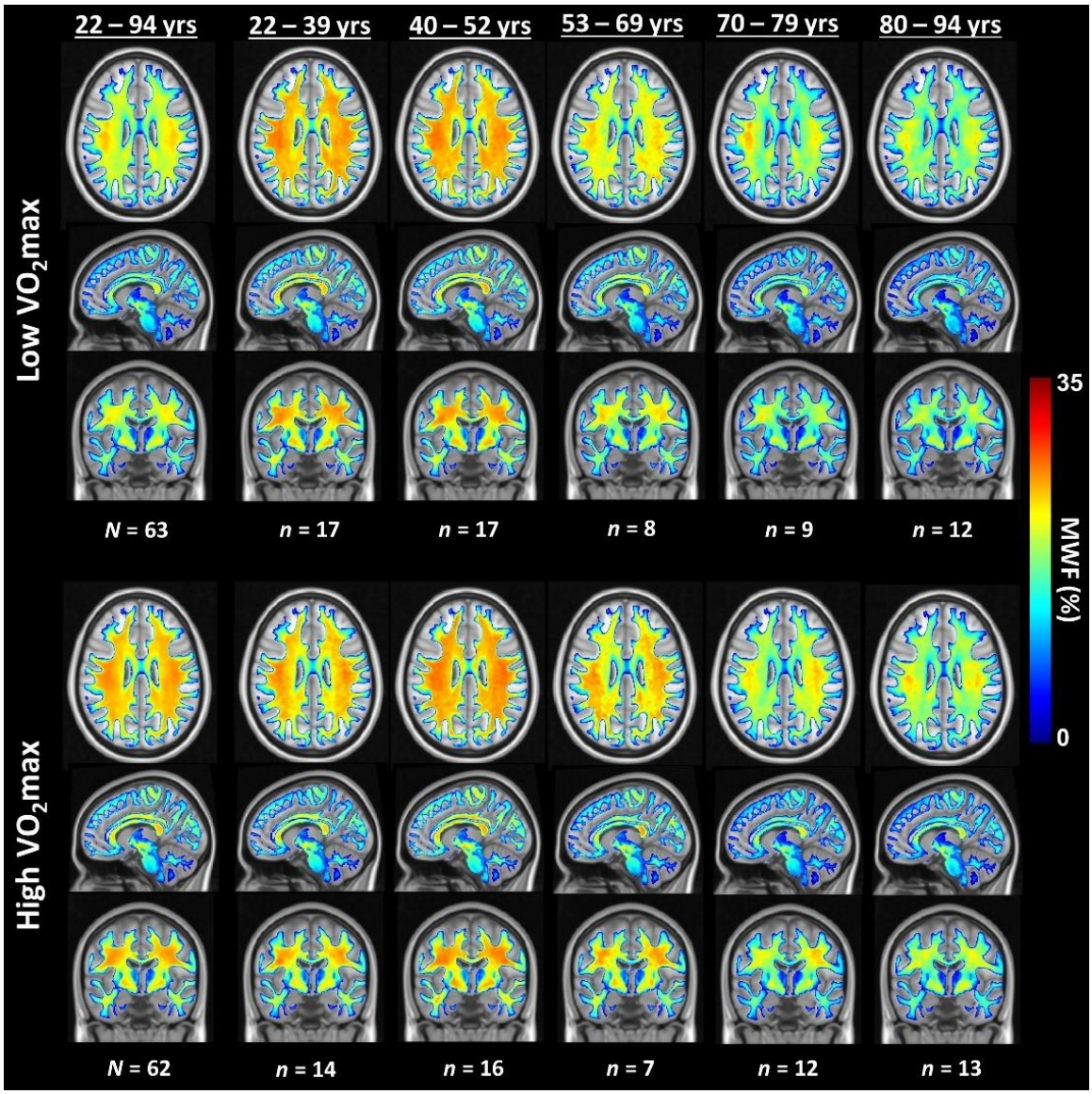

Fig. S1. Examples of axial, sagittal, and coronal myelin water fraction (MWF) parameter maps averaged across participants with either low or high levels of maximum rate of oxygen consumption (VO_2max). Participants were drawn from the full age range as well as from restricted age ranges to mitigate the effect of age. Within a given age range, low VO_2max corresponds to values less than the mean VO_2max, while high VO_2max corresponds to values equal to or greater than the mean VO_2max. Results are shown for representative slices. Visual inspection indicates that, overall, participants with higher VO_2max levels exhibit greater regional MWF values, especially at middle and older ages.

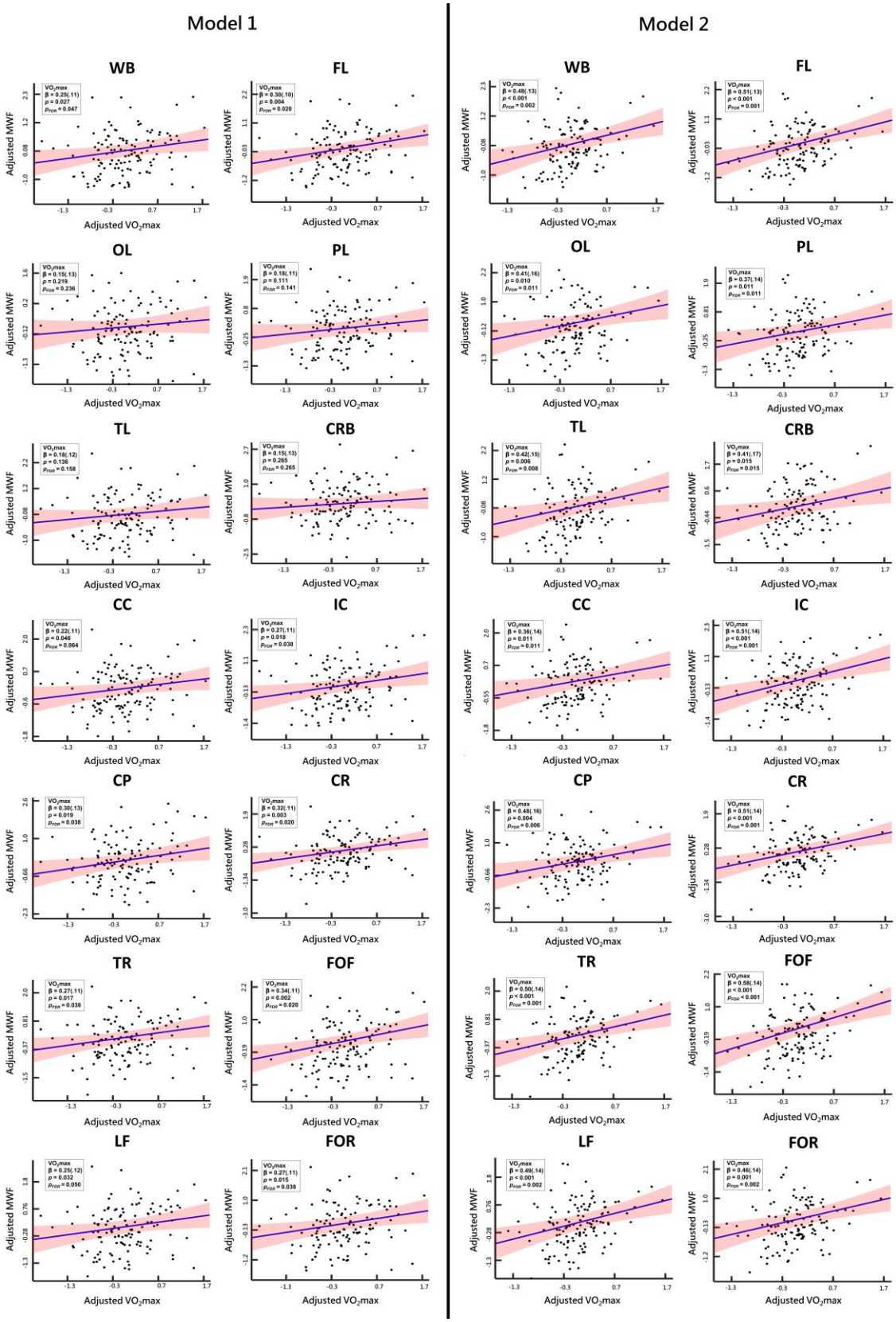
Model 1
Model 2
WB
FL
OL
PL
TL
CRB
CC
IC
CP
CR
TR
FOF
LF
FOR
Adjusted MWF
Adjusted VO2max

Fig. S2. Association of myelin water fraction (MWF) with maximum rate of oxygen consumption (VO_2max) within all 14 white matter ROIs derived using model #1 or model #2. The line of best fit (blue solid line), confidence intervals (shaded red), regression coefficients (standard error), *p* value, and FDR-corrected *p* value derived from the linear regression models adjusted for covariates are also displayed. The adjusted response function describes the relationship between the fitted response and MWF, with the remaining z-scored predictors set to 0.

Notes. ROI, region-of-interest; WB, whole brain; FL, frontal lobe; OL, occipital lobe; PL, parietal lobe; TL, temporal lobe; CRB, cerebellum; CC, corpus callosum; IC, internal capsule; CP, cerebral peduncle; CR, corona radiata; TR, thalamic radiation; FOF, fronto-occipital fasciculus; LF, longitudinal fasciculus; FOR, forceps.

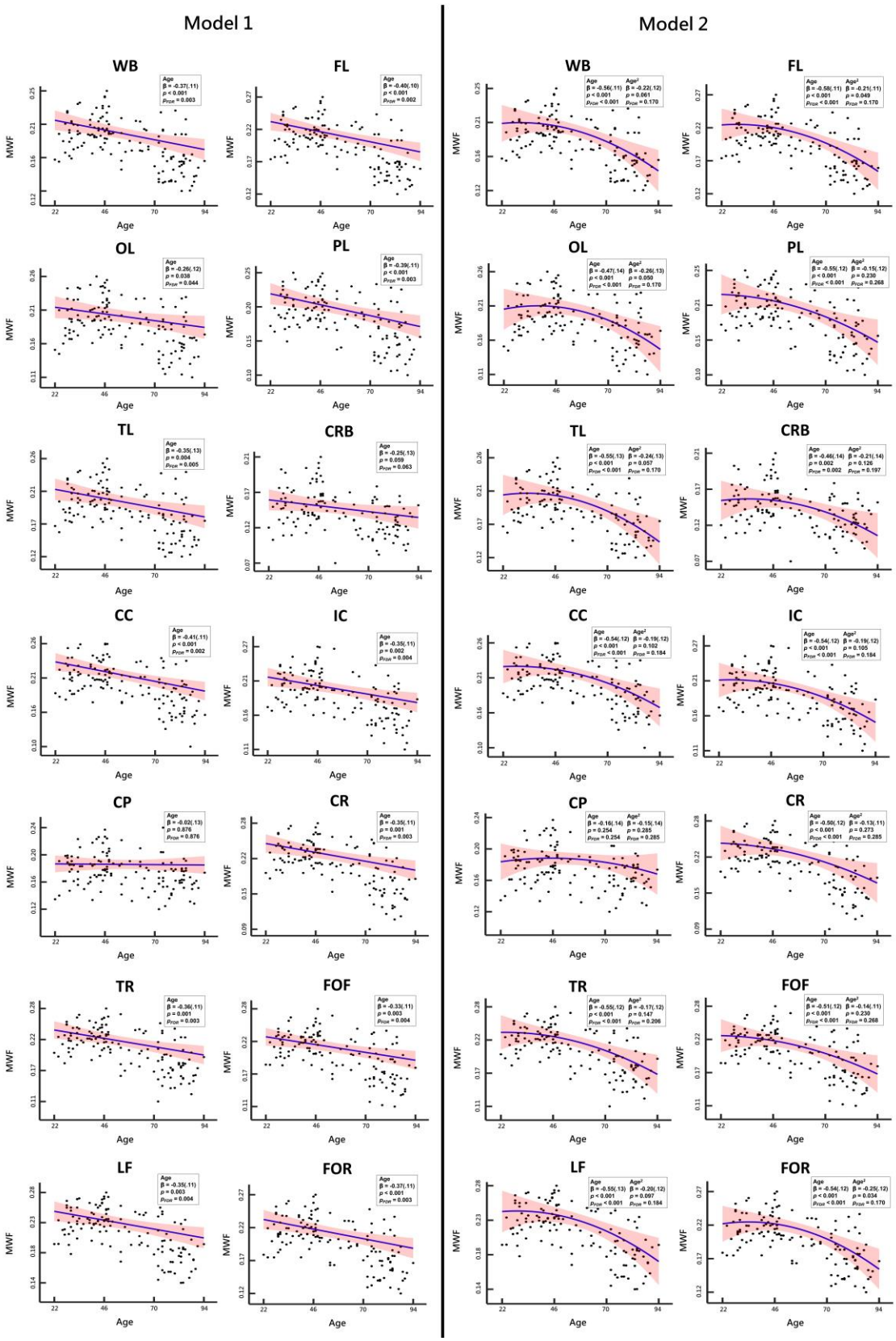
Model 1
Model 2
WB
FL
OL
PL
TL
CRB
CC
IC
CP
CR
TR
FOF
LF
FOR
MWF
Age

Fig. S3. Association of myelin water fraction (MWF) with age in all 14 white matter ROIs derived using model #1 and model #2. The line of best fit (blue solid line), confidence intervals (shaded red), regression coefficients (standard error), *p* value, and FDR-corrected *p* value derived from the linear regression models adjusted for covariates are also displayed.

Notes. ROI, region-of-interest; WB, whole brain; FL, frontal lobe; OL, occipital lobe; PL, parietal lobe; TL, temporal lobe; CRB, cerebellum; CC, corpus callosum; IC, internal capsule; CP, cerebral peduncle; CR, corona radiata; TR, thalamic radiation; FOF, fronto-occipital fasciculus; LF, longitudinal fasciculus; FOR, forceps.

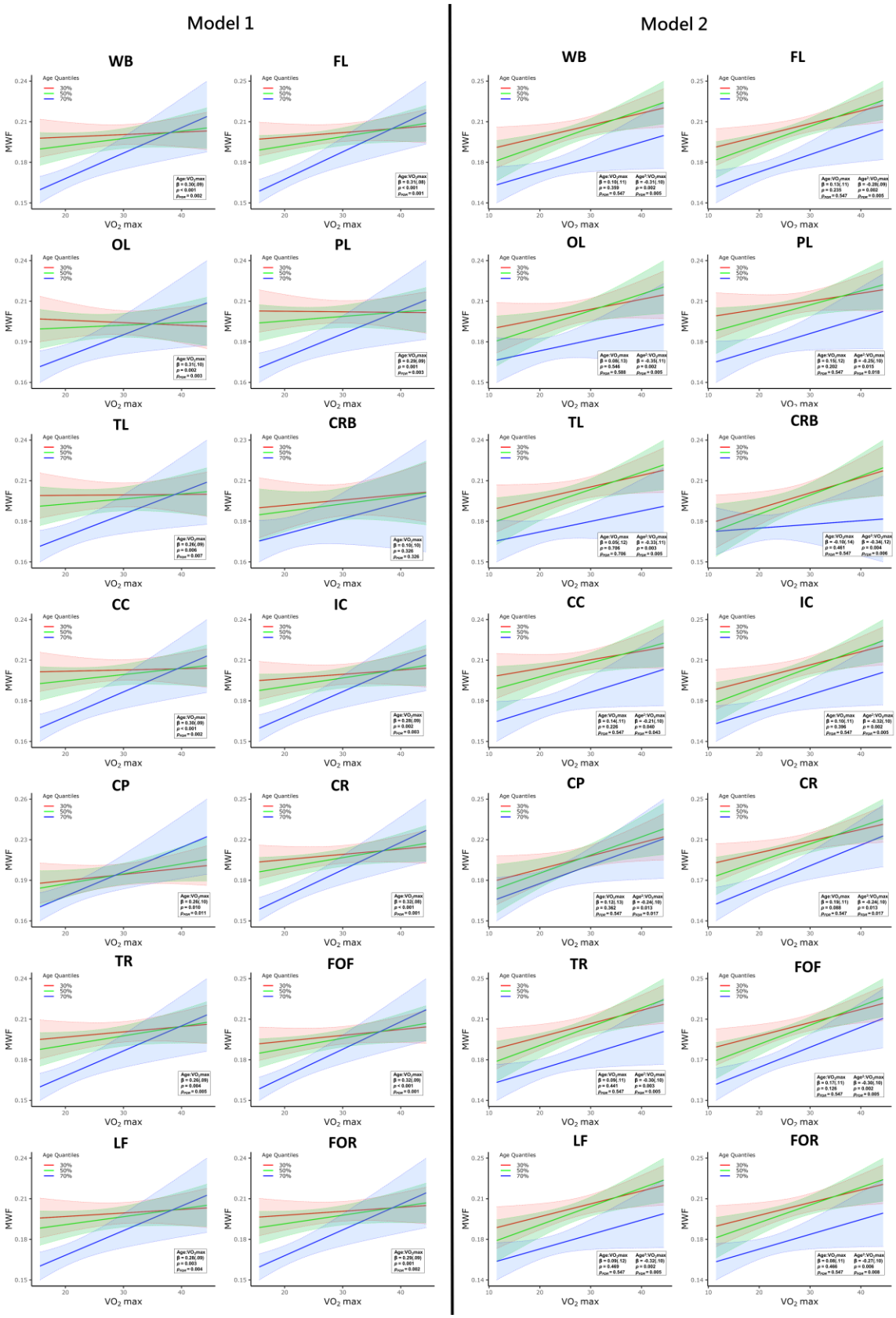
Model 1
Model 2
WB
FL
OL
PL
TL
CRB
CC
IC
CP
CR
TR
FOF
LF
FOR
MWF
VO2 max
Age Quantiles
30%
50%
70%

Fig. S4. Age-stratified associations between myelin water fraction (MWF) and maximum rate of oxygen consumption (VO_2max) in all 14 white matter ROIs derived using model #1 and model #2. The colored lines correspond to the 30th (red), 50th (green), and 70th (blue) quantiles of age. The line of best fit (solid line), confidence intervals (shaded regions), regression coefficients (standard error), *p* value, and FDR-corrected *p* value derived from the linear regression models adjusted for covariates are also displayed.

Notes. ROI, region-of-interest; WB, whole brain; FL, frontal lobe; OL, occipital lobe; PL, parietal lobe; TL, temporal lobe; CRB, cerebellum; CC, corpus callosum; IC, internal capsule; CP, cerebral peduncle; CR, corona radiata; TR, thalamic radiation; FOF, fronto-occipital fasciculus; LF, longitudinal fasciculus; FOR, forceps.

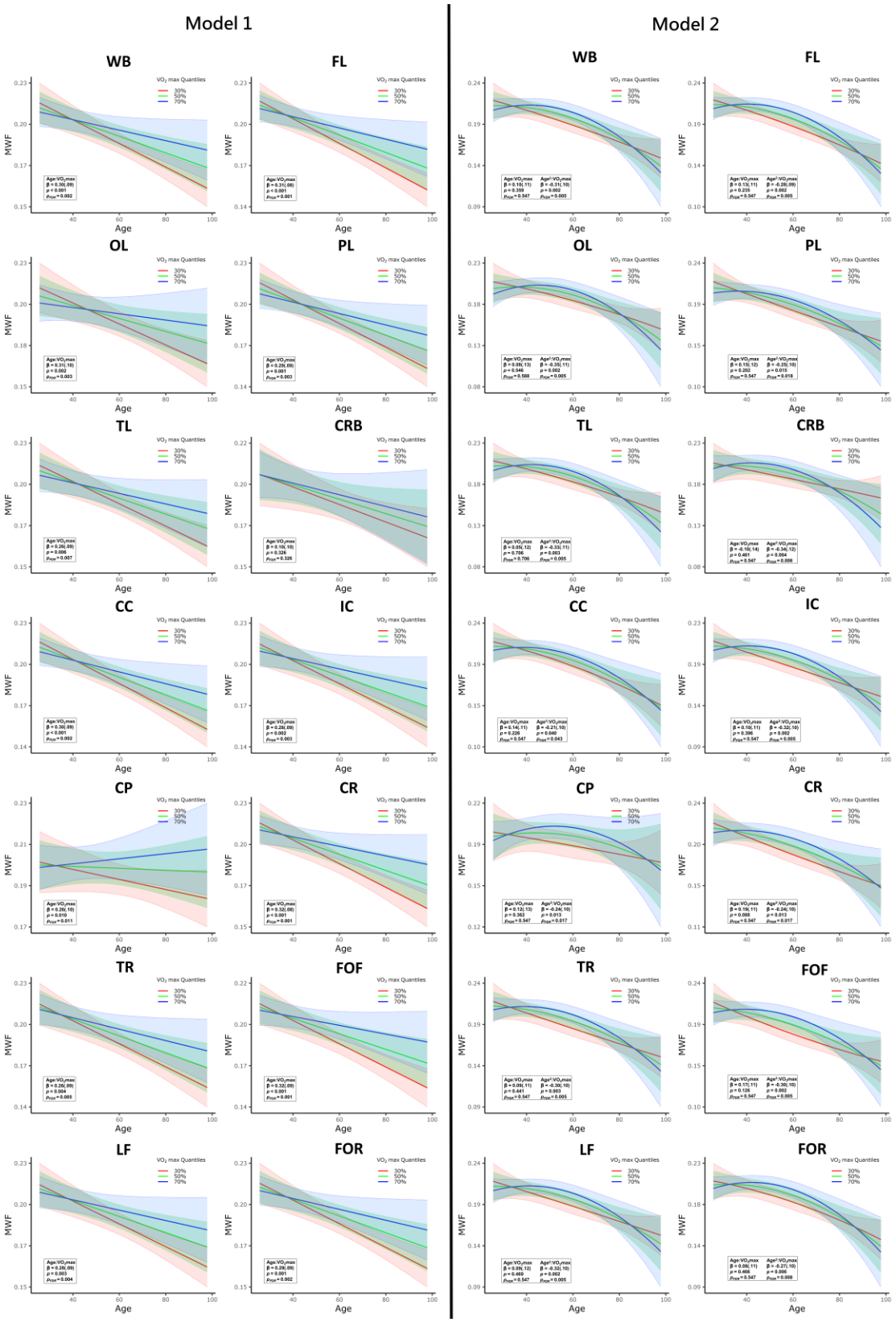

Fig. S5. VO_2max-stratified associations between myelin water fraction (MWF) and age in all 14 white matter ROIs derived using model #1 and model #2. The colored lines correspond to the 30th

(red), 50th (green), and 70th (blue) quantiles of maximum rate of oxygen consumption (VO_2max). The line of best fit (solid line), confidence intervals (shaded regions), regression coefficients (standard error), *p* value, and FDR-corrected *p* value derived from the linear regression models adjusted for covariates are also displayed.

Notes. ROI, region-of-interest; WB, whole brain; FL, frontal lobe; OL, occipital lobe; PL, parietal lobe; TL, temporal lobe; CRB, cerebellum; CC, corpus callosum; IC, internal capsule; CP, cerebral peduncle; CR, corona radiata; TR, thalamic radiation; FOF, fronto-occipital fasciculus; LF, longitudinal fasciculus; FOR, forceps.

Table 1S. Regression coefficient (standard error) and *p*-values (before, *p*, and after FDR correction, p_{FDR}) of age, VO_2max, age×VO_2max, sex, and SBP with respect to MWF (Model 1) for each of the 14 WM ROIs investigated.

ROIs	MWF				
	Model 1				
	Age	VO_2max	Age × VO_2max	Sex	SBP
WB	-0.37*(0.11)*, ***p*<0.001** ***p_{FDR}=0.003***	0.25*(0.11)*, ***p*=0.027** ***p_{FDR}=0.047***	0.30*(0.09)*, ***p*<0.001** ***p_{FDR}=0.002***	-0.28*(0.16)*, *p*=0.076 p_{FDR}=0.191	0.01*(0.08)*, *p*=0.881 p_{FDR}=0.959
FL	-0.40*(0.10)*, ***p*<0.001** ***p_{FDR}=0.002***	0.30*(0.10)*, ***p*=0.004** ***p_{FDR}=0.020***	0.31*(0.08)*, ***p*<0.001** ***p_{FDR}=0.001***	-0.31*(0.14)*, ***p*=0.035** p_{FDR}=0.191	0.08*(0.07)*, *p*=0.289 p_{FDR}=0.959
OL	-0.26*(0.12)*, ***p*=0.038** ***p_{FDR}=0.044***	0.15*(0.13)*, *p*=0.219 p_{FDR}=0.236	0.31*(0.09)*, ***p*=0.002** ***p_{FDR}=0.003***	-0.19*(0.18)*, *p*=0.285 p_{FDR}=0.360	-0.06*(0.09)*, *p*=0.465 p_{FDR}=0.959
PL	-0.39*(0.11)*, ***p*<0.001** ***p_{FDR}=0.003***	0.18*(0.11)*, *p*=0.111 p_{FDR}=0.141	0.29*(0.08)*, ***p*=0.001** ***p_{FDR}=0.003***	-0.28*(0.16)*, *p*=0.082 p_{FDR}=0.191	-0.01*(0.08)*, *p*=0.891 p_{FDR}=0.959
TL	-0.35*(0.12)*, ***p*=0.004** ***p_{FDR}=0.005***	0.18*(0.12)*, *p*=0.136 p_{FDR}=0.158	0.26*(0.09)*, ***p*=0.006** ***p_{FDR}=0.007***	-0.22*(0.17)*, *p*=0.194 p_{FDR}=0.302	-0.03*(0.08)*, *p*=0.704 p_{FDR}=0.959
CRB	-0.25*(0.13)*, *p*=0.059 p_{FDR}=0.063	0.15*(0.13)*, *p*=0.265 p_{FDR}=0.265	0.10*(0.10)*, *p*=0.326 p_{FDR}=0.326	-0.18*(0.18)*, *p*=0.335 p_{FDR}=0.360	0.01*(0.09)*, *p*=0.885 p_{FDR}=0.959
CC	-0.41*(0.11)*, ***p*<0.001** ***p_{FDR}=0.002***	0.22*(0.11)*, ***p*=0.046** p_{FDR}=0.064	0.30*(0.09)*, ***p*<0.001** ***p_{FDR}=0.002***	-0.34*(0.15)*, ***p*=0.028** p_{FDR}=0.191	0.05*(0.08)*, *p*=0.540 p_{FDR}=0.959
IC	-0.35*(0.11)*, ***p*=0.002** ***p_{FDR}=0.004***	0.27*(0.11)*, ***p*=0.018** ***p_{FDR}=0.038***	0.28*(0.09)*, ***p*=0.002** ***p_{FDR}=0.003***	-0.15*(0.16)*, *p*=0.329 p_{FDR}=0.360	-0.04*(0.08)*, *p*=0.628 p_{FDR}=0.959
CP	-0.02*(0.13)*, *p*=0.876 p_{FDR}=0.876	0.30*(0.13)*, ***p*=0.019** ***p_{FDR}=0.038***	0.26*(0.10)*, ***p*=0.010** ***p_{FDR}=0.011***	-0.37*(0.18)*, ***p*=0.042** p_{FDR}=0.191	-0.06*(0.09)*, *p*=0.523 p_{FDR}=0.959
CR	-0.35*(0.11)*, ***p*=0.001** ***p_{FDR}=0.003***	0.32*(0.11)*, ***p*=0.003** ***p_{FDR}=0.020***	0.32*(0.08)*, ***p*<0.001** ***p_{FDR}=0.001***	-0.27*(0.15)*, *p*=0.075 p_{FDR}=0.191	0.04*(0.07)*, *p*=0.632 p_{FDR}=0.959
TR	-0.36*(0.11)*, ***p*=0.001** ***p_{FDR}=0.003***	0.27*(0.11)*, ***p*=0.017** ***p_{FDR}=0.038***	0.26*(0.09)*, ***p*=0.004** ***p_{FDR}=0.005***	-0.16*(0.16)*, *p*=0.312 p_{FDR}=0.360	<0.01*(0.08)*, *p*=0.968 p_{FDR}=0.968
FOF	-0.33*(0.11)*, ***p*=0.003** ***p_{FDR}=0.004***	0.34*(0.11)*, ***p*=0.002** ***p_{FDR}=0.020***	0.32*(0.09)*, ***p*<0.001** ***p_{FDR}=0.001***	-0.07*(0.15)*, *p*=0.638 p_{FDR}=0.638	0.02*(0.07)*, *p*=0.828 p_{FDR}=0.959
LF	-0.35*(0.11)*, ***p*=0.003**	0.25*(0.12)*, ***p*=0.032**	0.28*(0.09)*, ***p*=0.003**	-0.27*(0.16)*, *p*=0.097	0.01*(0.08)*, *p*=0.861

	$\boldsymbol{p_{FDR}=0.004}$	$p_{FDR}=0.050$	$\boldsymbol{p_{FDR}=0.004}$	$p_{FDR}=0.194$	$p_{FDR}=0.959$
FOR	-0.37*(0.11)*, $\boldsymbol{p<0.001}$ $\boldsymbol{p_{FDR}=0.003}$	0.27*(0.11)*, $\boldsymbol{p=0.015}$ $\boldsymbol{p_{FDR}=0.038}$	0.29*(0.09)*, $\boldsymbol{p=0.001}$ $\boldsymbol{p_{FDR}=0.002}$	-0.25*(0.15)*, $p=0.111$ $p_{FDR}=0.194$	0.02*(0.08)*, $p=0.777$ $p_{FDR}=0.959$

Notes. VO_2max, maximum volume rate of oxygen; MWF, myelin water fraction; SBP, systolic blood pressure; WM, white matter; ROI, region-of-interest; WB, whole brain; FL, frontal lobe; OL, occipital lobe; PL, parietal lobe; TL, temporal lobe; CRB, cerebellum; CC, corpus callosum; IC, internal capsule; CP, cerebral peduncle; CR, corona radiata; TR, thalamic radiation; FOF, fronto-occipital fasciculus; LF, longitudinal fasciculus; FOR, forceps. Bolded values indicate statistical significance (p or $p_{FDR} < 0.05$). Standard error (SE) values are italicized.

Table 2S. Regression coefficient (standard error) and *p*-values (before, *p*, and after FDR correction, p_{FDR}) of age, age^2, VO_2max, age×VO_2max, age^2×VO_2max, sex, and SBP with respect to MWF (Model 2) for each of the 14 WM ROIs investigated.

ROIs	MWF						
	Model 2						
	Age	Age^2	VO_2max	Age × VO_2max	Age^2 × VO_2max	Sex	SBP
WB	-0.56*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.22*(0.12)*, p=0.061 p_{FDR}=0.170	0.48*(0.13)*, **p<0.001** **p_{FDR}=0.002**	0.10*(0.11)*, p=0.359 p_{FDR}=0.547	-0.31*(0.10)*, **p=0.002** **p_{FDR}=0.005**	-0.33*(0.15)*, **p=0.031** p_{FDR}=0.085	0.02*(0.07)*, p=0.763 p_{FDR}=0.873
FL	-0.58*(0.11)*, **p<0.001** **p_{FDR}<0.001**	-0.21*(0.11)*, **p=0.049** p_{FDR}=0.170	0.51*(0.13)*, **p<0.001** **p_{FDR}=0.001**	0.13*(0.11)*, p=0.235 p_{FDR}=0.547	-0.28*(0.09)*, **p=0.002** **p_{FDR}=0.005**	-0.35*(0.14)*, **p=0.013** p_{FDR}=0.085	0.08*(0.07)*, p=0.228 p_{FDR}=0.873
OL	-0.47*(0.14)*, **p <0.001** **p_{FDR}<0.001**	-0.26*(0.12)*, **p=0.049** p_{FDR}=0.170	0.41*(0.16)*, **p=0.010** **p_{FDR}=0.011**	0.08*(0.13)*, p=0.546 p_{FDR}=0.588	-0.35*(0.11)*, **p=0.002** **p_{FDR}=0.005**	-0.24*(0.17)*, p=0.154 p_{FDR}=0.202	-0.05*(0.08)*, p=0.540 p_{FDR}=0.873
PL	-0.55*(0.12)*, **p <0.001** **p_{FDR}<0.001**	-0.15*(0.12)*, p=0.230 p_{FDR}=0.268	0.37*(0.14)*, **p=0.011** **p_{FDR}=0.011**	0.15*(0.12)*, p=0.202 p_{FDR}=0.547	-0.25*(0.10)*, **p=0.015** **p_{FDR}=0.018**	-0.32*(0.16)*, **p=0.043** p_{FDR}=0.085	<0.01*(0.08)*, p=0.983 p_{FDR}=0.983
TL	-0.55*(0.13)*, **p <0.001** **p_{FDR}<0.001**	-0.24*(0.13)*, p=0.057 p_{FDR}=0.170	0.42*(0.15)*, **p=0.006** **p_{FDR}=0.008**	0.05*(0.12)*, p=0.706 p_{FDR}=0.706	-0.33*(0.11)*, **p=0.003** **p_{FDR}=0.005**	-0.27*(0.16)*, p=0.098 p_{FDR}=0.153	-0.02*(0.08)*, p=0.799 p_{FDR}=0.873
CRB	-0.46*(0.14)*, **p=0.002** **p_{FDR}=0.002**	-0.21*(0.14)*, p=0.126 p_{FDR}=0.197	0.41*(0.17)*, **p=0.015** **p_{FDR}=0.015**	-0.10*(0.14)*, p=0.461 p_{FDR}=0.547	-0.34*(0.12)*, **p=0.004** **p_{FDR}=0.006**	-0.24*(0.18)*, p=0.190 p_{FDR}=0.205	0.03*(0.09)*, p=0.749 p_{FDR}=0.873
CC	-0.54*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.19*(0.12)*, p=0.095 p_{FDR}=0.184	0.36*(0.14)*, **p=0.011** **p_{FDR}=0.011**	0.14*(0.11)*, p=0.226 p_{FDR}=0.547	-0.21*(0.10)*, **p=0.040** **p_{FDR}=0.043**	-0.37*(0.15)*, **p=0.016** p_{FDR}=0.085	0.05*(0.08)*, p=0.519 p_{FDR}=0.873
IC	-0.54*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.19*(0.12)*, p=0.098 p_{FDR}=0.184	0.51*(0.14)*, **p<0.001** **p_{FDR}=0.001**	0.10*(0.11)*, p=0.396 p_{FDR}=0.547	-0.32*(0.10)*, **p=0.002** **p_{FDR}=0.005**	-0.21*(0.15)*, p=0.173 p_{FDR}=0.202	-0.02*(0.08)*, p=0.766 p_{FDR}=0.873
CP	-0.16*(0.14)*, p=0.254 p_{FDR}=0.254	-0.15*(0.14)*, p=0.285 p_{FDR}=0.285	0.48*(0.16)*, **p=0.004** **p_{FDR}=0.006**	0.12*(0.13)*, p=0.362 p_{FDR}=0.547	-0.24*(0.12)*, **p=0.045** **p_{FDR}=0.045**	-0.41*(0.18)*, **p=0.024** p_{FDR}=0.085	-0.05*(0.09)*, p=0.607 p_{FDR}=0.873
CR	-0.50*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.13*(0.11)*, p=0.273 p_{FDR}=0.285	0.51*(0.14)*, **p<0.001** **p_{FDR}=0.001**	0.19*(0.11)*, p=0.088 p_{FDR}=0.547	-0.24*(0.10)*, **p=0.013** **p_{FDR}=0.017**	-0.31*(0.15)*, **p=0.037** p_{FDR}=0.085	0.05*(0.07)*, p=0.508 p_{FDR}=0.873
TR	-0.55*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.17*(0.12)*, p=0.147 p_{FDR}=0.206	0.50*(0.14)*, **p<0.001** **p_{FDR}=0.001**	0.09*(0.11)*, p=0.441 p_{FDR}=0.547	-0.30*(0.10)*, **p=0.003** **p_{FDR}=0.005**	-0.21*(0.15)*, p=0.168 p_{FDR}=0.202	0.02*(0.08)*, p=0.810 p_{FDR}=0.873
FOF	-0.51*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.14*(0.11)*, p=0.230 p_{FDR}=0.268	0.58*(0.14)*, **p<0.001** **p_{FDR}<0.001**	0.17*(0.11)*, p=0.126 p_{FDR}=0.547	-0.30*(0.10)*, **p=0.002** **p_{FDR}=0.005**	-0.13*(0.15)*, p=0.390 p_{FDR}=0.390	0.04*(0.07)*, p=0.635 p_{FDR}=0.873
LF	-0.55*(0.13)*, **p<0.001** **p_{FDR}<0.001**	-0.20*(0.12)*, p=0.097 p_{FDR}=0.184	0.49*(0.14)*, **p<0.001** **p_{FDR}=0.002**	0.09*(0.12)*, p=0.469 p_{FDR}=0.547	-0.32*(0.10)*, **p=0.002** **p_{FDR}=0.005**	-0.33*(0.16)*, **p=0.041** p_{FDR}=0.085	0.03*(0.08)*, p=0.719 p_{FDR}=0.873
FOR	-0.54*(0.12)*, **p<0.001** **p_{FDR}<0.001**	-0.25*(0.12)*, **p=0.034** p_{FDR}=0.170	0.46*(0.14)*, **p=0.001** **p_{FDR}=0.002**	0.08*(0.11)*, p=0.466 p_{FDR}=0.547	-0.27*(0.10)*, **p=0.006** **p_{FDR}=0.008**	-0.29*(0.15)*, p=0.058 p_{FDR}=0.102	0.03*(0.07)*, p=0.730 p_{FDR}=0.873

Notes. VO_2max, maximum volume rate of oxygen; MWF, myelin water fraction; SBP, systolic blood pressure; WM, white matter; ROI, region-of-interest; WB, whole brain; FL, frontal lobe; OL, occipital lobe; PL, parietal lobe; TL, temporal lobe; CRB, cerebellum; CC, corpus callosum; IC, internal capsule; CP, cerebral peduncle; CR, corona radiata; TR, thalamic radiation; FOF, fronto-occipital fasciculus; LF, longitudinal fasciculus; FOR, forceps. Bolded values indicate statistical significance (p or $p_{FDR} < 0.05$). Standard error (SE) values are italicized.