

**STIMULANTS AS SPECIFIC INDUCERS OF DOPAMINE-INDEPENDENT SIGMA AGONIST SELF-
ADMINISTRATION IN RATS**

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TABLES

Table 1: Statistical analyses of dose-effect curves of various compounds compared to saline availability as shown in the Figure 2a-c.

Treatment	Drug	Dose	Interaction	Post-hoc test
<i>d</i> -Methamphetamine vs. saline substitution	$F_{1,20}=30.5$; $p=0.003$	$F_{4,20}=26.4$; $p<0.001$	$F_{4,20}=32.0$; $p<0.001$	0.032 mg/kg/inj, $t=3.28$, $p=0.004$, 0.10 mg/kg/inj, $t=7.65$, $p<0.001$
PRE-084 vs. saline substitution	$F_{1,20}=6.10$; $p=0.057$	$F_{4,20}=5.05$; $p=0.006$	$F_{4,20}=5.43$; $p=0.004$	0.1 mg/kg/inj, $t=2.55$, $p=0.019$, 0.32 mg/kg/inj, $t=4.66$, $p<0.001$
(+)-Pentazocine vs. saline substitution	$F_{1,20}=15.6$; $p=0.011$	$F_{4,20}=13.8$; $p<0.001$	$F_{4,20}=15.1$; $p<0.001$	0.1 mg/kg/inj, $t=3.33$, $p=0.003$, 0.32 mg/kg/inj, $t=8.02$, $p<0.001$
<i>d</i> -Amphetamine vs. saline substitution	$F_{1,20}=24.8$; $p=0.004$	$F_{4,20}=18.3$; $p<0.001$	$F_{4,20}=20.1$; $p<0.001$	0.032 mg/kg/inj, $t=4.54$, $p<0.001$, 0.10 mg/kg/inj, $t=9.24$, $p<0.001$
BD 1008 vs. saline substitution	$F_{1,20}=7.12$; $p=0.044$	$F_{4,20}=0.859$; ; $p=0.505$	$F_{4,20}=0.255$; $p=0.903$	0.032 mg/kg/inj, $t=2.13$, $p=0.043$
(+)-Butaclamol vs. saline substitution	$F_{1,20}=1.58$; $p=0.264$	$F_{4,20}=0.038$ 3; $p=0.997$	$F_{4,20}=0.552$; $p=0.700$	N.S.
Naltrexone vs. saline substitution	$F_{1,20}=6.10$; $p=0.057$	$F_{4,20}=0.400$; ; $p=0.806$	$F_{4,20}=0.474$; $p=0.755$	N.S.
Heroin vs. saline substitution	$F_{1,20}=28.3$; $p=0.003$	$F_{4,20}=25.0$; $p<0.001$	$F_{4,20}=35.1$; $p<0.001$	3.2 μ g/kg/injection, $t=6.66$, $p<0.001$, 10 μ g/kg/injection, $t=10.6$, $p<0.001$
PRE-084 (0.032-1.0 mg/kg/inj) vs. saline substitution	$F_{1,20}=0.0224$; ; $p=0.887$	$F_{4,20}=8.20$; $p<0.001$	$F_{4,20}=5.21$; $p=0.005$	N.S.
PRE-084 substitution (0.32-10 mg/kg/inj) vs. saline substitution	$F_{1,20}=0.0016$ 0; $p=0.970$	$F_{4,20}=10.1$; $p<0.001$	$F_{4,20}=5.27$; $p=0.005$	3.2 mg/kg/inj, $t=2.32$, $p=0.031$, 10 mg/kg/inj, $t=2.61$, $p=0.016$
(+)-Pentazocine (0.032-1.0 mg/kg/inj) vs. saline substitution	$F_{1,20}=0.248$; $p=0.640$	$F_{4,20}=8.19$; $p<0.001$	$F_{4,20}=3.70$; $p=0.021$	0.1 mg/kg/injection, $t=2.76$, $p=0.011$
(+)-Pentazocine (0.32-10 mg/kg/inj) vs. saline substitution	$F_{1,20}=0.354$; $p=0.578$	$F_{4,20}=6.23$; $p=0.002$	$F_{4,20}=14.6$; $p<0.001$	0.32 mg/kg/inj, $t=3.74$, $p=0.001$, 1.0 mg/kg/inj, $t=4.23$, $p<0.001$,

				0 mg/kg/inj, t=3.45, p=0.003
Remifentanil vs. saline substitution	F _{1,20} =13.4; p=0.015	F _{4,20} =9.77; p<0.001	F _{4,20} =9.96; p<0.001	0.32 µg/kg/inj, t=3.71, p=0.001, 1.0 µg/kg/inj, t=6.37, p<0.001
BD 1008 vs. saline substitution	F _{1,20} =0.0271 ; p=0.876	F _{4,20} =2.98; p=0.044	F _{4,20} =6.19; p=0.002	0.32 mg/kg/inj, t=2.73, p=0.012, 1.0 mg/kg/inj, t=3.18, p=0.004
(+)-Butaclamol vs. saline substitution	F _{1,20} =0.0823 ; p=0.786	F _{4,20} =2.79; p=0.055	F _{4,20} =8.62; p<0.001	0.1 µg/kg/inj, t=2.72, p=0.013, 1.0 µg/kg/inj, t=2.31, p=0.031, 3.2 µg/kg/inj, t=3.19, p=0.004
Naltrexone vs. saline substitution	F _{1,20} =0.177; p=0.692	F _{4,20} =4.57; p=0.009	F _{4,20} =12.0; p<0.001	0.32 mg/kg/inj, t=2.78, p=0.019, 1.0 mg/kg/inj, t=3.20, p=0.009
Ketamine vs. saline substitution	F _{1,20} =15.9; p=0.011	F _{4,20} =11.9; p<0.001	F _{4,20} =12.3; p<0.001	0.1 mg/kg/inj, t=3.51, p=0.002, 0.32 mg/kg/inj, t=7.40, p<0.001
PRE-084 (0.032-1.0 mg/kg/inj) vs. saline substitution	F _{1,20} =6.19; p=0.055	F _{4,20} =2.48; p=0.077	F _{4,20} =6.74; p=0.001	0.32 mg/kg/inj, t=5.34, p<0.001
PRE-084 (0.32-10 mg/kg/inj) vs. saline substitution	F _{1,20} =3.64; p=0.115	F _{4,20} =4.55; p=0.009	F _{4,20} =2.38; p=0.086	1.0 mg/kg/inj, t=2.44, p=0.023
(+)-Pentazocine (0.032-1.0 mg/kg/inj) vs. saline substitution	F _{1,20} =2.26; p=0.193	F _{4,20} =1.28; p=0.310	F _{4,20} =1.63; p=0.205	N.S.
(+)-Pentazocine (0.32-10 mg/kg/inj) vs. saline substitution	F _{1,20} =2.47; p=0.177	F _{4,20} =1.54; p=0.230	F _{4,20} =2.46; p=0.079	N.S.
(+)-MK 801 vs. saline substitution	F _{1,20} =27.2; p=0.003	F _{4,20} =22.4; p<0.001	F _{4,20} =34.7; p<0.001	1.0 µg/kg/inj, t=6.76, p<0.001, 3.2 µg/kg/inj, t=10.1, p<0.001, 10 µg/kg/inj, t=2.28, p=0.038
BD 1008 vs. saline substitution	F _{1,20} =1.52; p=0.272	F _{4,20} =7.06; p=0.001	F _{4,20} =1.54; p=0.229	0.32 mg/kg/inj, t=2.44, p=0.026
(+)-Butaclamol vs. saline substitution	F _{1,20} =3.03; p=0.142	F _{4,20} =4.67; p=0.008	F _{4,20} =8.02; p<0.001	0 µg/kg/inj, t=2.72, p=0.012, 0.1 µg/kg/inj, t=2.31, p=0.031, 1.0 µg/kg/inj, t=2.64, p=0.015,

				3.2 µg/kg/inj, t=3.36, p=0.003
Naltrexone vs. saline substitution	F _{1,20} =4.28; p=0.093	F _{4,20} =3.69; p=0.021	F _{4,20} =2.07; p=0.123	0 mg/kg/inj, t=2.30, p=0.031, 0.1 mg/kg/inj, t=2.19, p=0.038

N.S. non-significant

Table 2: Statistical analyses of effects of BD 1008, (+)-butaclamol, or naltrexone on self-administration of *d*-methamphetamine, heroin, ketamine, and PRE-084 substitution for *d*-methamphetamine as shown in Figures 3-4.

Treatment	Self-Administered Drug Dose	Antagonist Dose (i.p.)	Interaction	Post-hoc test
(+)-Butaclamol (i.p.) before <i>d</i> -methamphetamine self-administration	F _{4,80} =31.3; p<0.001	F _{4,80} =30.5; p<0.001	F _{16,80} =31.2; p<0.001	3.2 µg/kg (i.p.) at 0.032 mg/kg/inj, t=7.19, p<0.001, 10 µg/kg (i.p.) at 0.032 mg/kg/inj, t=6.86, p<0.001, 32 µg/kg (i.p.) at 0.032 mg/kg/inj, t=7.02, p<0.001, 3.2 µg/kg (i.p.) at 0.1 mg/kg/inj, t=5.18, p<0.001, 10 µg/kg (i.p.) at 0.1 mg/kg/inj, t=10.8, p<0.001, 32 µg/kg (i.p.) at 0.1 mg/kg/inj, t=11.3, p<0.001, 3.2 µg/kg (i.p.) at 0.32 mg/kg/inj, t=11.3, p<0.001, 10 µg/kg (i.p.) at 0.32 mg/kg/inj, t=6.03, p<0.001, 32 µg/kg (i.p.) at 0.32 mg/kg/inj, t=2.93, p=0.043
BD 1008 (i.p.) before <i>d</i> -methamphetamine self-administration	F _{4,80} =36.2; p<0.001	F _{4,80} =3.38; p=0.029	F _{16,80} =2.44; p=0.005	N.S. (vs. Vehicle, i.p.)
Naltrexone (i.p.) before <i>d</i> -methamphetamine self-administration	F _{4,60} =34.9; p<0.001	F _{3,60} =1.28; p=0.317	F _{12,60} =0.776; p=0.673	N.S. (vs. Vehicle, i.p.)
(+)-Butaclamol (i.p.) before PRE-084 substitution for <i>d</i> -methamphetamine self-administration	F _{4,60} =5.36; p=0.004	F _{3,60} =2.99; p=0.064	F _{12,60} =3.12; p=0.002	10 µg/kg (i.p.) at 0.1 mg/kg/inj, t=5.04, p<0.001 32 µg/kg (i.p.) at 0.32 mg/kg/inj, t=3.06, p=0.019 100 µg/kg (i.p.) at 0.32 mg/kg/inj, t=3.76, p=0.002
BD 1008 (i.p.) before PRE-084 substitution for <i>d</i> -methamphetamine self-administration	F _{4,60} =6.24; p=0.002	F _{3,60} =5.82; p=0.008	F _{12,60} =4.77; p<0.001	10 mg/kg (i.p.) at 0.1 mg/kg/inj, t=3.29, p=0.010, 3.2 mg/kg (i.p.) at 0.32 mg/kg/inj, t=4.39, p<0.001, 10 mg/kg (i.p.) at 0.32 mg/kg/inj, t=5.60, p<0.001

Naltrexone (i.p.) before PRE-084 substitution for <i>d</i> -methamphetamine self-administration	F _{4,60} =5.55; p=0.004	F _{3,60} =3.45; p=0.044	F _{12,60} =3.50; p<0.0001	1.0 mg/kg (i.p.) at 0.1 mg/kg/inj, t=5.78, p<0.001 3.2 mg/kg (i.p.) at 0.1 mg/kg/inj, t=3.54, p=0.005 10 mg/kg (i.p.) at 0.1 mg/kg/inj, t=5.78, p<0.001 1.0 mg/kg (i.p.) at 0.32 mg/kg/inj, t=3.56, p=0.004
(+)-Butaclamol (i.p.) before heroin self-administration	F _{4,100} =30.4; p<0.001	F _{5,100} =6.57; p<0.001	F _{20,100} =4.24; p<0.001	1.0 µg/kg (i.p.) at 3.2 µg/kg/inj, t=4.23, p=0.001 3.2 µg/kg (i.p.) at 10 µg/kg/inj, t=5.75, p<0.001
BD 1008 (i.p.) before heroin self-administration	F _{4,80} =32.7; p<0.001	F _{4,80} =3.27; p=0.033	F _{16,80} =0.855; p=0.621	N.S. (vs. Vehicle, i.p.)
Naltrexone (i.p.) before heroin self-administration	F _{4,80} =32.9; p<0.001	F _{4,80} =26.3; p<0.001	F _{16,80} =32.9; p<0.001	0.32 µg/kg (i.p.) at 3.2 µg/kg/inj, t=7.72, p<0.001, 1.0 µg/kg (i.p.) at 3.2 µg/kg/inj, t=7.88, p<0.001, 3.2 µg/kg (i.p.) at 3.2 µg/kg/inj, t=7.24, p<0.001, 0.32 µg/kg (i.p.) at 10 µg/kg/inj, t=3.07, p=0.028, 1.0 µg/kg (i.p.) at 10 µg/kg/inj, t=10.8, p<0.001, 3.2 µg/kg (i.p.) at 10 µg/kg/inj, t=10.8, p<0.001, 0.32 µg/kg (i.p.) at 32 µg/kg/inj, t=9.75, p<0.001, 1.0 µg/kg (i.p.) at 32 µg/kg/inj, t=8.44, p<0.001, 3.2 µg/kg (i.p.) at 32 µg/kg/inj, t=2.89, p=0.047
(+)-Butaclamol (i.p.) before ketamine self-administration	F _{4,100} =12.5; p<0.001	F _{5,100} =6.83; p<0.001	F _{20,100} =6.68; p<0.001	1.0 µg/kg (i.p.) at 0.1 mg/kg/inj, t=3.90, p=0.002 1.0 µg/kg (i.p.) at 0.32 mg/kg/inj, t=6.36, p<0.001 32 µg/kg (i.p.) at 0.32 mg/kg/inj, t=3.11, p=0.035 100 µg/kg (i.p.) at 0.32 mg/kg/inj, t=3.23, p=0.024
BD 1008 (i.p.) before ketamine self-administration	F _{4,80} =12.5; p<0.001	F _{4,80} =5.85; p=0.003	F _{16,80} =5.47; p<0.001	1.0 mg/kg (i.p.) at 0.32 mg/kg/inj, t=5.90, p<0.001, 3.2 mg/kg (i.p.) at 0.32 mg/kg/inj, t=3.27, p=0.015, 32 mg/kg (i.p.) at 0.32 mg/kg/inj, t=3.28, p=0.015
Naltrexone (i.p.) before ketamine self-administration	F _{4,100} =11.3; p<0.001	F _{5,100} =5.74; p=0.001	F _{20,100} =4.75; p<0.001	3.2 mg/kg (i.p.) at 0.32 mg/kg/inj, t=8.85, p<0.001

N.S.: non-significant