

## **Antidepressant-like effects of fenofibrate in mice via the hippocampal BDNF signaling pathway**

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**Running title:** Fenofibrate has antidepressant-like effects

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## Supplemental Figure Legends

Figure S1. The antidepressant-like actions of fenofibrate occur independent of the cannabinoid system. The vehicle refers to 5% dextrose (pH 7.0) with 2.5% DMSO and 10% Cremaphor EL (i.p.) + ACSF with 1% DMSO (i.c.v.). (A) Blocking cannabinoid system with rimonabant/AM630 had no influence on the antidepressant-like effects of fenofibrate in the FST. (B) Rimonabant/AM630 pretreatment could not eliminate the antidepressant-like effects of fenofibrate in the TST. (C) Rimonabant and AM630 did not influence the locomotor activity of mice in the open field test. (D) Co-treatment fenofibrate with rimonabant/AM630 did not block the effects of fenofibrate in the sucrose preference test, since CSDS + fenofibrate + rimonabant/AM630 mice had as much sucrose consumption as CSDS + fenofibrate mice. (E) Also, in the social interaction test, CSDS + fenofibrate + rimonabant/AM630 mice did not differ significantly from CSDS + fenofibrate mice. Results are expressed as means  $\pm$  S.E.M. ( $n = 10-12$ );  $**P < 0.01$ ; n.s., no significance. Comparison was made by two-way ANOVA followed by post-hoc Bonferroni's test.

Figure S2. Blockade of BDNF signaling cascade by K252a prevents the antidepressant actions of fenofibrate. The vehicle refers to 5% dextrose (pH 7.0) with 2.5% DMSO and 10% Cremaphor EL (i.p.) + ACSF with 1% DMSO (i.c.v.). (A) K252a pretreatment before fenofibrate administration prevented the fenofibrate-induced decrease of immobility in the FST test. (B) K252a pretreatment also prevented the fenofibrate-induced decrease of immobility in the TST test. (C) K252a did not influence the locomotor activity of mice in the open field test. (D) CSDS mice were co-injected with fenofibrate and K252a for 14 d. CSDS + fenofibrate + K252a mice displayed significantly lower sucrose preference than CSDS + fenofibrate mice. (E) Co-treatment fenofibrate with K252a also blocked the effects of fenofibrate in the social interaction test. CSDS + fenofibrate + K252a mice displayed significantly lower social interaction than CSDS + fenofibrate mice. Results are expressed as means  $\pm$  S.E.M. ( $n = 12$ );  $*P < 0.05$ ;  $**P < 0.01$ ; n.s., no significance.

Comparison was made by two-way ANOVA followed by post-hoc Bonferroni's test.