

Supplementary materials for

Sestrin modulator NV-5138 produces rapid antidepressant effects via direct mTORC1 activation

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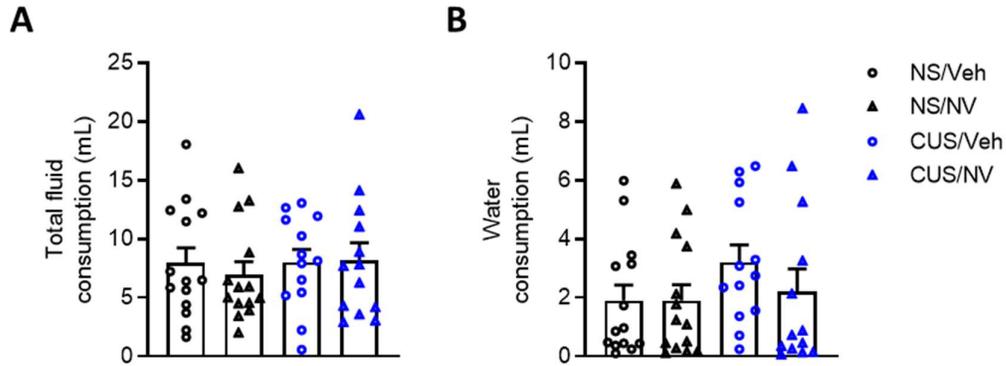
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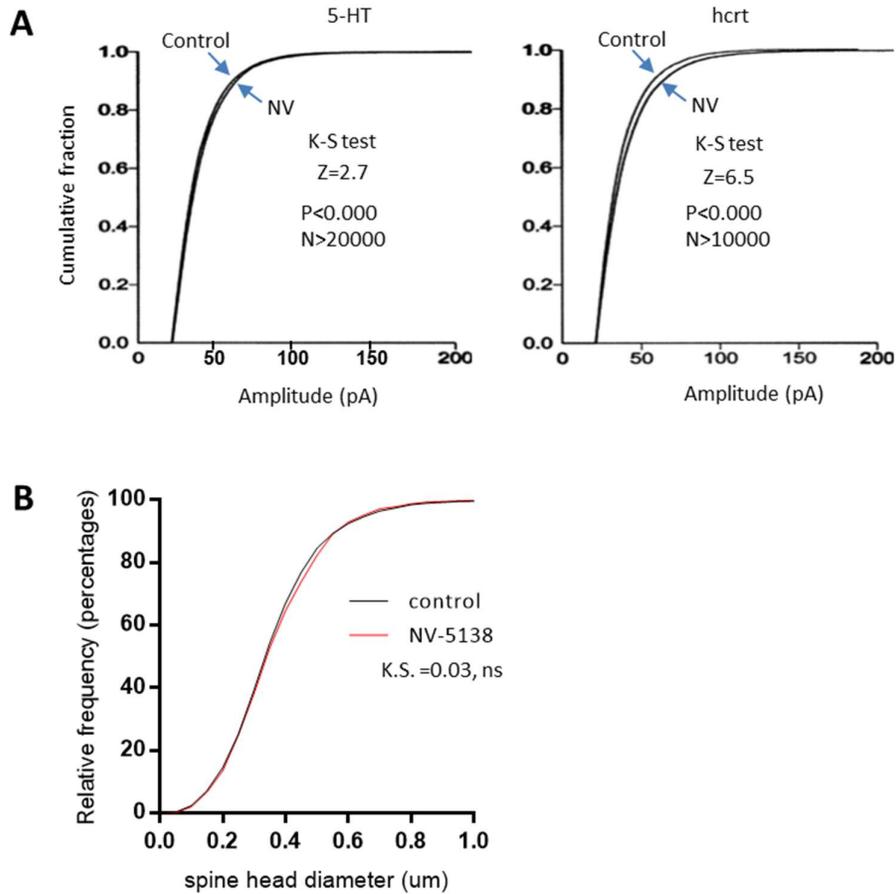
Fig. S1. Effect of NV-5138 on the total fluid and water consumption in naïve or CUS rats

Fig. S2. Influence of NV-5138 on spine number and function in the PFC

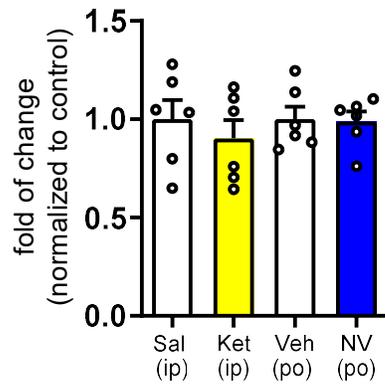
Fig. S3. Effect of NV-5138 on the GAPDH levels



Supplemental Figure 1. Effect of NV-5138 on total fluid and water consumption in naïve and CUS rats. Neither CUS nor NV-5138 treatment altered total fluid (A) or water (B) consumption (in mL) on the test day. There were no statistically significant effects observed on total fluid consumption (effect of CUS: $F_{1,50} = 0.287$, $p = 0.59$, effect of NV-5138: $F_{1,50} = 0.1$, $p = 0.75$, interaction (CUS vs. NV-5138): $F_{1,50} = 0.23$, $p = 0.64$) or water consumption (effect of CUS: $F_{1,50} = 1.72$, $p = 0.20$, effect of NV-5138: $F_{1,50} = 0.68$, $p = 0.41$, interaction (CUS vs. NV-5138): $F_{1,50} = 0.70$, $p = 0.41$). Results are expressed as mean \pm S.E.M. $n = 13-14$ /group. $p > 0.05$, Two-way ANOVA and post hoc Tukey's multiple comparison test.



Supplemental Figure 2. Influence of NV-5138 on spine number and function in the PFC. Layer V pyramidal neurons in mPFC brain slices were recorded 24 hr after vehicle or NV5138 administration as described in Figure 6. (A) Cumulative probability distributions showing significantly increased amplitudes for 5-HT and hypocretin (hcrt) (Kolmogorov–Smirnov two-sample test; $p = 0.0000$, z value = 2.7 for 5-HT; $p = 0.000$, z value = 6.5 for hypocretin). (B) Cumulative probability distribution showing the effect of NV-5138 on spine head diameter in layer V neurons (Kolmogorov–Smirnov two-sample test; $p = 0.03$, not significant).



Supplemental Figure 3. Effect of NV-5138 on GAPDH levels in PFC. (a) Rats were administered saline or ketamine (10 mg/kg) or vehicle or NV-5138 (160 mg/kg) and PFC dissections were collected 24 hr later. Levels of the GAPDH as determined by western blot analysis were unaltered by ketamine or NV-5138 treatments. The results are shown as mean \pm S.E.M. n = 6/group. p > 0.05, Student's t-test.