Antidiabetic Drug Metformin Ameliorates Depressive-Like Behavior in Mice with Chronic Restraint Stress via Activation of AMP-Activated Protein Kinase

Heng Ai¹,#, Weiqing Fang²,#, Hanyi Hu³, Xupang Hu⁴, Wen Lu⁵*

¹Department of Physiology, Hangzhou Medical College, Hangzhou, Zhejiang, China
²Department of Pharmacy, Women's Hospital, School of Medicine, Zhejiang University, Zhejiang, China
³Department of Ophthalmology, Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou, China
⁴Department of Neurobiology, Key Laboratory of Medical Neurobiology of Ministry of Health of China, Zhejiang University School of Medicine, Zhejiang, China
⁵Department of Biochemistry and Molecular Biology, Hainan Medical University, Haikou, Hainan, China
Supplementary Figure 1. Measurement of the corticosterone levels in non-stressed and stressed mice with chronic restraint stress. Data was presented as the mean ± SEM, n = 7 mice per group, unpaired student t test, ¹P < 0.001.

Supplementary Figure 2. Compound C (CC) exerted minimal effects on the mice. A-B. The total distance (A) and the mean velocity (B) measured by the OFT at 1 h or 24 h after injection in the mice treated with saline or compound C (10 mg/kg). C-D. The immobility time in the FST (C) and TST (D) in the mice treated with saline or compound C. One-way analysis of variance (ANOVA) with Bonferroni post hoc analysis, n = 7 mice per group, n.s. represents not significant.
Supplementary Figure 3. Inhibition of AMPK activity by AAV-mediated knock down in the hippocampus. A. Representative blots of hippocampal proteins in AAV-NC- and AAV-shRNA-injected mice. B. Statistical analysis of the pS79-ACC, ACC and AMPKα levels in the hippocampus, n = 5 mice per group. Unpaired student t test, *P < 0.001, n.s. represents not significant.