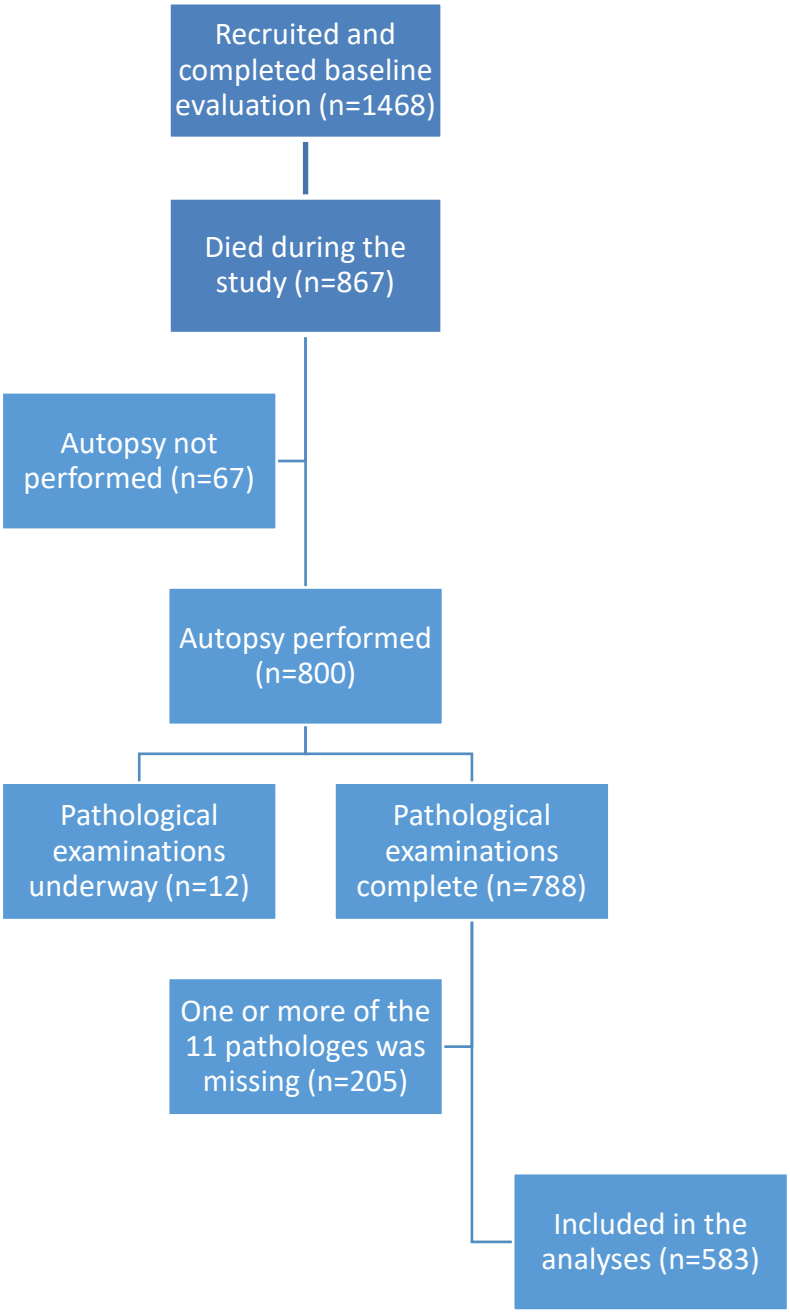
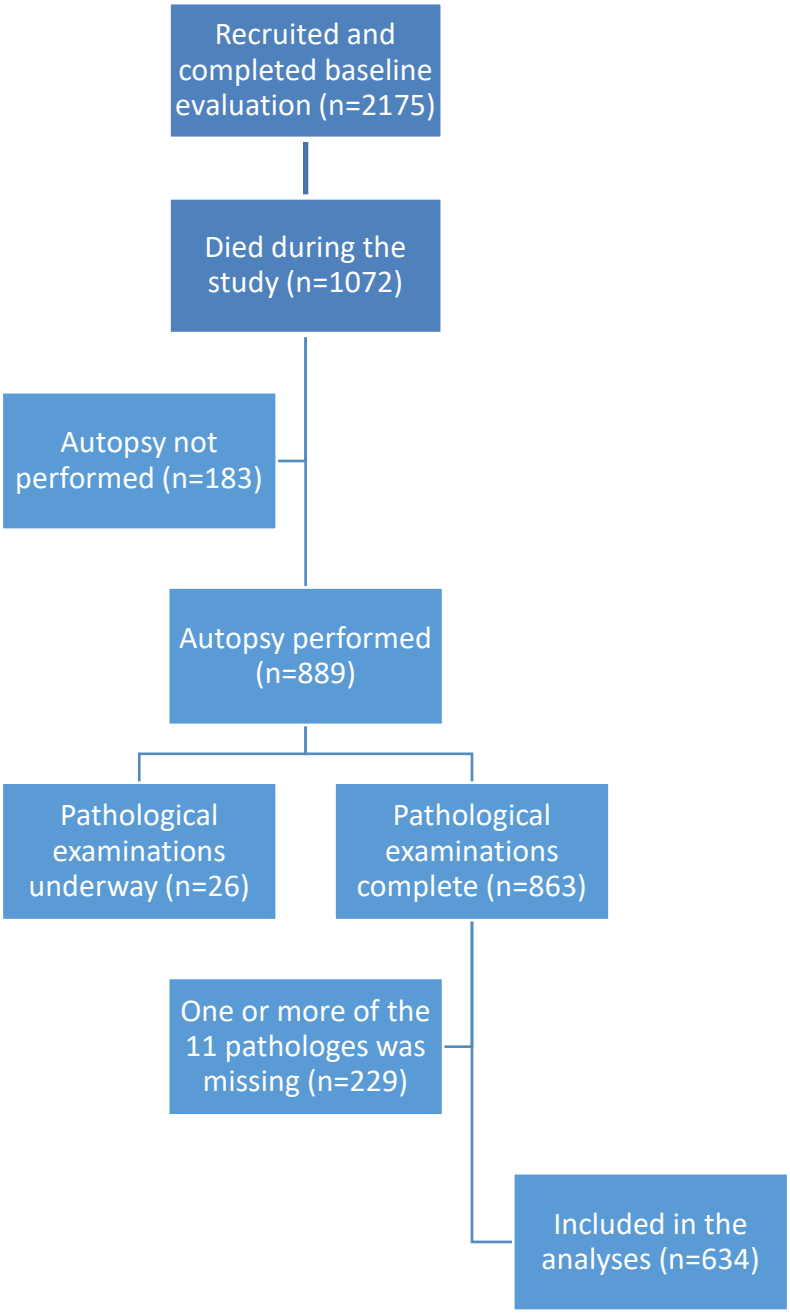
Supplementary Materials

Supplementary Figure e-1. Flow chart of the Religious Orders Study (ROS) participants included in the current study.



Supplementary Figure e-2. Flow chart of the Rush Memory and Aging Project (MAP) participants included in the current study.



Supplementary Table e-1. Association of demographic and clinical characteristics of participants with grip strength and gait function at the last visit before death.

Covariates	Association with Grip strength[a]	Association with Gait function[a]
Age at last visit (years), mean (SD)	$r = -0.34$, $p < 0.001$	$r = -0.28$, $p < 0.001$
Age at death (years), mean (SD_	$r = -0.32$, $p < 0.001$	$r = -0.25$, $p < 0.001$
Female, n (%)	$t_{1215} = -22.8$, $p < 0.001$	$t_{1215} = -4.64$, $p < 0.001$
Years of education, mean (SD)	$r = 0.08$, $p = 0.007$	$r = -0.07$, $p = 0.014$
Presence of ApoE ε4, n (%)	$t_{1206} = -1.07$, $p = 0.284$	$t_{1206} = -0.22$, $p = 0.823$
Hypertension n (%)	$t_{1215} = -2.71$, $p = 0.007$	$t_{1215} = -1.75$ $p = 0.081$
Diabetes Mellitus n (%)	$t_{1214} = 1.55$, $p = 0.121$	$t_{1215} = -1.04$, $p = 0.299$
Smoking history n (%)	$t_{1215} = 7.78$, $p < 0.001$	$t_{1215} = 5.72$, $p < 0.001$
Number of vascular risk factors, median (IQR)	$r = 0.11$, $p < 0.001$	$r = 0.08$, $p = 0.003$
History of stroke n (%)	$t_{1214} = -2.10$, $p = 0.036$	$t_{1214} = -4.59$, $p < 0.001$
Dementia prior to death n (%)	$t_{1210} = -14.1$, $p < 0.001$	$t_{1215} = -10.3$, $p < 0.001$
Years of follow up prior to death, mean (SD)	$r = -0.03$, $p = 0.298$	$r = -0.11$. $p < 0.001$

Estimates are either Spearman correlation coefficients, p-values or t(degree of freedom), p-values derived from t-tests.

Supplementary Table e-2. Descriptive summary of neurodegenerative and vascular brain pathologies identified in postmortem examination of 1217 decedents.

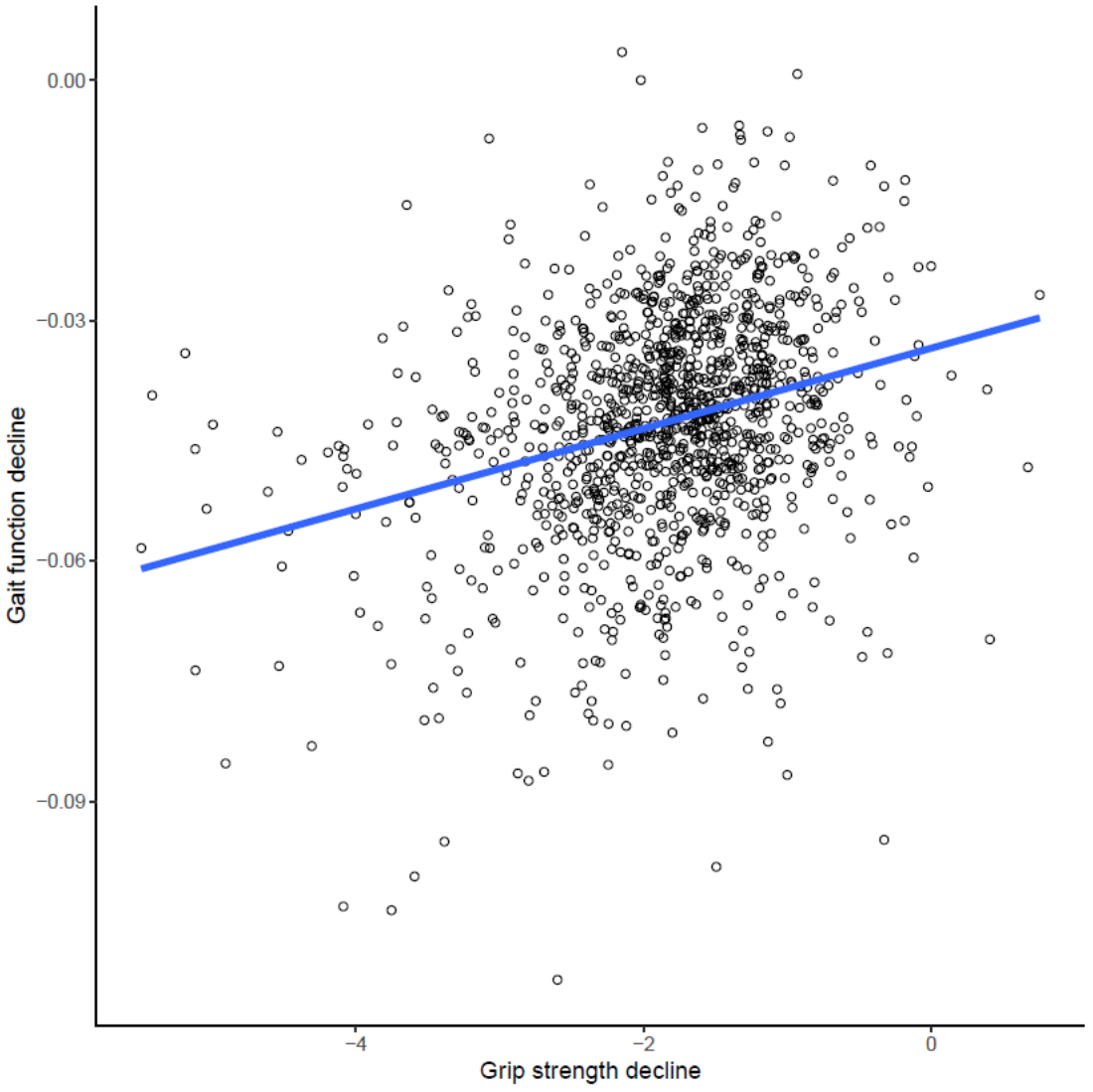
Postmortem pathologies	**N(%) or Mean (SD)**				
	No stroke (n=969)	**History of stroke (n=247)**	**No dementia (n=556)**	**Dementia (n=661)**	**All (n=1217)**
Neurodegenerative					
Alzheimer's disease, n (%)	637 (66)	162 (66)	341 (52)	458 (82)	799 (66)
Amyloid, mean (SD)	1.6 (1.1)	1.6 (1.1)	1.3 (1.1)	1.9 (1.1)	1.6 (1.1)
Tangles, mean (SD)	1.7 (1.4)	1.5 (1.1)	1.1 (0.9)	2.3 (1.5)	1.7 (1.3)
TDP-43 in the hippocampus or neocortex, n (%)	333 (34)	71 (29)	144 (22)	260 (47)	404 (33)
Hippocampal sclerosis, n (%)	104 (11)	17 (7)	25 (4)	96 (17)	121 (10)
Lewy bodies (present in one or more sites), n (%)	263 (27)	65 (26)	124 (19)	204 (37)	328 (27)
Moderate to severe nigral neuronal loss, n (%)	119 (12)	27 (11)	49 (7)	97 (17)	146 (12)
Cerebrovascular					
Macroinfarcts (1 or more), n (%)	298 (31)	144 (58)	204 (31)	238 (43)	442 (36)
Microinfarcts (1 or more), n (%)	277 (29)	96 (39)	181 (27)	192 (35)	373 (31)
Moderate to severe atherosclerosis, n (%)	287 (30)	105 (43)	177 (27)	215 (39)	392 (32)
Moderate to severe arteriolosclerosis, n (%)	288 (30)	88 (36)	167 (25)	210 (38)	377 (31)
Moderate to severe cerebral amyloid angiopathy, n (%)	354 (37)	93 (38)	197 (30)	250 (45)	447 (37)
Number of pathologies	3.1 (1.8)	3.5 (1.7)	2.4 (1.5)	4.0 (1.6)	3.1 (1.8)

Supplementary Table e-3. Linear mixed effects models examining grip strength and gait function in the years prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.268 (0.488), <0.001	0.571 (0.011), <0.001
Age at death	-0.732 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.482 (0.883), <0.001	-0.096 (0.020), <0.001
Education	0.034 (0.114), 0.766	-0.007 (0.003), 0.007
Time	-1.845 (0.054), <0.001	-0.043 (0.001), <0.001
Age at death×Time	0.019 (0.007), 0.008	-0.000 (0.000), 0.840
Sex×Time	1.008 (0.097), <0.001	0.000 (0.002), 0.997
Education×Time	0.007 (0.012), 0.560	-0.001 (0.000), 0.040

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Figure e-3. Correlation of estimated person-specific decline rates of grip strength and gait function adjusted for demographics.



Scatterplot showing the relationship of the annual rates of grip strength decline (X axis) and gait function decline (Y axis) with a corresponding regression line. The person-specific annual rates of grip strength and gait function decline are estimated from 2 separate linear mixed effects models with grip strength and gait function as the outcomes and age at death, sex, education, time (the rate of change of either grip strength or gait function), and the interaction of the demographics with time as the model's terms.

Supplementary Table e-4. Association of the *ε4* allele of *apolipoprotein E* (*ApoE)* with the longitudinal changes of grip strength and gait function.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.759 (0.545), <0.001	0.578 (0.013), <0.001
Age at death	-0.744 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.433 (0.886), <0.001	-0.097 (0.021), <0.001
Education	0.052 (0.115), 0.649	-0.007 (0.003), 0.015
Time	-1.738 (0.060), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.017 (0.007), 0.019	-0.000 (0.000), 0.781
Sex×Time	1.040 (0.096), <0.001	0.000 (0.002), 0.979
Education×Time	0.012 (0.012), 0.328	-0.001 (0.000), 0.047
ApoE ε4	-1.543 (0.936), 0.099	-0.026 (0.022), 0.237
ApoE ε4 ×Time	-0.343 (0.100), <0.001	-0.001 (0.002), 0.676

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-5. Association of vascular risk factors with the longitudinal changes of grip strength and gait function.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.026 (0.698), <0.001	0.570 (0.011), <0.001
Age at death	-0.729 (0.065), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.455 (0.892), <0.001	-0.097 (0.021), <0.001
Education	0.040 (0.116), 0.727	-0.007 (0.003), 0.010
Time	-1.871 (0.076), <0.001	-0.043 (0.002), <0.001
Age at death×Time	0.020 (0.007), 0.008	-0.000 (0.000), 0.903
Sex×Time	1.007 (0.098), <0.001	0.000 (0.002), 0.954
Education×Time	0.007 (0.012), 0.554	-0.001 (0.000), 0.050
Number of vascular risk factors	0.236 (0.486), 0.625	0.001 (0.011), 0.934
Number of vascular risk factors ×Time	0.026 (0.052), 0.619	0.001 (0.001), 0.477

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-6. Association of history of stroke with the longitudinal changes of grip strength and gait function.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.452 (0.533), <0.001	0.597 (0.012), <0.001
Age at death	-0.730 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.442 (0.885), <0.001	-0.091 (0.020), <0.001
Education	0.031 (0.114), 0.783	-0.007 (0.003), 0.007
Time	-1.864 (0.059), <0.001	-0.041 (0.001), <0.001
Age at death×Time	0.019 (0.007), 0.009	-0.000 (0.000), 0.871
Sex×Time	1.007 (0.097), <0.001	0.000 (0.002), 0.868
Education×Time	0.007 (0.012), 0.561	-0.001 (0.000), 0.030
History of stroke	-0.853 (0.996), 0.392	-0.123 (0.023), <0.001
History of stroke ×Time	0.094 (0.109), 0.387	-0.007 (0.002), 0.003

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-7. Association of presence of dementia with the longitudinal changes of grip strength and gait function.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	28.906 (0.582), <0.001	0.651 (0.014), <0.001
Age at death	-0.576 (0.061), <0.001	-0.011 (0.002), <0.001
Sex (women vs. men)	-19.010 (0.825), <0.001	-0.089 (0.020), <0.001
Education	0.075 (0.106), 0.481	-0.006 (0.003), 0.021
Time	-1.411 (0.066), <0.001	-0.037 (0.001), <0.001
Age at death×Time	0.034 (0.007), 0.008	0.000 (0.000), 0.251
Sex×Time	1.078 (0.093), <0.001	0.001 (0.002), 0.783
Education×Time	0.012 (0.012), 0.302	-0.000 (0.000), 0.084
Dementia	-9.759 (0.767), <0.001	-0.179 (0.019), <0.001
Dementia ×Time	-0.901 (0.084), <0.001	-0.012 (0.002), <0.001

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-8. Association of postmortem amyloid-β level with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	26.838 (0.764), <0.001	0.588 (0.018), <0.001
Age at death	-0.702 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.150 (0.879), <0.001	-0.094 (0.020), <0.001
Education	0.010 (0.113), 0.928	-0.007 (0.003), 0.009
Time	-1.545 (0.085), <0.001	-0.041 (0.002), <0.001
Age at death×Time	0.023 (0.007), 0.002	-0.000 (0.000), 0.952
Sex×Time	1.048 (0.097), <0.001	0.000 (0.002), 0.914
Education×Time	0.005 (0.012), 0.687	-0.001 (0.000), 0.034
Amyloid	-1.541 (0.356), <0.001	-0.10 (0.008), 0.219
Amyloid×Time	-0.176 (0.039), <0.001	-0.001 (0.001), 0.140

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2). Level of amyloid-β was square root transformed.

Supplementary Table e-9. Association of postmortem tau tangles level with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	**Model2-Gait function**
Intercept	27.556 (0.728), <0.001	0.606 (0.017), <0.001
Age at death	-0.689 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-18.743 (0.877), <0.001	-0.089 (0.021), <0.001
Education	0.011 (0.112), 0.923	-0.007 (0.003), 0.008
Time	-1.494 (0.080), <0.001	-0.039 (0.002), <0.001
Age at death×Time	0.024 (0.007), 0.001	0.000 (0.000), 0.878
Sex×Time	1.092 (0.096), <0.001	-0.001 (0.002), 0.700
Education×Time	0.005 (0.012), 0.680	-0.001 (0.000), 0.031
Tangles	-1.849 (0.308), <0.001	-0.021 (0.007), 0.005
Tangles×Time	-0.195 (0.033), <0.001	-0.002 (0.001), 0.003

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2). Level of tau tangles was square root transformed.

Supplementary Table e-10. Association of postmortem TDP-43 stages with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	25.554 (0.567), <0.001	0.577 (0.013), <0.001
Age at death	-0.670 (0.065), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.322 (0.876), <0.001	-0.095 (0.020), <0.001
Education	0.028 (0.113), 0.807	-0.007 (0.003), 0.011
Time	-1.706 (0.063), <0.001	-0.041 (0.001), <0.001
Age at death×Time	0.026 (0.007), <0.001	0.000 (0.000), 0.851
Sex×Time	1.027 (0.097), <0.001	0.000 (0.002), 0.918
Education×Time	0.007 (0.012), 0.562	-0.001 (0.000), 0.043
TDP-43	-3.776 (0.868), <0.001	-0.018 (0.021), 0.369
TDP-43×Time	-0.402 (0.093), <0.001	-0.004 (0.002), 0.065

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-11. Association of postmortem hippocampal sclerosis with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.818 (0.503), <0.001	0.572 (0.012), <0.001
Age at death	-0.710 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.379 (0.877), <0.001	-0.096 (0.020), <0.001
Education	0.031 (0.113), 0.786	-0.007 (0.003), 0.011
Time	-1.789 (0.056), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.021 (0.007), 0.004	-0.000 (0.000), 0.880
Sex×Time	1.023 (0.097), <0.001	0.000 (0.002), 0.969
Education×Time	0.007 (0.012), 0.591	-0.001 (0.000), 0.041
Hippocampal sclerosis	-5.317 (1.346), <0.001	-0.018 (0.033), 577
Hippocampal sclerosis×Time	-0.504 (0.138), <0.001	-0.003 (0.003), 0.405

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-12. Association of postmortem presence of Lewy bodies with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	**Model2-Gait function**
Intercept	25.282 (0.535), <0.001	0.585 (0.013), <0.001
Age at death	-0.731 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.654 (0.877), <0.001	-0.099 (0.020), <0.001
Education	0.039 (0.113), 0.731	-0.007 (0.003), 0.012
Time	-1.743 (0.059), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.019 (0.007), 0.008	-0.000 (0.000), 0.872
Sex×Time	0.996 (0.097), <0.001	-0.000 (0.002), 0.925
Education×Time	0.008 (0.012), 0.498	-0.001 (0.000), 0.047
Lewy bodies	-3.961 (0.897), <0.001	-0.057 (0.021), 0.007
Lewy bodies×Time	-0.387 (0.097), <0.001	-0.005 (0.002), 0.019

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-13. Association of postmortem moderate to severe nigral neuronal loss with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.721 (0.502), <0.001	0.583 (0.012), <0.001
Age at death	-0.736 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.682 (0.881), <0.001	-0.101 (0.020), <0.001
Education	0.049 (0.113), 0.667	-0.006 (0.003), 0.017
Time	-1.784 (0.056), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.018 (0.007), 0.012	-0.000 (0.000), 0.734
Sex×Time	0.987 (0.097), <0.001	-0.000 (0.002), 0.850
Education×Time	0.009 (0.012), 0.444	-0.000 (0.000), 0.062
Nigral neuronal loss	-4.263 (1.229), <0.001	-0.114 (0.029), <0.001
Nigral neuronal loss×Time	-0.539 (0.131), <0.001	-0.010 (0.003), <0.001

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-14. Association of postmortem presence of macroinfarcts with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.931 (0.570), <0.001	0.620 (0.013), <0.001
Age at death	-0.712 (0.065), <0.001	-0.013 (0.002), <0.001
Sex (women vs. men)	-19.563 (0.882), <0.001	-0.102 (0.020), <0.001
Education	0.015 (0.114), 0.896	-0.008 (0.003), 0.002
Time	-1.782 (0.062), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.022 (0.007), 0.004	0.000 (0.000), 0.635
Sex×Time	0.999 (0.097), <0.001	-0.000 (0.002), 0.821
Education×Time	0.005 (0.012), 0.661	-0.001 (0.000), 0.016
Macroinfarcts	-1.884 (0.842), 0.025	-0.142 (0.019), <0.001
Macroinfarcts×Time	-0.183 (0.092), 0.046	-0.010 (0.002), <0.001

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-15. Association of postmortem presence of microinfarcts with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.693 (0.553), <0.001	0.594 (0.013), <0.001
Age at death	-0.721 (0.064), <0.001	-0.013 (0.002), <0.001
Sex (women vs. men)	-19.540 (0.884), <0.001	-0.100 (0.020), <0.001
Education	0.018 (0.114), 0.871	-0.008 (0.003), 0.004
Time	-1.820 (0.061), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.020 (0.007), 0.007	-0.000 (0.000), 0.989
Sex×Time	1.004 (0.098), <0.001	-0.000 (0.002), 0.940
Education×Time	0.006 (0.012), 0.616	-0.001 (0.000), 0.029
Microinfarcts	-1.422 (0.875), 0.104	-0.080 (0.020), <0.001
Microinfarcts×Time	-0.078 (0.093), 0.402	-0.004 (0.002), 0.047

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-16. Association of postmortem moderate to severe atherosclerosis with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.261 (0.560), <0.001	0.596 (0.013), <0.001
Age at death	-0.732 (0.064), <0.001	-0.013 (0.002), <0.001
Sex (women vs. men)	-19.475 (0.884), <0.001	-0.096 (0.020), <0.001
Education	0.035 (0.114), 0.761	-0.007 (0.003), 0.009
Time	-1.818 (0.060), <0.001	-0.040 (0.001), <0.001
Age at death×Time	0.020 (0.007), 0.006	0.000 (0.000), 0.865
Sex×Time	1.009 (0.097), <0.001	-0.000 (0.002), 0.979
Education×Time	0.007 (0.012), 0.541	-0.001 (0.000), 0.042
Atherosclerosis	-0.021 (0.863), 0.981	-0.079 (0.020), <0.001
Atherosclerosis×Time	-0.100 (0.097), 0.304	-0.008 (0.002), <0.001

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-17. Association of postmortem moderate to severe arteriolosclerosis with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.628 (0.565), <0.001	0.585 (0.013), <0.001
Age at death	-0.723 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.412 (0.885), <0.001	-0.099 (0.020), <0.001
Education	0.032 (0.114), 0.776	-0.007 (0.003), 0.010
Time	-1.774 (0.061), <0.001	-0.041 (0.001), <0.001
Age at death×Time	0.021 (0.007), 0.004	0.000 (0.000), 0.871
Sex×Time	1.025 (0.097), <0.001	0.000 (0.002), 0.811
Education×Time	0.007 (0.012), 0.546	-0.001 (0.000), 0.040
Arteriolosclerosis	-1.149 (0.874), 0.189	-0.057 (0.020), 0.005
Atrteriolosclerosis×Time	-0.237 (0.097), 0.014	-0.006 (0.002), 0.001

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-18. Association of postmortem moderate to severe cerebral amyloid angiopathy with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	24.379 (0.581), <0.001	0.531 (0.013), <0.001
Age at death	-0.730 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-19.450 (0.884), <0.001	-0.095 (0.020), <0.001
Education	0.037 (0.114), 0.745	-0.007 (0.003), 0.011
Time	-1.753 (0.064), <0.001	-0.042 (0.001), <0.001
Age at death×Time	0.021 (0.007), 0.004	-0.000 (0.000), 0.928
Sex×Time	1.022 (0.097), <0.001	0.000 (0.002), 0.943
Education×Time	0.008 (0.012), 0.495	-0.001 (0.000), 0.042
Cerebral amyloid angiopathy	-0.272 (0.835), 0.745	-0.029 (0.019), 0.135
Cerebral amyloid angiopathy×Time	-0.237 (0.090), 0.009	-0.003 (0.002), 0.107

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-19. Association of postmortem neurodegenerative brain pathologies with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	29.349 (0.835), <0.001	0.617 (0.020), <0.001
Age at death	-0.648 (0.064), <0.001	-0.014 (0.002), <0.001
Sex (women vs. men)	-18.920 (0.868), <0.001	-0.095 (0.021), <0.001
Education	0.016 (0.111), 0.887	-0.007 (0.003), 0.013
Time	-1.276 (0.094), <0.001	-0.038 (0.002), <0.001
Age at death×Time	0.028 (0.007), <0.001	0.000 (0.000), 0.830
Sex×Time	1.082 (0.095), <0.001	0.000 (0.002), 0.841
Education×Time	0.006 (0.012), 0.586	-0.000 (0.000), 0.053
Amyloid	-0.596 (0.394), 0.131	0.002 (0.009), 0.798
Amyloid×Time	-0.082 (0.043), 0.057	000 (0.001), 0.939
Tangles	-1.279 (0.353), <0.001	-0.020 (0.009), 0.017
Tangles×Time	-0.132 (0.038), <0.001	-0.002 (0.001), 0.018
TDP-43	-1.976 (0.922), 0.032	-0.010 (0.022), 0.964
TDP-43×Time	-0.229 (0.099), 0.020	-0.002 (0.002), 0.339
Hippocampal Sclerosis	-3.096 (1.403), 0.028	-0.001 (0.034), 0.986
Hippocampal sclerosis×Time	-0.245 (0.146), 0.093	0.000 (0.003), 0.931
Lewy bodies	-2.080 (0.983), 0.035	-0.018 (0.023), 0.450
Lewy bodies×Time	-0.153 (0.105), 0.144	-0.001 (0.002), 0.649
Nigral neuronal loss	-2.709 (1.324), 0.041	-0.103 (0.032), 0.001
Nigral neuronal loss×Time	-0.402 (0.140), 0.004	-0.009 (0.003), 0.002

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-20. Association of postmortem cerebrovascular disease pathologies with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	**Estimate (SE), p-value**	
	Model1-Grip strength	**Model2-Gait function**
Intercept	25.395 (0.745), <0.001	0.661 (0.017), <0.001
Age at death	-0.700 (0.065), <0.001	-0.012 (0.002), <0.001
Sex (women vs. men)	-19.492 (0.886), <0.001	-0.101 (0.020), <0.001
Education	0.009 (0.114), 0.937	-0.008 (0.003), 0.001
Time	-1.622 (0.081), <0.001	-0.036 (0.002), <0.001
Age at death×Time	0.025 (0.008), <0.001	0.000 (0.000), 0.298
Sex×Time	1.029 (0.098), <0.001	0.000 (0.002), 0.966
Education×Time	0.007 (0.012), 0.572	-0.001 (0.000), 0.019
Macroinfarcts	-1.667 (0.879), 0.058	-0.121 (0.020), <0.001
Macroinfarcts×Time	-0.145 (0.096), 0.129	-0.008 (0.002), <0.001
Microinfarcts	-1.063 (0.894), 0.235	-0.051 (0.020), 0.012
Microinfarcts×Time	-0.039 (0.096), 0.686	-0.002 (0.002), 0.410
Atherosclerosis	0.639 (0.909), 0.482	-0.047 (0.021), 0.023
Atherosclerosis×Time	-0.027 (0.101), -.793	-0.005 (0.002), 0.011
Arteriolosclerosis	-1.026 (0.911), 0.261	-0.023 (0.021), 0.277
Arteriolosclerosis×Time	-0.209 (0.100), 0.038	-0.004 (0.002), 0.059
Cerebral amyloid angiopathy	-0.280 (0.834), 0.737	-0.033 (0.019), 0.086
Cerebral amyloid angiopathy×Time	-0.240 (0.090), 0.008	-0.003 (0.002), 0.076

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-21. Association of postmortem neurodegenerative and cerebrovascular disease pathologies with the longitudinal changes of grip strength and gait function prior to death.

Models' terms	Estimate (SE), p-value	
	Model1-Grip strength	Model2-Gait function
Intercept	30.051 (0.951), <0.001	0.696 (0.022), <0.001
Age at death	-0.624 (0.065), <0.001	-0.012 (0.002), <0.001
Sex (women vs. men)	-18.982 (0.868), <0.001	-0.102 (0.020), <0.001
Education	0.021 (0.111), 0.850	-0.008 (0.003), 0.002
Time	-1.156 (0.106), <0.001	-0.032 (0.002), <0.001
Age at death×Time	0.032 (0.007), <0.001	0.000 (0.000), 0.193
Sex×Time	1.081 (0.096), <0.001	0.000 (0.002), 0.913
Education×Time	0.005 (0.012), 0.665	-0.001 (0.000), 0.026
Amyloid	-0.673 (0.398), 0.092	0.004 (0.009), 0.645
Amyloid×Time	-0.079 (0.043), 0.068	0.000 (0.001), 0.810
Tangles	-1.421 (0.362), <0.001	-0.019 (0.009), 0.026
Tangles×Time	-0.121 (0.039), 0.002	-0.002 (0.001), 0.043
TDP-43	-2.019 (0.921), 0.029	0.000 (0.022), 0.986
TDP-43×Time	-0.231 (0.099), 0.020	-0.002 (0.002), 0.343
Hippocampal Sclerosis	-2.952 (1.402), 0.036	0.003 (0.034), 0.925
Hippocampal sclerosis×Time	-0.222 (0.147), 0.130	0.001 (0.003), 0.864
Lewy bodies	-2.139 (0.982), 0.030	-0.022 (0.023), 0.336
Lewy bodies×Time	-0.166 (0.105), 0.113	-0.001 (0.002), 0.564
Nigral neuronal loss	-2.666 (1.324), 0.044	-0.099 (0.031), 0.001
Nigral neuronal loss×Time	-0.389 (0.140), 0.006	-0.009 (0.003), 0.003
Macroinfarcts	-1.683 (0.852), 0.048	-0.124 (0.020), <0.001
Macroinfarcts×Time	-0.153 (0.093), 0.101	-0.009 (0.002), <0.001
Microinfarcts	-1.269 (0.867), 0.144	-0.053 (0.020), 0.009
Microinfarcts×Time	-0.063 (0.093), 0.495	-0.002 (0.002), 0.379
Atherosclerosis	0.699 (0.882), 0.428	-0.043 (0.020), 0.034
Atherosclerosis×Time	-0.011 (0.099), 0.912	-0.005 (0.002), 0.019
Arteriolosclerosis	-0.466 (0.890), 0.600	-0.016 (0.021), 0.454
Arteriolosclerosis×Time	-0.140 (0.099), 0.156	-0.003 (0.002), 0.121
Cerebral amyloid angiopathy	1.528 (0.855), 0.074	-0.021 (0.020), 0.295
Cerebral amyloid angiopathy×Time	-0.075 (0.093), 0.419	-0.002 (0.002), 0.290

In 2 mixed effects models, we examined the levels and rates of changes in 2 motor variables: grip strength (model1) and gait function (model2).

Supplementary Table e-22: Neurodegenerative vs. cerebrovascular pathologies and declining grip strength and gait function controlling for history of stroke, dementia, and their interaction with time.

Group of pathologies	Neuropathology	Grip strength decline Estimates (SE), p-values			Gait function decline Estimates (SE), p-values		
		Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Neurodegenerative	Amyloid×Time	-0.067 (0.042), 0.112		-0.065 (0.043), 0.126	0.001 (0.001), 0.573		0.001 (0.001), 0.545
	Tangles×Time	-0.035 (0.039), 0.367		-0.028 (0.040), 0.486	-0.001 (0.001), 0.529		-0.001 (0.001), 0.582
	TDP-43×Time	-0.132 (0.097), 0.176		-0.137 (0.098), 0.160	-0.000 (0.002), 0.647		-0.001 (0.002), 0.605
	Hippocampal sclerosis×Time	-0.096 (0.144), 0.504		-0.078 (0.144), 0.588	0.002 (0.003), 0.460		0.002 (0.003), 0.453
	Lewy bodies×Time	-0.066 (0.103), 0.519		-0.080 (0.103), 0.436	0.000 (0.002), 0.890		-0.000 (0.002), 0.946
	Nigral neuronal loss×Time	**-0.289 (0.137), 0.035**		**-0.286 (0.138), 0.038**	**-0.008 (0.003), 0.008**		**-0.008 (0.003), 0.009**
Cerebrovascular Disease	Macroinfarcts×Time		-0.096 (0.093), 0.321	-0.107 (0.093), 0.252		**-0.007 (0.002), <0.001**	**-0.007 (0.002), <0.001**
	Microinfarcts×Time		-0.013 (0.091), 0.882	-0.030 (0.091), 0.739		-0.001 (0.002), 0.632	-0.001 (0.002), 0.597
	Atherosclerosis×Time		-0.019 (0.097), 0.848	0.022 (0.097), 0.819		**-0.004 (0.002), 0.047**	-0.004 (0.002), 0.062
	Arteriolosclerosis×Time		-0.109 (0.097), 0.261	-0.101 (0.097), 0.298		-0.003 (0.002), 0.161	-0.003 (0.002), 0.214
	Cerebral amyloid angiopathy×Time		-0.119 (0.087), 0.172	-0.069 (0.091), 0.449		-0.002 (0.002), 0.375	-0.002 (0.002), 0.363
Model derived variance component							
Variance in the person-specific motor function decline rate		**1.009**	**1.028**	**1.015**	**0.000384**	**0.000369**	**0.000367**

Each model shows a single mixed-effects model with the outcome of grip strength decline (Models 1-3) or gait function decline (Models 4-6). The terms for pathologies included in each model were different: either neurodegenerative (Model 1 or 4), cerebrovascular disease pathologies (Model 2 or 5), or both together (Model 3 or 6). Each model included a term for time (the rate of change of either grip strength or gait function) with cross-sectional terms for age, sex, education, history of stroke, dementia, and each of the pathologies listed in the left column as well as their interaction with time. Each cell in a column shows the Estimate, Standard

Error and p-Value for the interaction of the pathology with Time to show whether the pathology metric was associated with either grip strength or gait function decline. Bolded cells were significant. The last row indicates variance of the person specific grip strength (models 1-3) and gait function (models 4-6) decline rates derived from the corresponding models, which were used to determine the percentage of variance in a motor function decline rate explained by pathologies.

Supplementary Table e-23: Neurodegenerative vs. cerebrovascular pathologies and declining grip strength and gait function in participants without history of stroke.

Group of pathologies	Neuropathology	Grip strength decline Estimates (SE), p-values			Gait function decline Estimates (SE), p-values		
		Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Neurodegenerative	Amyloid×Time	**-0.117 (0.049), 0.018**		**-0.117 (0.050), 0.019**	0.000 (0.001), 0.869		0.000 (0.001), 0.732
	Tangles×Time	**-0.113 (0.043), 0.008**		**-0.010 (0.044), 0.024**	**-0.002 (0.001), 0.042**		-0.002 (0.001), 0.092
	TDP-43×Time	**-0.283 (0.113), 0.012**		**-0.287 (0.113), 0.011**	-0.004 (0.002), 0.059		-0.004 (0.002), 0.069
	Hippocampal sclerosis×Time	-0.297 (0.162), 0.066		-0.256 (0.163), 0.116	0.001 (0.003), 0.801		0.001 (0.003), 0.669
	Lewy bodies×Time	-0.219 (0.119), 0.065		**-0.240 (0.119), 0.044**	-0.003 (0.002), 0.280		-0.003 (0.002), 0.242
	Nigral neuronal loss×Time	**-0.391 (0.158), 0.014**		**-0.377 (0.159), 0.017**	**-0.009 (0.003), 0.008**		**-0.009 (0.003), 0.004**
Cerebrovascular Disease	Macroinfarcts×Time		-0.146 (0.114), 0.200	-0.128 (0.110), 0.246		**-0.007 (0.002), 0.003**	**-0.007 (0.002), 0.003**
	Microinfarcts×Time		-0.079 (0.111), 0.480	-0.101 (0.108), 0.350		-0.001 (0.002), 0.654	-0.001 (0.002), 0.605
	Atherosclerosis×Time		0.037 (0.119), 0.754	0.047 (0.115), 0.686		**-0.005 (0.002), 0.026**	**-0.005 (0.002), 0.043**
	Arteriolosclerosis×Time		**-0.255 (0.116), 0.028**	-0.190 (0.114), 0.096		-0.002 (0.002), 0.359	-0.002 (0.002), 0.468
	Cerebral amyloid angiopathy×Time		**-0.251 (0.104), 0.016**	-0.049 (0.107), 0.645		-0.004 (0.002), 0.063	-0.002 (0.002), 0.271
Model derived variance component							
Variance in the person-specific motor function decline rate		**1.183**	**1.318**	**1.188**	**0.000375**	**0.000363**	**0.000355**

Each model shows a single mixed-effects model with the outcome of grip strength decline (Models 1-3) or gait function decline (Models 4-6). The terms for pathologies included in each model were different: either neurodegenerative (Model 1 or 4), cerebrovascular disease pathologies (Model 2 or 5), or both together (Model 3 or 6). Each model included a term for time (the rate of change of either grip strength or gait function) with cross-sectional terms for age, sex, education, and each of the pathologies listed in the left column as well as their interaction with time. Each cell in a column shows the Estimate, Standard Error and p-Value for the

interaction of the pathology with Time to show whether the pathology metric was associated with either grip strength or gait function decline. Bolded cells were significant. The last row indicates variance of the person specific grip strength (models 1-3) and gait function (models 4-6) decline rates derived from the corresponding models, which were used to determine the percentage of variance in a motor function decline rate explained by pathologies.

Supplementary Table e-24: Neurodegenerative vs. cerebrovascular pathologies and declining grip strength and gait function in participants without dementia.

Group of pathologies	Neuropathology	Grip strength decline Estimates (SE), p-values			Gait function decline Estimates (SE), p-values		
		Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Neurodegenerative	Amyloid×Time	-0.060 (0.052), 0.245		-0.059 (0.052), 0.258	-0.000 (0.001), 0.986		0.000 (0.001), 0.980
	Tangles×Time	0.023 (0.067), 0.733		0.026 (0.068), 0.702	-0.001 (0.001), 0.308		-0.001 (0.001), 0.430
	TDP-43×Time	**-0.273 (0.130), 0.035**		**-0.280 (0.131), 0.033**	0.001 (0.003), 0.794		0.001 (0.003), 0.609
	Hippocampal sclerosis×Time	0.270 (0.273), 0.321		0.279 (0.276), 0.313	0.007 (0.005), 0.175		0.007 (0.005), 0.203
	Lewy bodies×Time	-0.177 (0.143), 0.216		-0.194 (0.144), 0.178	-0.000 (0.003), 0.980		-0.000 (0.003), 0.945
	Nigral neuronal loss×Time	0.088 (0.205), 0.667		0.076 (0.207), 0.712	**-0.010 (0.004), 0.011**		**-0.010 (0.004), 0.012**
Cerebrovascular Disease	Macroinfarcts×Time		0.075 (0.119), 0.526	0.081 (0.119), 0.498		**-0.005 (0.002), 0.054**	**-0.005 (0.002), 0.037**
	Microinfarcts×Time		**-0.229 (0.115), 0.046**	**-0.250 (0.116), 0.031**		-0.003 (0.002), 0.172	-0.003 (0.002), 0.142
	Atherosclerosis×Time		0.003 (0.126), 0.981	0.034 (0.128), 0.790		**-0.006 (0.003), 0.022**	**-0.005 (0.003), 0.044**
	Arteriolosclerosis×Time		-0.077 (0.129), 0.550	-0.084 (0.130), 0.518		-0.001 (0.003), 0.592	-0.001 (0.003), 0.665
	Cerebral amyloid angiopathy×Time		-0.119 (0.111), 0.284	-0.087 (0.115), 0.446		-0.003 (0.002), 0.153	-0.003 (0.002), 0.176
Model derived variance component							
Variance in the person-specific motor function decline rate		**0.738**	**0.746**	**0.749**	**0.000246**	**0.000239**	**0.000231**

Each model shows a single mixed-effects model with the outcome of grip strength decline (Models 1-3) or gait function decline (Models 4-6). The terms for pathologies included in each model were different: either neurodegenerative (Model 1 or 4), cerebrovascular disease pathologies (Model 2 or 5), or both together (Model 3 or 6). Each model included a term for time (the rate of change of either grip strength or gait function) with cross-sectional terms for age, sex, education, and each of the pathologies listed in the left column as well as their interaction with time. Each cell in a column shows the Estimate, Standard Error and p-Value for the

interaction of the pathology with Time to show whether the pathology metric was associated with either grip strength or gait function decline. Bolded cells were significant. The last row indicates variance of the person specific grip strength (models 1-3) and gait function (models 4-6) decline rates derived from the corresponding models, which were used to determine the percentage of variance in a motor function decline rate explained by pathologies.

Supplementary Table e-25: Neurodegenerative vs. cerebrovascular pathologies and declining grip strength and gait function controlling for parental cohort (MAP vs. ROS) and its interaction with time.

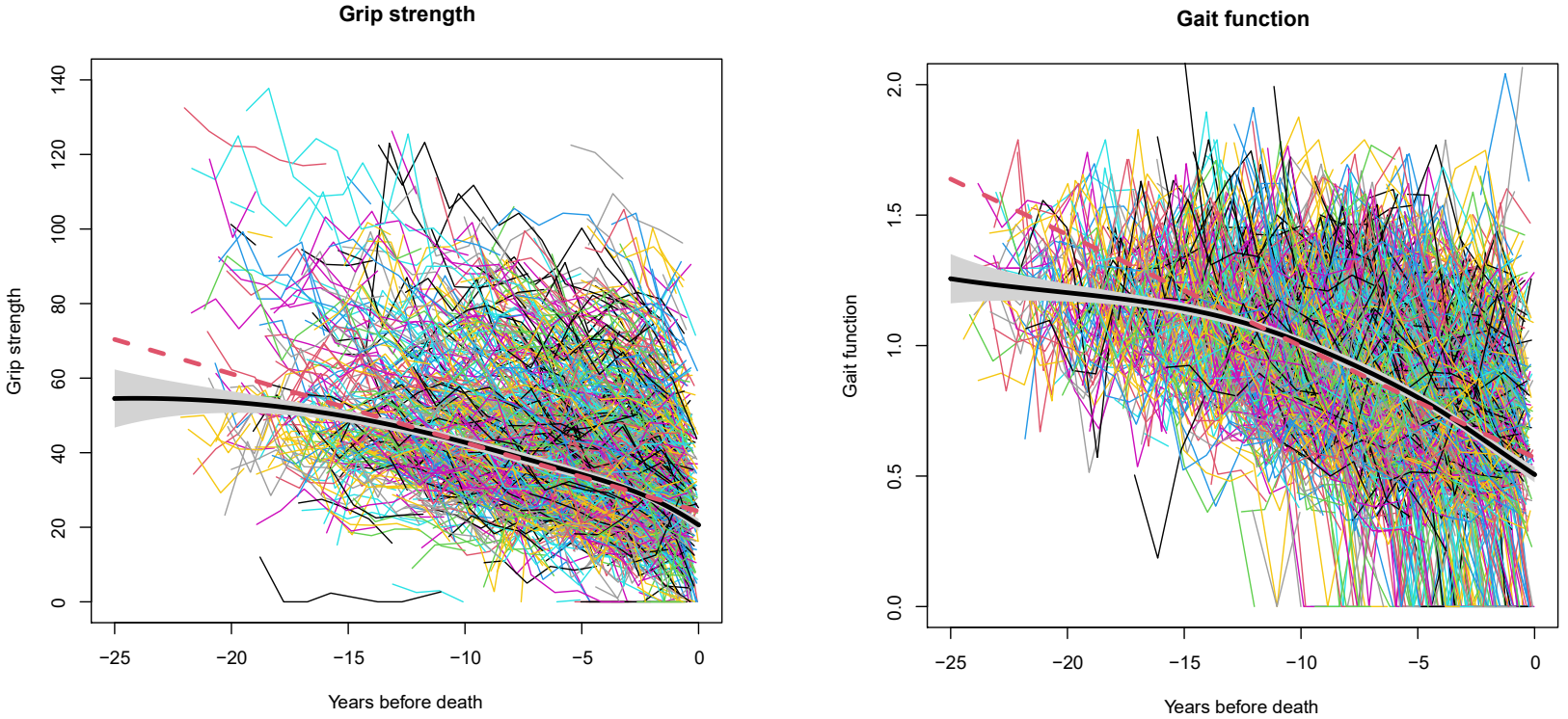
Group of pathologies	Neuropathology	Grip strength decline Estimates (SE), p-values			Gait function decline Estimates (SE), p-values		
		Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Neurodegenerative	Amyloid×Time	-0.077 (0.043), 0.072		-0.074 (0.044), 0.091	-0.000 (0.001), 0.839		0.000 (0.001), 0.986
	Tangles×Time	**-0.132 (0.038), <0.001**		**-0.121 (0.039), 0.002**	**-0.002 (0.001), 0.042**		-0.001 (0.001), 0.089
	TDP-43×Time	**-0.227 (0.099), 0.022**		**-0.228 (0.099), 0.021**	-0.002 (0.002), 0.309		-0.002 (0.002), 0.314
	Hippocampal sclerosis×Time	-0.240 (0.146), 0.100		-0.217 (0.147), 0.138	0.000 (0.003), 0.882		0.001 (0.003), 0.811
	Lewy bodies×Time	-0.152 (0.105), 0.146		-0.165 (0.105), 0.115	-0.001 (0.002), 0.630		-0.001 (0.002), 0.549
	Nigral neuronal loss×Time	**-0.411 (0.140), 0.003**		**-0.398 (0.140), 0.005**	**-0.009 (0.003), 0.003**		**-0.008 (0.003), 0.004**
Cerebrovascular Disease	Macroinfarcts×Time		-0.144 (0.095), 0.132	-0.152 (0.093), 0.103		**-0.008 (0.002), <0.001**	**-0.009 (0.002), <0.001**
	Microinfarcts×Time		-0.040 (0.095), 0.677	-0.064 (0.093), 0.491		-0.001 (0.002), 0.526	-0.001 (0.002), 0.497
	Atherosclerosis×Time		-0.045 (0.102), 0.657	-0.028 (0.099), 0.781		**-0.005 (0.002), 0.011**	**-0.005 (0.002), 0.018**
	Arteriolosclerosis×Time		**-0.201 (0.100), 0.045**	-0.134 (0.099), 0.176		-0.004 (0.002), 0.068	-0.003 (0.002), 0.124
	Cerebral amyloid angiopathy×Time		**-0.245 (0.090), 0.007**	-0.083 (0.093), 0.371		-0.003 (0.002), 0.067	-0.002 (0.002), 0.251
Model derived variance component							
Variance in the person-specific motor function decline rate		**1.095**	**1.195**	**1.095**	**0.000395**	**0.000373**	**0.000367**

Each model shows a single mixed-effects model with the outcome of grip strength decline (Models 1-3) or gait function decline (Models 4-6). The terms for pathologies included in each model were different: either neurodegenerative (Model 1 or 4), cerebrovascular disease pathologies (Model 2 or 5), or both together (Model 3 or 6). Each model included a term for time (the rate of change of either grip strength or gait function) with cross-sectional terms for age, sex, education, history of stroke, dementia, and each

of the pathologies listed in the left column as well as their interaction with time. Each cell in a column shows the Estimate, Standard Error and p-Value for the interaction of the pathology with Time to show whether the pathology metric was associated with either grip strength or gait function decline. Bolded cells were significant. The last row indicates variance of the person specific grip strength (models 1-3) and gait function (models 4-6) decline rates derived from the corresponding models, which were used to determine the percentage of variance in a motor function decline rate explained by pathologies.

Supplementary Figure e-4. Using functional mixed effects (FME) models to examine non-linear trajectories of grip strength and gait function changes over time.

Solid black line is the nonlinear trajectory of motor function decline estimated by a FME model (with shaded gray area indicating its 95% pointwise confidence interval), and red dashed line is the trajectory of the motor function decline estimated by a linear mixed effects model; both models were controlled for age at death, sex, education.



Supplementary Table e-26. Variance of grip strength decline rate explained by brain pathologies associated with it.

Neuropathology	**Variance component of the decline rate in a model including the pathology of interest alone**	**Variance component of the decline rate in a model including all pathologies except the pathology of interest**	**Variance component of the decline rate in a model including All pathologies**	**Variance explained in the grip strength decline rate by the pathology of interest**
Tangles	1.142	1.119	1.095	22% - 61%
TDP-43	1.186	1.101	1.095	6% - 24%
Nigral neuronal loss	1.193	1.103	1.095	7% - 18%

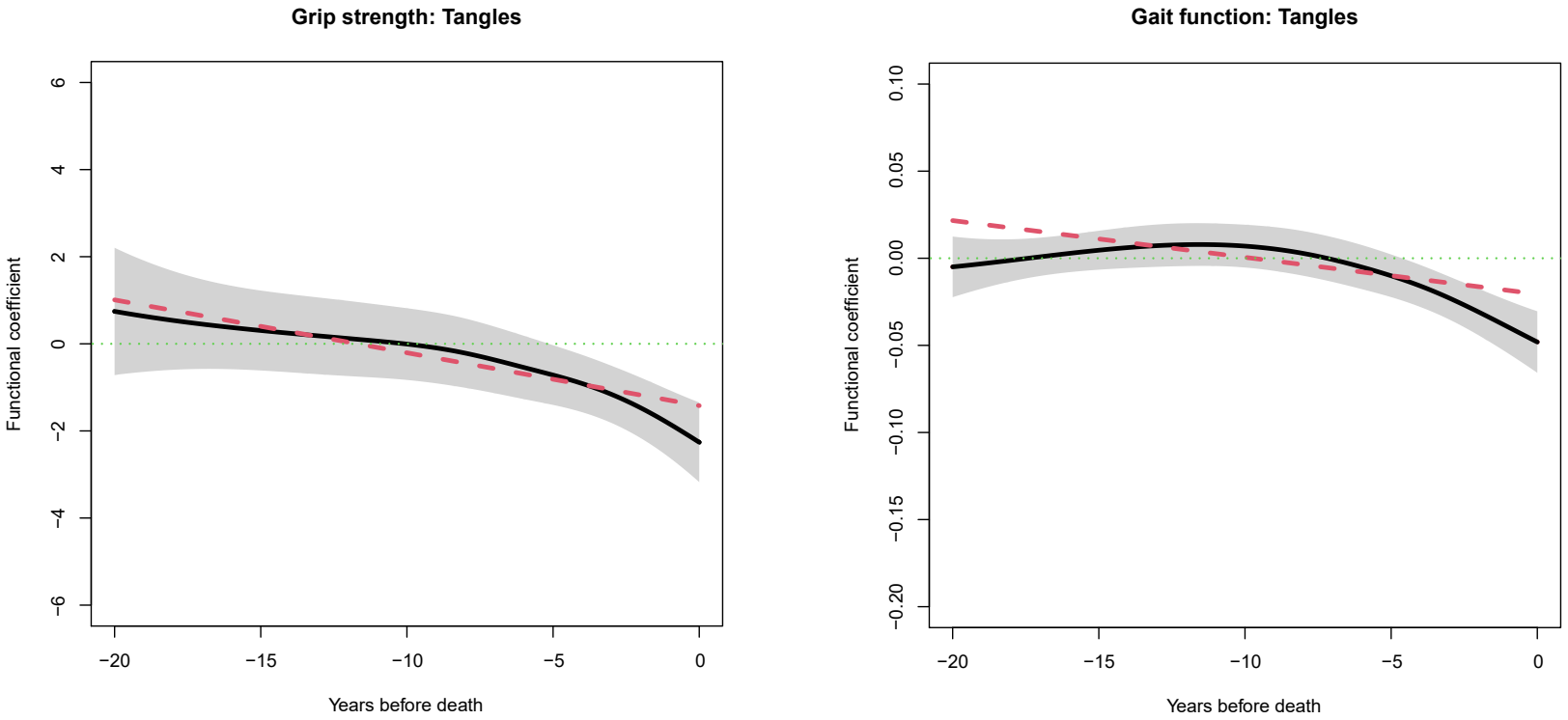
All the models were controlled for age at death, sex, education, and their interaction with time. The range of explained variance in the last column is due to the order at which the pathology of interest or the other pathologies were included in the models. Higher percentages result from when the pathology of interest is included first.

Supplementary Table e-27. Variance of gait function decline rate explained by brain pathologies associated with it.

Neuropathology	**Variance component of the decline rate in a model including the pathology of interest alone**	**Variance component of the decline rate in a model including all pathologies except the pathology of interest**	**Variance component of the decline rate in a model including All pathologies**	**Variance explained in the grip strength decline rate by the pathology of interest**
Macroinfarcts	0.000397	0.000399	0.000381	49% - 59%
Atherosclerosis	0.000405	0.000388	0.000381	19% - 38%
Nigral neuronal loss	0.000408	0.000390	0.000381	25% - 31%
Tangles	0.000417	0.000382	0.000381	3% - 8%

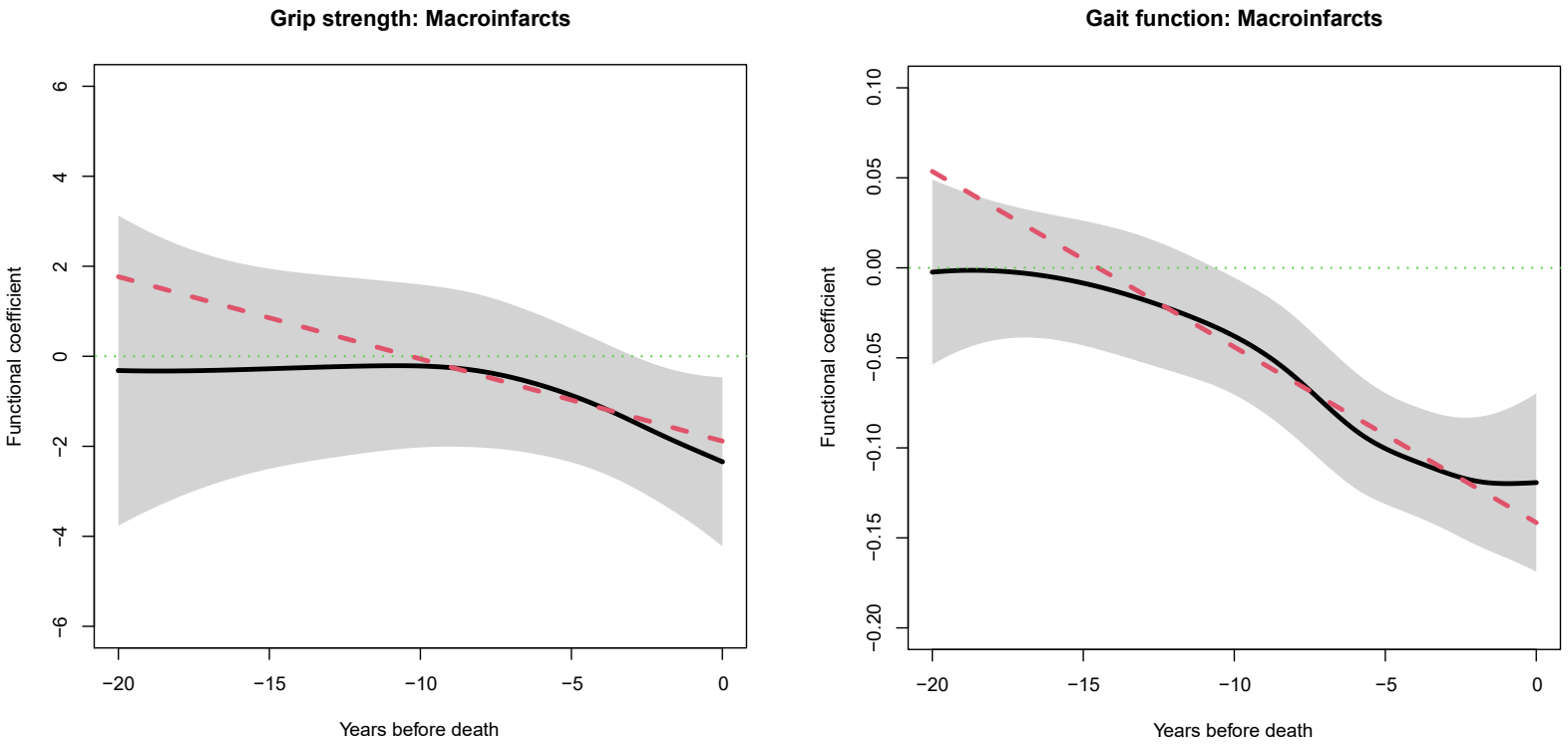
All the models were controlled for age at death, sex, education, and their interaction with time. The range of explained variance in the last column is due to the order at which the pathology of interest or the other pathologies were included in the models. Higher percentages result from when the pathology of interest is included first.

Supplementary Figure e-5. The association of tangles with change in grip strength and gait function assessments.



Solid black line is the nonlinear association of tangles with motor function decline estimated by a functional mixed effects model (with shaded gray area indicating its 95% pointwise confidence interval), and red dashed line is the linear association of tangles with motor function decline estimated by a linear mixed effects model; both models were controlled for age at death, sex, education. The dotted green line is the flat line of zero. If the dotted green line is not completely covered by the gray shaded area, the association between the pathology and the motor function decline is significantly non-zero. Similarly, if the dashed red line is not completely covered by the gray shaded area, the association of the pathology with the motor decline is significantly nonlinear.

Supplementary Figure e-6. The association of macroinfarcts with change in grip strength and gait function assessments.



Solid black line is the nonlinear association of macroinfarcts with motor function decline estimated by a functional mixed effects model (with shaded gray area indicating its 95% pointwise confidence interval), and red dashed line is the linear association of macroinfarcts with motor function decline estimated by a linear mixed effects model; both models were controlled for age at death, sex, education. The dotted green line is the flat line of zero. If the dotted green line is not completely covered by the gray shaded area, the association between the pathology and the motor function decline is significantly non-zero. Similarly, if the dashed red line is not completely covered by the gray shaded area, the association of the pathology with the motor decline is significantly nonlinear.