

Supplementary Table 1

Figure 1	Subfigure	Experiment	Strain	Young	Aged	Statistical test	Day/Trial	Young Mean	SEM	Aged Mean	SEM	Units	p-value	Significance						
1	B	Barnes maze-Latency to find target hole (Training)	C57/BL6	N=5	N=5	Two-way ANOVA w/ Tukey	0	52.56833	10.65164	60.74167	14.97003	seconds	0.6694	ns						
							1	39.665	8.752984	37.915	10.89164	seconds	0.9036	ns						
							2	22.99	2.62284	71.065	14.01323	seconds	0.0252	*						
							3	20.255	6.099116	35.91	9.389098	seconds	0.2055	ns						
	Group	33.87		51.41		seconds	0.1021	ns												
C	Barnes maze-Latency to find target hole (Probe trail)	C57/BL6	N=5	N=5	Student t-test	Probe	8.16	1.892	42.02	14.5	seconds	0.0493	*							
D	Barnes maze-Target hole entries (Probe trial)	C57/BL6	N=5	N=5	Student t-test	Probe	7.2	1.53	1.2	0.4899	# of entries	0.0057	**							
Figure 2	Subfigure	Experiment	Strain	Young	Aged	Statistical test	Comparison	Young Mean	SEM	Aged Mean	SEM	Units	p-value	Significance						
2	B	Hippocampal cell counts	C57/BL6	N=5, 2-7 sections/mouse	N=5, 3-4 sections/mouse	Student t-test	PV ⁺ Cells	29.91	1.874	34.88	2.595	# of cells/mm ²	0.1586	ns						
							WFA ⁺ Cells	20.69	0.7683	25.96	1.876	# of cells/mm ²	0.0318	*						
							ACAN ⁺ Cells	15.04	0.9128	18.58	1.95	# of cells/mm ²	0.1388	ns						
							PV ⁺ :WFA ⁺ Cells	14.19	1.386	19.47	1.69	# of cells/mm ²	0.0421	*						
							PV ⁺ :ACAN ⁺ Cells	7.308	0.8589	9.777	0.9607	# of cells/mm ²	0.0917	ns						
							WFA ⁺ :ACAN ⁺ Cells	6.248	0.4854	9.77	0.8901	# of cells/mm ²	0.0084	**						
							PV ⁺ :WFA ⁺ :ACAN ⁺ Cells	4.907	0.5917	7.666	0.6379	# of cells/mm ²	0.0125	*						
	C	Percentage of PV ⁺ Cells with a WFA ⁺ PNN (Hippocampus)	C57/BL6	N=5, 2-7 sections/mouse	N=5, 3-4 sections/mouse	Student t-test	Young vs Aged	47.95	2.102	57.27	2.783	% of PV cells	0.0282	*						
	D	WFA ⁺ PNNs by hippocampal subregion	C57/BL6	N=5, 2-7 sections/mouse	N=5, 3-4 sections/mouse	Two-way ANOVA w/ Tukey	[A] vs [B]	[A] Mean	[A] SEM	[B] Mean	[B] SEM	Units	p-value	Significance						
							CA1 (Young) vs. CA1 (Aged)	0.0001594	0.00001243	0.0002128	0.00003012	# of cells/mm ²	0.7598	ns						
							CA1 (Young) vs. CA2 (Young)	0.0001594	0.00001243	0.0003036	0.00004165	# of cells/mm ²	0.001	***						
							CA1 (Young) vs. CA2 (Aged)	0.0001594	0.00001243	0.000396	0.0000353	# of cells/mm ²	<0.0001	****						
							CA1 (Young) vs. CA3 (Young)	0.0001594	0.00001243	0.0001864	0.00003831	# of cells/mm ²	0.9926	ns						
							CA1 (Young) vs. CA3 (Aged)	0.0001594	0.00001243	0.0002106	0.00001688	# of cells/mm ²	0.7967	ns						
							CA1 (Young) vs. DG (Young)	0.0001594	0.00001243	0.0001336	0.00001486	# of cells/mm ²	0.9944	ns						
							CA1 (Young) vs. DG (Aged)	0.0001594	0.00001243	0.0001283	0.00002307	# of cells/mm ²	0.9833	ns						
							CA1 (Aged) vs. CA2 (Young)	0.0002128	0.00003012	0.0003036	0.00004165	# of cells/mm ²	0.1364	ns						
							CA1 (Aged) vs. CA2 (Aged)	0.0002128	0.00003012	0.000396	0.0000353	# of cells/mm ²	<0.0001	****						
							CA1 (Aged) vs. CA3 (Young)	0.0002128	0.00003012	0.0001864	0.00003831	# of cells/mm ²	0.9938	ns						
							CA1 (Aged) vs. CA3 (Aged)	0.0002128	0.00003012	0.0002106	0.00001688	# of cells/mm ²	>0.9999	ns						
CA1 (Aged) vs. DG (Young)							0.0002128	0.00003012	0.0001336	0.00001486	# of cells/mm ²	0.2785	ns							
CA1 (Aged) vs. DG (Aged)							0.0002128	0.00003012	0.0001283	0.00002307	# of cells/mm ²	0.2086	ns							
CA2 (Young) vs. CA2 (Aged)							0.0003036	0.00004165	0.000396	0.0000353	# of cells/mm ²	0.1222	ns							
CA2 (Young) vs. CA3 (Young)							0.0003036	0.00004165	0.0001864	0.00003831	# of cells/mm ²	0.0156	*							
CA2 (Young) vs. CA3 (Aged)							0.0003036	0.00004165	0.0002106	0.00001688	# of cells/mm ²	0.1172	ns							
CA2 (Young) vs. DG (Young)							0.0003036	0.00004165	0.0001336	0.00001486	# of cells/mm ²	<0.0001	****							
CA2 (Young) vs. DG (Aged)							0.0003036	0.00004165	0.0001283	0.00002307	# of cells/mm ²	<0.0001	****							
CA2 (Aged) vs. CA3 (Young)							0.000396	0.0000353	0.0001864	0.00003831	# of cells/mm ²	<0.0001	****							
CA2 (Aged) vs. CA3 (Aged)							0.000396	0.0000353	0.0002106	0.00001688	# of cells/mm ²	<0.0001	****							
CA2 (Aged) vs. DG (Young)							0.000396	0.0000353	0.0001336	0.00001486	# of cells/mm ²	<0.0001	****							
CA2 (Aged) vs. DG (Aged)							0.000396	0.0000353	0.0001283	0.00002307	# of cells/mm ²	<0.0001	****							
CA3 (Young) vs. CA3 (Aged)							0.0001864	0.00003831	0.0002106	0.00001688	# of cells/mm ²	0.9964	ns							
CA3 (Young) vs. DG (Young)							0.0001864	0.00003831	0.0001336	0.00001486	# of cells/mm ²	0.7665	ns							
CA3 (Young) vs. DG (Aged)							0.0001864	0.00003831	0.0001283	0.00002307	# of cells/mm ²	0.6725	ns							
CA3 (Aged) vs. DG (Young)							0.0002106	0.00001688	0.0001336	0.00001486	# of cells/mm ²	0.3133	ns							
CA3 (Aged) vs. DG (Aged)							0.0002106	0.00001688	0.0001283	0.00002307	# of cells/mm ²	0.2376	ns							
DG (Young) vs. DG (Aged)							0.0001336	0.00001486	0.0001283	0.00002307	# of cells/mm ²	>0.9999	ns							
E							ACAN ⁺ PNNs by hippocampal subregion	C57/BL6	N=5, 2-7 sections/mouse	N=5, 3-4 sections/mouse	Two-way ANOVA w/ Tukey	CA1 (Young) vs. CA1 (Aged)	0.0000944	0.000008325	0.0001058	0.00001013	# of cells/mm ²	>0.9999	ns	
												CA1 (Young) vs. CA2 (Young)	0.0000944	0.000008325	0.0002196	0.00002244	# of cells/mm ²	0.0049	**	
												CA1 (Young) vs. CA2 (Aged)	0.0000944	0.000008325	0.0002832	0.00003419	# of cells/mm ²	<0.0001	****	
												CA1 (Young) vs. CA3 (Young)	0.0000944	0.000008325	0.0001626	0.0000346	# of cells/mm ²	0.4268	ns	
												CA1 (Young) vs. CA3 (Aged)	0.0000944	0.000008325	0.000183	0.0000324	# of cells/mm ²	0.1318	ns	
												CA1 (Young) vs. DG (Young)	0.0000944	0.000008325	0.0001194	0.00001358	# of cells/mm ²	0.9944	ns	
												CA1 (Young) vs. DG (Aged)	0.0000944	0.000008325	0.0001271	0.00001779	# of cells/mm ²	0.9737	ns	
												CA1 (Aged) vs. CA2 (Young)	0.0001058	0.00001013	0.0002196	0.00002244	# of cells/mm ²	0.0161	*	
												CA1 (Aged) vs. CA2 (Aged)	0.0001058	0.00001013	0.0002832	0.00003419	# of cells/mm ²	<0.0001	****	
												CA1 (Aged) vs. CA3 (Young)	0.0001058	0.00001013	0.0001626	0.0000346	# of cells/mm ²	0.6645	ns	
												CA1 (Aged) vs. CA3 (Aged)	0.0001058	0.00001013	0.000183	0.0000324	# of cells/mm ²	0.2777	ns	
												CA1 (Aged) vs. DG (Young)	0.0001058	0.00001013	0.0001194	0.00001358	# of cells/mm ²	0.9999	ns	
												CA1 (Aged) vs. DG (Aged)	0.0001058	0.00001013	0.0001271	0.00001779	# of cells/mm ²	0.9981	ns	
												CA2 (Young) vs. CA2 (Aged)	0.0002196	0.00002244	0.0002832	0.00003419	# of cells/mm ²	0.5255	ns	
												CA2 (Young) vs. CA3 (Young)	0.0002196	0.00002244	0.0001626	0.0000346	# of cells/mm ²	0.6567	ns	
	CA2 (Young) vs. CA3 (Aged)	0.0002196	0.00002244	0.000183	0.0000324	# of cells/mm ²						0.9517	ns							
	CA2 (Young) vs. DG (Young)	0.0002196	0.00002244	0.0001194	0.00001358	# of cells/mm ²						0.0526	ns							
	CA2 (Young) vs. DG (Aged)	0.0002196	0.00002244	0.0001271	0.00001779	# of cells/mm ²						0.0995	ns							
	CA2 (Aged) vs. CA3 (Young)	0.0002832	0.00003419	0.0001626	0.0000346	# of cells/mm ²						0.0083	**							
	CA2 (Aged) vs. CA3 (Aged)	0.0002832	0.00003419	0.000183	0.0000324	# of cells/mm ²						0.056	ns							
	CA2 (Aged) vs. DG (Young)	0.0002832	0.00003419	0.0001194	0.00001358	# of cells/mm ²						<0.0001	****							
	CA2 (Aged) vs. DG (Aged)	0.0002832	0.00003419	0.0001271	0.00001779	# of cells/mm ²						0.0002	***							
	CA3 (Young) vs. CA3 (Aged)	0.0001626	0.0000346	0.000183	0.0000324	# of cells/mm ²						0.9985	ns							
	CA3 (Young) vs. DG (Young)	0.0001626	0.0000346	0.0001194	0.00001358	# of cells/mm ²						0.8879	ns							
	CA3 (Young) vs. DG (Aged)	0.0001626	0.0000346	0.0001271	0.00001779	# of cells/mm ²						0.9589	ns							
	CA3 (Aged) vs. DG (Young)	0.000183	0.0000324	0.0001194	0.00001358	# of cells/mm ²						0.5263	ns							
	CA3 (Aged) vs. DG (Aged)	0.000183	0.0000324	0.0001271	0.00001779	# of cells/mm ²						0.6876	ns							
	DG (Young) vs. DG (Aged)	0.0001194	0.00001358	0.0001271	0.00001779	# of cells/mm ²						>0.9999	ns							
	3	B	Dorsal striatum cell counts	C57/BL6	N=5, 5-8 sections/mouse	N=5, 4-6 sections/mouse						Student t-test	PV ⁺ Cells	36.97	4.323	37.83	2.641	# of cells/mm ²	0.8697	ns
													WFA ⁺ Cells	23.94	4.733	28.3	1.46	# of cells/mm ²	0.4048	ns
													ACAN ⁺ Cells	9.538	2.039	6.139	0.3701	# of cells/mm ²	0.1071	ns
													PV ⁺ :WFA ⁺ Cells	16.14	3.782	18.48	1.35	# of cells/mm ²	0.5762	ns
PV ⁺ :ACAN ⁺ Cells							1.009	0.1641	0.9083	0.1583	# of cells/mm ²		0.6693	ns						
WFA ⁺ :ACAN ⁺ Cells							0.691	0.1275	0.6805	0.05578	# of cells/mm ²		0.9419	ns						
PV ⁺ :WFA ⁺ :ACAN ⁺ Cells							0.532	0.1155	0.4588	0.06843	# of cells/mm ²		0.6009	ns						
C		Percentage of PV ⁺ Cells with a WFA ⁺ PNN (Total striatum)	C57/BL6	N=5, 5-8 sections/mouse	N=5, 4-6 sections/mouse	Student t-test	Young vs Aged	40.8	4.118	49.15	1.271	% of PV cells	0.0886	ns						
D		PV ⁺ Cells with a WFA ⁺ PNN (Striatal regions)	C57/BL6	N=5, 5-8 sections/mouse	N=5, 4-6 sections/mouse	Two-way ANOVA w/ Tukey	[A] vs [B]	[A] Mean	[A] SEM	[B] Mean	[B] SEM	Units	p-value	Significance						
							DMS (Young) vs DLS (Young)	22.07	1.986	39.44	4.552	% of PV cells	<0.0001	****						
	DMS (Young) vs DMS (Aged)						22.07	1.986	21.7	2.037	% of PV cells	0.9992	ns							
	DMS (Young) vs DLS (Aged)						22.07	1.986	27.41	2.306	% of PV cells	0.2568	ns							
	DLS (Young) vs DMS (Aged)						39.44	4.552	21.7	2.037	% of PV cells	<0.0001	****							
	DLS (Aged) vs DLS (Aged)						39.44	4.552	27.41	2.306	% of PV cells	0.0005	***							
DMS (Aged) vs DLS (Aged)	21.7	2.037	27.41	2.306	% of PV cells	0.1529	ns													

Figure 3	Subfigure	Experiment	Strain	Young	Aged	Statistical test	Comparison	Young Mean	SEM	Aged Mean	SEM	Units	p-value	Significance
3	E	Percentage of PV+ Cells with a WFA+ PNN (Striatal regions)	C57/BL6	N=5, 5-8 sections/mouse	N=5, 4-6 sections/mouse	Two-way ANOVA w/ Tukey	[A] vs [B]	[A] Mean	[A] SEM	[B] Mean	[B] SEM	Units	p-value	Significance
							DMS (Young) vs DLS (Young)	38.19	3.572	44.34	4.776	% of PV cells	0.2719	ns
							DMS (Young) vs DMS (Aged)	38.19	3.572	50.4	1.777	% of PV cells	0.0058	**
							DMS (Young) vs DLS (Aged)	38.19	3.572	48.67	0.9025	% of PV cells	0.0239	*
							DLS (Young) vs DMS (Aged)	44.34	4.776	50.4	1.777	% of PV cells	0.3421	ns
	DLS (Young) vs DLS (Aged)	44.34	4.776	48.67	0.9025	% of PV cells	0.6308	ns						
	DMS (Aged) vs DLS (Aged)	50.4	1.777	48.67	0.9025	% of PV cells	0.9688	ns						
	F	Colocalization of PV+:WFA+	C57/BL6	N=5, 2 sections/mouse	N=5, 2 sections/mouse	Two-way ANOVA w/ Tukey	DMS (Young) vs DLS (Young)	0.2629	0.2915	0.4233	0.02819	Pearson's r	0.0011	**
							DMS (Young) vs DMS (Aged)	0.2629	0.2915	0.366	0.02362	Pearson's r	0.053	ns
							DMS (Young) vs DLS (Aged)	0.2629	0.2915	0.4798	0.02539	Pearson's r	<0.0001	****
							DLS (Young) vs DMS (Aged)	0.4233	0.2819	0.366	0.02362	Pearson's r	0.4112	ns
							DLS (Young) vs DLS (Aged)	0.4233	0.2819	0.4798	0.02539	Pearson's r	0.4076	ns
DMS (Aged) vs DLS (Aged)	0.366	0.02362	0.4798	0.02539	Pearson's r	0.0256	*							
Figure 4	Subfigure	Experiment	Region	Young	Aged	Statistical test	Age group	Equation	R ²	Y-intercept	Slope	p-value	Significance	
4	A	Linear regression of WFA+ vs PV+ intensity	Striatum	N=5, 2-7 sections/mouse	N=5, 3-8 sections/mouse	Linear regression/ Coefficient difference t-test of slopes	Young	Y = 0.7525*X + 0.2125	0.5681	0.2125	0.7525	0.1412	ns	
			Aged				Y = 0.9409*X + 0.08875	0.974	0.08875	0.9409	0.0018	**		
			Young				Y = 1.011*X + 0.01704	0.3062	0.01704	1.011	0.0093	**		
	B	Hippocampus	Aged	Y = 0.7325*X + 0.2406	0.4345	0.2406	0.7325	0.0029	**					
			C	Linear regression of WFA+ vs ACAN+ intensity	Striatum	Young	Y = 0.001760*X + 0.7824	0.000002881	0.7824	0.00176	0.9978	ns		
					Aged	Y = 0.4923*X + 0.4269	0.5271	0.4269	0.4923	0.1649	ns			
	Hippocampus	Young			Y = 0.09677*X + 0.7287	0.005889	0.7287	0.09677	0.7409	ns				
	Aged	Y = 0.5204*X + 0.4462	0.5328	0.4462	0.5204	0.0006	***							
Figure 5 (See supplementary table 2)														
Figure 6	Subfigure	Experiment	Strain	Young	Aged	Statistical test	[A] vs [B]	[A] Mean	[A] SEM	[B] Mean	[B] SEM	Units	p-value	Significance
6	B	Iba1 Intensity per cell	C57/BL6	N=5, 4-17 cells/region/mouse	N=5, 4-15 cells/region/mouse	Two-way ANOVA w/ Tukey	Str. (Young) vs Str. (Aged)	42.07	3.766	64.66	7.634	A.U./cell	<0.0001	****
							Str. (Young) vs Hpc. (Young)	42.07	3.766	32.56	4.155	A.U./cell	0.3364	ns
							Str. (Young) vs Hpc. (Aged)	42.07	3.766	47.45	5.76	A.U./cell	0.7456	ns
							Str. (Aged) vs Hpc. (Young)	64.66	7.634	32.56	4.155	A.U./cell	<0.0001	****
							Str. (Aged) vs Hpc. (Aged)	64.66	7.634	47.45	5.76	A.U./cell	0.0089	**
							Str. (Young) vs Hpc. (Young)	32.56	4.155	47.45	5.76	A.U./cell	0.0959	ns
	C	Striatal mean Iba1 intensity	C57/BL6	N=5, 3-4 sections/mouse	N=5, 4 sections/mouse	Student t-test	Young vs Aged	202.9	3.82	215.3	3.245	A.U.	0.0391	*
	D	Striatal Iba1 intensity per cell	C57/BL6	N=5, 2-12 cells/region/mouse	N=5, 3-12 cells/region/mouse	Two-way ANOVA w/ Tukey	DMS (Young) vs DLS (Young)	47.05	8.569	40.47	4.353	A.U./cell	0.6523	ns
							DMS (Young) vs DMS (Aged)	47.05	8.569	54.74	7.97	A.U./cell	0.557	ns
							DMS (Young) vs DLS (Aged)	47.05	8.569	72.21	12.19	A.U./cell	0.0005	***
							DLS (Young) vs DMS (Aged)	40.47	4.353	54.74	7.97	A.U./cell	0.032	*
							DLS (Young) vs DLS (Aged)	40.47	4.353	72.21	12.19	A.U./cell	<0.0001	****
							DMS (Aged) vs DLS (Aged)	54.74	7.97	72.21	12.19	A.U./cell	0.0128	*
	E	Average cell body area	C57/BL6	N=5, 4-17 cells/region/mouse	N=5, 4-15 cells/region/mouse	Two-way ANOVA w/ Tukey	Str. (Young) vs Str. (Aged)	36.36	2.217	51.73	3.09	µm ²	<0.0001	****
							Str. (Young) vs Hpc. (Young)	36.36	2.217	37.07	2.388	µm ²	0.9978	ns
							Str. (Young) vs Hpc. (Aged)	36.36	2.217	40.5	4.369	µm ²	0.6817	ns
							Str. (Aged) vs Hpc. (Young)	51.73	3.09	37.07	2.388	µm ²	0.0022	**
							Str. (Aged) vs Hpc. (Aged)	51.73	3.09	40.5	4.369	µm ²	0.0227	*
							Hpc. (Young) vs Hpc. (Aged)	37.07	2.388	40.5	4.369	µm ²	0.8782	ns
	F	Average cell body perimeter	C57/BL6	N=5, 4-17 cells/region/mouse	N=5, 4-15 cells/region/mouse	Two-way ANOVA w/ Tukey	Str. (Young) vs Str. (Aged)	23.72	0.7215	29.45	1.1	µm	<0.0001	****
							Str. (Young) vs Hpc. (Young)	23.72	0.7215	24.22	0.9237	µm	0.9871	ns
							Str. (Young) vs Hpc. (Aged)	23.72	0.7215	26.51	1.971	µm	0.2028	ns
							Str. (Aged) vs Hpc. (Young)	29.45	1.1	24.22	0.9237	µm	0.0035	**
							Str. (Aged) vs Hpc. (Aged)	29.45	1.1	26.51	1.971	µm	0.1721	ns
							Str. (Young) vs Hpc. (Young)	24.22	0.9237	26.51	1.971	µm	0.5338	ns
	G	Striatal cell body area	C57/BL6	N=5, 2-12 cells/region/mouse	N=5, 3-12 cells/region/mouse	Two-way ANOVA w/ Tukey	DMS (Young) vs DLS (Young)	36.47	2.478	38.12	2.034	µm ²	0.9849	ns
							DMS (Young) vs DMS (Aged)	36.47	2.478	48.15	2.874	µm ²	0.0674	ns
							DMS (Young) vs DLS (Aged)	36.47	2.478	57.03	5.583	µm ²	0.0005	***
							DLS (Young) vs DMS (Aged)	38.12	2.034	48.15	2.874	µm ²	0.0693	ns
							DLS (Young) vs DLS (Aged)	38.12	2.034	57.03	5.583	µm ²	0.0003	***
							DMS (Aged) vs DLS (Aged)	48.15	2.874	57.03	5.583	µm ²	0.1997	ns
	H	Striatal cell body perimeter	C57/BL6	N=5, 2-12 cells/region/mouse	N=5, 3-12 cells/region/mouse	Two-way ANOVA w/ Tukey	DMS (Young) vs DLS (Young)	23.55	0.9868	24.2	0.7286	µm	0.9813	ns
							DMS (Young) vs DMS (Aged)	23.55	0.9868	28.71	1.256	µm	0.0216	*
							DMS (Young) vs DLS (Aged)	23.55	0.9868	30.54	1.321	µm	0.0014	**
							DLS (Young) vs DMS (Aged)	24.2	0.7286	28.71	1.256	µm	0.0219	*
							DLS (Young) vs DLS (Aged)	24.2	0.7286	30.54	1.321	µm	0.001	**
							DMS (Aged) vs DLS (Aged)	28.71	1.256	30.54	1.321	µm	0.7006	ns
	I	Microglia morphology characterization	C57/BL6	N=5, 25-64 cells/mouse	N=5, 29-58 cells/mouse	No statistical tests	Group	Branch	No Branch		Units		N.A.	
							Striatum (Young)	30	46.88%	34	53.13%	# of cells		
							Striatum (Aged)	19	32.76%	39	67.24%	# of cells		
							Hippocampus (Young)	20	80.00%	5	20.00%	# of cells		
	Hippocampus (Aged)	20	68.97%	9	31.03%	# of cells								
	J	Average number of endpoints	C57/BL6	N=5, 4-17 cells/region/mouse	N=5, 4-15 cells/region/mouse	Two-way ANOVA w/ Tukey	[A] vs [B]	[A] Mean	[A] SEM	[B] Mean	[B] SEM	Units	p-value	Significance
							Str. (Young) vs Str. (Aged)	8.997	0.634	6.951	0.9349	# of endpoints	*	0.0293
							Str. (Young) vs Hpc. (Young)	8.997	0.634	5.193	0.7651	# of endpoints	***	0.0005
							Str. (Young) vs Hpc. (Aged)	8.997	0.634	4.406	0.641	# of endpoints	****	<0.0001
							Str. (Aged) vs Hpc. (Young)	6.951	0.9349	5.193	0.7651	# of endpoints	ns	0.2809
							Str. (Aged) vs Hpc. (Aged)	6.951	0.9349	4.406	0.641	# of endpoints	*	0.0384
	Str. (Young) vs Hpc. (Young)	5.193	0.7651	4.406	0.641	# of endpoints	ns	0.8946						
	K	Sholl analysis	C57/BL6	N=5, 5-26 cells/mouse	N=5, 5-29 cells/mouse	Three-way ANOVA w/ Tukey by region	Source of Variation	SS (Type III)	DF	MS	F (DFn, DFd)	p-value	Significance	
							Distance from Soma	367.8	19	19.36	F (19, 1220) = 39.62	<0.0001	****	
							Region	7.732	1	7.732	F (1, 1220) = 15.82	<0.0001	****	
							Age	0.4463	1	0.4463	F (1, 1220) = 0.9134	0.3394	ns	
Distance from Soma x Region							72.53	19	3.817	F (19, 1220) = 7.812	<0.0001	****		
Distance from Soma x Age							2.543	19	0.1338	F (19, 1220) = 0.2739	0.9992	ns		
Region x Age							0.2107	1	0.2107	F (1, 1220) = 0.4313	0.5115	ns		
Distance from Soma x Region x Age							1.9	19	0.1	F (19, 1220) = 0.2047	>0.9999	ns		
Distance from Soma (µm)							Young-Str	Young-Hpc	Aged-Str	Aged-Hpc	p-value (Hpc.)	p-value (Str.)	Significance	
0							0	1.8	0	1.655172414	0.4702	>0.9999	ns	
5							3.765757576	2.32	3.225826649	1.965517241	0.0773	0.0022	##	
10							2.943030303	1.12	2.164455214	1.206896552	0.6648	<0.0001	####	
15		1.706969697	0.56	1.926363636	0.517241379	0.8311	0.2088	ns						
20		1.079696967	0.16	0.992942291	0.275862069	0.5634	0.6184	ns						
25		0.789696967	0.12	0.558786765	0.103448276	0.9342	0.186	ns						
30		0.35	0	0.223902629	0.034482759	0.8635	0.4693	ns						
35		0.206666667	0	0.164622326	0	>0.9999	0.8092	ns						
40		0.166666667	0	0.071657754	0	>0.9999	0.5855	ns						
45		0.04	0	0	0	>0.9999	0.8183	ns						
50		0.013333333	0	0	0	>0.9999	0.939	ns						
55-100		0	0	0	0	>0.9999	>0.9999	ns						

Supplementary Table 2

Supplementary Table 2								Hippocampus						Striatum					
								Young		Aged		p-value	Significance	Young		Aged		p-value	Significance
Figure 5	Strain	Young	Aged	Statistical test	Subfigure	Experiment	Marker	Fold Change	ΔCt	Fold Change	ΔCt			Fold Change	ΔCt	Fold Change	ΔCt		
5	C57/BL6	N=5	N=5	Student t-test	A	Glial marker expression	GFAP	1.064	14.43	1.814	13.64	0.0514	ns	1.018	10.57	2.428	9.382	0.0031	**
							AQP4	1.015	16.42	1.003	16.44	0.9120	ns	1.004	11.17	1.176	10.97	0.2289	ns
							Iba1	1.030	18.87	1.307	18.51	0.1278	ns	1.007	13.13	1.480	12.59	0.0075	**
							TREM2	1.036	17.99	1.251	17.68	0.1855	ns	1.003	12.68	1.524	12.12	0.0206	*
							CD68	1.016	11.19	1.159	10.98	0.1472	ns	1.006	10.79	1.407	10.31	0.0026	**
							TLR2	1.015	16.68	2.209	15.61	0.0033	**	1.015	16.68	2.209	15.61	0.0033	**
					B	Neuroinflammatory marker expression	TLR4	1.013	16.24	1.291	15.89	0.0508	ns	1.018	16.21	1.266	15.89	0.1001	ns
							IL-1β	1.024	24.48	2.335	23.33	0.0046	**	1.047	19.83	2.022	19.05	0.1150	ns
							IL-6	1.027	18.05	1.761	17.24	0.0022	**	1.021	18.23	2.133	17.14	0.0002	***
							IL-10	Failed assumptions of ΔΔCt Method				NA	ND	Failed assumptions of ΔΔCt Method				NA	ND
							TNF-α	1.090	24.97	2.923	23.50	0.0056	**	1.066	18.99	3.707	17.28	0.0054	**
							TGF-β	1.021	20.43	1.219	20.15	0.1062	ns	1.009	20.05	1.073	19.95	0.4233	ns
					C	Complement and senescence-related marker expression	CCL2	1.055	24.45	2.714	23.04	0.0013	**	1.169	19.17	2.950	17.76	0.0286	*
							CCL5	1.007	16.71	1.774	16.04	0.0756	ns	1.027	16.54	2.508	15.36	0.0126	*
							C1qa	1.007	9.029	1.251	8.569	0.0085	**	1.000	8.871	1.353	8.445	0.0012	**
							C3	1.019	14.76	2.595	13.58	0.0163	*	1.090	15.60	4.291	13.62	0.0015	**
							C3ar1	1.007	14.92	1.383	14.60	0.0253	*	1.006	14.76	1.360	14.36	0.0912	ns
							P16	1.027	24.85	2.874	23.37	0.0002	***	1.052	13.99	2.737	12.55	0.0004	***
					D	PNN component and matrix metalloproteinase marker expression	P21	1.003	13.08	1.045	13.03	0.6630	ns	1.003	13.09	0.981	13.14	0.7251	ns
							HAPLN1	1.024	18.51	1.044	18.47	0.8103	ns	1.006	22.86	1.001	22.89	0.8450	ns
							PV	1.069	15.44	0.880	15.66	0.4806	ns	1.020	10.29	1.112	10.16	0.5205	ns
							ACAN	1.014	20.77	1.094	20.66	0.5009	ns	1.014	15.70	1.236	15.42	0.1167	ns
							MMP3	0.836	19.94	18.340	15.25	0.0004	***	1.259	18.15	2.336	17.60	0.5605	ns
							MMP3 (Retest)	1.085	16.35	19.341	12.24	<0.0001	****	1.441	15.69	3.001	15.20	0.6241	ns
							MMP9	1.007	14.80	0.844	15.06	0.0835	ns	1.009	16.14	1.274	15.80	0.0461	*
							TIMP1	1.021	17.62	1.749	16.84	0.0062	**	1.129	17.74	1.811	17.13	0.2841	ns
					Not shown	Other markers tested but not shown in Figure 5	ADAM17	1.003	8.397	0.8422	8.65	0.0165	*	1.001	10.72	1.205	10.46	0.0222	*
							IFN-γ	1.047	18.92	1.000	19.72	0.4438	ns	1.017	18.61	0.994	19.01	0.5365	ns
							TMEM119	1.004	12.17	1.211	11.92	0.0980	ns	1.004	12.17	1.211	11.92	0.0980	ns
							MMP2	1.050	15.07	0.869	15.28	0.3763	ns	1.013	15.42	1.140	15.25	0.3254	ns
							MMP13	1.015	17.18	0.674	18.00	0.0971	ns	1.418	17.26	0.654	18.02	0.2661	ns
							TLR3	1.008	13.17	1.121	13.02	0.3156	ns	1.009	13.18	1.130	13.02	0.2870	ns
							TLR5	1.032	17.34	1.160	17.17	0.5130	ns	1.047	17.30	1.175	17.12	0.5490	ns
							NFE212	1.005	13.23	1.171	13.02	0.1382	ns	1.005	13.23	1.171	13.02	0.1328	ns

Supplementary Table 3

Gene	Gene name	Company	Cat. #	Species	Color
<i>Acan</i>	<i>Aggrecan</i>	Applied Biosystems-ThermoFisher	Mm00645794_m1	Mouse	FAM
<i>Adam17</i>	<i>A disintegrin and metallopeptidase domain 17</i>	Applied Biosystems-ThermoFisher	Mm00456428_m1	Mouse	FAM
<i>Aif (Iba1)</i>	<i>Allograt inflammatory factor 1/Ionized calcium-binding adaptor molecule 1</i>	Applied Biosystems-ThermoFisher	Mm00479862_g1	Mouse	FAM
<i>Aqp4</i>	<i>Aquaporin 4</i>	Applied Biosystems-ThermoFisher	Mm00802131_m1	Mouse	FAM
<i>C1qa</i>	<i>Complement component 1, q subcomponen, alpha polypeptide</i>	Applied Biosystems-ThermoFisher	Mm00432142_m1	Mouse	FAM
<i>C3</i>	<i>Complement component 3</i>	Applied Biosystems-ThermoFisher	Mm01232779_m1	Mouse	FAM
<i>C3ar1</i>	<i>Complement component 3a receptor 1</i>	Applied Biosystems-ThermoFisher	Mm02620006_s1	Mouse	FAM
<i>Ccl2</i>	<i>Chemokine (C-C motif) ligand 2</i>	Applied Biosystems-ThermoFisher	Mm00441242_m1	Mouse	FAM
<i>Ccl5</i>	<i>Chemokine (C-C motif) ligand 5</i>	Applied Biosystems-ThermoFisher	Mm01302427_m1	Mouse	FAM
<i>Cd68</i>	<i>CD68 antigen</i>	Applied Biosystems-ThermoFisher	Mm03047343_m1	Mouse	FAM
<i>Cdkn1a (P21)</i>	<i>Cyclin-dependent kinase inhibitor 1A</i>	Applied Biosystems-ThermoFisher	Mm04205640_g1	Mouse	FAM
<i>Cdkn2a (P16)</i>	<i>Cyclin-dependent kinase inhibitor 2A</i>	Applied Biosystems-ThermoFisher	Mm00494449_m1	Mouse	FAM
<i>Gapdh</i>	<i>Glyceraldehyde-3-phosphate dehydrogenase</i>	Applied Biosystems-ThermoFisher	Mm99999915_g1	Mouse	FAM
<i>Gfap</i>	<i>Glial fibrillary acidic protein</i>	Applied Biosystems-ThermoFisher	Mm01253030_m1	Mouse	FAM
<i>Hapln1</i>	<i>Hyaluronan and proteoglycan link protein 1</i>	Applied Biosystems-ThermoFisher	Mm00488952_m1	Mouse	FAM
<i>Ifng</i>	<i>Interferon gamma</i>	Applied Biosystems-ThermoFisher	Mm01168134_m1	Mouse	FAM
<i>Il1b</i>	<i>Interleukin 1 beta</i>	Applied Biosystems-ThermoFisher	Mm00434228_m1	Mouse	FAM
<i>Il2</i>	<i>Interleukin 2</i>	Applied Biosystems-ThermoFisher	Mm00434256_m1	Mouse	FAM
<i>Il6</i>	<i>Interleukin 6</i>	Applied Biosystems-ThermoFisher	Mm00446190_m1	Mouse	FAM
<i>Il10</i>	<i>Interleukin 10</i>	Applied Biosystems-ThermoFisher	Mm00439614_m1	Mouse	FAM
<i>Mmp2</i>	<i>Matrix metallopeptidase 2</i>	Applied Biosystems-ThermoFisher	Mm00439498_m1	Mouse	FAM
<i>Mmp3</i>	<i>Matrix metallopeptidase 3</i>	Applied Biosystems-ThermoFisher	Mm00440295_m1	Mouse	FAM
<i>Mmp9</i>	<i>Matrix metallopeptidase 9</i>	Applied Biosystems-ThermoFisher	Mm00442991_m1	Mouse	FAM
<i>Mmp13</i>	<i>Matrix metallopeptidase 13</i>	Applied Biosystems-ThermoFisher	Mm00439491_m1	Mouse	FAM
<i>Nfe2l2</i>	<i>Nuclear factor, erythroid derived 2, like 2</i>	Applied Biosystems-ThermoFisher	Mm00477784_m1	Mouse	FAM
<i>Pvalb (PV)</i>	<i>Parvalbumin</i>	Applied Biosystems-ThermoFisher	Mm0043100_m1	Mouse	FAM
<i>Timp1</i>	<i>Tissue inhibitor of metalloproteinase 1</i>	Applied Biosystems-ThermoFisher	Mm01341361_m1	Mouse	FAM
<i>Tgfb1</i>	<i>Transforming growth factor, beta 1</i>	Applied Biosystems-ThermoFisher	Mm01178820_m1	Mouse	FAM
<i>Tmem119</i>	<i>Transmembrane protein 119</i>	Applied Biosystems-ThermoFisher	Mm00525305_m1	Mouse	FAM
<i>Tnf</i>	<i>Tumor necrosis factor alpha</i>	Applied Biosystems-ThermoFisher	Mm00443258_m1	Mouse	FAM
<i>Tlr2</i>	<i>Toll-like receptor 2</i>	Applied Biosystems-ThermoFisher	Mm00442346_m1	Mouse	FAM
<i>Tlr3</i>	<i>Toll-like receptor 3</i>	Applied Biosystems-ThermoFisher	Mm01207404_m1	Mouse	FAM
<i>Tlr4</i>	<i>Toll-like receptor 4</i>	Applied Biosystems-ThermoFisher	Mm00445273_m1	Mouse	FAM
<i>Tlr5</i>	<i>Toll-like receptor 5</i>	Applied Biosystems-ThermoFisher	Mm00546288_s1	Mouse	FAM
<i>Trem2</i>	<i>Triggering receptor expressed on myeloid cells 2</i>	Applied Biosystems-ThermoFisher	Mm04209422_m1	Mouse	FAM
<i>18S</i>	<i>Eukaryotic 18S rRNA</i>	Applied Biosystems-ThermoFisher	4333760F	Eukaryotic	FAM

Supplementary Table 4

Figure(s)	Experiment	Microscope Model	Objective	Pixel Size (µm) (x*y*z)	Imaging Parameters	Channel	Wavelength (nm)		Light Source		Z-Stacks		
							Excitation	Emission	Exposure time (ms)	Intensity (%)	Z-stack (µm)	Z-steps (µm)	Number of Slices
Fig. 2, Sup. Fig. 1A/C/E	Hippocampus Cell Counts & Intensity	Zeiss-Axio Imager.Z2	Plan-Apocromat 20X/0.8 M27	0.173 µm x 0.173 µm	Tiled images with 30% overlap and stitched using Zen Blue.	49 DAPI	353.0	465.0	40.0	25.0	NA	NA	NA
						38 eGFP	488.0	509.0	390.0	32.0			
						71 HcRed	590.0	618.0	40.0	25.0			
						50 Cy5	650.0	673.0	225.0	25.0			
Fig. 3A-D, Sup. Fig. 1B/D/F	Dorsal Striatum Cell Counts	Zeiss-Axio Imager.Z2	Plan-Apocromat 20X/0.8 M27	0.173 µm x 0.173 µm	Tiled images with 30% overlap and stitched using Zen Blue.	49 DAPI	353.0	465.0	40.0	25.0	NA	NA	NA
						38 eGFP	488.0	509.0	390.0	32.0			
						71 HcRed	590.0	618.0	40.0	25.0			
						50 Cy5	650.0	673.0	225.0	25.0			
Fig. 3E	Colocalization Analysis	Zeiss-Axio Imager.Z2	Plan-Apocromat 40X/0.95 Korr M27	0.086 µm x 0.086 µm x 0.340 µm	Subtract background = 20 pixels, Average projection, analyzed with JaCoP on FIJI.	49 DAPI	353.0	465.0	40.0	25.0	14.96	0.34	45
						38 eGFP	488.0	509.0	275.0	32.0			
						71 HcRed	590.0	618.0	40.0	25.0			
						50 Cy5	650.0	673.0	225.0	25.0			
Fig. 4	Regression Analysis	Zeiss-Axio Imager.Z2	Plan-Apocromat 20X/0.8 M27	0.173 µm x 0.173 µm	Regions of interests intensities normalized before plotting.	49 DAPI	353.0	465.0	40.0	25.0	NA	NA	NA
						38 eGFP	488.0	509.0	390.0	32.0			
						71 HcRed	590.0	618.0	40.0	25.0			
						50 Cy5	650.0	673.0	225.0	25.0			
Fig. 5B, Sup. Fig. 2A-C	Microglia Cell Counts & Intensity	Zeiss-Axio Imager.Z2	Plan-Apocromat 20X/0.8 M27	0.173 µm x 0.173 µm	Tiled images with 30% overlap and stitched using Zen Blue.	49 DAPI	353.0	465.0	26.0	25.0	NA	NA	NA
						50 Cy5	650.0	673.0	200.0	25.0			
Fig. 5C-K	Microglia Morphology	Leica LSM 880, AxioObserver	Plan-Apochromat 63x/1.40 Oil DIC M27	0.22 µm x 0.22 µm x 0.30 µm	Subtract background = 50 pixels, Average 2D projections.	49 DAPI	405.0	455.0	1.02 µs/pixel	2.2	15.00	0.30	51
						38 eGFP	488.0	537.0	1.02 us/pixel	2.0			