

Online Appendix

Supplemental Table 1

Supplemental Table 2

Supplemental Fig. 1 and legend

Supplemental Fig. 2 and legend

Supplemental Fig. 3 and legend

Supplemental Fig. 4 and legend

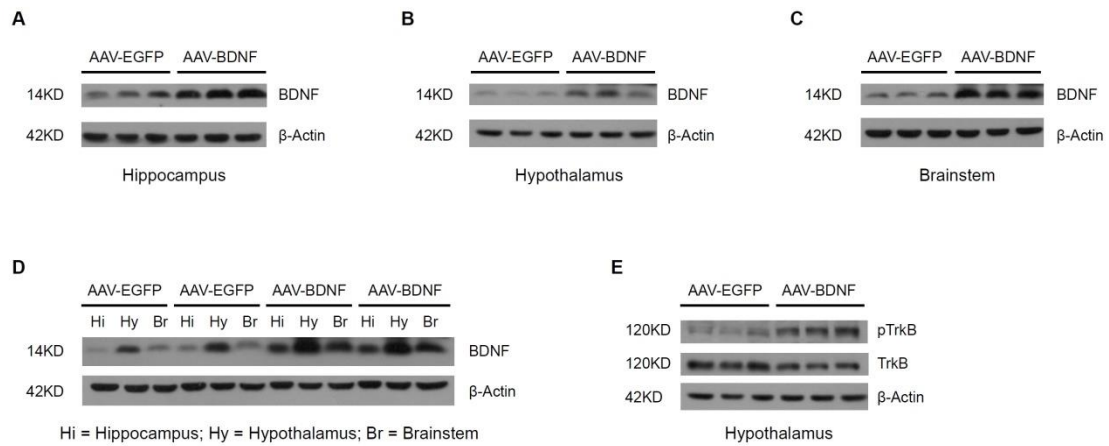
Supplemental table 1. Daily schedule of the CUMS paradigm

Swim stress (16°C/3min)	D7, D11, D13, D24, D26
Food and water deprivation	D2, D8, D26, D33,
Light on overnight	D1, D4, D6, D8, D11, D13, D17, D18, D21, D28, D30, D32, D35
Light off in the daytime	D1, D4, D7, D10, D15, D18, D19, D22, D28, D35
Wet bedding overnight	D2, D7, D16, D24, D31,
Crowding	D2, D5, D9, D11, D17, D23, D29,
Tilt cage at 45 degree overnight	D5, D10, D12, D14, D16, D20, D25, D30, D34,
Empty cage overnight	D3, D5, D9, D12, D15, D17, D22, D27, D31,
Hot stress (45°C/10 min)	D4, D8, D14, D19, D25, D33,
Elevated platform (30 min)	D1, D3, D6, D21, D27,
Restraint stress (1h)	D3, D6, D9, D10, D12, D13, D14, D18, D20, D23, D29, D32, D34,

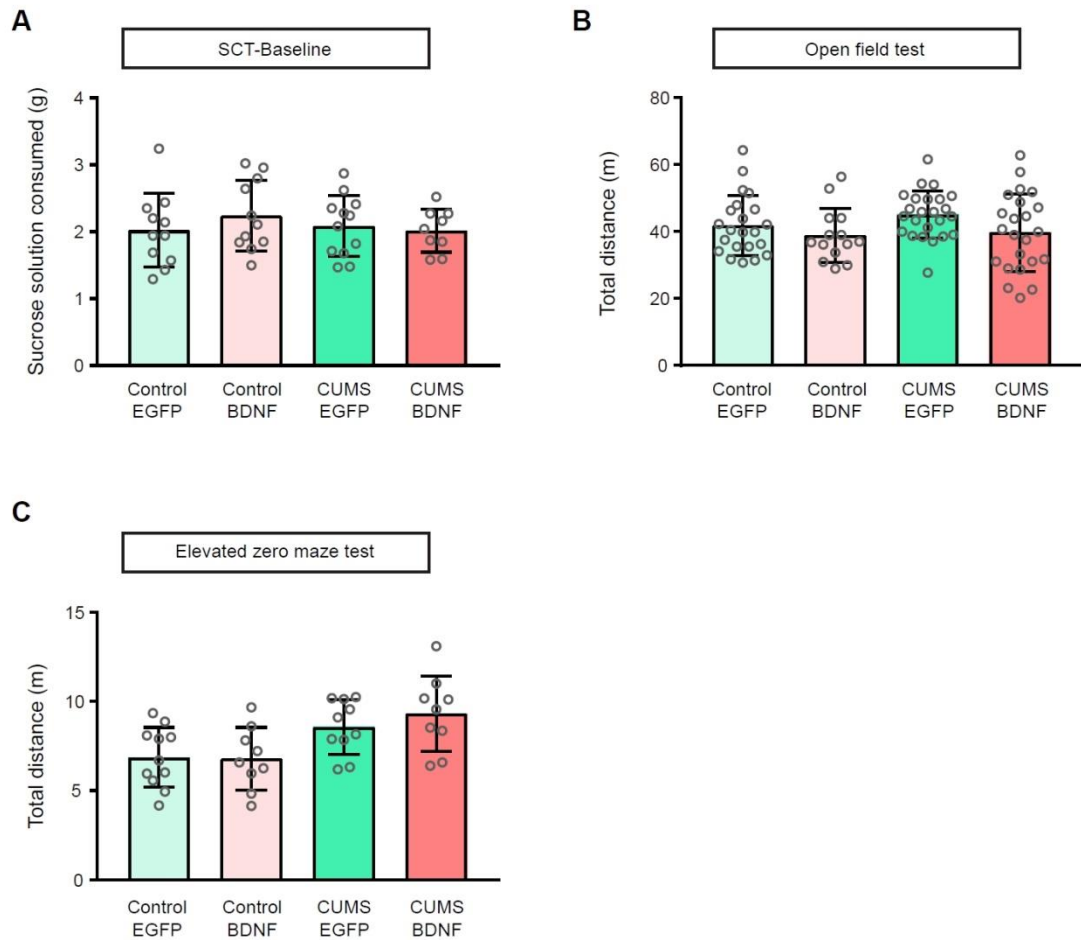
Supplemental table 2. Primers used in the real-time quantitative PCR analyses

Gene	Forward primer	Reverse primer
<i>Tph2</i>	5'-TCTACACCCCGGAACCAGAT-3'	5'-GCAAAGGCCGAACTCGATTG-3'
<i>Vmat2</i>	5'-GGGGTATGCTATCGGTCCCT-3'	5'-TAATGGGGCAGTTGTGGTCC-3'
<i>Sert</i>	5'-GACATCAGGAGGGGCGTATG-3'	5'-AGAAACAGAGGGCTGATGGC-3'
<i>Maoa</i>	5'-ATGGGCTTCATACTTGCCCG-3'	5'-CTGCCGAATCACCTTCCATA-3'
<i>Maob</i>	5'-GGAAGGGTTCTACGTCAGCC-3'	5'-TCGTGCAGGGACATCCAAAG-3'
<i>Htr1a</i>	5'-TACTCCACTTTCGGCGCTTT-3'	5'-GGCTGACCATTGAGGCTCTT-3'
<i>Htr1b</i>	5'-GCTTTGTGAACACCGACCAC-3'	5'-GAGCCCGGGAGTTAATGGAG-3'
<i>Ntrk2</i>	5'-CCTGATGGCCAAGAACGAGT-3'	5'-CGGCATAGACCGAGAGATGC-3'
<i>Agrp</i>	5'-AGACAACCTGCAGACCGAGC-3'	5'-CATTGAAGAAGCGGCAGTAGC-3'
<i>Npy</i>	5'-CCGCCACGATGCTAGGTAAC-3'	5'-AGTGTCTCAGGGCTGGATCT-3'
<i>Pomc</i>	5'-ATAGATGTGTGGAGCTGGTGC-3'	5'-ACTTCCGGGGGTTTTTCAGTC-3'
<i>Cartpt</i>	5'-GGACATCTACTCTGCCGTGG-3'	5'-CTGTGTCGCCCTTCACAAGCA-3'
<i>Crh</i>	5'-ACCAAGGGAGGAGAAGAGAGC-3'	5'-TTCTTCACCCATGCGGATCA-3'
<i>Trh</i>	5'-CTGGAAGCAGCCCAGGAG-3'	5'-CCGGATGCTGGCGTTTTG-3'
<i>Mc4r</i>	5'-TGAGCAACTTTTTGTTTCCCCC-3'	5'-AGGTTCTTGTTCTTGGCTATCG-3'
<i>Lepr</i>	5'-TATGTGGTCCAGGTTTCGCTG-3'	5'-TTTCGTCAGGGGCTTCCAAA-3'
<i>Insr</i>	5'-GCCGATATGGTGATGAGGAGC-3'	5'-TGGCAATATTTGATGGGACATCT-3'
<i>Htr2c</i>	5'-ATCGCTGGACCGGTATGTAG-3'	5'-ACGCAGGTAGTATTATTCACGAAC-3'
<i>G6pc</i>	5'-TTACCAAGACTCCCAGGACTG-3'	5'-GAGCTGTTGCTGTAGTAGTCG-3'
<i>Pck1</i>	5'-TAAGGAGGAAGGGTGGCTGG-3'	5'-GCCAGGAGCAACTCCAAAAA-3'
<i>Acox1</i>	5'-CTTCGAGGGGGAGAACAACCTG-3'	5'-TACCAATCTGGCTGCACGTA-3'
<i>Cpt1a</i>	5'-CCATGATGGACCCCAACAACA-3'	5'-CATGGCTCAGACAGTACCTCC-3'
<i>Fasn</i>	5'-AGATGGAAGGCTGGGCTCTA-3'	5'-CCTCTGAACCACTCACACCC-3'
<i>Gpam</i>	5'-GTTGCCGTGTACGCTGAGAG-3'	5'-CTCGCTCGAGATAGGTGCTG-3'
<i>Scd1</i>	5'-CCTGCCTCTTCGGGATTTT-3'	5'-GCCCATTCGTACACGTCATT-3'
<i>Pparg</i>	5'-CGAGTCTGTGGGGATAAAGCA-3'	5'-ACCTGATGGCATTGTGAGAC-3'

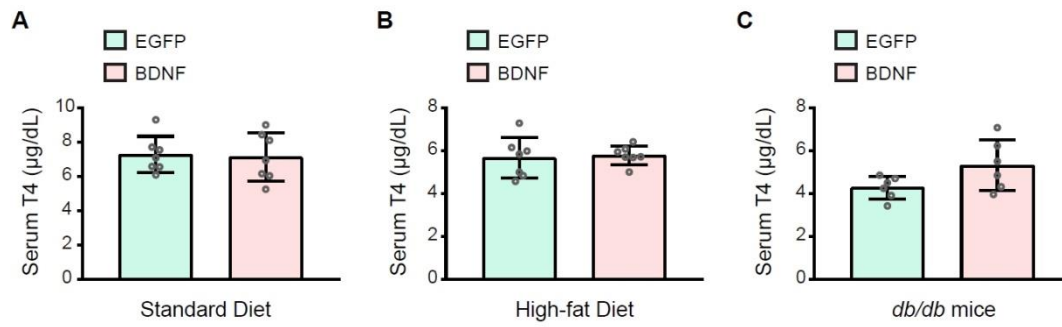
<i>Ucp2</i>	5'-GCGGTCCGGACACAATAGTA-3'	5'-GGGACCTTCAATCGGCAAGA-3'
<i>Adrb1</i>	5'-CCGCTACCTCGCCATCAC-3'	5'-CAGGAAGGACACCAACGC-3'
<i>Adrb2</i>	5'-TGGTTGGGCTACGTCAACTC-3'	5'-CCAGCTGACAAGTGTTTGGC-3'
<i>Adrb3</i>	5'-AGGGAAAAGAGAGCACCCCT-3'	5'-GCCATAGTGAGGAGACAGGGA-3'
<i>Gapdh</i>	5'-AGGTCGGTGTGAACGGATTTG-3'	5'-TGTAGACCATGTAGTTGAGGTCA-3'



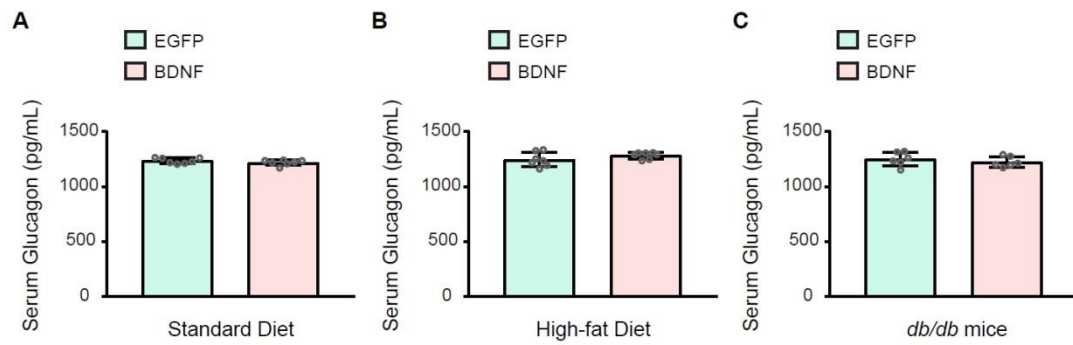
Supplemental figure 1. Protein levels of BDNF are elevated in the hippocampus, hypothalamus, and brainstem after BDNF gene transfer in the DRN. (A) Western blot assay of BDNF in the hippocampus. n = 3 mice per group. (B) Western blot assay of BDNF in the hypothalamus. n = 3 mice per group. (C) Western blot assay of BDNF in the brainstem (at the level posterior to the DRN). n = 3 mice per group. (D) Western blot assay of relative BDNF protein levels in the hippocampus (Hi), hypothalamus (Hy), and brainstem (Br). n = 2 mice per group. (E) Western blot assay of phosphorylated TrkB (pTrkB) in the hypothalamus. n = 3 mice per group.



Supplemental figure 2. BDNF-expressing mice exhibit antidepressant and anxiolytic behaviors in the CUMS model. **(A)** Sucrose consumption at baseline. $n = 9-12$ mice per group. **(B)** Total distance travelled by mice in the open field test after CUMS. $n = 14-24$ mice per group. **(C)** Total distance travelled by mice in the elevated zero maze test after CUMS. $n = 9-11$ mice per group. Two-way ANOVA followed by Tukey's multiple comparisons test. Data are presented as mean \pm SD.



Supplemental figure 3. BDNF gene transfer in the DRN does not affect serum levels of T4. **(A)** Serum levels of T4 from standard-diet mice. **(B)** Serum levels of T4 from high-fat diet mice. **(C)** Serum levels of T4 from *db/db* mice. $n = 6-7$ mice per group. Unpaired two-tailed Student's t test. Data are presented as mean \pm SD.



Supplemental figure 4. BDNF gene transfer in the DRN does not affect serum levels of glucagon. (A) Serum levels of glucagon from standard-diet mice. (B) Serum levels of glucagon from high-fat diet mice. (C) Serum levels of glucagon from *db/db* mice. $n = 6-7$ mice per group. Unpaired two-tailed Student's t test. Data are presented as mean \pm SD.