

Supplementary Table 1. Diet composition of different treatment groups.

Ingredients (g/kg diet)	Normal diet	EPA-rich diet	DHA-rich diet
	C, S, SR	SRE	SRD
Casein	140.0	140.0	140.0
L-cystine	1.80	1.80	1.80
Corn starch	465.7	465.7	465.7
Dextrinized corn starch	155.0	155.0	155.0
Sucrose	100.0	100.0	100.0
Cellulose	50.0	50.0	50.0
Soybean oil	40.0	20.0	20.0
EPA-rich oil	-	20.0	-
DHA-rich oil	-	-	20.0
t-Butylhydroquinone	0.008	0.008	0.008
AIN-93M mineral mix	35.0	35.0	35.0
AIN-93 vitamin mix	10.0	10.0	10.0
Choline bitartrate	2.50	2.50	2.50

C, control; S, sleep deprivation; SR, sleep deprivation treated with RMT; SRE, sleep deprivation treated with RMT and EPA; SRD, sleep deprivation treated with RMT and DHA. EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; AIN, American Institute of Nutrition.

Supplementary Table 2. EPA and DHA content of different fish oil.

Ingredients (mg/g)	EPA-rich oil	DHA-rich oil
EPA	800	3
DHA	2	700

EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Supplementary Table3: The sequences of primers.

Genes	Primer sequence (5'→3')	bp
MT1	F: TTCCCTGTGCTACGTGTTCC	122
	R: TGACGGACTGGGTGAAGGTA	
MT2	F: GGCCATTCTCCATGACGGTT	131
	R: AGATGCACCAGTAGCGGTTG	
BDNF	F: CGCTTTTTCTAGCTCTGTGGTG	143
	R: CCGTGGACGTTTGCTTCTTTC	
SOD1	F: TGCTTTTTGCTCTCCCAGGT	120
	R: CTGCTCGAAGTGAATGACGC	
SOD2	F: GGGATTGATGTGTGGGAGCA	138
	R: GGAAGGGCTTCACTTCTTGC	
CAT	F: CCCTCAGAAACCCGATGTCC	134
	R: CAAAGTGTGCCATCTCGTCG	
GPX1	F: AGTGCGAGGTGAATGGTGAG	125
	R: CACCGGGACCAAATGATGT	
GAPDH	F: GTGCCAGCCTCGTCTCATAG	122
	R: CGTTGATGGCAACAATGTCCA	

MT1, melatonin receptor 1; MT2, melatonin receptor 2; BDNF, brain-derived neurotrophic factor; SOD, superoxide dismutase; CAT, catalase; GPX, glutathione peroxidase; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; bp, base pair.

Supplementary Table 4. Summary of potential biomarkers of sleep deprivation induced anxiety-like behaviors.

Lipid metabolites	Group S/C		Group SR/S		Group SRE/S		Group SRD/S	
	FC	p value	FC	p value	FC	p value	FC	p value
NAE 18:1	2.62	0.04	0.95	0.80	0.74	0.19	0.99	0.94
Oleamide	0.62	0.02	1.11	0.53	1.11	0.29	1.27	0.05
PA 34:0	0.79	0.01	1.02	0.78	1.16	0.06	1.14	0.07
PC 44:12	0.51	0.02	0.32	0.00	0.51	0.02	0.48	0.01
PC 48:2	1.68	0.03	0.26	0.00	0.40	0.01	0.27	0.00
PC O-32:2	0.55	0.01	1.41	0.01	1.15	0.18	0.82	0.15
PC O-44:1	0.57	0.04	0.58	0.04	0.58	0.03	0.47	0.01
PE 32:4	0.55	0.00	2.71	0.00	2.91	0.00	1.15	0.31
PE 40:4	3.51	0.00	0.72	0.12	0.66	0.06	0.75	0.17
PE-NMe2 40:6	0.62	0.04	1.82	0.00	2.22	0.00	2.49	0.00
PS 40:0	0.74	0.02	1.52	0.01	1.75	0.00	1.28	0.16
PS 40:4	1.31	0.01	1.21	0.36	0.78	0.01	0.60	0.00
PS 41:6	0.66	0.01	1.14	0.39	0.91	0.50	1.12	0.44
PS 42:6	0.43	0.00	2.43	0.00	2.04	0.01	0.13	0.01
PS 44:10	0.48	0.00	2.63	0.00	3.58	0.00	1.26	0.26
CL 60:4	1.60	0.03	0.18	0.00	0.07	0.00	0.10	0.00
Cer 34:0;O2	4.04	0.01	0.34	0.02	0.26	0.01	1.00	0.99
SHexCer 38:1;O2	0.48	0.00	1.03	0.90	4.68	0.00	6.22	0.00
SHexCer 40:1;O2	2.71	0.04	1.15	0.53	0.90	0.69	1.47	0.14
GA2 36:2;O2	3.91	0.00	1.10	0.64	0.89	0.61	1.61	0.13
GM3 36:1;O2	1.88	0.00	0.50	0.12	0.44	0.00	0.51	0.00
MG 16:0	1.33	0.02	0.75	0.01	0.66	0.00	0.59	0.00
MG 18:3	0.69	0.02	1.98	0.00	2.37	0.00	1.37	0.07
DG 30:0	2.13	0.01	0.40	0.00	0.38	0.00	0.50	0.01
DG 36:1	0.74	0.03	1.55	0.07	1.53	0.01	1.30	0.23
DG 38:8	1.93	0.01	0.91	0.72	0.75	0.42	1.15	0.71
DG 40:6	1.51	0.02	0.63	0.01	1.15	0.31	1.18	0.42
DG 42:6	1.50	0.04	0.77	0.21	0.63	0.03	0.52	0.01
DG 48:1	0.18	0.01	2.39	0.15	2.69	0.01	3.87	0.00
TG 60:8	0.65	0.05	0.43	0.03	0.27	0.01	0.33	0.01
TG 62:4	0.49	0.01	1.37	0.25	1.89	0.01	1.31	0.34

C, control; S, sleep deprivation; SR, sleep deprivation treated with RMT; SRE, sleep deprivation treated with RMT and EPA; SRD, sleep deprivation treated with RMT and DHA. FC, fold change; NAE, N-acyl ethanolamines (endocannabinoids); PA, phosphatidic acid; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PS, phosphatidylserine; CL, cardiolipin; Cer, ceramide; SHexCer, sulfohexosylceramide; MG, monoacylglycerol; DG, diacylglycerol; TG, triacylglycerol. Lipid metabolites with fold change >2 and <0.5 are highlighted in yellow and blue, respectively. $P < 0.05$ shows significant differences. C: n=5; S: n=5; SR: n=5; SRE: n=5; SRD: n=5.

Supplementary Table 5. Summary of potential biomarkers of sleep deprivation induced depression-like behaviors.

Lipid metabolites	Group S/C		Group SR/S		Group SRE/S		Group SRD/S	
	FC	p value	FC	p value	FC	p value	FC	p value
FA 5:2;O2	0.31	0.01	5.43	0.00	7.76	0.00	1.83	0.08
PC 44:2	0.71	0.02	0.99	0.96	0.87	0.23	0.98	0.82
PC 48:2	1.68	0.03	0.26	0.00	0.40	0.01	0.27	0.00
PE 32:4	0.55	0.00	2.71	0.00	2.91	0.00	1.15	0.31
PE 40:4	3.51	0.00	0.72	0.12	0.66	0.06	0.75	0.17
PS 42:6	0.43	0.00	2.43	0.00	2.04	0.01	0.13	0.01
PS 44:10	0.48	0.00	2.63	0.00	3.58	0.00	1.26	0.26
CL 52:0	0.71	0.01	0.66	0.04	0.77	0.08	0.69	0.10
CL 60:4	1.60	0.03	0.18	0.00	0.07	0.00	0.10	0.00
Cer 34:0;O2	4.04	0.01	0.34	0.02	0.26	0.01	1.00	0.99
GM3 32:1;O2	0.26	0.04	1.43	0.18	2.04	0.02	1.40	0.30
GM3 36:1;O2	1.88	0.00	0.50	0.12	0.44	0.00	0.51	0.00
MG 18:3	0.69	0.02	1.98	0.00	2.37	0.00	1.37	0.07
DG 30:0	2.13	0.01	0.40	0.00	0.38	0.00	0.50	0.01
DG 36:4	0.59	0.00	0.94	0.70	0.86	0.18	0.71	0.03
DG 40:7	1.75	0.01	0.54	0.03	0.46	0.00	1.46	0.07
DG 42:6	1.50	0.04	0.77	0.21	0.63	0.03	0.52	0.01
TG 62:4	0.49	0.01	1.37	0.25	1.89	0.01	1.31	0.34

C, control; S, sleep deprivation; SR, sleep deprivation treated with RMT; SRE, sleep deprivation treated with RMT and EPA; SRD, sleep deprivation treated with RMT and DHA. FC, fold change; FA, fatty acid; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PS, phosphatidylserine; CL, cardiolipin; Cer, ceramide; MG, monoacylglycerol; DG, diacylglycerol; TG, triacylglycerol. Lipid metabolites with fold change >2 and <0.5 are highlighted in yellow and blue, respectively. $P < 0.05$ shows significant differences. C: n=5; S: n=5; SR: n=5; SRE: n=5; SRD: n=5.

Supplementary Figure 1. Overview of identified lipid specie

