

Table S1. Comparison of retinal measures between cognitively normal group and cognitive impairment group.

Items	CN (21)	CI (27)	t	p-value
Vessel Density				
Center Ring	5.44 ± 2.63	3.8 ± 3.08	0.495	0.486
Inner Ring	13.87 ± 3.07	13.11 ± 3.69	0.705	0.407
Outer Ring	15.4 ± 2.47	14.42 ± 3.13	2.865	0.099
Full Ring	14.75 ± 2.51	13.65 ± 3.47	2.146	0.152
TI	13.52 ± 3.63	13.61 ± 3.01	0.635	0.431
SI	16.45 ± 12.82	12.74 ± 4.08	1.172	0.286
NI	14.16 ± 2.88	12.86 ± 3.34	0.449	0.507
II	13.91 ± 3.36	13.91 ± 2.94	0.091	0.765
TO	13.59 ± 3.3	13.81 ± 2.93	0.485	0.491
SO	15.03 ± 2.8	14.08 ± 3.58	3.005	0.092
NO	17.43 ± 2.75	16.39 ± 2.55	1.108	0.299
IO	15.48 ± 2.72	14.69 ± 2.76	4.144	0.049*
FAZ Area	0.23 ± 0.09	0.28 ± 0.16	0.026	0.874
RNFL Thickness				
Full	95 ± 8.23	92.5 ± 10.25	0.026	0.874
T	70.29 ± 13.72	70.13 ± 13.01	0.297	0.589
S	117.37 ± 15.22	103.3 ± 30.68	0.052	0.821
N	82.97 ± 43.85	65.93 ± 12.08	0.289	0.594
I	122.29 ± 14.49	118.2 ± 18.29	0.085	0.772
ILM-RPE Thickness				
TI	320.15 ± 14.46	317.5 ± 14.7	0.017	0.898
SI	280.15 ± 12.47	276.84 ± 9.54	0.030	0.864
NI	314.45 ± 14.58	311.94 ± 15.52	0.038	0.846
II	266.2 ± 12.35	266.35 ± 12.81	0.101	0.752
TO	307.2 ± 14.95	305.68 ± 14.44	0.187	0.668
SO	263.65 ± 14.41	264.26 ± 9.8	0.273	0.605
NO	320.4 ± 16.12	318.76 ± 16.06	0.017	0.897
IO	294.4 ± 12.87	294.94 ± 11.84	0.006	0.939

Data are expressed as the mean ± standard deviation (SD). All data were analyzed by covariance (ANCOVA), accounting for sex, age, years of education. CN: cognitively normal; CI: cognitive impairment; TI, temporal inner; TO, temporal outer; NI, nasal inner; NO, nasal outer; SI, superior inner; SO, superior outer, II, inferior inner, IO, inferior outer; FAZ, foveal avascular zone; RNFL, retinal nerve fiber layer; ILM-RPE, inner limiting membrane - retinal pigment epithelium. * < 0.05.

Table S2. Comparison of white matter integrity between cognitively normal group and cognitive impairment group.

Items	CN (21)	CI (27)	F	p-value
FA				
ATR	0.42 ± 0.03	0.43 ± 0.026	3.27	0.148
CST	0.6 ± 0.04	0.6 ± 0.028	0.35	0.704
CgC	0.54 ± 0.04	0.53 ± 0.043	0.11	0.896
CgH	0.48 ± 0.04	0.46 ± 0.039	1.77	0.183
Fma	0.57 ± 0.03	0.56 ± 0.033	0.37	0.692
IFO	0.49 ± 0.02	0.47 ± 0.035	0.03	0.970
ILF	0.47 ± 0.02	0.46 ± 0.03	0.22	0.800
SLF	0.46 ± 0.04	0.47 ± 0.026	1.83	0.174
UF	0.48 ± 0.03	0.46 ± 0.032	0.85	0.434
tSLF	0.5 ± 0.03	0.49 ± 0.06	2.24	0.119
MD				
ATR	0.0008 ± 0.000074	0.00081 ± 0.000079	0.65	0.426
CST	0.00072 ± 0.000031	0.00072 ± 0.000026	0.03	0.875
CgC	0.00074 ± 0.000032	0.00076 ± 0.000044	0.35	0.559
CgH	0.00073 ± 0.000046	0.00077 ± 0.000051	4.25	0.046*
Fma	0.00078 ± 0.000029	0.00079 ± 0.000046	0.06	0.807
IFO	0.00078 ± 0.000031	0.0008 ± 0.000048	0.04	0.834
ILF	0.00079 ± 0.000028	0.00081 ± 0.000053	0.28	0.597
SLF	0.00075 ± 0.000047	0.00075 ± 0.000033	0.43	0.515
UF	0.00076 ± 0.00003	0.00078 ± 0.00005	0.05	0.833
tSLF	0.00078 ± 0.000029	0.00079 ± 0.000049	0.35	0.555
AxD				
ATR	0.00118 ± 0.000077	0.00121 ± 0.000089	0	1
CST	0.00128 ± 0.000041	0.00128 ± 0.000026	0	1
CgC	0.00123 ± 0.000054	0.00125 ± 0.000055	0.295	0.59
CgH	0.00115 ± 0.000062	0.00119 ± 0.000056	5.043	0.03*
Fma	0.00136 ± 0.000039	0.00138 ± 0.000041	0.953	0.335
IFO	0.00124 ± 0.000033	0.00125 ± 0.000042	0.026	0.873
ILF	0.00123 ± 0.000042	0.00126 ± 0.000056	1.19	0.282
SLF	0.00114 ± 0.000043	0.00116 ± 0.00004	0.691	0.411
UF	0.00121 ± 0.000039	0.00121 ± 0.000054	0.01	0.922
tSLF	0.00125 ± 0.000054	0.00126 ± 0.000086	0.178	0.676
RD				
ATR	0.00061 ± 0.000076	0.00061 ± 0.000076	1.43	0.239
CST	0.00044 ± 0.000041	0.00044 ± 0.000035	0.03	0.872
CgC	0.0005 ± 0.00004	0.00052 ± 0.000054	0.16	0.691
CgH	0.00052 ± 0.000047	0.00057 ± 0.000057	2.55	0.118
Fma	0.00048 ± 0.000037	0.0005 ± 0.000054	0.02	0.885
IFO	0.00055 ± 0.000034	0.00057 ± 0.000056	0.04	0.838
ILF	0.00057 ± 0.000028	0.00059 ± 0.000056	0.02	0.895

SLF	0.00056 ± 0.000057	0.00055 ± 0.000036	1.53	0.224
UF	0.00053 ± 0.000037	0.00056 ± 0.000054	0.11	0.739
tSLF	0.00054 ± 0.000029	0.00056 ± 0.000059	0.22	0.638

Data are expressed as the mean \pm standard deviation (SD). All data were analyzed by covariance (ANCOVA), accounting for sex, age, years of education. Abbreviations: CN: cognitive normal; CI: cognitive impairment; CgH: Cingulum hippocampus; UF: Uncinate fasciculus; FA: fractional anisotropy; MD: mean diffusivity; AxD: Axial Diffusivity; RD: Radial Diffusivity. ATR: anterior thalamic radiation; CgC: cingulum in the cingulated cortex area; CgH: cingulum in the hippocampal area; CST: corticospinal tract; FMa: forceps major; IFO: inferior fronto-occipital fasciculus; ILF: inferior longitudinal fasciculus; SLF: superior longitudinal fasciculus; tSLF: the temporal projection of the SLF; UF: uncinate fasciculus. * < 0.05 .

Table S3. Relationship Between hippocampal subfield volumes and retinal parameters in CI group.

Partial Correlation						
Control	Items	Subiculum	Presubiculum	Molecular_layer_HP	GC-ML-DG	Whole hippocampus
Age,						
Gender,	Vessel density					
Years of education, eTIV						
Center Ring	0.142	0.417	0.051	0.060	0.157	
Inner Ring	0.017	0.250	-0.057	0.019	0.024	
Outer Ring	0.293	0.435*	0.257	0.310	0.305	
Full Area	0.220	0.398	0.170	0.231	0.231	
FAZ Area	0.041	0.252	-0.009	-0.001	-0.008	
VD_TI	0.245	0.400	0.108	0.168	0.175	
VD_SI	0.150	0.438	0.062	0.044	0.130	
VD_NI	-0.033	0.176	-0.152	-0.129	-0.084	
VD_II	0.198	0.356	0.189	0.189	0.197	
VD_TO	0.196	0.300	0.155	0.174	0.180	
VD_SO	0.523*	0.593**	0.463*	0.452*	0.487*	
VD_NO	0.440	0.559*	0.339	0.301	0.348	
VD_IO	0.142	0.417	0.051	0.060	0.157	
Thickness						
RNFL	0.264	0.160	0.317	0.271	0.284	
RNFL_T	0.011	-0.113	-0.039	-0.099	-0.056	
RNFL_S	0.235	0.162	0.277	0.267	0.236	
RNFL_N	0.276	0.176	0.357	0.339	0.329	
RNFL_I	0.215	0.253	0.291	0.274	0.296	
ILM-RFE_TI	0.303	0.336	0.299	0.248	0.355	
ILM-RFE_SI	0.309	0.287	0.293	0.224	0.350	
ILM-RFE_NI	0.307	0.278	0.312	0.234	0.363	
ILM-RFE_II	0.388	0.381	0.342	0.273	0.375	
ILM-RFE_TO	0.222	0.218	0.223	0.192	0.209	
ILM-RFE_SO	0.198	0.157	0.205	0.134	0.187	
ILM-RFE_NO	0.284	0.258	0.297	0.207	0.274	
ILM-RFE_IO	0.009	0.028	0.042	-0.008	0.039	

Partial correlation was conducted controlling for age, gender, years of education, and eTIV. FAZ: foveal avascular zone; TI: temporal inner; TO: temporal outer; NI: nasal inner; NO: nasal outer; SI: superior inner; SO: superior outer; II: inferior inner, IO: inferior outer; VD: vessel density; RNFL: retinal nerve fiber layer; T: temporal, S: superior; N: nasal; I: inferior; ILM-RPE: inner limiting membrane - retinal pigment epithelium; GC-ML-DG: Molecular and Granule Cell Layers of the Dentate. * < 0.05.

Table S4. Relationship Between hippocampal subfield volumes and retinal parameters in CN group.

Control	Items	Partial Correlation				
		Subiculu m	Presubiculu m	Molecular_ layer_HP	GC-ML- DG	Whole hippocam- pus
Age,						
Gender,	Vessel density					
Years of educa- tion, eTIV						
Center Ring	0.200	0.548*	-0.041	0.105	-0.041	
Inner Ring	0.264	0.445	0.073	0.237	0.018	
Outer Ring	0.333	0.239	0.177	0.278	0.135	
Full Area	0.323	0.315	0.150	0.273	0.104	
FAZ Area	0.187	0.339	0.029	0.246	-0.017	
VD_TI	0.186	0.392	-0.066	0.081	-0.088	
VD_SI	0.305	0.502*	0.094	0.175	0.010	
VD_NI	0.328	0.442	0.233	0.377	0.175	
VD_II	0.216	0.250	0.115	0.323	0.106	
VD_TO	0.254	0.139	0.053	0.171	0.060	
VD_SO	0.261	0.166	0.106	0.053	0.039	
VD_NO	0.367	0.197	0.310	0.354	0.236	
VD_IO	0.200	0.548*	-0.041	0.105	-0.041	
Thickness						
RNFL	-0.105	-0.210	0.030	-0.073	-0.028	
RNFL_T	-0.037	0.334	-0.046	-0.158	-0.163	
RNFL_S	-0.192	-0.202	-0.037	-0.105	-0.018	
RNFL_N	0.021	-0.334	0.235	0.200	0.198	
RNFL_I	-0.086	-0.307	-0.097	-0.139	-0.081	
ILM-RFE_TI	-0.084	0.196	0.081	0.015	-0.029	
ILM-RFE_SI	-0.098	0.148	0.014	-0.053	-0.078	
ILM-RFE_NI	-0.012	0.297	0.061	-0.088	-0.046	
ILM-RFE_II	0.013	0.133	0.198	0.087	0.075	
ILM-RFE_TO	-0.043	-0.072	0.093	0.160	0.027	
ILM-RFE_SO	-0.064	-0.052	0.097	0.097	0.017	
ILM-RFE_NO	-0.127	-0.150	0.147	0.017	0.021	
ILM-RFE_IO	-0.112	-0.157	0.231	0.155	0.136	

Partial correlation was conducted controlling for age, gender, years of education, and eTIV. FAZ: foveal avascular zone; TI: temporal inner; TO: temporal outer; NI: nasal inner; NO: nasal outer; SI: superior inner; SO: superior outer; II: inferior inner, IO: inferior outer; VD: vessel density; RNFL: retinal nerve fiber layer; T: temporal, S: superior; N: nasal; I: inferior; ILM-RPE: inner limiting membrane - retinal pigment epithelium; GC-ML-DG: Molecular and Granule Cell Layers of the Dentate. * < 0.05.

Table S5. Relationship Between Diffusion Metrics and retinal parameters in CN group.

Control	Items	Partial Correlation	
		CgH (MD)	CgH (AxD)
Age,			
Gender,			
Years of education	Vessel density		
	Center Ring	-0.397	-0.194
	inner Ring	-0.072	-0.216
	Outer Ring	-0.235	-0.323
	Full Area	-0.156	-0.366
	FAZ Area	0.175	-0.013
	VD_TI	-0.268	-0.354
	VD_SI	-0.094	-0.217
	VD_NI	0.207	-0.135
	VD_II	-0.098	-0.100
	VD_TO	-0.174	-0.320
	VD_SO	-0.283	-0.210
	VD_NO	-0.272	-0.102
	VD_IO	-0.397	-0.194
	Thickness		
	RNFL	-0.158	0.108
	RNFL_T	0.115	0.205
	RNFL_S	-0.091	-0.033
	RNFL_N	-0.463	-0.138
	RNFL_I	-0.076	0.230
	ILM-RFE_TI	-0.331	0.015
	ILM-RFE_SI	-0.128	0.139
	ILM-RFE_NI	-0.287	-0.041
	ILM-RFE_II	0.121	0.147
	ILM-RFE_TO	-0.361	-0.147
	ILM-RFE_SO	-0.149	-0.004
	ILM-RFE_NO	-0.321	-0.068
	ILM-RFE_IO	-0.087	0.028

Partial correlation was conducted controlling for age, gender, years of education. FAZ: foveal avascular zone; TI: temporal inner; TO: temporal outer; NI: nasal inner; NO: nasal outer; SI: superior inner; SO: superior outer; II: inferior inner, IO: inferior outer; VD: vessel density; RNFL: retinal nerve fiber layer; T: temporal, S: superior; N: nasal; I: inferior; ILM-RPE: inner limiting membrane - retinal pigment epithelium; All data were analyzed via two-sample t-test. CN: cognitively normal; CI: cognitive impairment; CgH: Cingulum hippocampus; UF: Uncinate fasciculus; FA: fractional anisotropy; MD: mean diffusivity; AxD: Axial Diffusivity; RD: Radial Diffusivity. * <0.05.

Table S6. Relationship Between Diffusion Metrics and retinal parameters in CN group.

Control	Items	Partial Correlation	
		CgH (MD)	CgH (AxD)
Age,			
Gender,			
Years of	Vessel density		
education			
	Center Ring	-0.263	-0.334
	inner Ring	-0.387	-0.304
	Outer Ring	-0.205	-0.179
	Full Area	-0.267	-0.227
	FAZ Area	-0.397	-0.337
	VD_TI	0.454	0.495*
	VD_SI	-0.309	-0.225
	VD_NI	-0.383	-0.284
	VD_II	-0.350	-0.362
	VD_TO	-0.193	-0.223
	VD_SO	0.013	0.032
	VD_NO	-0.127	0.004
	VD_IO	-0.263	-0.334
	Thickness		
	RNFL	0.043	0.130
	RNFL_T	0.158	0.265
	RNFL_S	-0.290	-0.208
	RNFL_N	-0.007	0.057
	RNFL_I	-0.035	0.016
	ILM-RFE_TI	-0.043	0.141
	ILM-RFE_SI	0.058	0.126
	ILM-RFE_NI	0.015	0.143
	ILM-RFE_II	0.155	0.088
	ILM-RFE_TO	0.029	0.171
	ILM-RFE_SO	0.185	0.168
	ILM-RFE_NO	-0.015	0.114
	ILM-RFE_IO	0.186	0.238

Partial correlation was conducted controlling for age, gender, years of education. FAZ: foveal avascular zone; TI: temporal inner; TO: temporal outer; NI: nasal inner; NO: nasal outer; SI: superior inner; SO: superior outer; II: inferior inner, IO: inferior outer; VD: vessel density; RNFL: retinal nerve fiber layer; T: temporal, S: superior; N: nasal; I: inferior; ILM-RPE: inner limiting membrane - retinal pigment epithelium; All data were analyzed via two-sample t-test. CN: cognitively normal; CI: cognitive impairment; CgH: Cingulum hippocampus; UF: Uncinate fasciculus; FA: fractional anisotropy; MD: mean diffusivity; AxD: Axial Diffusivity; RD: Radial Diffusivity. * <0.05.

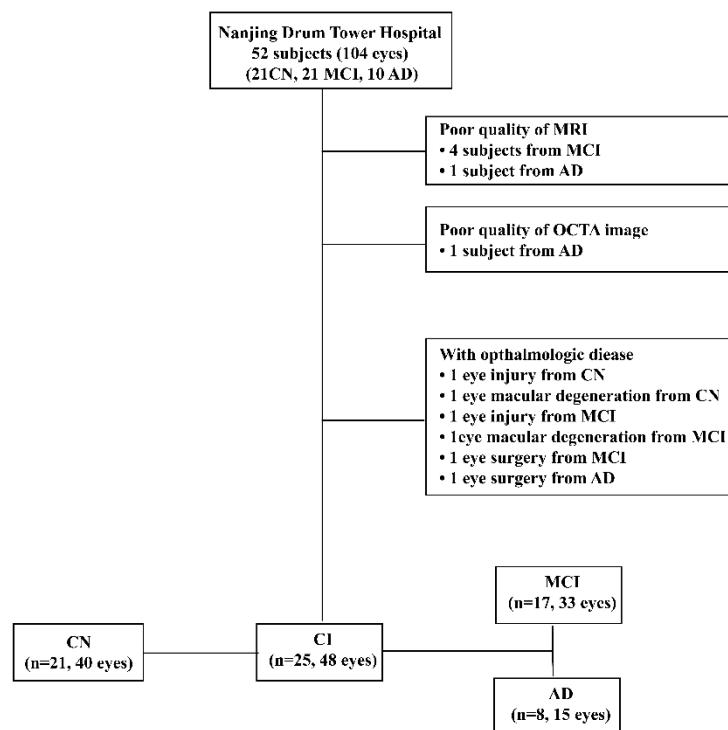


Figure S1. Flow Diagram of the Inclusion Process. CN, cognitively normal; MCI; mild cognitive impairment. AD, Alzheimer's Disease; CI; cognitive impairment. MRI, magnetic resonance imaging.

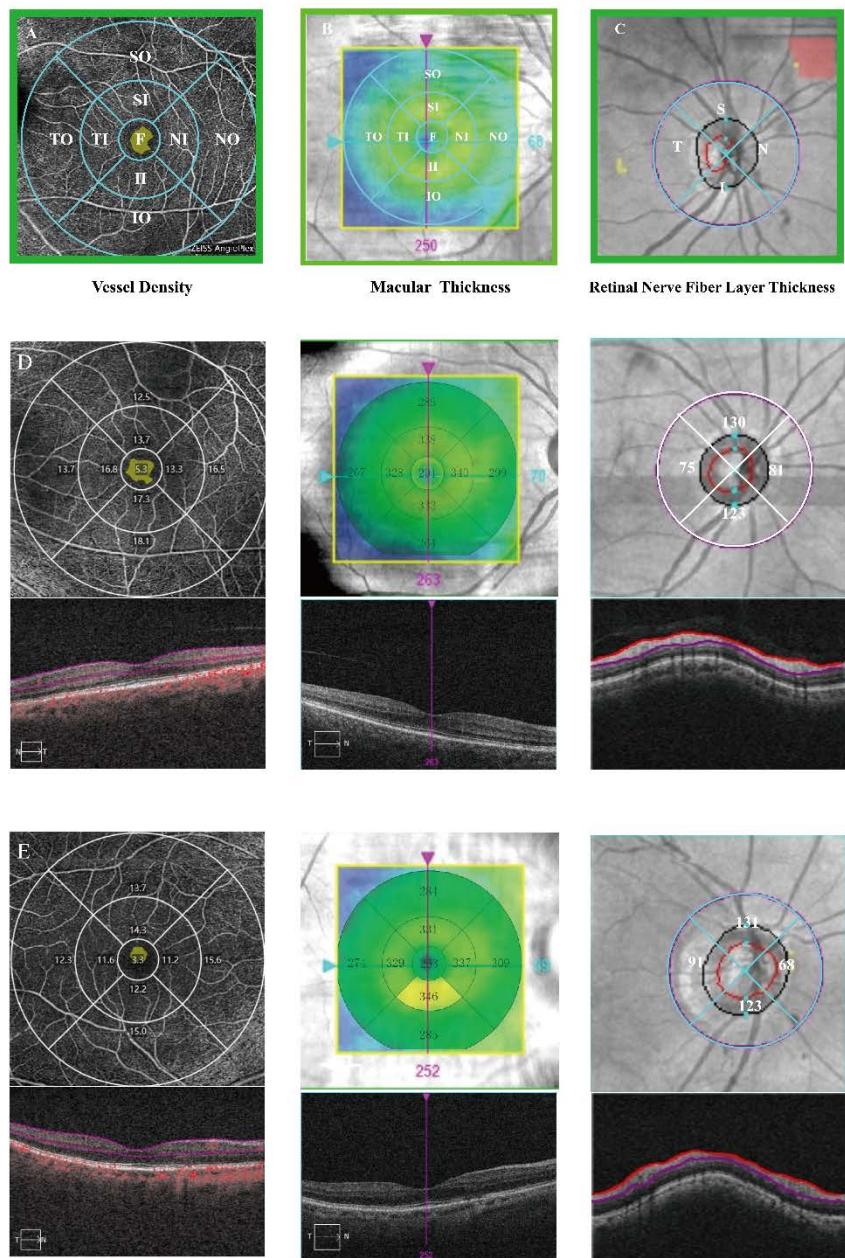


Figure S2. OCTA images. (A, B) In the macula, vessel density and retinal macular thickness are measured in the fovea (F) (\varnothing 1 mm), inner ring (\varnothing 3 mm), and outer ring (\varnothing 6 mm) following the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. The inner ring and outer ring are subdivided into four sectors (superior, nasal, inferior, and temporal). (C) Around the optic nerve head (peripapillary): retinal nerve fiber layer (RNFL) thickness was measured in the following sectors: temporal (T), superior (S), nasal (N), inferior (I), and mean RNFL thickness (RNFL). (D) Retinal scan images and B-scans from healthy eye. (E) Retinal scan images and B-scans from patient eye.