

Supplemental Materials

Dissociable effects of the prodrug phendimetrazine and its metabolite phenmetrazine at dopamine transporters

Ernesto Solis Jr¹, Julie A Suyama², Matthew F Lazenka², Louis J De Felice¹, S Stevens Negus^{2,3},
Bruce E Blough⁴, Matthew L Banks^{2,3*}

¹Department of Physiology and Biophysics, Virginia Commonwealth University, Richmond, VA, USA 23298

²Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA, USA 23298

³Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, VA, USA 23298

⁴Center for Drug Discovery, Research Triangle Institute, Research Triangle Park, NC, USA 27709

Number of Figures: 4

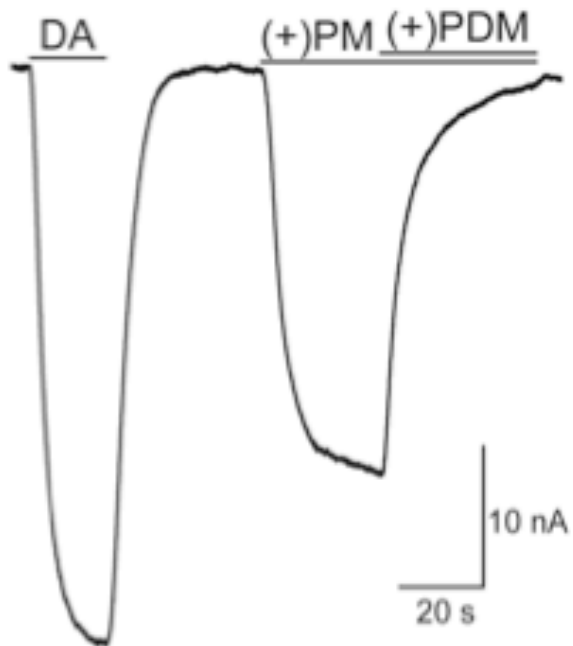


Figure 1: (+)-Phendimetrazine (PDM) effects on (+)-phenmetrazine (PM) -induced inward currents at hDAT in *Xenopus laevis* oocytes voltage-clamped to -60 mV. The initial DA-induced response was $5 \mu\text{M}$ DA. This representative trace shows application of $200 \mu\text{M}$ (+)-PDM attenuated the current induced by $2 \mu\text{M}$ (+)-PM.

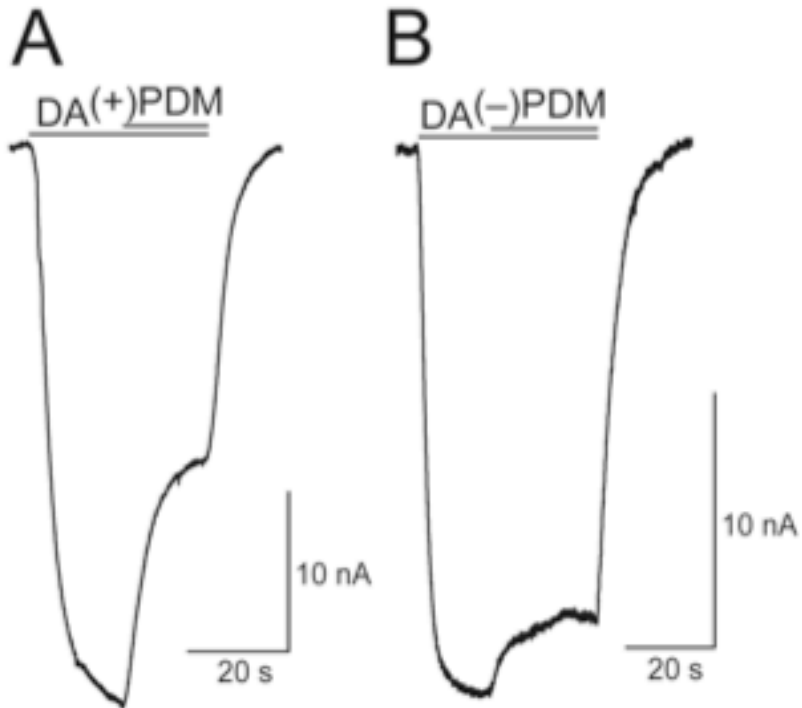


Figure 2: (+)-Phendimetrazine (PDM) and (-)-PDM effects on dopamine- (DA) -induced inward currents at hDAT in *Xenopus laevis* oocytes voltage-clamped to -60 mV. Panel A shows application of 50 μ M (+)-PDM attenuated the current induced by 5 μ M DA. Panel B shows application of 100 μ M (-)-PDM attenuated the current induced by 5 μ M DA; however, this effect was weaker than (+)-PDM due to the lower potency of (-)-PDM.

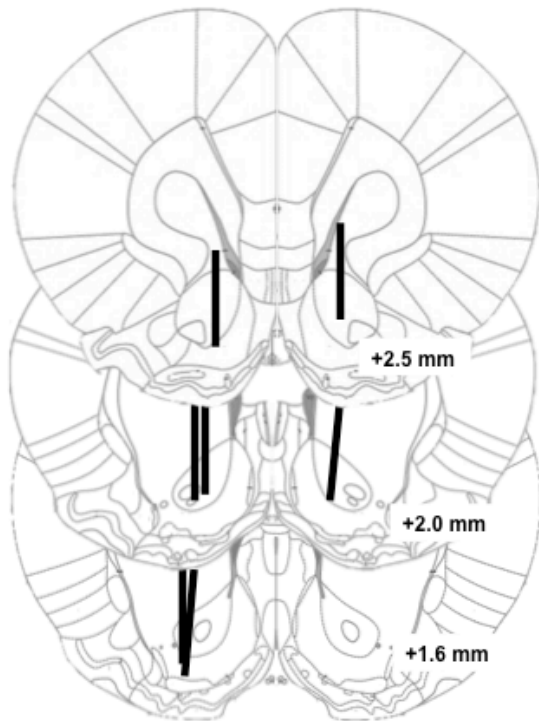


Figure 3: Coronal section depiction of the rat brain (adapted by authors from Paxinos and Watson, 2006) showing the positions of the microdialysis probes. Number in the bottom right indicates anterior-posterior position relative to bregma.

Paxinos, G. and Watson, C. *The Rat Brain in Stereotaxic Coordinates*, 6th edition, (Academic Press, San Diego 2006).

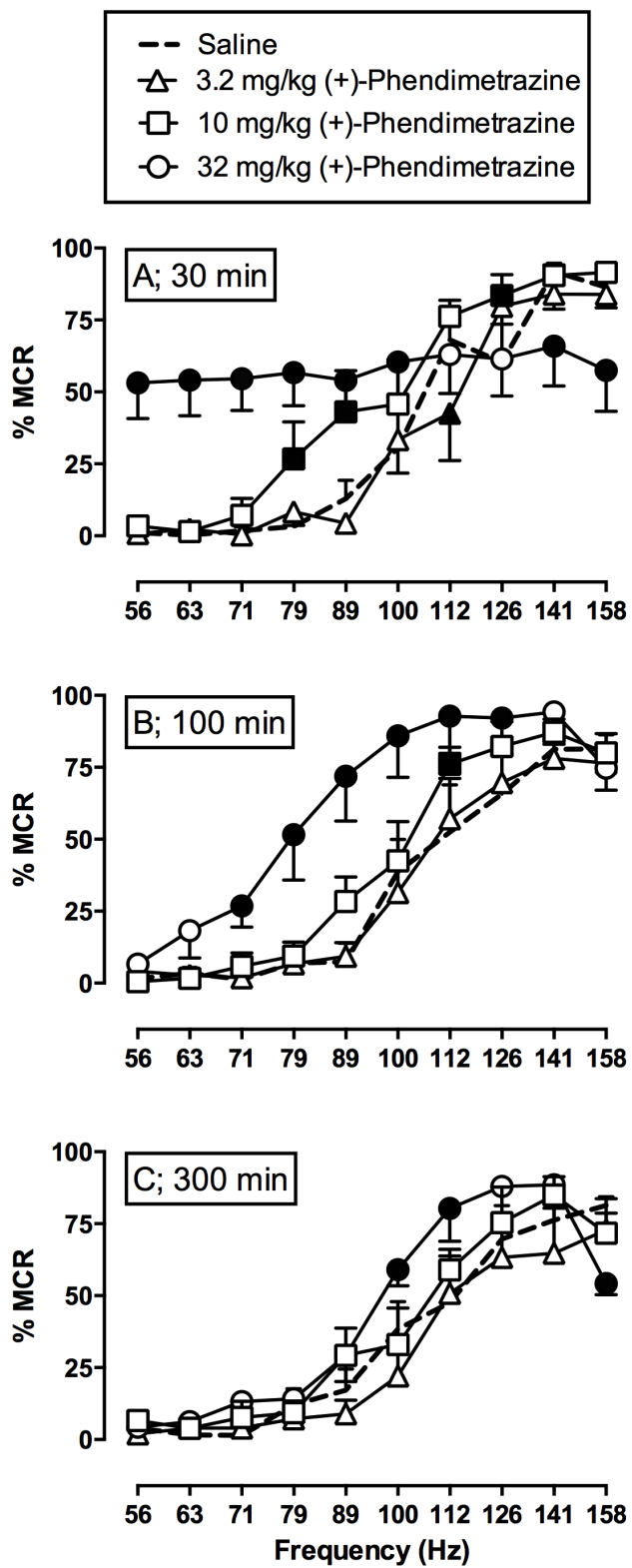


Figure 4: (+)-Phendimetrazine (PDM; 3.2-32 mg/kg, ip) effects on intracranial self-stimulation (ICSS) at 30 min (Panel A), 100 min (Panel B), and 300 min (Panel C). *Abscissa:* frequency of electrical brain stimulation in Hz. *Ordinate:* ICSS rate maintained by each brain stimulation frequency, expressed as percent maximum control reinforcement rate (%MCR). Filled points represent frequencies at which ICSS rates were statistically different from vehicle rates ($p < 0.05$). All data show mean \pm SEM for 6 rats. 30 min (frequency: $F_{9,45}=49.3$, $p < 0.0001$; dose \times frequency interaction: $F_{27,135}=8.0$, $p < 0.0001$). 100 min (frequency: $F_{9,45}=51.7$, $p < 0.0001$; dose: $F_{3,15}=4.8$, $p=0.0152$; dose \times frequency interaction: $F_{27,135}=2.6$, $p=0.0002$). 300 min (frequency: $F_{9,45}=52.5$, $p < 0.0001$; dose: $F_{3,15}=7.1$, $p=0.0034$; dose \times frequency interaction: $F_{27,135}=1.9$, $p=0.0071$).