Supplementary

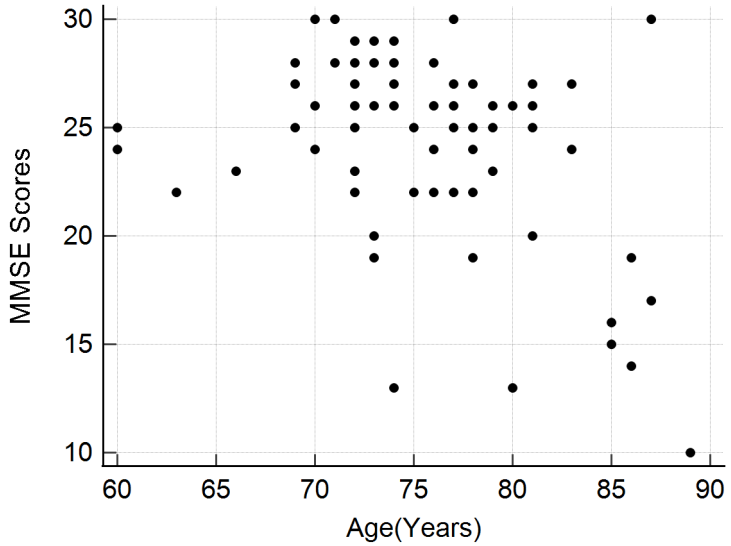

Figure S1 Scatter plot of MMSE versus age for the 77 participants.

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Table S1 Result of voxel-based multiple regression between Mini-Mental State Examination (MMSE) scores and conductivity indices

Group analysis	Cluster size	Cluster location	BA	Talairach coordinates	Z score
(–)HFC	11751	Lt Parietal Postcentral Gyrus		–55.95, –24.91, 21.69	4.86
		Lt Frontal Sub-Gyral		–28.95, 13.58, 21.29	4.28
		Lt Frontal Precentral Gyrus		–36.5, –6.64, 26.45	4.02
	27038	Rt Temporal Supramarginal Gyrus		50.37, –53.67, 23.47	4.79
		Rt Sub-lobar Insula	13	37.63, –5.4, 20.62	4.48
	971	Lt Middle Temporal Gyrus		–56.93, –60.98, 15.55	4.02
	1164	Lt Temporal Sub-Gyral		–31.87, –53.22, 12.21	3.64
		Lt Sub-lobar Lateral Ventricle		–19.83, –38.64, 16.5	2.74
	784	Lt Sub-lobar Extra-Nuclear		–34.36, –26.49, –1.52	3.38
		Lt Limbic Parahippocampal Gyrus		–36.07, –25.43, –12.26	3.18
	263	Left Brainstem Midbrain		–2.83, –11.48, –2.26	3.37
	227	Lt Inferior Frontal Gyrus		–33.03, 27.68, –17.08	3.07
	100	Lt Temporal Fusiform Gyrus	37	–38.98, –58.37, –11.82	3.06
(–)EC	140134	Rt Frontal Lobe Sub-Gyral		33.82, –6.16, 28.59	5.27
		Lt Frontal Lobe Sub-Gyral		–31.7, 18.34, 20.79	5.18
	743	Rt Occipital Lingual Gyrus		6.22, –90.72, –9.62	3.05
		Lt Occipital Lingual Gyrus	18	–6.72, –96.06, –12.14	2.67
(–)EC_WM	8525	Rt Frontal Lobe Sub-Gyral		33.82, –7.1, 28.5	4.68
		Rt Sub-lobar Extra-Nuclear		28.44, 7.95, 19.02	4.18
	10642	Lt Sub-lobar Insula		–40.17, –21.94, 19.54	4.63
		Lt Sub-lobar Extra-Nuclear		–37.41, –13.83, 23.05	4.37
		Lt Frontal Lobe Sub-Gyral		–37.22, 18.63, 18.02	4.28
	371	Lt Superior Temporal Gyrus		–30.99, 4.44, –39.07	3.81
	331	Rt Parahippocampal Gyrus	Amygdala	26.93, –6.02, –11.15	3.5
		Rt Temporal Lobe Sub-Gyral		38.01, –13.53, –11.68	3.32
	279	Lt Brainstem Pons		–3.44, –21.06, –29.31	3.34

Age was used as a covariate. A significance level of α=0.05 was applied with correction for multiple comparisons using the false-discovery rate (FDR) method and clusters with at least 100 contiguous voxels. BA, Brodmann area; Lt, left; Rt, right.

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Table S2 Result of voxel-based multiple regression between Mini-Mental State Examination (MMSE) scores and diffusion indices

Group analysis	Cluster size	Cluster location	BA	Talairach coordinates	Z score
(–)ED	18508	Rt Occipital Lingual Gyrus		20.98, –57.37, 4.6	5.36
		Rt Sub-lobar Insula		34.14, 17.18, 10.99	5.06
		Rt Temporal Hippocampus		31.46, –27.73, –10.43	5.14
	4250	Lt Occipital Lingual Gyrus		–22.51, –57.99, 2.91	5.79
		Lt Limbic Parahippocampal Gyrus	36	–28.7, –33.01, –11.95	5.10
	487	Rt Middle Frontal Gyrus		36.48, 3.02, 40.31	5.62
	967	Lt Middle Temporal Gyrus		–61.23, –32.02, –1.59	4.90
		Lt Superior Temporal Gyrus		–58.71, –42.16, 15.5	3.43
	654	Lt Inferior Frontal Gyrus		–41.65, 23.77, 4.02	4.84
	479	Rt Middle Frontal Gyrus		37.65, 29.48, 29.33	4.23
	128	Rt Parietal Supramarginal Gyrus		47.45, –52.84, 34.31	4.00
	119	Lt Superior Temporal Gyrus		–55.56, –5.62, –2.6	3.83
	193	Lt Middle Temporal Gyrus		–56.88, –63.34, 10.83	3.70
	115	Lt Inferior Temporal Gyrus		–44.76, –69.14, 2.38	3.67
	183	Lt Inferior Frontal Gyrus	47	–25.66, 28.31, –14.19	3.61
	124	Rt Medial Frontal Gyrus		6.7, 6.05, –18.46	3.30
(–)ED_EV	209218	Rt Sub-lobar Insula		31.35, 17.11, 11.83	5.47
		Rt Limbic Parahippocampal Gyrus		29.67, –22.72, –13.59	5.43
		Lt Occipital Lobe Lingual Gyrus		–20.66, –58, 2.94	5.40
(–)MD	145767	Lt Inferior Frontal Gyrus		–38.87, 26.55, 4.33	5.90
		Rt Frontal Lobe Sub-Gyral		32.24, 18.7, 14.7	5.57
		Rt Occipital Lingual Gyrus		20.07, –52.62, 4.14	5.26
	426	Lt Temporal Fusiform Gyrus	20	–49.7, –3.38, –25.71	4.02
	701	Lt Superior Temporal Gyrus	38	–21.71, 12.77, –38.12	2.66
(+)FA	598	Rt Middle Frontal Gyrus		34.51, 43.67, –9.92	4.88
	465	Lt Occipital Lobe Cuneus	18	–12.69, –98.15, 19.09	4.52
	3374	Lt Sub-lobar Extra-Nuclear		–13.83, 26.77, 1.17	4.28
		Lt Middle Frontal Gyrus	11	–24.7, 41.35, –12.94	4.19
		Lt Superior Frontal Gyrus	10	–25.72, 57.17, –1.55	4.10
		Rt Limbic Parahippocampal Gyrus		26.56, –47.15, 5.66	3.57
	1967	Rt Sub-lobar Extra-Nuclear		15.78, 26.62, 1.66	4.16
		Rt Frontal Lobe Sub-Gyral		32.14, 20.71, 23	3.90
	219	Lt Middle Occipital Gyrus		–53.13, –76.72, 3.32	4.16
	371	Lt Middle Occipital Gyrus		–28.24, –99.47, 4.29	4.09
		Lt Occipital Lingual Gyrus	18	–17.95, –99.67, –3.67	3.73
	198	Rt Parietal Postcentral Gyrus	3	55.73, –13.96, 49.84	3.78
	237	Lt Middle Frontal Gyrus		–42.5, 49.02, 5.5	3.69
	133	Lt Sub-lobar Corpus Callosum		–12.46, –37.08, 19.47	3.45
(–)RD	144652	Lt Inferior Frontal Gyrus		–38.87, 26.55, 4.33	5.78
		Rt Frontal Sub-Gyral		32.24, 18.7, 14.7	5.60
		Rt Limbic Parahippocampal Gyrus		21, –52.62, 4.15	5.34
	421	Lt Temporal Fusiform Gyrus	20	–49.7, –3.38, –25.71	4.01
	514	Lt Superior Temporal Gyrus	38	–21.71, 12.77, –38.12	2.60
(–)AxD	124572	Lt Inferior Frontal Gyrus		–39.79, 26.56, 4.32	6.01
		Rt Sub-lobar Insula	13	34.92, –4.86, 15.22	5.04
	411	Lt Temporal Fusiform Gyrus	20	–49.7, –3.38, –25.71	3.95
	890	Lt Inferior Parietal Lobule	40	–39.61, –52.07, 39.21	3.04
	148	Rt Occipital Lobe		3.51, –90.27, –14.12	2.72

Age was used as a covariate. A significance level of α=0.05 was applied with correction for multiple comparisons using the false-discovery rate (FDR) method and clusters with at least 100 contiguous voxels. BA, Brodmann area; Lt, left; Rt, right.

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Table S3 Result of multiple regression analysis between high-frequency conductivity (HFC) and diffusion indices and gray matter volume (GMV) brain tissue volume (BTV) index

HFC and ROI	Age (β/p)	MMSE (β/p)	Diffusion (β/p)	GMV BTV (β/p)	ANOVA (F/P)
Hippocampus	–0.0004/0.763	0.001/0.561	***AxD 245.1/<0.0001***	0.100/0.574	9.717/<0.0001
	–0.0003/0.823	0.001/0.509	***MD 266.0/<0.0001***	0.152/0.387	10.98/<0.0001
	–0.0002/0.855	0.001/0.489	***RD 274.4/<0.0001***	0.174/0.319	11.61/<0.0001
	–0.001/0.445	0.001/0.793	***ED EV 240.8/<0.0001***	0.114/0.527	9.802/<0.0001
Amygdala	0.002/0.544	–0.004/0.261	***AxD 433.1/0.002***	–0.152/0.441	5.708/0.001
	0.002/0.526	–0.004/0.225	***MD 463.7/0.004***	–0.169/0.397	5.299/0.001
	0.002/0.518	–0.004/0.200	***RD 458.0/0.007***	–0.187/0.349	4.945/0.001
	0.002/0.459	–0.004/0.218	ED EV 240.4/0.057	–0.225/0.281	3.818/0.007
Thalamus	0.001/0.664	0.003/0.308	AxD 218.5/0.047	–0.434/0.074	3.256/0.016
	0.001/0.688	0.003/0.304	MD 249.4/0.023	–0.383/0.117	3.623/0.010
	0.001/0.717	0.002/0.310	RD 259.1/0.017	–0.360/0.142	3.789/0.008
	–0.0002/0.889	0.002/0.346	ED EV 174.7/0.063	–0.456/0.059	3.109/0.020
Insula	–0.001/0.609	–0.001/0.687	***AxD 308.4/<0.0001***	–0.264/0.054	15.16/<0.0001
	–0.001/0.573	–0.001/0.566	***MD 318.5/<0.0001***	–0.291/0.037	13.64/<0.0001
	–0.001/0.565	–0.001/0.498	***RD 318.3/<0.0001***	–0.306/0.031	12.66/<0.0001
	0.0001/0.882	–0.0003/0.849	***ED EV 326.9/<0.0001***	–0.268/0.054	14.01/<0.0001
Corpus callosum	0.002/0.380	–0.001/0.670	AxD 127.4/0.081	–0.129/0.837	1.377/0.250
	0.002/0.346	–0.001/0.679	MD 106.7/0.094	–0.194/0.760	1.313/0.273
	0.002/0.336	–0.001/0.677	RD 95.25/0.106	–0.208/0.745	1.262/0.293
	0.002/0.299	–0.001/0.629	ED EV 52.49/0.241	–0.133/0.837	0.933/0.450

In this analysis, we used the model as HFC ≈ β1* age + β2* MMSE + β3* diffusion index + β4* gray matter volume (GMV) index + ε (error). For the diffusion indices, we used axial diffusivity (AxD or ADC), mean diffusivity (MD), radial diffusivity (RD), and extra-neurite diffusivity (ED) at extracellular volume (EV). For the BTV index, we used gray matter (GMV) volume. Therefore, the four tested models were ADC and GMV, MD and GMV, RD and GMV, and ED_EV and GMV for each ROI. For each ROI, $\alpha<0.05$ divided by 4 tested models (P=0.05/4=0.0125) was used to determine the significance level. Italic and bold characters in each column indicate a significant association between conductivity value and other indices.

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Table S4 Result of multiple regression analysis between extra-neurite conductivity (EC) and diffusion indices and gray matter volume (GMV) brain tissue volume (BTV) index

EC and ROI	Age (β/p)	MMSE (β/p)	Diffusion (β/p)	GMV BTV (β/p)	ANOVA (F/P)
Hippocampus	–0.001/0.752	0.002/0.300	***AxD 247.6/<0.0001***	–0.128/0.487	14.03/<0.0001
	–0.004/0.795	0.002/0.281	***MD 257.5/<0.0001***	–0.103/0.575	14.56/<0.0001
	–0.0003/0.817	0.002/0.275	***RD 260.5/<0.0001***	–0.095/0.605	14.77/<0.0001
	–0.001/0.447	0.001/0.479	***ED EV 232.1/0.0001***	–0.143/0.448	13.36/<0.0001
Amygdala	0.001/0.603	–0.002/0.417	AxD 212.2/0.059	–0.566/0.001	7.931/<0.0001
	0.001/0.591	–0.002/0.384	MD 226.2/0.079	–0.575/0.001	7.759/<0.0001
	0.001/0.585	–0.003/0.360	RD 223.13/0.101	–0.584/0.001	7.615/<0.0001
	0.002/0.431	–0.002/0.553	***ED EV 265.2/0.007***	–0.509/0.002	9.332/<0.0001
Thalamus	0.002/0.201	0.002/0.445	AxD 121.8/0.213	–0.608/0.006	3.735/0.008
	0.002/0.200	0.002/0.436	MD 144.7/0.138	–0.573/0.010	3.932/0.006
	0.002/0.204	0.002/0.438	RD 153.1/0.113	–0.557/0.013	4.030/0.005
	0.001/0.352	0.003/0.142	***ED EV 348.5/<0.0001***	–0.375/0.049	10.03/<0.0001
Insula	–0.001/0.521	–0.001/0.514	***AxD 310.1/<0.0001***	–0.283/0.031	17.44/<0.0001
	–0.001/0.495	–0.001/0.404	***MD 317.2/<0.0001***	–0.312/0.021	15.34/<0.0001
	–0.001/0.492	–0.001/0.345	***RD 315.1/<0.0001***	–0.328/0.017	14.09/<0.0001
	0.0001/0.944	–0.0002/0.870	***ED EV 379.4/<0.0001***	–0.260/0.034	22.94/<0.0001
Corpus callosum	–0.0003/0.778	–0.002/0.364	***AxD 265.0/<0.0001***	0.459/0.357	7.636/<0.0001
	–0.0001/0.926	–0.002/0.402	***MD 246.3/<0.0001***	0.258/0.603	8.705/<0.0001
	–0.00002/0.989	–0.002/0.410	***RD 229.2/<0.0001***	0.195/0.695	8.846/<0.0001
	0.001/0.568	–0.002/0.379	***ED EV 188.3/<0.0001***	0.112/0.816	10.73/<0.0001

In this analysis, we used the model as EC ≈ β1* age + β2* MMSE + β3* diffusion index + β4* gray matter volume (GMV) index + ε (error). For the diffusion indices, we used axial diffusivity (AxD or ADC), mean diffusivity (MD), radial diffusivity (RD), and extra-neurite diffusivity (ED) at extracellular volume (EV). For the BTV index, we used gray matter (GMV) volume. Therefore, the four tested models were ADC and GMV, MD and GMV, RD and GMV, and ED_EV and GMV for each ROI. For EC ROI, $\alpha<0.05$ divided by 4 tested models (P=0.05/4=0.0125) was used to determine the significance level. Italic and bold characters in each column indicate a significant association between conductivity value and other indices.

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Table S5 Result of multiple regression analysis between extra-neurite conductivity (EC) at white matter (WM) (EC_WM) and diffusion indices and brain tissue volume (BTV) index

EC WM and ROI	Age (β/p)	MMSE (β/p)	ED EV WM Diffusion (β/p)	BTV (β/p)	ANOVA (F/P)
Hippocampus	–0.0002/0.417	0.0003/0.374	***258.6/<0.0001***	***WMV 0.216/0.005***	42.73/<0.0001
	–0.0002/0.442	0.0003/0.395	***313.1/<0.0001***	CSF 0.024/0.059	39.16/<0.0001
Amygdala	0.0004/0.420	<0.0001/0.993	***494.3/0.003***	WMV 0.080/0.737	5.466/0.001
	0.0004/0.451	–0.0002/0.842	***562.8/<0.0001***	CSF –0.137/0.372	5.692/0.0005
Thalamus	0.001/0.056	0.001/0.231	***571.8/<0.0001***	***WMV 0.445/0.0003***	69.44/<0.0001
	0.001/0.142	0.002/0.043	***693.5/<0.0001***	CSF 0.323/0.135	57.39/<0.0001
Insula	–0.0002/0.405	–0.0004/0.120	***442.0/<0.0001***	WMV 0.088/0.320	26.31/<0.0001
	–0.0002/0.248	–0.0002/0.502	***425.5/<0.0001***	***CSF 0.073/0.0004***	34.09/<0.0001
Corpus callosum	0.001/0.343	–0.001/0.672	***154.9/<0.0001***	WMV –0.112/0.144	7.061/<0.0001
	0.001/0.434	–0.0005/0.686	***113.2/0.002***	***CSF 0.118/0.025***	8.104/<0.0001

In this analysis, we used the model as EC_WM ≈ β1* age + β2* MMSE + β3* ED EV WM diffusion index + β4* brain tissue volume (BTV) index + ε (error). For the diffusion index, we used extra-neurite diffusivity (ED) at extracellular volume (EV) at white matter (WM). For the BTV index, we used white matter volume (WMV) and cerebrospinal fluid (CSF) volume. Therefore, the two tested models were between ED_EV_WM and WMV and between ED_EV_WM and CSF for each ROI. For EC_WM ROI data, $\alpha<0.05$ divided by 2 tested models (P=0.05/2=0.025) was used to determine the significance level. Italic and bold characters in each column indicate a significant association between conductivity value and other indices.

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Table S6 Result of multiple regression analysis between intra-neurite conductivity (IC) at white matter (WM) (IC_WM) and diffusion indices and brain tissue volume (BTV) index

IC WM and ROI	Age (β/p)	MMSE (β/p)	Diffusion (β/p)	WMV BTV (β/p)	ANOVA (F/P)
Hippocampus	–0.0001/0.458	0.0001/0.655	ID –0.225/0.971	***0.259/<0.0001***	12.00/<0.0001
	–0.0001/0.329	–<0.0001/0.848	***ID IV 49.26/<0.0001***	***0.124/<0.0001***	80.40/<0.0001
	–0.0001/0.221	<0.0001/0.724	***ID IV WM 158.5/<0.0001***	0.009/0.708	123.8/<0.0001
Amygdala	0.0001/0.402	0.0003/0.180	***ID 30.20/<0.0001***	***0.263/<0.0001***	17.41/<0.0001
	0.0001/0.506	0.0001/0.750	***ID IV 45.71/<0.0001***	***0.219/0.0001***	19.97/<0.0001
	0.0001/0.468	0.0001/0.634	***ID IV WM 190.7/<0.0001***	0.043/0.440	25.53/<0.0001
Thalamus	0.0003/0.411	0.001/0.047	***ID 82.53/<0.0001***	***0.541/<0.0001***	48.80/<0.0001
	0.0003/0.291	0.001/0.211	***ID IV 108.7/<0.0001***	***0.534/<0.0001***	91.03/<0.0001
	0.0004/0.210	0.0005/0.194	***ID IV WM 196.1/<0.0001***	***0.271/<0.0001***	117.8/<0.0001
Insula	–0.0001/0.483	0.0004/0.010	***ID 37.67/<0.0001***	***0.253/<0.0001***	25.96/<0.0001
	–0.0001/0.249	0.0001/0.563	***ID IV 50.84/<0.0001***	***0.207/<0.0001***	44.31/<0.0001
	<0.0001/0.939	0.0001/0.597	***ID IV WM 151.2/<0.0001***	0.062/0.052	86.74/<0.0001
	0.002/0.024	0.002/0.074	***ID 11.29/0.751***	0.124/0.092	2.608/0.043
Corpus callosum	0.001/0.144	0.0004/0.593	***ID IV 183.5/<0.0001***	–0.013/0.772	40.35/<0.0001
	0.001/0.184	0.0002/0.795	***ID IV WM 192.5/<0.0001***	–0.047/0.300	40.50/<0.0001

In this analysis, we used the model as IC ≈ β1* age + β2* MMSE + β3* diffusion index + β4* WMV brain tissue volume (BTV) index + ε (error). For the diffusion indices, we used intra-neurite diffusivity (ID), ID at intracellular volume (IV), and ID_IV at white matter (WM). For the BTV index, we used white matter volume. Therefore, the three tested models were between ID and WMV, between ID_IV and WMV, and between ID_IV_WM and WMV for each ROI. For IC ROI data, $\alpha<0.05$ divided by 3 tested models (P=0.05/3=0.0166) was used to determine the significance level. Italic and bold characters in each column indicate a significant association between conductivity value and other indices.

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