

## Inducible Schizophrenia Rat Models

The most widely validated animal models of the positive, negative and cognitive symptoms of schizophrenia involve administration of the dopamine-releasing drug, d-amphetamine in combination with the benzodiazepine Chlordiazepoxide (AMPH) or an open channel NMDA receptor blocker, phencyclidine (PCP). Pretreatment with Clozapine (CZP) can reverse the observed effects.

- PCP decreases social interaction of Sprague Dawley rats in the Three Chamber Social test. Effect can not be prevented or decreased by CZP
- PCP increases startle response in the prepulse inhibition test, effect can be prevented by CZP
- PCP decreases prepulse inhibition in the prepulse inhibition test, effect can be reversed by CZP, effect of PCP depends on prepulse intensity

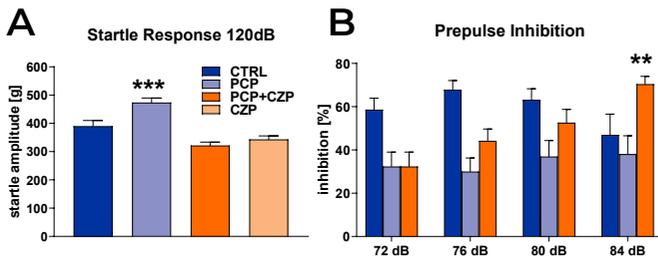


Figure 1: Startle response and prepulse inhibition of PCP-treated Sprague Dawley rats. A: Startle amplitude in gram at 120 dB; One-way ANOVA. B: Prepulse inhibition in percent using 4 different dB intensities; Two-way ANOVA. n = 10; Mean + SEM; \*\*p<0.01; \*\*\*p<0.001.

- AMPH increases activity in the Open Field test 10 minutes after treatment
- AMPH effect can be decreased by CZP

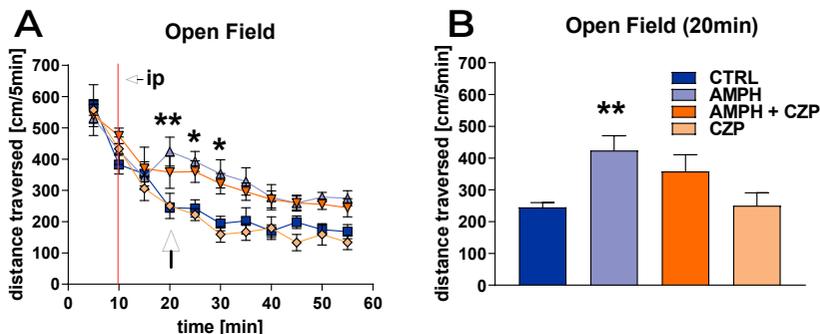


Figure 2: Open field behavior of amphetamine (AMPH)-treated Sprague Dawley rats. A: Distance traversed in cm/5min over time; Two-way repeated measurements ANOVA with Bonferroni's *post hoc* test. Mean ± SEM. B: distance traversed in cm/5min, 20 minutes after start of the analysis; One-way ANOVA with Bonferroni's *post hoc* test. Mean + SEM. CTRL = Control; CTRL, AMPH, AMPH+CZP: n = 8 - 10; \*p<0.05; \*\*p<0.01.