

SUPPLEMENTARY INFORMATION

Fig. S1: Battery of behavioral tests. Mice were subjected to a battery of behavioral tests over a period of 3 weeks consisting of hindlimb claspings, open field, elevated plus maze, Y-maze spontaneous alternation, and object location memory. A description of the characteristics of each test and the sequence time in the performance is indicated

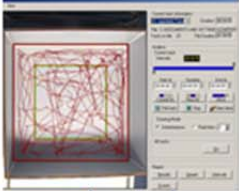
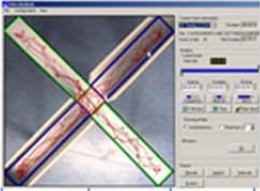
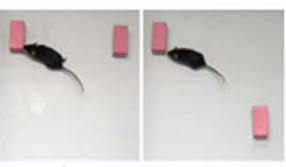
REFLECTION		ANXIETY TEST		COGNITIVE TEST	
Hindlimb claspings		Open Field	Elevated Plus Maze	Y-maze	Object location
					
1 day		1 day	1 day	1 day	2 days
Week 1		Week 2		Week 3	
<u>Clasping trial:</u> 10 sec		<u>Open Field trial:</u> 5 min	<u>Elevated plus maze trial:</u> 5 min	<u>Alternation trial:</u> 5 min	<u>Habituation trial:</u> 10 min on day 1 <u>Sample trial:</u> 5 min on day 2 <u>Object location trial:</u> 5 min on day 2

Table S1: Descriptive and inferential statistical summary table of behavioral and histopathological variables analyzed throughout this study. The table details the behavioral test or histological analysis with the variable name and the statistical test used (^a) no parametric or ^b) parametric or ^c) parametric equal variances not assumed), the corresponding test statistic (chi-squared for non-parametric test or F test for a parametric test) and significance (p-value): *p<0.05, **p<0.01, ***p<0.001. To assess the effect size of the interventions in multiple comparisons, Cohen's delta coefficient (d) was calculated and scored as negligible (d < 0.20), small (d≥0.20), medium (d≥0.50), large (d≥0.80), and much larger (d≥1.00) size effect (see Materials and Methods). Table shows mean ± sem for each variable with the significance (p-value) and the effect size of the multiple comparisons between-groups and within-groups. In bold, significant values p<0.05 and large or much large delta coefficients.

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Openfield: % Travelled distance in center ^{b)}	F = 0.376 p=0.544		Water	Riluzole	within-group effects	
		WT	20.61 ± 4.00	21.21 ± 2.17	p=0.9986	d = - 0.0699 negligible
		KO	27.58 ± 2.69	24.71 ± 2.34	p=0.8964	d = 0.3864 small
		between-group effect	p=0.4197	p=0.7406		
			d = - 0.7735 medium	d = - 0.4666 small		
Openfield: % Travelled distance in center ^{a)}	$\sigma^2d = 6.273$ p=0.099		Saline	Memantine	within-group effects	
		WT	19.97 ± 2.13			
		KO	26.17 ± 2.49	24.36 ± 2.79	p=0.5930	d = 0.1794 negligible
		between-group effect	p=0.0730			
			d = - 0.7132 medium			
Openfield: % Travelled distance in center ^{a)}	$\sigma^2d = 10.14$ p=0.017*		Vehicle	Resveratrol	within-group effects	
		WT	16.38 ± 2.27	22.5 ± 2.31	p=0.1084	d = - 0.6892 medium
		KO	22.10 ± 2.77	14.64 ± 2.15	p=0.0108*	d = 0.7939 large
		between-group effect	p=0.1661	p=0.0053**		
			d = - 0.5954 small	d = 0.9075 large		
Openfield: % Travelled distance in center ^{a)}	$\sigma^2d = 6.273$ p=0.099		Saline	Minocycline	within-group effects	
		WT	19.97 ± 2.13			
		KO	26.17 ± 2.49	18.01 ± 2.24	p=0.0320*	d = 0.9525 large
		between-group effect	p=0.0730			
			d = - 0.7132 medium			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Openfield: Entries into center (n°) ^{b)}	F = 0.376 p=0.544		Water	Riluzole	within-group effects	
		WT	15.42 ± 3.21	12.5 ± 1.99	p=0.8944	d = 0.3960 small
		KO	22.83 ± 4.44	18.68 ± 2.73	p=0.7773	d = 0.4274 small
		between-group effect	p=0.4219	p=0.3475		
			d = - 0.7657 medium	d = - 0.7784 medium		
Openfield: Entries into center (n°) ^{a)}	$\sigma^2d = 9.966$ p=0.018*		Saline	Memantine	within-group effects	
		WT	16.92 ± 2.19			
		KO	21.92 ± 2.53	17.46 ± 2.92	p=0.1669	d = 0.4295 small
		between-group effect	p=0.2386			
			d = - 0.5642 medium			
Openfield: Entries into center (n°) ^{a)}	$\sigma^2d = 4.028$ p=0.258		Vehicle	Resveratrol	within-group effects	
		WT	10.86 ± 2.30	15.93 ± 2.24	p=0.0570	d = - 0.5749 medium
		KO	13.42 ± 1.51	12.00 ± 1.63	p=0.5310	d = 0.2369 small
		between-group effect	p=0.1710	p=0.2530		
			d = - 0.3402 small	d = 0.5163 medium		
Openfield: Entries into center (n°) ^{a)}	$\sigma^2d = 9.966$ p=0.018*		Saline	Minocycline	within-group effects	
		WT	16.92 ± 2.19			
		KO	21.92 ± 2.53	9.63 ± 1.47	p=0.0017**	d = 1.5724 much large
		between-group effect	p=0.2386			
			d = - 0.5642 medium			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Elevated plus maze: %Permanence time in open arms ^{a)}	$\sigma^2d = 4.658$ $p=0.198$		Water	Riluzole	within-group effects	
		WT	9.18 ± 2.61	18.47 ± 4.99	p=0.1830	d = - 0.7139 medium
		KO	23.88 ± 5.60	20.03 ± 6.46	p=0.4010	d = 0.2002 small
		between-group effect	p=0.0340*	p=0.8200		
			d = - 1.3906 much large	d = - 0.0825 negligible		
Elevated plus maze: %Permanence time in open arms ^{a)}	$\sigma^2d = 5.675$ $p=0.339$		Saline	Memantine	within-group effects	
		WT	18.26 ± 3.48			
		KO	20.56 ± 3.77	18.53 ± 3.51	p=0.8500	d = 0.1409 negligible
		between-group effect	p=0.7500			
			d = - 0.1605 negligible			
Elevated plus maze: %Permanence time in open arms ^{b)}	F = 2.766 $p=0.101$		Vehicle	Resveratrol	within-group effects	
		WT	19.30 ± 3.02	13.28 ± 1.83	p=0.3772	d = 0.6216 medium
		KO	14.79 ± 2.39	17.60 ± 3.12	p=0.8795	d = - 0.2629 small
		between-group effect	p=0.6352	p=0.6533		
			d = 0.4305 small	d = - 0.4360 small		
Elevated plus maze: %Permanence time in open arms ^{a)}	$\sigma^2d = 5.675$ $p=0.339$		Saline	Minocycline	within-group effects	
		WT	18.26 ± 3.48			
		KO	20.56 ± 3.77	26.00 ± 5.27	p=0.8500	d = - 0.3063 small
		between-group effect	p=0.7500			
			d = - 0.1605 negligible			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Elevated plus maze: Entries into arms ^{b)}	F = 0.744 p=0.394		Water	Riluzole	within-group effects	
		WT	32.71 ± 5.72	33.54 ± 5.75	p=0.9995	d = - 0.0469 negligible
		KO	41.00 ± 6.40	32.63 ± 2.88	p=1.0000	d = 0.6991 medium
		between-group effect	p=0.7621	p=0.9995		
			d = - 0.5383 medium	d = 0.0601 negligible		
Elevated plus maze: Entries into arms ^{a)}	σ^2d = 4.329 p=0.228		Saline	Memantine	within-group effects	
		WT	32.93 ± 4.23			
		KO	38.53 ± 4.38	38.75 ± 6.04	p=0.6600	d = - 0.0103 negligible
		between-group effect	p=0.3100			
			d = - 0.3300 small			
Elevated plus maze: Entries into arms ^{b)}	F = 0.229 p=0.633		Vehicle	Resveratrol	within-group effects	
		WT	31.73 ± 3.41	34.4 ± 3.51	p=0.9601	d = - 0.1987 negligible
		KO	34.35 ± 3.15	33.33 ± 4.97	p=0.9976	d = 0.0635 negligible
		between-group effect	p=0.9637	p=0.9972		
			d = - 0.2090 small	d = 0.0639 negligible		
Elevated plus maze: Entries into arms ^{a)}	σ^2d = 4.329 p=0.228		Saline	Minocycline	within-group effects	
		WT	32.93 ± 4.23			
		KO	38.53 ± 4.38	25.33 ± 3.33	p=0.0500	d = 0.8753 large
		between-group effect	p=0.3100			
			d = - 0.3300 small			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Y-maze: % Alternations ^{b)}	F = 0.597 p=0.445		Water	Riluzole	within-group effects	
		WT	70.66 ± 6.42	62.01 ± 4.97	p=0.5683	d = 0.5493 medium
		KO	58.43 ± 2.51	56.98 ± 3.20	p=0.9960	d = 0.1550 negligible
		between-group effect	p=0.3689	p=0.8069		
			d = 1.0232 much large	d = 0.3732 small		
Y-maze: % Alternations ^{a)}	σ^2d = 1.050 p=0.789		Saline	Memantine	within-group effects	
		WT	55.89 ± 4.64			
		KO	49.22 ± 3.81	54.61 ± 5.57	p=0.7200	d = - 0.2832 small
		between-group effect	p=0.3100			
			d = 0.4055 small			
Y-maze: % Alternations ^{b)}	F = 0.187 p=0.666		Vehicle	Resveratrol	within-group effects	
		WT	60.24 ± 3.84	52.37 ± 4.09	p=0.5813	d = 0.5208 medium
		KO	60.23 ± 5.45	48.55 ± 4.05	p=0.2562	d = 0.6492 medium
		between-group effect	p=1.0000	p=0.9286		
			d = 0.0008 negligible	d = 0.2504 small		
Y-maze: % Alternations ^{a)}	σ^2d = 1.050 p=0.789		Saline	Minocycline	within-group effects	
		WT	55.89 ± 4.64			
		KO	49.22 ± 3.81	54.65 ± 7.35	p=0.7100	d = - 0.2583 small
		between-group effect	p=0.3100			
			d = 0.4055 small			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Y-maze: % Incomplete alternations ^{b)}	F = 0.944 p=0.339		Water	Riluzole	within-group effects	
		WT	33.14 ± 7.03	39.48 ± 8.51	p=0.9497	d = - 0.2650 small
		KO	53.54 ± 9.10	43.74 ± 6.56	p=0.8342	d = 0.4459 small
		between-group effect	p=0.4271	p=0.9736		
			d = - 1.0233 much large	d = - 0.1751 negligible		
Y-maze: % Incomplete alternations ^{a)}	σ^2d = 6.958 p=0.073		Saline	Memantine	within-group effects	
		WT	15.03 ± 5.90			
		KO	40.38 ± 7.40	19.11 ± 6.18	p=0.0350*	d = 0.7955 medium
		between-group effect	p=0.0170*			
			d = - 0.9767 large			
Y-maze: % Incomplete alternations ^{b)}	F = 0.264 p=0.609		Vehicle	Resveratrol	within-group effects	
		WT	37.83 ± 6.75	27.11 ± 7.27	p=0.7410	d = 0.4016 small
		KO	35.04 ± 8.90	32.07 ± 7.06	p=0.9924	d = 0.0988 negligible
		between-group effect	p=0.9934	p=0.9670		
			d = 0.0934 negligible	d = - 0.1846 negligible		
Y-maze: % Incomplete alternations ^{a)}	σ^2d = 6.958 p=0.073		Saline	Minocycline	within-group effects	
		WT	15.03 ± 5.90			
		KO	40.38 ± 7.40	20.46 ± 6.06	p=0.0780	d = 0.7955 medium
		between-group effect	p=0.0170*			
			d = - 0.9767 large			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
OLM: DI ^{b)}	F = 3.197 p=0.083		Water	Riluzole	within-group effects	
		WT	-30.26 ± 11.38	-14.88 ± 11.97	p=0.8405	d = - 0.4222 small
		KO	19.78 ± 8.34	-12.95 ± 14.26	p=0.3508	d = 0.8106 large
		between-group effect	p=0.1100	p=0.9994		
			d = - 1.9123 much large	d = - 0.0442 negligible		
OLM: DI ^{b)}	F = 0.659 p=0.580		Saline	Memantine	within-group effects	
		WT	-10.79 ± 7.68			
		KO	-2.93 ± 7.74	-14.36 ± 5.97	p=0.6742	d = 0.4265 small
		between-group effect	p=0.8596			
			d = - 0.2585 small			
OLM: DI ^{a)}	σ^2d = 2.632 p=0.451		Vehicle	Resveratrol	within-group effects	
		WT	-23.74 ± 7.09	-15.17 ± 6.12	p=0.2200	d = - 0.3334 small
		KO	-13.77 ± 9.56	-7.31 ± 10.02	p=0.5700	d = - 0.1727 negligible
		between-group effect	p=0.3500	p=0.7500		
			d = - 0.3138 small	d = - 0.2444 small		
OLM: DI ^{b)}	F = 0.659 p=0.580		Saline	Minocycline	within-group effects	
		WT	-10.79 ± 7.68			
		KO	-2.93 ± 7.74	-2.59 ± 6.97	p=0.9999	d = - 0.0122 negligible
		between-group effect	p=0.8596			
			d = - 0.2585 small			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
OLM: Activity time (s) ^{b)}	F = 0.0001 p=0.991		Water	Riluzole	within-group effects	
		WT	107.85 ± 21.21	138.45 ± 14.17	p=0.4728	d = - 0.6042 medium
		KO	102 ± 9.80	132.90 ± 11.40	p=0.5056	d = - 0.9131 large
		between-group effect	p=0.9949	p= 0.9904		
			d = 0.1315 negligible	d = 0.1299 negligible		
OLM: Activity time (s) ^{a)}	σ2d = 6.619 p=0.085		Saline	Memantine	within-group effects	
		WT	157 ± 12.22			
		KO	196.86 ± 14.10	145.26 ± 15.73	p=0.0160*	d = 0.8917 large
		between-group effect	p=0.0480*			
			d = - 0.7706 medium			
OLM: Activity time (s) ^{a)}	σ2d = 1.832 p=0.608		Vehicle	Resveratrol	within-group effects	
		WT	87.66 ± 9.21	73.33 ± 7.70	p=0.2000	d = 0.4356 small
		KO	80.35 ± 10.78	81.53 ± 11.08	p=0.9200	d = - 0.0282 negligible
		between-group effect	p=0.3900	p=0.7600		
			d = 0.1923 negligible	d = - 0.2218 small		
OLM: Activity time (s) ^{a)}	σ2d = 6.619 p=0.085		Saline	Minocycline	within-group effects	
		WT	157 ± 12.22			
		KO	196.86 ± 14.10	168.00 ± 12.15	p=0.331	d = 0.5725 medium
		between-group effect	p=0.0480*			
			d = - 0.7706 medium			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
PAS: % PGs number vs KO ^{c)}	F =20.68 p=0.0008***		Water	Riluzole	within-group effects	
		WT	1.18 ± 0.77	0.78 ± 0.21	p=0.9500	d = 0.4103 small
		KO	100.00 ± 17.31	60.23 ± 9.26	p=0.2600	d = 1.1345 much large
		between-group effect	p=0.0100**	p=0.0010**		
			d = - 2.7564 much large	d = - 2.1199 much large		
PAS: % PGs number vs KO ^{a)}	σ2d = 8.714 p=0.033*		Saline	Memantine	within-group effects	
		WT	3.54 ± 0.26			
		KO	100.00 ± 4.71	84.76 ± 8.79	p=0.2642	d = 0.8801 large
		between-group effect	p=0.0056**			
			d = - 9.8801 much large			
PAS: % PGs number vs KO ^{a)}	σ2d = 14.44 p=0.002**		Vehicle	Resveratrol	within-group effects	
		WT	12.22 ± 2.95	124.65 ± 3.15	p=0.9021	d = - 0.4583 small
		KO	100.00 ± 7.26	98.34 ± 8.58	p=0.8640	d = 0.0548 negligible
		between-group effect	p=0.0051**	p=0.0101*		
			d = - 3.6061 much large	d = - 2.6847 much large		
PAS: % PGs number vs KO ^{a)}	σ2d = 8.714 p=0.033*		Saline	Minocycline	within-group effects	
		WT	3.54 ± 0.26			
		KO	100.00 ± 4.71	98.03 ± 4.51	p=0.7801	d = 0.1738 negligible
		between-group effect	p=0.0056**			
			d = - 9.8801 much large			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Astrogliosis: % GFAP area vs KO ^{a)}	$\sigma^2d = 6.390$ $p=0.094$		Water	Riluzole	within-group effects	
		WT	78.47 ± 15.55	51.77 ± 8.31	p=0.1859	d = 0.8091 large
		KO	100.00 ± 14.22	93.44 ± 13.29	p=0.6434	d = 0.1589 negligible
		between-group effect	p=0.3161	p=0.0331*		
			d = - 0.5604 medium	d = - 1.1148 much large		
Astrogliosis: % GFAP area vs KO ^{a)}	$\sigma^2d = 9.553$ $p=0.022^*$		Saline	Memantine	within-group effects	
		WT	38.98 ± 7.05			
		KO	100.00 ± 9.57	89.10 ± 14.95	p=0.3691	d = 0.3541 small
		between-group effect	p=0.0062**			
			d = - 2.9610 much large			
Astrogliosis: % GFAP area vs KO ^{b)}	F = 0.324 $p=0.576$		Vehicle	Resveratrol	within-group effects	
		WT	57.13 ± 9.65	54.95 ± 4.67	p=0.9980	d = 0.1290 negligible
		KO	100.00 ± 10.25	107.88 ± 9.61	p=0.9207	d = - 0.3545 small
		between-group effect	p=0.0163*	p=0.0031**		
			d = - 1.6245 much large	d = - 3.1300 much large		
Astrogliosis: % GFAP area vs KO ^{a)}	$\sigma^2d = 9.553$ $p=0.022^*$		Saline	Minocycline	within-group effects	
		WT	38.98 ± 7.05			
		KO	100.00 ± 9.57	90.67 ± 7.17	p=0.9025	d = 0.4500 small
		between-group effect	p=0.0062**			
			d = - 2.9610 much large			

Variable Statistical test	Test statistic P-value	Genotype	Control	Treatment	P value / delta	
Microgliosis: % Iba1+ cells vs KO ^{a)}	$\sigma^2d = 12.54$ $p=0.005^{**}$		Water	Riluzole	within-group effects	
		WT	75.64 ± 4.49	55.67 ± 4.26	p=0.0200*	d = 1.7217 much large
		KO	100.00 ± 13.71	71.75 ± 4.82	p=0.0900	d = 1.2078 much large
		between-group effect	p=0.2123	p=0.0250*		
			d = - 1.0024 much large	d = - 1.1157 much large		
Microgliosis: % Iba1+ cells vs KO ^{b)}	F = 1.051 p=0.391		Saline	Memantine	within-group effects	
		WT	77.18 ± 8.13			
		KO	100.00 ± 11.48	105.42 ± 13.91	p=0.9881	d = - 0.1736 negligible
		between-group effect	p=0.5432			
			d = - 0.9355 large			
Microgliosis: % Iba1+ cells vs KO ^{b)}	F = 1.838 p=0.193		Vehicle	Resveratrol	within-group effects	
		WT	78.82 ± 7.61	92.88 ± 7.61	p=0.4968	d = -0.8259 large
		KO	100.00 ± 4.54	95.27 ± 7.44	p=0.9619	d = 0.3426 small
		between-group effect	p=0.1763	p=0.9946		
			d = - 1.5103 much large	d = - 0.1421 negligible		
Microgliosis: % Iba1+ cells vs KO ^{b)}	F = 1.051 p=0.391		Saline	Minocycline	within-group effects	
		WT	77.18 ± 8.13			
		KO	100.00 ± 11.48	92.96 ± 13.37	p=0.9750	d = 0.2302 small
		between-group effect	p=0.5432			
			d = - 0.9355 large			

Table S2: Contingency tables and inferential statistical summary of hindlimb clasping test. The summary table details the contingency tables of the relative frequency of the hindlimb clasping score (from absent to severe) for each group of treatment. Pearson's Chi-square test ^{a)} was used to estimate the chi-squared statistic (χ^2) and the p-value (p) for multiple and paired comparisons between-groups and within-groups. Fischer's exact test ^{b)} was used when sample sizes were zero. Significance (p-value): ***p<0.001, ****p<0.0001.

Test statistic P-value	Genotype	Control				Treatment				P value / chi square	
$\sigma^2d = 131.9$ $p=2.20e-16^{****}$		Water				Riluzole				within-group effects	
	WT	Ab	Mi	Mo	Se	Ab	Mi	Mo	Se	$p=5.335e-06^{****\ b)}$	$\sigma^2d = NA^{\ b)}$
		85.71	14.29	0.00	0.00	72.73	9.09	18.18	0.00		
	KO	Ab	Mi	Mo	Se	Ab	Mi	Mo	Se	$p=2.143e-10^{****}$	$\sigma^2d = 47.99$
		66.67	16.67	16.67	0.00	27.27	9.09	54.55	9.09		
	between-group effect	$p=7.551e-06^{****\ b)}$				$p=2.205e-10^{****}$					
$\sigma^2d = NA^{\ b)}$				$\sigma^2d = 47.93$							
$\sigma^2d = 84.02$ $p=2.55e-14^{****}$		Saline				Memantine				within-group effects	
	WT	Ab	Mi	Mo	Se						
		68.75	33.33	43.75	66.66						
	KO	Ab	Mi	Mo	Se	Ab	Mi	Mo	Se	$p=0.0007^{***}$	$\sigma^2d = 16.938$
		33.33	33.33	40.00	6.66	43.75	12.50	43.75	0.00		
	between-group effect	$p=9.97e-08^{****}$									
$\sigma^2d = 35.410$											
$\sigma^2d = 84.93$ $p=1.67e-14^{****}$		Vehicle				Resveratrol				within-group effects	
	WT	Ab	Mi	Mo	Se	Ab	Mi	Mo	Se	$p= 0.4208^{\ b)}$	$\sigma^2d = NA^{\ b)}$
		80.00	6.66	13.33	0.00	73.33	6.66	20.00	0.00		
	KO	Ab	Mi	Mo	Se	Ab	Mi	Mo	Se	$p=1.634e-07^{****}$	$\sigma^2d = 34.397$
		35.71	28.57	21.42	14.28	73.33	6.66	6.66	13.33		
	between-group effect	$p=3.94e-10^{****}$				$p=0.0001^{***}$					
$\sigma^2d = 46.742$				$\sigma^2d = 20.005$							
$\sigma^2d = 84.02$ $p=2.55e-14^{****}$		Saline				Minocycline				within-group effects	
	WT	Ab	Mi	Mo	Se						
		68.75	33.33	43.75	66.66						
	KO	Ab	Mi	Mo	Se	Ab	Mi	Mo	Se	$p=4.731e-09^{****}$	$\sigma^2d = 41.663$
		33.33	33.33	40.00	6.66	66.66	26.66	6.66	0.00		
	between-group effect	$p=9.97e-08^{****}$									
$\sigma^2d = 35.410$											