

Figure S1. Effect of acute AC-263093 treatment on locomotor activity in mice. Mice were injected with AC-263093 (30 mg/kg, IP) 60 min prior to the behavioral test. The activity was evaluated by tracking the mice movement in 30 min (EthoVision, Noldus, The Netherlands). **(A)** Distance mice moved in every 5 min. **(B)** Total distance mice moved; **(C,D)** Representative mouse tracks after injection with vehicle or AC-263093. Data are expressed as mean \pm S.E.M. and were analyzed using an unpaired Student's *t*-test ($N = 4$ per group).

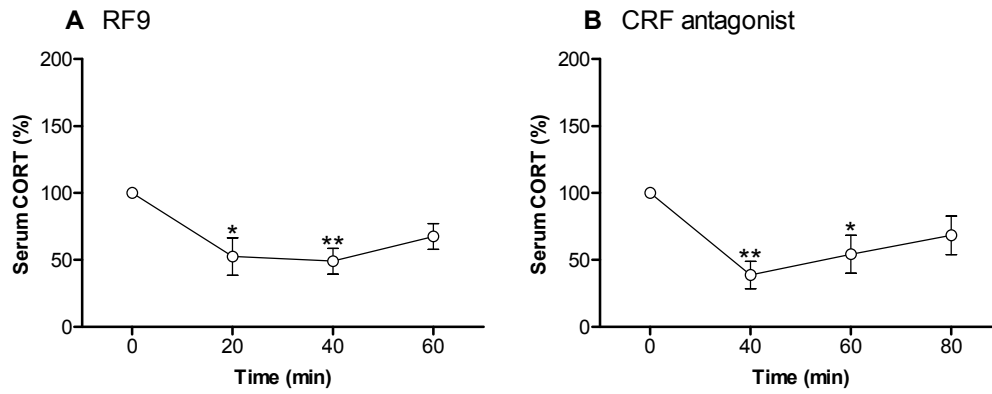


Figure S2. Time-dependent effect of RF9 or CRF antagonist on serum CORT levels in rats. Rats were injected with (A) RF9 (10 nmol, ICV) or (B) CRF antagonist α -helical CRF9-41 (200 μ g, IV) and serum CORT was monitored for up to 80 min post-drug administration. Data are expressed as mean \pm S.E.M and were analyzed using one-way ANOVA. ($N = 6$ per group). *, $p < 0.05$; **, $p < 0.01$, compared to time zero.

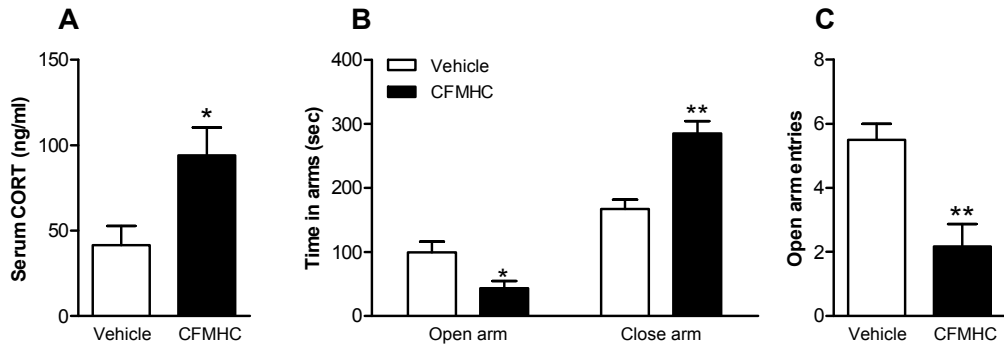


Figure S3. Effect of acute CFMHC treatment on serum CORT level and anxiety-like behaviors. Mice were injected with CFMHC (30 mg/kg, IP) 60 min prior to behavioral testing or serum collection. **(A)** Levels of serum CORT were measured to indicate the activity of the HPA axis. Anxiety-like behavior was evaluated by elevated plus maze; **(B)** Time that mice stayed in open versus closed arms; **(C)** Number of entries in open arms. Data are expressed as mean \pm S.E.M. and were analyzed using an unpaired Student's *t*-test. *, $p < 0.05$; **, $p < 0.01$, compared to vehicle controls ($N = 4-6$ per group).