References on the Administration of Cocaine
Using ALZET® Osmotic Pumps

Agents: Cocaine Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML2; Duration: Not Stated;
ALZET Comments: Dose (4 mg/kg); Controls received mp w/ vehicle; dependence;

Agents: Cocaine hydrochloride Vehicle: Saline; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Dose (30 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (12 weeks old); neurodegenerative (Huntington's Disease);

Agents: Cocaine Vehicle: Not Stated; Route: Not Stated; Species: Not Stated; Pump: Not Stated;
ALZET Comments:

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, Holtzmann/Harlan SD); 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 37°C for at least 4 hours;

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); MRI; pumps primed 24 hr 37°C saline;

Agents: Cocaine Vehicle: Not Stated; 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 37°C saline;

Agents: Nicotine; cocaine hydrochloride Vehicle: Saline, sterile; Route: SC; IP; Species: Mice; Pump: 2004; 1003D; Duration: 3, 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (mGlu5 KO, wt

**Agents:** Cocaine hydrochloride  
**Vehicle:** Saline, sterile  
**Route:** IP  
**Species:** Mice  
**Pump:** 1003D  
**Duration:** 3 days  

**ALZET Comments:** Controls received mp w/ saline; animal info (C57BL/6, male, 7-8 wks old) withdrawal; “continuous cocaine administration via intraperitoneal osmotic minipumps is an excellent tool for the assessment of the effects of cocaine administration and withdrawal on various behavioral measures.” pg 180


**Agents:** Cocaine  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML4  
**Duration:** 28 days  

**ALZET Comments:** Controls received mp w/ saline; good methods pg. 243; animal info (male, Sprague Dawley, 250-300 g); microdialysis fiber attached to exit port to prevent development of necrotic skin


**Agents:** Cocaine; Fluoxetine; GBR12909; Nisoxetine  
**Vehicle:** Water, sterile  
**Route:** SC; CSF/CNS  
**Species:** Rat  
**Pump:** 2001; 2ML1  
**Duration:** 7 days  

**ALZET Comments:** Controls received mp w/ vehicle; no stress (see pg. 37); animal info (male, Sprague-Dawley, 200-250 grams)


**Agents:** Cocaine  
**Vehicle:** Water, sterile  
**Route:** CSF/CNS  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 7 days  

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 200-250 grams)


**Agents:** Cocaine, hydrochloride  
**Vehicle:** Saline, isotonic  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML2  
**Duration:** 2 weeks  

**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by residual volume; comparison of IP injections vs. SC mp; tolerance; “The cocaine pumps were slightly modified by adding a microdialysis fiber to the output portal to minimize tissue necrosis from the cocaine.” p. 151; behavioral study


**Agents:** Cocaine HCL  
**Vehicle:** Saline, isotonic  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML2  
**Duration:** 3,7 days  

**ALZET Comments:** Controls received mp w/ vehicle; dose-response; tolerance; “mp slightly modified by adding a microdialysis fiber to the output portal to eliminate tissue necrosis from the cocaine.” (pg. 294); mp primed 37C water for 4 hours


**Agents:** Cocaine HCl  
**Vehicle:** Saline, isotonic  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML2  
**Duration:** 14 days  

**ALZET Comments:** Controls received mp w/ vehicle; tolerance; dependence; “The pumps were slightly modified by adding a microdialysis fiber to the output portal to eliminate tissue necrosis from the cocaine.” (p. 112)


**Agents:** Cocaine  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Rat  
**Pump:** 2001  
**Duration:** 7 days  

**ALZET Comments:** Tolerance
**Agents:** Cocaine; pramipexole  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 14 days;  
**ALZET Comments:** Functionality of mp verified by measuring residual volume; pulsed delivery - drugs administered either continuously or for 16 or 20 hrs per day (p. 409); study included behavioral testing; pramipexole is a direct dopamine agonist; microdialysis fiber attached to pump via catheter to minimize tissue necrosis caused by the cocaine (p. 408); intermittent delivery made possible by disconnecting and reconnecting an externalized catheter.

**Agents:** Cocaine; RTI-117; GBR 12909  
**Vehicle:** Saline; DMSO; water, sterile;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML1; 2ML2;  
**Duration:** 7, 14 days;  
**ALZET Comments:** Controls received mp w/ vehicle; brain tissue distribution; 50% DMSO used for GBR12909.

**Agents:** Cocaine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Monkey (pregnant);  
**Pump:** 2ML4;  
**Duration:** 180 days;  
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by cocaine serum levels; dose-response (table 4 p. 136); long-term study, pumps replaced every 28 days for up to 180 days (until birth); teratology.

**Agents:** Cocaine HCl  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 14 days;  
**ALZET Comments:** controls received mp w/ vehicle; functionality of mp verified by residual volume; “The pumps were modified by adding a microdialysis fiber to the output portal to eliminate cocaine-induced tissue necrosis”.  

P4517: T. H. Lee, et al. Altered activity of midbrain dopamine neurons following 7-day withdrawal from chronic cocaine abuse is normalized by D2 receptor stimulation during the early withdrawal phase. Neuropsychopharmacology 1999;21(127-136
**Agents:** Cocaine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 14 days;  
**ALZET Comments:** Comparison of SC injections vs. mp; tolerance; modified flow moderators used.

**Agents:** Cocaine HCl  
**Vehicle:** Saline, isotonic;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 14 day;  
**ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by measuring residual volume; comparison of SC injections vs. mp; tolerance; microdialysis; pumps were modified by adding a microdialysis fiber to eliminate tissue necrosis from cocaine administration.

**Agents:** Cocaine; GBR 12909; Fluoxetine HCl; Nisoxetine HCl, RTI-117  
**Vehicle:** DMSO; Water, sterile;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001; 2ML1; 2ML2;  
**Duration:** 7.14 days;  
**ALZET Comments:** Antidepressant; controls received mp w/ saline; RTI-117 is a dopamine uptake inhibitor; 2ML1 used to deliver GBR 12909, due to its limited solubility.

**Agents:** Cocaine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 2 weeks;  
**ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by residual volume; no stress (P. 448); tolerance; At the end of the experiment, the tissue surrounding the minipumps was inspected and found to be normal (p. 448);
Agents: Cocaine; Naltrexone HCl; Morphine sulfate Vehicle: Saline, Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp w/vehicle; functionality of mp verified by plasma levels; dose-response (p. 279-280); tolerance

Agents: Cocaine HCl Vehicle: Saline, sterile; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: controls received mp w/vehicle; functionality of mp verified by residual volume; good methods (p.265); dependence; microdialysis

Agents: Cocaine HCl; SKF-82958; Bromocriptine; Hydrobromide, R(+)-6-bromo-APB; PD 128907 Vehicle: Saline, Route: SC; Species: Rat; Pump: 2ML1; Duration: 24,48,66,72,90,96,168,336 hours;
ALZET Comments: controls received mp w/vehicle; dopamine agonists

P3484: M. S. Matell, et al. 5-HT(3) receptor mediated dopamine release in the nucleus accumbens during withdrawal from continuous cocaine. Psychopharmacology 1997;130(242-248
Agents: Cocaine HCl Vehicle: Saline, Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: controls received mp w/ saline; functionality of mp verified by residual solution; tolerance; microdialysis

Agents: Cocaine HCl Vehicle: Saline, Route: SC; Species: Rat; Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: functionality of mp verified by measuring residual volume; no stress (see p. 936) - no observed skin necrosis
Agents: Cocaine Vehicle: Not Stated; Route: IV (femoral); Species: Rat; Pump: 2001; Duration: 3 days;
ALZET Comments: no comment posted

Agents: Cocaine HCl Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: no comment posted

Agents: Cocaine HCl Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: controls received saline infusion; comparison of intermittent sc injections vs. mp; pump connected to 3 cm of dialysis tubing

Agents: Cocaine HCl; Eticlopride; SCH-23390 Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 3 days;
ALZET Comments: controls received mp w/ saline; eticlopride is a D1 & D2 receptor antagonist

Agents: Hydrobromide, R(+)-6-bromo-APB-SKF-38393; Nafadotride, (5)-bromocriptine; Cocaine HCl Vehicle: Saline; Route: Not Stated; Species: Rat; Pump: 2ML1; Duration: 3 days;
ALZET Comments: controls received mp w/ saline

Agents: Cocaine HCl Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: controls received mp w/ saline; comparison of sc injections vs. mp; tolerance

P3070: J. L. Neisewander, et al. Time-dependent changes in sensitivity to apomorphine and monoamine receptors following withdrawal from continuous cocaine administration in rats. Synapse 1994;16(1-10
Agents: Cocaine HCl Vehicle: Saline, sterile; Route: SC; Species: Rat; Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: controls received mp w/ saline; functionality of mp verified by residual volume; possible minipump failure noted

Agents: Cocaine Vehicle: Not Stated; Route: Not Stated; Species: Sheep (fetus); Pump: Not Stated; Duration: Not Stated;
ALZET Comments: functionality of mp verified by plasma, amniotic fluid, and meconium samples; stability verified by in vitro testing at 39 degrees; teratology; pump released drug into amniotic fluid; pump placed on fetal back; ampicillin added to amniotic fluid

Agents: Cocaine Vehicle: Saline; Route: SC; Species: Rat (pregnant); Pump: 2ML2; Duration: 14 days;
ALZET Comments: controls received mp w/ saline; comparison of sc injections vs. mp
**Agents:** Cocaine HCl **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** functionality of mp verified by measuring residual amount; comparison of ip injections vs mp; no stress (pg. 400); good methods: "minipumps were modified by adding a microdialysis fiber... to increase surface area over which cocaine is delivered." This allowed higher dose delivery without necrotic skin lesion

**Agents:** Cocaine HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** functionality of mp verified by residual volume; comparison of sc injections vs. mp; tolerance; microdialysis fiber added to pump's outflow portal to increase surface area distribution, and to avoid necrotic skin lesions

**Agents:** Cocaine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
**ALZET Comments:** controls received mp with saline; dependence; pump incision site covered with an antibiotic and 5% lignocaine to prevent discomfort and infection

P2339: G. R. King, et al. Dopamine efflux during withdrawal from continuous or intermittent cocaine. Psychopharmacology 1993;111(179-184
**Agents:** Cocaine HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** functionality of mp verified measuring residual amount; comparison of SC injections vs. mp; no stress (see pg. 180); tolerance; microdialysis fiber

**Agents:** Cocaine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ saline; comparison of sc injections vs. mp; tolerance

**Agents:** Cocaine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
**ALZET Comments:** Controls received mp with water; microdialysis; pump modified; modification eliminated necrosis

**Agents:** Cocaine **Vehicle:** Water, sterile; **Route:** Not Stated; **Species:** Rabbit (pregnant); **Pump:** Not Stated; **Duration:** 22 days;
**ALZET Comments:** Controls received mp with water; teratology; 2 mps implanted

**Agents:** Cocaine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** controls received sham op; functionality of mp verified by plasma levels; no stress (see p. 50)

**Agents:** Cocaine HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** controls received mp w/ saline; functionality of mp verified by residual volume; tolerance; gentamicin applied after surgery; no tissue necrosis seen
P2218: S. T. Cain, et al. Chronic continuous or intermittent infusion of cocaine differentially alter the concentration of neurotensin-like immunoreactivity in specific rat brain regions. Neuropsychopharmacology 1993;8(259-265

**Agents:** Cocaine HCl  
**Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;  
**ALZET Comments:** controls received mp w/saline; functionality of mp verified upon removal; stability verified upon removal; tolerance

P2185: L. Y. Burger, et al. Day/night differences in D1 but not D2 DA receptor protection from EEDQ denaturation in rats treated with continuous cocaine. Synapse 1993;13(20-29

**Agents:** SCH-23390; Cocaine HCl; Raclopride  
**Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;  
**ALZET Comments:** no comment posted


**Agents:** Cocaine HCl  
**Vehicle:** Saline; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2001; **Duration:** 2,4,6 days;  
**ALZET Comments:** comparison of intermittent injections vs mp


**Agents:** Cocaine HCl  
**Vehicle:** Sodium chloride; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;  
**ALZET Comments:** comparison of iv injections vs. mp


**Agents:** Cocaine HCl  
**Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;  
**ALZET Comments:** functionality of mp verified by residual volume upon explant; comparison of sc injections vs. mp; tolerance; advantages of mp (pg. 247)


**Agents:** Cocaine HCl; Nicotine tartrate  
**Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;  
**ALZET Comments:** tolerance


**Agents:** Cocaine  
**Vehicle:** Saline; **Route:** IV (vena cava); **Species:** Rat; **Pump:** 2ML2; **Duration:** 11,12 days;  
**ALZET Comments:** Controls received mp w/ saline; tolerance; loop of catheter tubing exposed to terminate infusion


**Agents:** Cocaine HCl  
**Vehicle:** Water; **Route:** SC; **Species:** Rabbit; **Pump:** 2ML4; **Duration:** 22 days;  
**ALZET Comments:** Teratology


**Agents:** Cocaine HCl  
**Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 3 weeks;  
**ALZET Comments:** no comment posted


**Agents:** Cocaine HCl  
**Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 8 days;  
**ALZET Comments:** controls received mp w/ saline; cardiovascular

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Agents: Cocaine HCl; Nicotine tartrate Vehicle: Saline; Route: SC; Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: no comment posted

Agents: Cocaine Vehicle: Not Stated; Route: IP; Species: Rat; Pump: Not Stated; Duration: 7,14 days;
ALZET Comments: Controls received mp w/saline; dose-response; comparison of injections vs. mp; tolerance

Agents: Cocaine Vehicle: Hank’s solution; Route: SC; Species: mice; Pump: 2001; Duration: 7 days;
ALZET Comments: no comment posted

Agents: Cocaine Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; Duration: 1, 2 weeks;
ALZET Comments: controls received plastic sham pumps; stress/adverse reaction (localized vasoconstriction); pump replaced

Agents: Cocaine HCl Vehicle: Saline; Route: SC; Species: Monkey; Pump: 2002; Duration: 14 days;
ALZET Comments: Dose-response; functionality of mp verified by plasma levels; pump replaced > than or = to 2 months elapsed between implants; toxicology/teratology

Agents: Cocaine Vehicle: Saline; Route: SC; Species: Rat (pregnant); Pump: 2ML4; Duration: 28 days;
ALZET Comments: toxicology/teratology

Agents: Amphetamine sulfate, d-; Cocaine HCl Vehicle: Saline; Route: IV (jugular); SC; Species: Rat; Pump: 2ML1; Duration: 3, 30 days;
ALZET Comments: controls received silastic plug implant

Agents: Cocaine Vehicle: Not Stated; Route: IV (jugular); Species: Rat; Pump: 2ML4; Duration: 21 days;
ALZET Comments: tolerance

Agents: Cocaine HCl Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: no comment posted

Agents: Cocaine HCl Vehicle: Saline; Route: SC; Species: Rat; Pump: Not Stated; Duration: 2 weeks;
ALZET Comments: pump model not stated; controls received mp w/ saline