

1 **Supplementary Table 1:** Statistical analysis for figure 1.

Experiment	Groups	2-way ANOVA			Tukey's multiple comparisons test	
		Factor	F (DFn, DFd)	P Value	Comparisons	P Value
PD15: Iba1+ area (%) Hippocampus	WT	Interaction Sex MS	F(1,13)=2.41 F(1,13)=16.4 F(1,13)=13.0	0.1445 0.0014** 0.0032**	Non-MS F vs. MS F	0.5103
					Non-MS M vs. MS M	0.0113*
					Non-MS F vs. Non-MS M	0.3093
					MS F vs. MS M	0.0093**
	5xFAD	Interaction Sex MS	F(1,13)=0.527 F(1,13)=0.577 F(1,13)=1.610	0.4806 0.4610 0.2272	Non-MS F vs. MS F	0.9815
					Non-MS M vs. MS M	0.4937
					Non-MS F vs. Non-MS M	0.7388
					MS F vs. MS M	>0.999
PD15: Iba1+ area (%) Prefrontal Cortex	WT	Interaction Sex MS	F(1,16)=1.59 F(1,16)=2.40 F(1,16)=0.548	0.2254 0.1411 0.4699	Non-MS F vs. MS F	0.9823
					Non-MS M vs. MS M	0.5085
					Non-MS F vs. Non-MS M	0.9969
					MS F vs. MS M	0.2337
	5xFAD	Interaction Sex MS	F(1,16)=0.420 F(1,16)=2.750 F(1,16)=0.014	0.5261 0.1169 0.9055	Non-MS F vs. MS F	0.9469
					Non-MS M vs. MS M	0.9817
					Non-MS F vs. Non-MS M	0.8903
					MS F vs. MS M	0.3906
PD15: Microglia morphology (%) Hippocampus	WT	Ramified With stout processes Round/ameboid			Non-MS F vs. MS F	0.9380 0.9969 0.8614
					Non-MS M vs. MS M	0.9999 0.9299 0.9072
					Non-MS F vs. Non-MS M	0.9529 0.9906 0.8435
					MS F vs. MS M	>0.9999 0.9143

						0.9072		
	5xFAD	Ramified With stout processes Round/ameboid				Non-MS F vs. MS F	0.9907 0.9828 0.9999	
Non-MS M vs. MS M						0.9936 0.7848 0.9057		
Non-MS F vs. Non-MS M						0.9874 0.9914 >0.9999		
MS F vs. MS M						0.9780 0.9947 0.9163		
PD15: Microglia morphology (%) Prefrontal Cortex	WT	Ramified With stout processes Round/ameboid				Non-MS F vs. MS F	0.9884 0.0055** 0.0021**	
						Non-MS M vs. MS M	0.7510 0.9800 0.5141	
						Non-MS F vs. Non-MS M	0.9780 0.0692 0.1611	
						MS F vs. MS M	0.3246 0.5285 0.0173*	
	5xFAD	Ramified With stout processes Round/ameboid					Non-MS F vs. MS F	0.9941 0.6262 0.7777
							Non-MS M vs. MS M	0.2831 0.9678 0.5373
							Non-MS F vs. Non-MS M	0.4133 0.6007 0.9897
							MS F vs. MS M	0.9573 0.9753 0.9997
PD15: CXCL1 Hippocampus	WT	Interaction Sex MS	F(1,16)=0.134 F(1,16)=8.93 F(1,16)=1.44	0.7190 0.0087** 0.2471		Non-MS F vs. MS F	0.6897	
						Non-MS M vs. MS M	0.9335	
						Non-MS F vs. Non-MS M	0.1231	
						MS F vs. MS M	0.2856	
	5xFAD	Interaction Sex MS	F(1,15)=1.12 F(1,15)=0.441 F(1,15)=0.0379	0.3048 0.5161 0.8481			Non-MS F vs. MS F	0.8114
							Non-MS M vs. MS M	0.9268
							Non-MS F vs. Non-MS M	0.9920

					MS F vs. MS M	0.6241
PD15: TNF-α Hippocampus	WT	Interaction Sex MS	F(1,16)=0.00114 F(1,16)=7.36 F(1,16)=0.00666	0.9735 0.0154* 0.9360	Non-MS F vs. MS F	>0.999
					Non-MS M vs. MS M	0.9998
					Non-MS F vs. Non-MS M	0.2502
					MS F vs. MS M	0.2690
	5xFAD	Interaction Sex MS	F(1,16)=4.54 F(1,16)=0.374 F(1,16)=0.033	0.0489* 0.5494 0.8581	Non-MS F vs. MS F	0.3876
					Non-MS M vs. MS M	0.5294
					Non-MS F vs. Non-MS M	0.2511
					MS F vs. MS M	0.7091

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4 **Supplementary Table 2:** Statistical analysis for figure 2.

Experiment	Groups	2-way ANOVA			Tukey's multiple comparisons test	
		Factor	F (DFn, DFd)	P Value	Comparisons	P Value
4 months: Open Field Test	WT	Interaction	F(1,26)=0.0434	0.8366	Non-MS F vs. MS F	0.6126
		Sex	F(1,26)=4.080	0.0537	Non-MS M vs. MS M	0.7368
		MS	F(1,26)=2.560	0.1216	Non-MS F vs. Non-MS M	0.3746
					MS F vs. MS M	0.6110
	5xFAD	Interaction	F(1,37)=4.890	0.0332*	Non-MS F vs. MS F	0.3750
		Sex	F(1,37)=0.453	0.5053	Non-MS M vs. MS M	0.4504
		MS	F(1,37)=0.0386	0.8453	Non-MS F vs. Non-MS M	0.1121
					MS F vs. MS M	0.7601
4 months: Forced Swim Test	WT	Interaction	F(1,24)=0.586	0.4513	Non-MS F vs. MS F	0.0707
		Sex	F(1,24)=1.920	0.1781	Non-MS M vs. MS M	0.003**
		MS	F(1,24)=20.80	0.0001***	Non-MS F vs. Non-MS M	0.4358
					MS F vs. MS M	0.9714
	5xFAD	Interaction	F(1,36)=1.40	0.244	Non-MS F vs. MS F	0.0269*
		Sex	F(1,36)=0.168	0.6845	Non-MS M vs. MS M	0.3792
		MS	F(1,36)=10.9	0.0022**	Non-MS F vs. Non-MS M	0.6567
					MS F vs. MS M	0.9502
4 months: Novel Object Recognition Memory Test	WT	Interaction	F(1,19)=0.0014	0.9698	Non-MS F vs. MS F	0.0390*
		Sex	F(1,19)=0.213	0.6498	Non-MS M vs. MS M	0.0426*
		MS	F(1,19)=17.00	0.0006***	Non-MS F vs. Non-MS M	0.9899
					MS F vs. MS M	0.9851
	5xFAD	Interaction	F(1,22)=0.0901	0.7668	Non-MS F vs. MS F	0.0400*
		Sex	F(1,22)=7.06	0.0144*	Non-MS M vs. MS M	0.0572
		MS	F(1,22)=15.7	0.0007***	Non-MS F vs. Non-MS M	0.1563
					MS F vs. MS M	0.4015
4 months: HP gene expression <i>Bdnf</i>	WT	Interaction	F(1,18)=1.68	0.2109	Non-MS F vs. MS F	0.4331
		Sex	F(1,18)=1.77	0.1998	Non-MS M vs. MS M	0.0160*
		MS	F(1,18)=12.1	0.0027**	Non-MS F vs. Non-MS M	0.2799
					MS F vs. MS M	>0.9999
	5xFAD	Interaction	F(1,19)=2.50	0.1307	Non-MS F vs. MS F	0.8942
		Sex	F(1,19)=0.072	0.7913	Non-MS M vs. MS M	0.034*
		MS	F(1,19)=6.72	0.0179*	Non-MS F vs. Non-MS M	0.5828
					MS F vs. MS M	0.7823
4 months: HP gene expression <i>Arc</i>	WT	Interaction	F(1,18)=1.180	0.2918	Non-MS F vs. MS F	0.6909
		Sex	F(1,18)=0.0909	0.7655	Non-MS M vs. MS M	0.9724
		MS	F(1,18)=0.228	0.6391	Non-MS F vs. Non-MS M	0.7618
					MS F vs. MS M	0.9440
	5xFAD	Interaction	F(1,22)=16.6	0.0005***	Non-MS F vs. MS F	0.0842
		Sex	F(1,22)=0.0931	0.7632	Non-MS M vs. MS M	0.0185*
		MS	F(1,22)=0.254	0.6194	Non-MS F vs. Non-MS M	0.0253*

					MS F vs. MS M	0.0634
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7 **Supplementary Table 3:** Statistical analysis for figure 3.

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Experiment	Groups	2-way ANOVA			Tukey's multiple comparisons test	
		Factor	F (DFn, DFd)	P Value	Comparisons	P Value
4 months: Iba1+ area (%) Prefrontal Cortex	WT	Interaction Sex MS	F(1,21)=0.898	0.3451	Non-MS F vs. MS F	0.4640
			F(1,21)=1.26	0.2749	Non-MS M vs. MS M	0.0365*
			F(1,21)=9.61	0.0054**	Non-MS F vs. Non-MS M	0.9994
					MS F vs. MS M	0.4542
	5xFAD	Interaction Sex MS	F(1,22)=5.49	0.0286*	Non-MS F vs. MS F	0.0829
			F(1,22)=4.77	0.0400*	Non-MS M vs. MS M	0.8893
			F(1,22)=1.87	0.1850	Non-MS F vs. Non-MS M	0.9995
					MS F vs. MS M	0.020*
4 months: CD68+ area related to Iba1+ area (%) Prefrontal Cortex	WT	Interaction Sex MS	F(1,15)=0.126	0.7278	Non-MS F vs. MS F	0.6945
			F(1,15)=0.763	0.3961	Non-MS M vs. MS M	0.4478
			F(1,15)=3.48	0.0819	Non-MS F vs. Non-MS M	0.8074
					MS F vs. MS M	0.9838
	5xFAD	Interaction Sex MS	F(1,16)=4.07	0.0606	Non-MS F vs. MS F	0.9183
			F(1,16)=4.56	0.0485*	Non-MS M vs. MS M	0.1608
			F(1,16)=1.25	0.2806	Non-MS F vs. Non-MS M	0.9998
					MS F vs. MS M	0.0431*
4 months: 6E10+ area (%) Prefrontal Cortex	5xFAD	Interaction Sex MS	F(1,23)=0.619	0.4396	Non-MS F vs. MS F	0.3647
			F(1,23)=0.246	0.6246	Non-MS M vs. MS M	0.9044
			F(1,23)=2.86	0.1043	Non-MS F vs. Non-MS M	0.8082
					MS F vs. MS M	0.9967
4 months: Gal-3+ area (%) Prefrontal Cortex	5xFAD	Interaction Sex MS	F(1,11)=2.76	0.1251	Non-MS F vs. MS F	0.1313
			F(1,11)=3.57	0.0853	Non-MS M vs. MS M	0.9875
			F(1,11)=4.30	0.0625	Non-MS F vs. Non-MS M	0.9985
					MS F vs. MS M	0.1029
4 months: Congo Red Prefrontal Cortex	5xFAD	Interaction Sex MS	F(1,23)=1.28	0.2967	Non-MS F vs. MS F	0.0276*
			F(1,23)=5.11	0.0336*	Non-MS M vs. MS M	0.4032
			F(1,23)=10.9	0.0031**	Non-MS F vs. Non-MS M	0.8289
					MS F vs. MS M	0.1365
4 months: Soluble Fraction Prefrontal Cortex	5xFAD	Interaction Sex MS	F(1,10)=0.964	0.3494	Non-MS F vs. MS F	0.3138
			F(1,10)=3.150	0.1061	Non-MS M vs. MS M	0.9690
			F(1,10)=2.60	0.1380	Non-MS F vs. Non-MS M	0.9411
					MS F vs. MS M	0.2684
4 months: Protofibrils Prefrontal Cortex	5xFAD	Interaction Sex MS	F(1,16)=1.72	0.2080	Non-MS F vs. MS F	0.0795
			F(1,16)=11.9	0.0033**	Non-MS M vs. MS M	0.8563
			F(1,16)=5.87	0.0276*	Non-MS F vs. Non-MS M	0.4105
					MS F vs. MS M	0.0256*
4 months: Dense Plaques Prefrontal Cortex	5xFAD	Interaction Sex MS	F(1,10)=1.270	0.2867	Non-MS F vs. MS F	0.4491
			F(1,10)=0.122	0.7343	Non-MS M vs. MS M	0.9987
			F(1,10)=0.804	0.3909	Non-MS F vs. Non-MS M	0.9447
					MS F vs. MS M	0.7296

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11 **Supplementary Table 4:** Statistical analysis for figure 4.

Experiment	Groups	2-way ANOVA			Tukey's multiple comparisons test	
		Factor	F (DFn, DFd)	P Value	Comparisons	P Value
4 months: Inflamm. Monocytes	WT	Interaction Sex MS	F(1, 32)=0.0145 F(1, 32)=0.783 F(1, 32)=9.61	0.9048 0.3827 0.0040**	Non-MS F vs. MS F	0.1092
					Non-MS M vs. MS M	0.1913
					Non-MS F vs. Non-MS M	0.8928
					MS F vs. MS M	0.9479
	5xFAD	Interaction Sex MS	F(1, 28)=2.75 F(1, 28)=12.4 F(1, 28)=13.2	0.1086 0.0015** 0.0011**	Non-MS F vs. MS F	0.3789
					Non-MS M vs. MS M	0.0123*
					Non-MS F vs. Non-MS M	0.5146
					MS F vs. MS M	0.0085*
4 months: Cytotoxic T Cells	WT	Interaction Sex MS	F(1, 32)=2.81 F(1, 32)=4.82 F(1, 32)=5.70	0.1033 0.0356* 0.0231*	Non-MS F vs. MS F	0.0281*
					Non-MS M vs. MS M	0.9611
					Non-MS F vs. Non-MS M	0.0478*
					MS F vs. MS M	0.9828
	5xFAD	Interaction Sex MS	F(1, 28)=0.0043 F(1, 28)=4.90 F(1, 28)=14.4	0.9478 0.0353* 0.0007***	Non-MS F vs. MS F	0.0227*
					Non-MS M vs. MS M	0.0940
					Non-MS F vs. Non-MS M	0.3924
					MS F vs. MS M	0.4323
4 months: Dendritic Cells	WT	Interaction Sex MS	F(1, 32)=1.10 F(1, 32)=2.40 F(1, 32)=1.59	0.3020 0.1312 0.2163	Non-MS F vs. MS F	0.3498
					Non-MS M vs. MS M	0.9989
					Non-MS F vs. Non-MS M	0.2777
					MS F vs. MS M	0.9844
	5xFAD	Interaction Sex MS	F(1, 28)=1.76 F(1, 28)=2.95 F(1, 28)=4.74	0.1957 0.0971 0.0381*	Non-MS F vs. MS F	0.8957
					Non-MS M vs. MS M	0.1470
					Non-MS F vs. Non-MS M	0.9911
					MS F vs. MS M	0.1958
4 months: Eosinophils	WT	Interaction Sex MS	F(1, 32)=0.343 F(1, 32)=5.04 F(1, 32)=5.17	0.5625 0.0317* 0.0298*	Non-MS F vs. MS F	0.1810
					Non-MS M vs. MS M	0.6544
					Non-MS F vs. Non-MS M	0.6493
					MS F vs. MS M	0.2062
	5xFAD	Interaction Sex MS	F(1, 28)=0.482 F(1, 28)=1.26 F(1, 28)=2.71	0.4932 0.2712 0.1107	Non-MS F vs. MS F	0.2393
					Non-MS M vs. MS M	0.9314
					Non-MS F vs. Non-MS M	0.9884
					MS F vs. MS M	0.6184
4 months: Neutrophils	WT	Interaction Sex MS	F(1, 32)=1.43 F(1, 32)=7.66 F(1, 32)=0.234	0.2407 0.0093** 0.6318	Non-MS F vs. MS F	0.6177
					Non-MS M vs. MS M	0.9608
					Non-MS F vs. Non-MS M	0.0413*
					MS F vs. MS M	0.6831
	5xFAD	Interaction Sex MS	F(1, 28)=0.980 F(1, 28)=7.14 F(1, 28)=5.59	0.3308 0.0124* 0.0253*	Non-MS F vs. MS F	0.6735
					Non-MS M vs. MS M	0.1747
					Non-MS F vs. Non-MS M	0.5962

					MS F vs. MS M	0.0882
4 months: Activated T helper	WT	Interaction Sex MS	F(1, 32)=1.75 F(1, 32)=1.51 F(1, 32)=7.80	0.1959 0.2287 0.0087**	Non-MS F vs. MS F	0.7094
					Non-MS M vs. MS M	0.0379*
					Non-MS F vs. Non-MS M	0.2947
					MS F vs. MS M	0.9999
	5xFAD	Interaction Sex MS	F(1, 28)=0.0238 F(1, 28)=1.42 F(1, 28)=0.24	0.8785 0.2441 0.6277	Non-MS F vs. MS F	0.9508
					Non-MS M vs. MS M	0.9966
					Non-MS F vs. Non-MS M	0.8654
					MS F vs. MS M	0.8028
4 months: Activated T cytotoxic	WT	Interaction Sex MS	F(1, 32)=2.02 F(1, 32)=0.0467 F(1, 32)=4.02	0.1650 0.8302 0.0536	Non-MS F vs. MS F	0.9739
					Non-MS M vs. MS M	0.1064
					Non-MS F vs. Non-MS M	0.8305
					MS F vs. MS M	0.6551
	5xFAD	Interaction Sex MS	F(1, 28)=2.34 F(1, 28)=0.398 F(1, 28)=0.835	0.1370 0.5332 0.3687	Non-MS F vs. MS F	0.9564
					Non-MS M vs. MS M	0.4293
					Non-MS F vs. Non-MS M	0.9065
					MS F vs. MS M	0.4777

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14 **Supplementary Table 5:** Statistical analysis for figure Supplementary 1.

Experiment	Groups	2-way ANOVA			Tukey's multiple comparisons test	
		Factor	F (DFn, DFd)	P Value	Comparisons	P Value
4 months: Iba1 Dentate Gyrus	WT	Interaction	F(1,24)=0.315	0.5800	Non-MS F vs. MS F	0.9977
		Sex	F(1,24)=1.140	0.2965	Non-MS M vs. MS M	0.8048
		MS	F(1,24)=0.646	0.4296	Non-MS F vs. Non-MS M	0.6469
					MS F vs. MS M	0.9848
	5xFAD	Interaction	F(1,22)=0.868	0.3617	Non-MS F vs. MS F	0.9557
		Sex	F(1,22)=2.22	0.1501	Non-MS M vs. MS M	0.8366
		MS	F(1,22)=0.0241	0.8780	Non-MS F vs. Non-MS M	0.9807
					MS F vs. MS M	0.3060
4 months: Iba1 CA1	WT	Interaction	F(1,24)=0.849	0.3660	Non-MS F vs. MS F	0.9360
		Sex	F(1,24)=0.934	0.3433	Non-MS M vs. MS M	0.8909
		MS	F(1,24)=0.025	0.8744	Non-MS F vs. Non-MS M	0.5328
					MS F vs. MS M	>0.999
	5xFAD	Interaction	F(1,22)=0.775	0.3882	Non-MS F vs. MS F	0.7631
		Sex	F(1,22)=2.560	0.1241	Non-MS M vs. MS M	0.9966
		MS	F(1,22)=0.368	0.5501	Non-MS F vs. Non-MS M	0.9608
					MS F vs. MS M	0.2873
4 months: Iba1 CA3	WT	Interaction	F(1,23)=1.78	0.1950	Non-MS F vs. MS F	0.9610
		Sex	F(1,23)=0.078	0.7826	Non-MS M vs. MS M	0.5378
		MS	F(1,23)=0.465	0.5021	Non-MS F vs. Non-MS M	0.6675
					MS F vs. MS M	0.8776
	5xFAD	Interaction	F(1,22)=0.274	0.6061	Non-MS F vs. MS F	0.9294
		Sex	F(1,22)=1.270	0.2716	Non-MS M vs. MS M	0.9997
		MS	F(1,22)=0.157	0.6953	Non-MS F vs. Non-MS M	0.9759
					MS F vs. MS M	0.6227
4 months: Iba1 Amygdala	WT	Interaction	F(1,21)=1.560	0.2252	Non-MS F vs. MS F	0.9659
		Sex	F(1,21)=0.307	0.5856	Non-MS M vs. MS M	0.5906
		MS	F(1,21)=0.384	0.5419	Non-MS F vs. Non-MS M	0.9642
					MS F vs. MS M	0.5544
	5xFAD	Interaction	F(1,24)=1.53	0.2281	Non-MS F vs. MS F	0.8512
		Sex	F(1,24)=0.35	0.5595	Non-MS M vs. MS M	0.7662
		MS	F(1,24)=0.0004	0.9845	Non-MS F vs. Non-MS M	0.9710
					MS F vs. MS M	0.5433
4 months: Congo Red HP	5xFAD	Interaction	F(1,25)=0.627	0.4359	Non-MS F vs. MS F	0.9936
		Sex	F(1,25)=17.6	0.0003***	Non-MS M vs. MS M	0.8083
		MS	F(1,25)=0.162	0.6906	Non-MS F vs. Non-MS M	0.0913
					MS F vs. MS M	0.0100
4 months: Congo Red Amygdala	5xFAD	Interaction	F(1,22)=1.54	0.2283	Non-MS F vs. MS F	0.9714
		Sex	F(1,22)=3.87	0.0620	Non-MS M vs. MS M	0.5402
		MS	F(1,22)=0.356	0.5570	Non-MS F vs. Non-MS M	0.9533

					MS F vs. MS M	0.1438
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