



**References on the Administration of Drugs of Abuse
(including Amphetamines, Barbiturates, Cocaine, GHB, Heroin, Nicotine, and PCP)
Using ALZET® Osmotic Pumps**

1. Amphetamines

Q7057: P. Petschner, *et al.* Gene expression analysis indicates reduced memory and cognitive functions in the hippocampus and increase in synaptic reorganization in the frontal cortex 3 weeks after MDMA administration in Dark Agouti rats. *BMC Genomics* 2018;19(1):580

Agents: Methamphetamine, 3,4-methylenedioxy- **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** ALZET
Comments: Controls received mp w/ vehicle; animal info (8-week old Dark Agouti rats weighing 152 +/- 3.58 g); 3,4-methylenedioxymethamphetamine aka MDMA or ecstasy;

Q7002: P. Petschner, *et al.* Gene expression analysis indicates reduced memory and cognitive functions in the hippocampus and increase in synaptic reorganization in the frontal cortex 3 weeks after MDMA administration in Dark Agouti rats. *BMC Genomics* 2018;19(1):580

Agents: Methamphetamine, 3,4-methylenedioxy- **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** ALZET
Comments: Controls received mp w/ vehicle;

Q7766: A. R. Johnson, *et al.* Amphetamine maintenance differentially modulates effects of cocaine, methylenedioxypyrovalerone (MDPV), and methamphetamine on intracranial self-stimulation and nucleus accumbens dopamine in rats. *Neuropsychopharmacology* 2018;43(8):1753-1762

Agents: amphetamine **Vehicle:** saline, bacteriostatic; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7, 13 days;
ALZET Comments: Dose (0.1 or 0.32 mg/kg/h), (2ML2 pump 0.5 µl/h); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 300-350g); behavioral testing (operant chambers); comparison of IP injection vs mp; dependence;

Q6700: D. Moller, *et al.* Discovery of G Protein-Biased Dopaminergics with a Pyrazolo[1,5-a]pyridine Substructure. *J Med Chem* 2017;60(7):2908-2929

Agents: Amphetamine **Vehicle:** DMSO; acetic acid; water; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (1.5 mg/kg/day); 2% acetic acid, 25% DMSO used; Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats weighing 300-350 g); dependence

Q6443: S. V. Kyosseva, *et al.* Chronic administration of MDMA ("ECSTASY") increases insulin-regulated glucose transporter GLUT4 in rat brain and heart. 2017;

Agents: Methamphetamine, 3,4-methylenedioxy **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 10 days;
ALZET Comments: Dose (0.3 or 3 mg/kg/day); animal info (Sprague-Dawley rats);

2. Cocaine

R0335: R. M. Post. Epigenetic basis of sensitization to stress, affective episodes, and stimulants: implications for illness progression and prevention. *Bipolar Disord* 2016;18(4):315-24

Agents: Cocaine **Vehicle:** **Route:** **Species:** **Pump:** **Duration:** **ALZET Comments:**

Q4278: A. K. Radke, *et al.* Cocaine withdrawal in rats selectively bred for low (LoS) versus high (HiS) saccharin intake. *PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR* 2015;129(51-55)

Agents: Cocaine hydrochloride **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Holtzman/Harlan Sprague Dawley); no stress (see pg.53); post op. care (topical antibiotic ointment); behavioral testing (saccharin intake); dependence; pumps removed after 2 weeks;

Q3606: C. M. Pudiak, *et al.* Tolerance to cocaine in brain stimulation reward following continuous cocaine infusions. *Pharmacology Biochemistry and Behavior* 2014;122(246-252)



Agents: Cocaine **Vehicle:** Saline; sodium metabisulfate; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Long-Evans, 275-350g); functionality of mp verified by residual volume; 0.3% sodium metabisulfate used to prevent degradation; stress/adverse reaction: (see pg.294); post op. care (neosporin); dependence; "Cocaine delivered continuously via osmotic minipump may better mimic the high drug-plasma concentrations maintained by an addict during a binge than daily administered cocaine injections." pg 250; pumps removed after 14 days; pumps primed at 37C for at least 4 hours;

Q3579: P. A. Narayana, *et al.* Chronic cocaine administration causes extensive white matter damage in brain: Diffusion tensor imaging and immunohistochemistry studies. *PSYCHIATRY RESEARCH-NEUROIMAGING* 2014;221(3):220-230

Agents: Cocaine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 280-300g); behavioral testing (fine motor movement; ambulation; rearing activities; general motor behavior); dependence; MRI; pumps primed for 24 hours in 37C saline;

Q3428: F. F. Caputi, *et al.* Dynorphin/KOP and nociceptin/NOP gene expression and epigenetic changes by cocaine in rat striatum and nucleus accumbens. *PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY* 2014;49(1):36-46

Agents: Cocaine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague Dawley, 200-250g); dependence; pumps primed overnight in 37C saline;

3. GHP (Gamma-hydroxybutyrate)

P6690: S. T. Szabo, M. S. Gold, B. A. Goldberger and P. Blier. Effects of sustained gamma-hydroxybutyrate treatments on spontaneous and evoked firing activity of locus coeruleus norepinephrine neurons. *Biological Psychiatry* 2004;55(9):934-939

ALZET Comments: Hydroxybutyrate, gamma-; Saline; SC; Rat; 2,10 days; Controls received mp w/ vehicle; dependence; agent is a drug of abuse, known as "liquid ecstasy" or GHB (sodium oxybate); pump model not listed.

4. Heroin

Q4818: S. Daniels, *et al.* Alterations of naltrexone-induced conditioned place avoidance by pre-exposure to high fructose corn syrup or heroin in Sprague–Dawley rats. *Psychopharmacology* 2016;233(1):425-433

Agents: Heroin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dalwley, 175-200g); behavioral testing (place conditioning); used wound clips; Dose (3.5 mg/kg/day);

Q2457: A. M. Williams, *et al.* The effect of intermittent alcohol vapor or pulsatile heroin on somatic and negative affective indices during spontaneous withdrawal in Wistar rats. *Psychopharmacology* 2012;223(1):75-88

Agents: Heroin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 30 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Wistar, male, 70 days old); pulsatile delivery; "By filling the pumps with saline and attaching polyethylene (PE60) tubing to the pump, based on the tubing inner diameter and pump flow rate characteristics, the volume needed for different infusion periods (e.g., 14- or 10-h periods) could be determined"; "the tubing was filled with alternating heroin solution and mineral oil"; pulsatile delivery; good methods, pg 78; image of pump with connected Lynch coil; wound clips used; post op. care (Baytril); behavioral testing (elevated plus mazet forced swim test)

P9748: G. Klein, *et al.* The contribution of MOR-1 exons 1-4 to morphine and heroin analgesia and dependence. *Neuroscience Letters* 2009;457(3):115-119

Agents: Heroin hydrochloride; morphine sulfate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** ALZET
Comments: Controls received mp w/vehicle; dependence; animal info (adult, male, CD-1)



Q0587: B. Kest, *et al.* Gnao1 (G- α_o PROTEIN) IS A LIKELY GENETIC CONTRIBUTOR TO VARIATION IN PHYSICAL DEPENDENCE ON OPIOIDS IN MICE. *Neuroscience* 2009;162(4):1255-1264

Agents: Morphine; heroin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Animal info (Naive, adult, 7-12 wks old, male, AcB/BcA)

P6278: M. R. Azar, *et al.* A non-invasive gating device for continuous drug delivery that allows control over the timing and duration of spontaneous opiate withdrawal. *Journal of Neuroscience Methods* 2004;135(1-2):129-135

Agents: Heroin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 192 hours;
ALZET Comments: Comparison of sc injections & pellet vs. mp; dependence; 3 day recovery period; pumps connected to a novel gating device to allow on-off delivery; assembly schematic (p. 131); infusions were delivered in 48 hour intervals; animal info (m, wistar, 300-380 grams)

5. Nicotine

Q8581: B. Kim, *et al.* Chronic nicotine impairs sparse motor learning via striatal fast-spiking parvalbumin interneurons. *Addict Biol* 2020;e12956

Agents: Nicotine ditartrate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2 weeks;
ALZET Comments: Dose (24 mg/kg/day); Controls received mp w/ vehicle; animal info (2- to 3-month-old C57BL/6J male mice); behavioral testing (Open field test; light-dark transition; rotarod test); dependence;

Q8553: G. Jia, *et al.* Nicotine induces cardiac toxicity through blocking mitophagic clearance in young adult rat. *Life Sci* 2020;257(118084)

Agents: Nicotine **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 6 weeks;
ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats, 2-4 months old); toxicology;

Q8474: K. Fukuyama, *et al.* Upregulated Connexin 43 Induced by Loss-of-Functional S284L-Mutant alpha4 Subunit of Nicotinic ACh Receptor Contributes to Pathomechanisms of Autosomal Dominant Sleep-Related Hypermotor Epilepsy. *Pharmaceuticals (Basel)* 2020;13(4):

Agents: Zonisamide; Nicotine **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (40 mg/kg/day Zonisamide, 10, 25 and 50 mg/kg/day Nicotine); animal info (Male S286L-TG and wild-type littermates); Zonisamide aka ZNS; neurodegenerative (Epilepsy);

Q8379: F. Diaz, *et al.* Simultaneous nicotine and oral contraceptive exposure alters brain energy metabolism and exacerbates ischemic stroke injury in female rats. *J Cereb Blood Flow Metab* 2020;271678X20925164

Agents: Nicotine Hydrogen Tartrate **Vehicle:** Saline; **Route:** CNS/CSF; **Species:** Rat; **Pump:** 2ML2; **Duration:** 21 days;
ALZET Comments: Dose (4.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley, 6 or 14 weeks old); ischemia (Stroke);

Q8388: D. Bhattacharya, *et al.* Concurrent nicotine exposure to prenatal alcohol consumption alters the hippocampal and cortical neurotoxicity. *Heliyon* 2020;6(1):e03045

Agents: Nicotine **Vehicle:** Alcohol, Saline; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** Not stated;
ALZET Comments: Dose (6 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague Dawley (Time pregnant) rats); behavioral testing (Y maze); toxicology;

6. Pentobarbital

P5450: Y. Kim, *et al.* Changes of the level of G protein alpha-subunit mRNA by tolerance to and withdrawal from pentobarbital in rats. *Neurochemical Research* 2002;27(6):527-533

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; tolerance; dependence; one week recovery period after cannula placement



P4317: C.-G. Jang, *et al.* Autoradiography of [³H] glutamate binding during pentobarbital tolerance and withdrawal in the rat. *Brain Research Bulletin* 1999;48(1):99-102

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: Controls received mp with vehicle; tolerance; dependence; animals allowed one week recovery after cannula placement

P4177: S. Oh, *et al.* Changes in (3H)forskolin binding to adenylate cyclase and (3H)phorbol dibutyrate binding to protein kinase c in pentobarbital tolerant/dependent rats. *Neurochem. Res* 1998;23(4):463-467

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: guide cannula implanted; rats were allowed 1 week recovery before implantation of pump; tolerance; dependence

P4188: C.-G. Jang, *et al.* Changes in NMDAR2 subunit mRNA levels during pentobarbital tolerance/withdrawal in the rat brain: an in situ hybridization study. *Neurochem. Res* 1998;23(11):1371-1377

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: controls received mp w/saline; tolerance

P3852: S. Oh, *et al.* Role of NMDA receptors in pentobarbital tolerance/dependence. *Neurochem. Res* 1997;22(7):767-774

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: controls received mp w/saline; tolerance; dependence

7. Penylcyclidine

Q2590: A. Balla, *et al.* Effects of novel, high affinity glycine transport inhibitors on frontostriatal dopamine release in a rodent model of schizophrenia. *European Neuropsychopharmacology* 2012;22(12):902-910

Agents: Phencyclidine hydrochloride **Vehicle:** Saline, sterile, physiological; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:**

ALZET Comments: Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, wks old, 160-200 g, 280-320 g)

Q0375: C. S. Pedersen, *et al.* Chronic infusion of PCP via osmotic mini-pumps: A new rodent model of cognitive deficit in schizophrenia characterized by impaired attentional set-shifting (ID/ED) performance. *Journal of Neuroscience Methods* 2009;185(1):66-69

Agents: Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 14 days;

ALZET Comments: Controls received mp w/saline; animal info (Lister hooded, male); post op. care (Bairril, Rimadyl); "Using PCP mini-pump infusion instead of the well described intraperitoneal dosing bears the advantage of reducing the animal's stress levels, bypasses the risk of potential mis-dosing that could arise from multiple dosing events and consequently may reduce the number of animals needed." pg 69

P7825: G. Pitas, *et al.* Anti-phencyclidine monoclonal antibody binding capacity is not the only determinant of effectiveness, disproving the concept that antibody capacity is easily surmounted. *Drug Metabolism and Disposition* 2006;34(6):906-912

Agents: Phencyclidine HCL **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 4 days;

ALZET Comments: Functionality of mp verified by serum PCP concentrations; half-life (pg. 907) 3.9 hours in rats; tolerance; animal info (male, Sprague-Dawley, 270-300g.)

P6979: F. Sams-Dodd. (+) MK-801 and phencyclidine induced neurotoxicity do not cause enduring behaviours resembling the positive and negative symptoms of schizophrenia in the rat. *BASIC & CLINICAL PHARMACOLOGY & TOXICOLOGY* 2004;95(5):241-246

Agents: MK-801; phencyclidine hydrochloride **Vehicle:** Sodium chloride; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 6 days;

ALZET Comments: Controls received mp w/ vehicle; dose-response; comparison of SC injections vs. mp; post op. care (wound plast); NMDA antagonists



P5913: E. M. Laurenzana, *et al.* Treatment of adverse effects of excessive phencyclidine exposure in rats with a minimal dose of monoclonal antibody. *Journal of Pharmacology and Experimental Therapeutics* 2003;306(3):1092-1098

Agents: Phencyclidine; phencyclidine HCL; **Vehicle:** Saline; sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days; **ALZET Comments:** Controls received mp w/ vehicle; serum levels taken; good methods p. 1093; half-life (p. 1093) =3.9 h in rats; dependence; behavioral study