

Supplementary Table 1 Effect size estimates, mean differences, and 95% confidence intervals for treatment-associated changes in behavioral, biochemical, and molecular parameters

Endpoint	Comparison	Mean difference	95%CI low	95%CI high	Cohen d	P value
Nrf2	PSNL vs Sham	0.601666667	0.572834594	0.630498739	26.86261755	1
Nrf2	PSNL vs PSNL+Gaba	0.198666667	0.171471518	0.225861815	9.400116438	1
Nrf2	PSNL vs PSNL+KP	0.236166667	0.211333806	0.260999528	12.36463397	0.9992
Nrf2	PSNL vs PSNL+KP+VNS	0.403	0.37727053	0.42872947	20.23448674	0.9993
Nrf2	PSNL vs PSNL+KP+TE	0.412133333	0.387845184	0.436421483	22.20708009	0.9778
Nrf2	PSNL vs PSNL+KP+TE+VNS	0.509833333	0.484663252	0.535003415	26.25833299	1
HO1	PSNL vs Sham	1.048333333	1.022266291	1.074400376	51.87904562	1
HO1	PSNL vs PSNL+Gaba	0.308333333	0.282266291	0.334400376	15.25854283	1
HO1	PSNL vs PSNL+KP	0.493333333	0.466083602	0.520583065	23.43016071	0.9999
HO1	PSNL vs PSNL+KP+VNS	0.721666667	0.69227682	0.751056514	32.00828103	0.9993
HO1	PSNL vs PSNL+KP+TE	0.758333333	0.732266291	0.784400376	37.5277675	0.9868
HO1	PSNL vs PSNL+KP+TE+VNS	0.88	0.846230549	0.913769451	34.51643978	1
Keap1	PSNL vs Sham	-1.365	-1.396499572	-1.333500428	-56.92443504	1
Keap1	PSNL vs PSNL+Gaba	-0.476666667	-0.549655211	-0.403678122	-9.018896453	1
Keap1	PSNL vs PSNL+KP	-0.706666667	-0.750055414	-0.663277919	-21.17883175	1

Keap1	PSNL vs PSNL+KP+VNS	-1.028333333	-1.064908231	-0.991758435	-36.16918055	0.9999
Keap1	PSNL vs PSNL+KP+TE	-1.088333333	-1.121765752	-1.054900914	-42.09837863	0.9975
Keap1	PSNL vs PSNL+KP+TE+VNS	-1.288333333	-1.321765752	-1.254900914	-49.83468098	1
Bax	PSNL vs Sham	-1.926666667	-1.990031311	-1.863302022	-43.04571987	1
Bax	PSNL vs PSNL+Gaba	-0.71	-0.780085425	-0.639914575	-13.14664542	1
Bax	PSNL vs PSNL+KP	-1.076666667	-1.146422473	-1.006910861	-20.05089862	1
Bax	PSNL vs PSNL+KP+VNS	-1.383333333	-1.449059592	-1.317607075	-28.02391331	1
Bax	PSNL vs PSNL+KP+TE	-1.466666667	-1.531420515	-1.401912818	-30.55997717	0.9993
Bax	PSNL vs PSNL+KP+TE+VNS	-1.76	-1.823638716	-1.696361284	-38.43686625	1
Bcl2	PSNL vs Sham	0.593333333	0.566083602	0.620583065	28.17951762	1
Bcl2	PSNL vs PSNL+Gaba	0.182333333	0.156949461	0.207717206	9.252598908	1
Bcl2	PSNL vs PSNL+KP	0.251166667	0.22657434	0.275758993	13.14156457	0.9994
Bcl2	PSNL vs PSNL+KP+VNS	0.412166667	0.38757434	0.436758993	21.56542083	0.9987
Bcl2	PSNL vs PSNL+KP+TE	0.42795	0.403543348	0.452356652	22.55853313	0.9722
Bcl2	PSNL vs PSNL+KP+TE+VNS	0.528583333	0.502572904	0.554593763	26.21150468	1
Caspase 3	SNT vs Sham	-2.105	-2.156965637	-2.053034363	-56.35922291	1
Caspase 3	SNT vs SNT+Gaba	-0.765	-0.825628422	-0.704371578	-16.25453574	1
Caspase 3	SNT vs SNT+KP	-1.185	-1.245628422	-1.124371578	-25.17859459	1

Caspase 3	SNT vs SNT+KP+VNS	-1.528333333	-1.586844475	-1.469822192	-33.76896648	1
Caspase 3	SNT vs SNT+KP+TE	-1.62	-1.675756065	-1.564243935	-37.97338571	0.9992
Caspase 3	SNT vs SNT+KP+TE+VNS	-1.943333333	-1.998561523	-1.888105143	-46.14791789	1
BDNF	PSNL vs Sham	0.64	0.610198787	0.669801213	27.62661423	1
BDNF	PSNL vs PSNL+Gaba	0.179	0.15071716	0.20728284	8.156047282	1
BDNF	PSNL vs PSNL+KP	0.259833333	0.23217575	0.287490917	12.1330489	0.9996
BDNF	PSNL vs PSNL+KP+VNS	0.406833333	0.377022403	0.436644264	17.55588174	0.9987
BDNF	PSNL vs PSNL+KP+TE	0.431266667	0.402654288	0.459879045	19.40974813	0.9728
BDNF	PSNL vs PSNL+KP+TE+VNS	0.527333333	0.497318277	0.55734839	22.60161446	1
CREB	PSNL vs Sham	0.563333333	0.536083602	0.590583065	26.75471054	1
CREB	PSNL vs PSNL+Gaba	0.163	0.134882577	0.191117423	7.52343307	1
CREB	PSNL vs PSNL+KP	0.221166667	0.193905206	0.248428128	10.49985049	0.999
CREB	PSNL vs PSNL+KP+VNS	0.3775	0.350457826	0.404542174	18.05517552	0.9969
CREB	PSNL vs PSNL+KP+TE	0.39795	0.37094443	0.42495557	19.05700451	0.9607
CREB	PSNL vs PSNL+KP+TE+VNS	0.496416667	0.46841766	0.524415673	23.00048003	1
MAO	PSNL vs Sham	-16.05	-16.63409374	-15.46590626	-37.39982094	1
MAO	PSNL vs PSNL+Gaba	-6.283333333	-6.884881059	-5.681785607	-13.83824054	1
MAO	PSNL vs PSNL+KP	-9.116666667	-9.722549545	-8.510783788	-19.85484214	1

MAO	PSNL vs PSNL+KP+VNS	-12.03333333	-12.62122246	-11.44544421	-27.63060799	1
MAO	PSNL vs PSNL+KP+TE	-12.8	-13.38026108	-12.21973892	-30.36735682	0.9988
MAO	PSNL vs PSNL+KP+TE+VNS	-15.2	-15.78026108	-14.61973892	-36.06123622	1
DOPAMINE	PSNL vs Sham	11.25	10.87774955	11.62225045	38.93223039	1
DOPAMINE	PSNL vs PSNL+Gaba	3.6	3.247700314	3.952299686	13.14534138	1
DOPAMINE	PSNL vs PSNL+KP	5.7	5.347700314	6.052299686	20.81345719	0.9995
DOPAMINE	PSNL vs PSNL+KP+VNS	8.016666667	7.645976636	8.387356697	27.85423638	0.9984
DOPAMINE	PSNL vs PSNL+KP+TE	8.583333333	8.24079893	8.925867737	32.25055099	0.9803
DOPAMINE	PSNL vs PSNL+KP+TE+VNS	10.21666667	9.845976636	10.5873567	35.4982264	1
ROS	PSNL vs Sham	-166.3333333	-171.8746078	-160.7920588	-41.11489374	1
ROS	PSNL vs PSNL+Gaba	-55	-60.83607588	-49.16392412	-12.37074829	1
ROS	PSNL vs PSNL+KP	-88.33333333	-94.25490855	-82.41175812	-19.47792389	1
ROS	PSNL vs PSNL+KP+VNS	-122.5	-128.1842421	-116.8157579	-28.70130428	1
ROS	PSNL vs PSNL+KP+TE	-129.6666667	-135.2839041	-124.0494293	-31.05547166	0.999
ROS	PSNL vs PSNL+KP+TE+VNS	-156.8333333	-162.4185055	-151.2481612	-38.01903831	1
ACHE	PSNL vs Sham	-8.766666667	-9.092709481	-8.440623852	-36.50665735	0.9999
ACHE	PSNL vs PSNL+Gaba	-3.183333333	-3.538286147	-2.82838052	-11.63682683	1
ACHE	PSNL vs PSNL+KP	-4.766666667	-5.119340831	-4.413992503	-17.56221434	1

ACHE	PSNL vs PSNL+KP+VNS	-6.333333333	-6.669053207	-5.99761346	-24.96975718	1
ACHE	PSNL vs PSNL+KP+TE	-6.733333333	-7.069053207	-6.39761346	-26.54679448	0.9994
ACHE	PSNL vs PSNL+KP+TE+VNS	-8.166666667	-8.492709481	-7.840623852	-34.00810285	1
NO	PSNL vs Sham	-30.25	-30.9630285	-29.5369715	-57.01461282	1
NO	PSNL vs PSNL+Gaba	-11.36666667	-12.18648676	-10.54684657	-17.85364784	1
NO	PSNL vs PSNL+KP	-17.16666667	-17.94863803	-16.38469531	-28.40150308	1
NO	PSNL vs PSNL+KP+VNS	-22.21666667	-22.9763963	-21.45693703	-38.05466192	1
NO	PSNL vs PSNL+KP+TE	-23.4	-24.15027265	-22.64972735	-40.73417149	0.9987
NO	PSNL vs PSNL+KP+TE+VNS	-28.51666667	-29.26085114	-27.77248219	-50.18911919	1
TNF	PSNL vs Sham	-89.88333333	-91.75462247	-88.0120442	-67.82601554	1
TNF	PSNL vs PSNL+Gaba	-30.73333333	-32.8120502	-28.65461647	-19.16844059	1
TNF	PSNL vs PSNL+KP	-48.43333333	-50.48060288	-46.38606379	-30.7758871	1
TNF	PSNL vs PSNL+KP+VNS	-63.53333333	-65.45950625	-61.60716042	-44.17294793	1
TNF	PSNL vs PSNL+KP+TE	-66.83333333	-68.77714249	-64.88952418	-45.72194899	0.9985
TNF	PSNL vs PSNL+KP+TE+VNS	-83.5	-85.3822009	-81.6177991	-61.34622337	1
NFKB	PSNL vs Sham	-79.83333333	-81.48794809	-78.17871857	-69.74183475	1
NFKB	PSNL vs PSNL+Gaba	-26.18333333	-28.00476523	-24.36190144	-18.67936361	1
NFKB	PSNL vs PSNL+KP	-41.25	-43.0435571	-39.4564429	-30.00892961	1

NFKB	PSNL vs PSNL+KP+VNS	-54.2	-55.88900551	-52.51099449	-43.40864494	1
NFKB	PSNL vs PSNL+KP+TE	-56.7	-58.40041183	-54.99958817	-44.78332113	0.9988
NFKB	PSNL vs PSNL+KP+TE+VNS	-73.78333333	-75.47180609	-72.09486057	-59.13399371	1
IL-1B	PSNL vs Sham	-75.46666667	-77.12775419	-73.80557914	-65.61905375	1
IL-1B	PSNL vs PSNL+Gaba	-24.05	-25.80131211	-22.29868789	-18.11722132	1
IL-1B	PSNL vs PSNL+KP	-38.58333333	-40.35853945	-36.80812722	-28.49956673	1
IL-1B	PSNL vs PSNL+KP+VNS	-51.23333333	-52.95211687	-49.5145498	-39.79675671	1
IL-1B	PSNL vs PSNL+KP+TE	-53.56666667	-55.29963804	-51.83369529	-41.02748426	0.9989
IL-1B	PSNL vs PSNL+KP+TE+VNS	-69.98333333	-71.66740257	-68.2992641	-56.74842504	1
IL-10	PSNL vs Sham	43.95	42.91432605	44.98567395	56.63703686	1
IL-10	PSNL vs PSNL+Gaba	14.5	13.71880546	15.28119454	24.01153745	1
IL-10	PSNL vs PSNL+KP	25.06666667	24.13777174	25.99556159	35.5445321	0.9998
IL-10	PSNL vs PSNL+KP+VNS	34.38333333	33.39349061	35.37317605	46.10473174	0.9989
IL-10	PSNL vs PSNL+KP+TE	37.11666667	36.20321483	38.03011851	53.41587467	0.9835
IL-10	PSNL vs PSNL+KP+TE+VNS	41.93333333	40.84339141	43.02327526	51.66858209	1
LDH	PSNL vs Sham	-66.125	-67.64654805	-64.60345195	-58.63318278	1
LDH	PSNL vs PSNL+Gaba	-23.54166667	-25.32378423	-21.7595491	-16.99988284	1
LDH	PSNL vs PSNL+KP	-37.54166667	-39.22924639	-35.85408695	-28.7491379	1

LDH	PSNL vs PSNL+KP+VNS	-48.625	-50.2608879	-46.9891121	-38.6305262	1
LDH	PSNL vs PSNL+KP+TE	-52.04166667	-53.66546084	-50.41787249	-41.73081911	0.9986
LDH	PSNL vs PSNL+KP+TE+VNS	-62.58333333	-64.19060961	-60.97605706	-50.85247608	1

Supplementary Table 2 One-way analysis of variance effect size summary showing *F* values, analysis of variance *P* values, and partial η^2 estimates for measured endpoints

Endpoint	<i>F</i> value	ANOVA <i>P</i> value	Partial η^2	Interpretation
Nrf2	699.670893	6.37025E-35	0.991731682	Large effect
HO1	1391.107316	4.12732E-40	0.995824208	Large effect
Keap1	1080.552354	3.3541E-38	0.994630513	Large effect
Bax	1681.04274	1.52377E-41	0.996541931	Large effect
Bcl2	628.3585932	4.10457E-34	0.990801943	Large effect
Caspase 3	2090.594203	3.40043E-43	0.997217489	Large effect
BDNF	583.7195672	1.47029E-33	0.990105496	Large effect
CREB	454.6428621	1.10439E-31	0.987331955	Large effect
MAO	1695.504535	1.31239E-41	0.996571326	Large effect
DOPAMINE	1162.357915	9.42136E-39	0.995006525	Large effect
ROS	1805.797721	4.37371E-42	0.996780065	Large effect

ACHE	1240.310526	3.04384E-39	0.995318893	Large effect
NO	2477.312775	1.75893E-44	0.99765083	Large effect
TNF	4217.52897	1.62018E-48	0.998618794	Large effect
NFKB	4442.822241	6.52587E-49	0.998688742	Large effect
IL-1B	4164.501895	2.02106E-48	0.998601232	Large effect
IL-10	2223.643374	1.15882E-43	0.997383541	Large effect
LDH	2544.651782	1.10139E-44	0.997712853	Large effect
