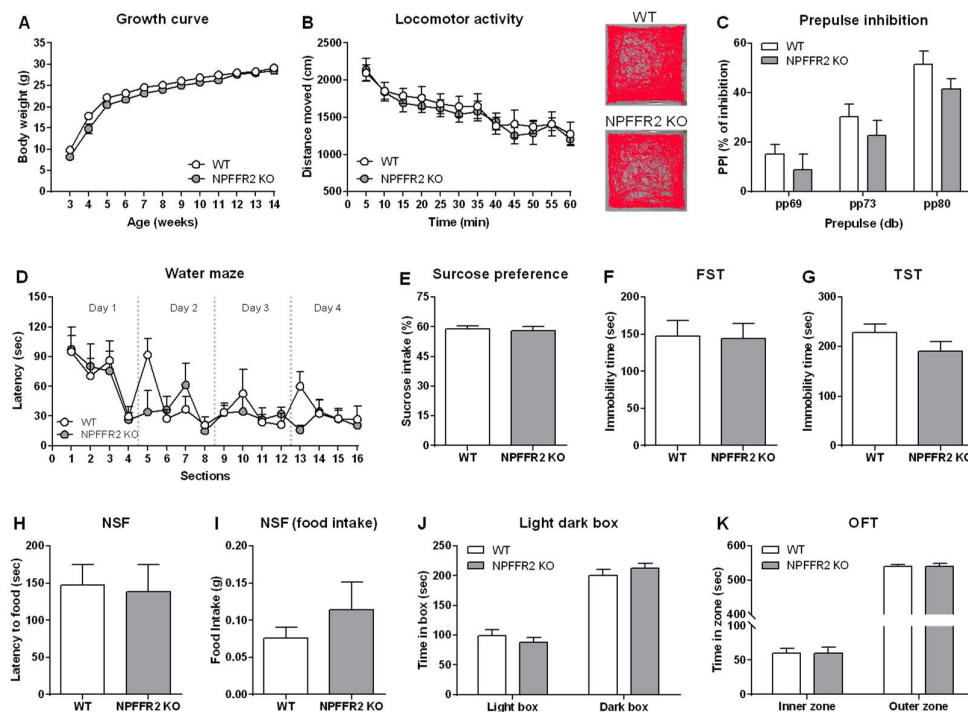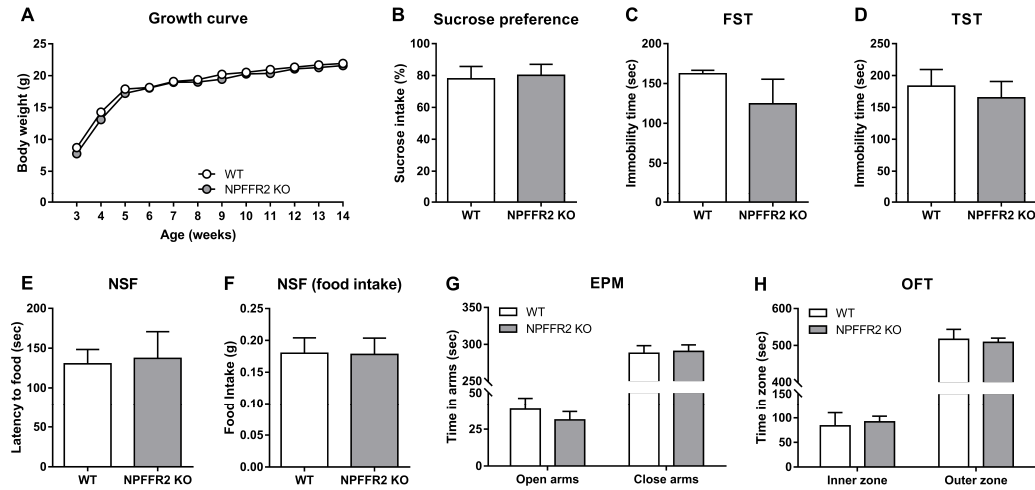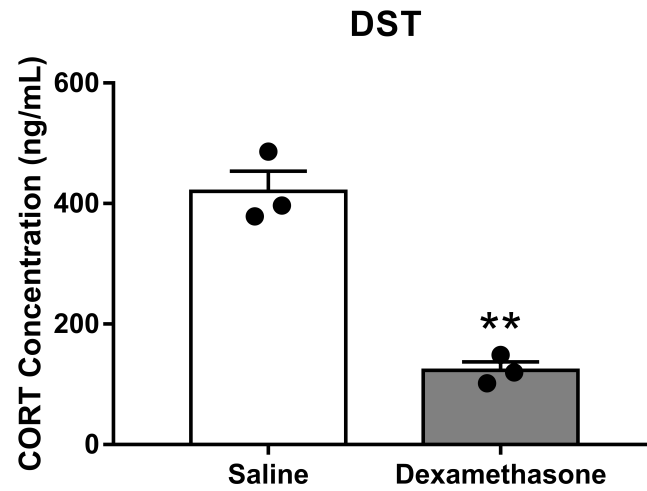# Supplementary Figures

Supplementary Figure S1. The behavioral profiles of male NPFFR2 knockout (KO) mice. (**A**) Growth curves of mice from 3 weeks of age to week 14 (wild-type (WT), $n = 11$; KO, $n = 7$). (**B**) Locomotor activity within 60 min (WT, $n = 9$; KO, $n = 10$). (**C**) Sensorimotor gating was tested by prepulse inhibition (WT, $n = 9$; KO, $n = 10$). (**D**) The water maze was tested for learning (WT, $n = 4$; KO, $n = 5$). The depressive-like behaviors were tested by (**E**) sucrose preference test (WT, $n = 9$; KO, $n = 10$), (**F**) forced swimming test (FST) (WT, $n = 9$; KO, $n = 10$), and (**G**) tail suspension test (TST) (WT, $n = 9$; KO, $n = 10$). Anxiety-like behaviors were tested by (**H** and **I**) novelty-suppressed feeding (NSF) (WT, $n = 9$; KO, $n = 10$), (**J**) light-dark box (WT, $n = 9$; KO, $n = 10$), and (**K**) open field test (OFT) (WT, $n = 9$; KO, $n = 10$). Data are presented as mean ± SEM. The data in S1E–I are analyzed by the unpaired Student's *t*-test. The data in S1A–D, S1J, S1K are analyzed by two-way ANOVA with Bonferroni's multiple comparison test.

Supplementary Figure S2. The behavioral profiles of female NPFFR2 KO mice. (**A**) Growth curves of mice from 3 weeks of age to week 14. The depressive-like behaviors were tested by sucrose preference (**B**), FST (**C**), and TST (**D**). The anxiety-like behaviors were tested by NSF (**E** and **F**), Elevated plus maze (EPM) (**G**), and OFT (**H**). Data are presented as mean ± SEM (WT, *n* = 5; KO, *n* = 5). The data in S2B–F are analyzed by the unpaired Student's *t*-test. The data in S2A, S2G, S2H are analyzed by two-way ANOVA with Bonferroni's multiple comparison test.

DST

Supplementary Figure S3. The dexamethasone suppression test in male WT mice. A pioneer test was performed to validate the effect of dexamethasone on the reduction of circulating CORT levels. WT mice were i.p. injected with saline or 0.1 mg/kg dexamethasone 1 h before mice were physically restrained for 10 min. Facial blood was collected immediately for CORT ELISA assay. Data are presented as mean ± SEM and are analyzed by the unpaired Student's *t*-test. ** $p < 0.01$, comparing saline to dexamethasone group ($n = 3$ per group). The black dots indicate the individual value of WT mice.