References on the Administration of Antipsychotics
Using ALZET® Osmotic Pumps

1. Chlorpromazine

ALZET Comments: Haloperidol; Chlorpromazine; Saline, sterile; SC; Rat; 2001; 2ML1; 8 days; controls received mp w/ vehicle.

ALZET Comments: Chlorpromazine HCl; IP; SC; mice; 2002; 7, 10 days; complications with sc delivery; no stress/stress.

ALZET Comments: Chlorpromazine; Haloperidol; SC; Rat; 2001; 2ML1; 8 days; controls received sham op; concomitant infusion of agents; comparison of agents effects; functionality of mp verified by gravimetric analyses.

ALZET Comments: Flupenthixol, cis-; Flupenthixol, trans-; Amitriptyline; Amphetamine; Atropine; Chlorpromazine; Clozapine; Fluphenazine; Haloperidol; Morphine; Prazosin; SC; Rat; 2 weeks; mp model not stated; comparison of sc injections vs. mp infusion; antihypertensive.

ALZET Comments: Chlorpromazine; haloperidol; phenobarbital; promethazine; SC; Rat; 2001; 8 days; Comparison of agents effects.

ALZET Comments: Chlorpromazine; Clozapine; Haloperidol; HCl; Saline; SC; Rat; 2ML2; 2ML4; 2 and 4 weeks; comparison of single injec vs. infusion; comparison of agents effects; Hal. given for 2 & 4 weeks, Chlor. & Cloz. for 2 weeks; saline & HCl vehicle used w/Cloz., others used saline only; stability of Hal., Chlor. & Cloz. by TLC.

2. Clozapine

ALZET Comments: Clozapine-N-oxide; Saline; SC; Mice (neonate); 1007D; 7 days; Controls received mp w/ vehicle; animal info (11-14 days); clozapine-N-oxide (CNO)
Therapeutic indication (learning and memory); Dose (1 mg/kg).

Q6104: K. Chikama, et al. Chronic atypical antipsychotics, but not haloperidol, increase neurogenesis in the hippocampus of adult mouse. Brain Res 2017;1676(77-82
ALZET Comments: Haloperidol; quetiapine; aripiprazole; clozapine; olanzapine; risperidone; IP; Mice; 1004; 21 days; Dose (haloperidol 1 mg/kg/d, quetiapine 20 mg/kg/d, aripiprazole 3 mg/kg/d, clozapine 20 mg/kg/d, olanzapine 2 mg/kg/d, risperidone 0.5 mg/kg/d); Controls received mp w/ vehicle; “It is known that osmotic pumps serve some preferable aspect such as to reduce stress to the animals, minimize unwanted experimental variables, and hold the drug concentration constant” pg. 80;
ALZET Comments: Clozapine-N-oxide; Saline, sterile; SC; Mice; 2004; 28 days; animal info (Adult male Swiss Webster mice); neurodegenerative (Alzheimer’s disease);

ALZET Comments: Haloperidol; clozapine; LY379268; Saline; acetic acid; water, sterile; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Wistar, 10-12 weeks old, 250-350g); functionality of mp verified by residual volume; behavioral testing (locomotor activity); LY379268 is a metabotropic glutamate 2/3 receptor agonist (mGluR 2/3);

ALZET Comments: Clozapine; Saline; CSF/CNS (lateral ventricle); Mice; 1002; 24 hours; Dose (0, 3, 7.5, 15 or 30 μg/day); Controls received mp w/ vehicle; animal info (DBA/2 mice (20–25 g)); comparison of once-per-day injection vs mp; ALZET brain infusion kit 3 used; Brain coordinates ([0.9 mm anterior to bregma, 0.1 mm lateral to midline and −2.0 mm from the brain surface); cyanoacrylate adhesive;

ALZET Comments: Clozapine; haloperidol; Acetic acid; saline; water; SC; Rat; 2ML4; Animal info (Hooded Long Evans, 186-248 g); pump functionality verified via residual volume.

ALZET Comments: Clozapine; HCl; saline; SC; Rat; 2ML1; 14 days; Controls received mp w/ vehicle; animal info (Wistar, male, 300 g); pumps replaced after 7 days; "The limited solubility of clozapine at the concentration that was required to deliver 4 mg/kg/day in the maximal volume that could be contained in the minipumps prevented the use of a single 14 day osmotic minipump; thus, two successive 7 day minipumps were used" pg 1423; wound clips used; post op. care (antibacterial ointment) pg 1423.

ALZET Comments: Clozapine; Acetic acid, glacial; water, sterile; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, hooded, Long-Evans, 333 g).

ALZET Comments: Clozapine; Hydrochloric acid; saline; SC; Rat; 2ML1; 14 days; Controls received mp w/ vehicle; pumps replaced after 7 days; post op. care (antibacterial ointment on incision area); animal info (Wistar rats, 300 g.); antipsychotic; subsequent pump implanted contralateral to the first minipump.

ALZET Comments: Nicotine tartrate; amphetamine; clozapine; HCL; saline; SC; Rat; 2ML1; 7,14 days; Controls received mp w/ vehicle; pumps replaced every 7 days for the 14 day study infusing clozapine; dependence; "in this experiment involving three pump implantations each pump was placed in a different part of the rats' body (left or right side of the back of the animal or at the shoulder area)," p. 1252; behavioral study.
ALZET Comments: Haloperidol; olanzapine; risperidone; quetiapine; clozapine; Water; acetic acid, glacial; SC; Rat; 2ML2; 7 days; Plasma levels taken; dose-response (p. 629); comparison of daily injections vs. chronic mp; half-life (p. 626) 2-4 hours; haloperidol and risperidone were dissolved in distilled water; olanzapine, quetiapine and clozapine were dissolved in 1% to 2% acetic acid; great dose information; "we propose that only administration by pump (or administration more than four times a day[injections]) can provide clinical-like occupancies for haloperidol, olanzapine, and risperidone." p. 630.

ALZET Comments: Clozapine; haloperidol; Acetic acid, glacial; water; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle.

ALZET Comments: Clozapine; Cyclodextrin, hydroxypropyl, beta; CSF/CNS; Rat; 28 days; Controls received mp w/ saline; ALZET brain infusion kit used; animal info (male, Sprague Dawley, 250-300g.); Schizophrenia.

ALZET Comments: Haloperidol; Clozapine; SC; Rat; 2ML2; 28 days; controls received mp with saline; pumps replaced at 14 days.

ALZET Comments: Clozapine; Haloperidol; Raclopride; Acetic acid, glacial; HCl; Sodium hydroxide; Water; SC; Rat; 2ML4; 28 days; controls received an empty plastic pellet of identical size.

ALZET Comments: Flupenthixol, cis-; Flupenthixol, trans-; Amitriptyline; Amphetamine; Atropine; Chlorpromazine; Clozapine; Fluphenazine; Haloperidol; Morphine; Prazosin; SC; Rat; 2 weeks; mp model not stated; comparison of sc injections vs. mp infusion; antihypertensive.

ALZET Comments: Chlorpromazine; Clozapine; Haloperidol; HCl; Saline; SC; Rat; 2ML2; 2ML4; 2 and 4 weeks; comparison of single injec vs. infusion; comparison of agents effects; Hal. given for 2 & 4 weeks, Chlor. & Cloz. for 2 weeks; saline & HCl vehicle used w/Cloz., others used saline only; stability of Hal., Chlor. & Cloz. by TLC.

3. Fluphenazine
ALZET Comments: Flupenthixol, cis-; Flupenthixol, trans-; Amitriptyline; Amphetamine; Atropine; Chlorpromazine; Clozapine; Fluphenazine; Haloperidol; Morphine; Prazosin; SC; Rat; 2 weeks; mp model not stated; comparison of sc injections vs. mp infusion; antihypertensive.
4. Haloperidol

**Q7103:** A. Calevro, *et al.* Effects of chronic antipsychotic drug exposure on the expression of Translocator Protein and inflammatory markers in rat adipose tissue. Psychoneuroendocrinology 2018;95(28-33)

**ALZET Comments:** Haloperidol, olanzapine; Cyclodextrin, 2-Hydroxypropyl-β-; SC; Rat; 2ML4; 8 weeks; Dose (Haloperidol-2mg/kg/day, Olanzapine-10mg/kg/day); Controls received mp w/vehicle; animal info (10-week old, male, Sprague-Dawley, 240–250 g); pumps replaced every 4 weeks; long-term study; dependence;

**Q5973:** A. Servonnet, *et al.* Neurotensin in the nucleus accumbens reverses dopamine supersensitivity evoked by antipsychotic treatment. Neuropharmacology 2017;123(10-21

**ALZET Comments:** Haloperidol; Acetic acid, water; SC; Rat; 2ML2; Controls received mp w/vehicle; animal info (200–225 g); Mp vs. intermittent administration by injection; Therapeutic indication (Anti-psychosis); Dose (0.5 mg/kg);


**ALZET Comments:** Haloperidol-Hcl; Saline; SC; Mice; 2004; 14 days; Controls received mp w/vehicle; animal info (hemizygous bacterial artificial chromosome (BAC) transgenic mice (p28-p38) expressing eGFP under either Drd1a or Drd2 control); Therapeutic indication (Schizophrenia); Dose (0.25 mg/kg/day);

**Q6192:** Y. Oda, *et al.* Alterations in glutamatergic signaling in the brain of dopamine supersensitivity psychosis and non-supersensitivity psychosis model rats. Psychopharmacology (Berl) 2017;1676(77-82

**ALZET Comments:** Haloperidol; quetiapine; aripiprazole; clozapine; olanzapine; risperidone; IP; Mice; 1004; 21 days; Dose (haloperidol 1 mg/kg/d, quetiapine 20 mg/kg/d, aripiprazole 3 mg/kg/d, clozapine 20 mg/kg/d, olanzapine 2 mg/kg/d, risperidone 0.5 mg/kg/d); Controls received mp w/vehicle; “It is known that osmotic pumps serve some preferable aspect such as to reduce stress to the animals, minimize unwanted experimental variables, and hold the drug concentration constant” pg. 80;

**ALZET Comments:** Haloperidol; Acetic acid, glacial; water; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Eleven-week-old male Wistar rats, 240–260 g ); functionality of mp verified by ELIZA testing; 2% acetic acid used; good methods (pg 1309); stress/ adverse reaction: “One animal did not recover from pump-implanting surgery and was excluded from analysis” (see pg. 1310); behavioral testing (MAP-induced locomotion test); Vehicle pH adjusted to 3.6-3.8 with NaOH; 9mm wound clips used; Dose (0.75 mg/kg/d);


**ALZET Comments:** Haloperidol; SC; Rat; 2002; 14 days; Controls received sham surgery; animal info (female, Sprague Dawley, 200-250g 2-3 months old, OVX); post op. care (Anafen 0.1 mL/rat; antibiotic ointment); MRI; PEEK; Dose (0.25 mg/kg/day);


**ALZET Comments:** Haloperidol; Olanzapine; Acetic acid; water; SC; Rat; 2ML2; 15 days; 17 days; Controls received sham surgery; animal info: Male Sprague-Dawley rats; %0.5 or %2 of acetic acid; behavioral testing (trained to associate the delivery of 100 ml water (the unconditioned stimulus; UCS) into a receptacle with a light/tone conditioned stimulus (CS)); Dose: 0.5 mg/kg/day (haloperidol); 10 mg/kg/day (olanzapine).

Q5134: A. Charron, et al. | 5-HT2 receptors modulate the expression of antipsychotic-induced dopamine supersensitivity. Eur Neuropsychopharmacol 2015;25(12):2381-93

**ALZET Comments:** Haloperidol; Acetic acid, glacial; water; SC; Rat; 2ML2; 15, 17 days; Controls received sham surgery consisting of an incision and sutures; animal info: Male Sprague-Dawley rats 200–225g; water (pH 5) used; half-life (p. 2383 ), 1.5 hours; models the kinetics of standard antipsychotic treatment in patients; Dose: 0.5 mg/ kg/day.

Q3580: S. Natesan, et al. | Effect of chronic antipsychotic treatment on striatal phosphodiesterase 10A levels: a [(11C)]MP-10 PET rodent imaging study with ex vivo confirmation. TRANSLATIONAL PSYCHIATRY 2014;4(U4-U10

**ALZET Comments:** Haloperidol; Cyclodextrin, 2-hydroxypropyl-beta; Ascorbic acid; SC; Rat; 2ML4; 3 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 308-456g); functionality of mp verified by plasma; 20% B-hydroxypropylcyclodextrin used; behavioral testing (chewing movements); “Daily intraperitoneal injections in rodents lead to plasma levels that dip to a negligible level during a 24-h period as most antipsychotics have a half-life of 2-4 h in rodents, whereas the half-life of most antipsychotics in humans is usually 12-24 h.14 Hence, the present study was designed taking into consideration a delivery method (subcutaneous mini-osmotic pumps) that maintained constant plasma levels to evaluate the effect of chronic antipsychotic treatment on striatal PDE10A levels in rodents” pg 1;


**ALZET Comments:** Haloperidol; Saline; SC; Rat; 2002; 12 days; Animal info (female, Sprague Dawley, ovariectomized); behavioral testing (motor activity); replacement therapy (ovariectomized); pump removed after 12 days;

Q3884: J. Gao, et al. | Differential effects of intermittent versus continuous haloperidol treatment throughout adolescence on haloperidol sensitization and social behavior in adulthood. PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY 2014;54(67-75

**ALZET Comments:** Haloperidol; Water, sterile; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, PND44-71); comparison of injection vs mp; post op. care (incision cleaned with 75% ethanol); behavioral testing (two-way avoidance conditioning apparatus; locomotor activity monitoring apparatus; avoidance training); dependence; used 9mm wound clips; pumps wiped with 75% ethanol; pumps removed after 28 days;

5. Olanzapine


ALZET Comments: Haloperidol, olanzapine; Cyclodextrin, 2-Hydroxypropyl-β-; SC; Rat; 2ML2; 15 days; 17 days; Controls received sham surgery; animal info: Male Sprague-Dawley rats; %0.5 or %2 of acetic acid; behavioral testing (trained to associate the delivery of 100 ml water (the unconditioned stimulus; UCS) into a receptacle with a light/tone conditioned stimulus (CS)); Dose: 0.5 mg/kg/day (haloperidol); 10 mg/kg/day (olanzapine).


ALZET Comments: Haloperidol; Acetic acid; water; SC; Rat; 2ML2; 15 days; 17 days; Controls received sham surgery; animal info: Male Sprague-Dawley rats; %0.5 or %2 of acetic acid; behavioral testing (trained to associate the delivery of 100 ml water (the unconditioned stimulus; UCS) into a receptacle with a light/tone conditioned stimulus (CS)); Dose: 0.5 mg/kg/day (haloperidol); 10 mg/kg/day (olanzapine).


ALZET Comments: Olanzapine; Saline; SC; Mice; 28 days; Animal info (female, C57Bl/6J, 8 wks old); functionality of mp verified by (oral glucose test); pumps replaced every (2 weeks); post op care (anesthesized with ketamine/xylazine (100/15 mg/kg/ip); antipsychotic.
**ALZET Comments:** Haloperidol; olanzapine; SC; Rat; 2ML4; 8 weeks; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 9 wks old, 240-250 g); pumps replaced after 28 days; long-term study.

**ALZET Comments:** Olanzapine; Acetic acid; sodium hydroxide; SC; Rat; 2ML2; 14 days; Dose (7.5 mg/kg/day); 2% acetic acid solution, buffered with 1 N NaOH used; Controls received mp w/ vehicle; animal info (Forty-eight female Sprague–Dawley rats weighing 200–225 g); comparison of IP and SC injections vs mp.

**ALZET Comments:** Haloperidol; olanzapine; Acetic acid; water, distilled; SC; Rat; 2ML2; 19 Days; Animal info (male, sprague-dawley, 200-225g); half-life (24hr, haloperidol); behavioral testing (lever pressing).

**ALZET Comments:** Haloperidol; olanzapine; Cyclodextrin, beta-hydroxypropyl; SC; Rat; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 240-250 g, 9 wks old); pumps replaced after 28 days; half-life 2.5 hours (p. 937); "MRI-safe" pumps; 20% cyclodextrin used; long-term study.

**ALZET Comments:** Olanzapine; Acetic acid, glacial; water, sterile; In vitro; 2ML4; Controls received vehicle; drug levels verified using a liquid-liquid extraction and liquid chromatography; "We suggest that olanzapine administration via (ALZET pumps) represents a viable option for (sub)chronic exposure with the caveats that a) duration be confined to 2 weeks..., and b) consideration be given to strategies in dissolving olanzapine that diminish the risk of oxidation." pg 89; "we strongly agree with van der Zwaal and colleagues (2008) that the issue of drug degradation is not specific to olanzapine, and that it is imperative to establish whether compounds being considered for minipump administration are capable of remaining stable in solution at body temperature."

**ALZET Comments:** Olanzapine; Acetic acid, glacial; SC; Rat; 2ML4; 4 weeks; Functionality of mp verified by residual volume; animal info (male, Sprague Dawley); stability verified for 4 weeks by electrospray MS/MS.

**ALZET Comments:** Olanzapine; Acetic acid; saline, isotonic; sodium hydroxide; SC; Mice; 2004; 30 days; Controls received mp w/ vehicle; animal info (CD-1, 11 wks old, female); functionality of mp verified by residual volume; "Although (degradation of AAP agents in mini-pump reservoir over time) is a serious concern, significant increases of body weight and food intake were found in female rats33Y35 and mice14 under constant OL infusion via implanted mini -pumps" pg 582.

**ALZET Comments:** Olanzapine; Lactic acid; SC; Rat; 2ML2; 12, 14 days; Controls received mp w/ vehicle; comparison of SC injections vs. mp; no stress (see pg. 2923); animal info (female, Sprague Dawley, 230-275 g.); "Mini-pumps were used to chronically deliver OLZ in order to minimize stress-related changes in food intake and body weight associated with daily handling and intraperitoneal (IP) injection." (p. 2923).

**ALZET Comments:** Olanzapine; Acetic acid, glacial; saline; hydrochloric acid; water, distilled; SC; Rat; 2ML4; 4 weeks; Controls received mp w/vehicle; comparison of SC injections vs. mp; half-life (p.130) "2-5 h in rats"; animal info (male, Wistar); "...at the end of the study, we noticed a strong discoloration of the solution remaining in the minipumps of the olanzapine-treated rats (from bright orange to dark green), as well as a dark precipitate in the pumps interior, which was most notable in the highest dose group" pg 132; "...this suggests that lower plasma levels of olanzapine occur over time only when osmotic minipumps are used and not with daily s.c. injections." pg 135; "Only drugs that are (relatively) stable in a solution at body temperature will result in truly constant drug delivery from an osmotic minipump and, therefore, enable accurate and reliable experimental results." pg 136.

**P9427:** K. Lykkegaard, et al. The once-daily human GLP-1 analog, liraglutide, reduces olanzapine-induced weight gain and glucose intolerance. SCHIZOPHRENIA RESEARCH 2008;103(1-3):94-103

**ALZET Comments:** Olanzapine; PBS; NaOH; lactic acid; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; stress/adverse reaction: (see pg. 96) 6 animals out of 40 developed local irritation/wounds at implantation site; post op. care (carprofen); animal info (male, Sprague Dawley, 240 g.); "we used continuous subcutaneous administration of olanzapine via osmotic minipumps in order to obtain a steady-state of olanzapine with no sedation. The result of this... is an animal model that mimics the side effect profile encountered in schizophrenic patients treated with olanzapine. This may be a valuable, rapid, and inexpensive model for screening." (p. 100).


**ALZET Comments:** Olanzapine; Acetic acid; SC; Rat; 2ML4; 4 weeks; Controls received no treatment; dose-response (fig. 2); animal info (male, Sprague Dawley, 225-275 g.); "The choice of administration by osmotic pump acknowledged the rapid metabolism of antipsychotics reported in rodents... and an effort to more closely approximate the human condition by providing sustained exposure." (p. 24); behavioral testing (locomotor activity).


**ALZET Comments:** Haloperidol; olanzapine; Acetic acid, glacial; water; NaOH; SC; Rat; 2ML2; 2,12,13 days; Controls received mp w/ vehicle; dose-response (fig. 4); comparison of SC injections vs. mp; half-life (p. 2985), 24 hours in humans, 1.4 hours in rats; tolerance; animal info (male, Sprague-Dawley, 225-275 grams); "Animal studies that use a mode of drug administration that more closely mimics clinical antipsychotic treatment (i.e., relatively continuous treatment) might be more informative about the true effects of these drugs in humans." (p. 2985).

**P8543:** K. Rasmussen, et al. The orexin-1 receptor antagonist SB-334867 blocks the effects of antipsychotics on the activity of A9 and A10 dopamine neurons: Implications for antipsychotic therapy. Neuropsychopharmacology 2007;32(4):786-792

**ALZET Comments:** Olanzapine; haloperidol; Water, distilled; sodium hydroxide; lactic acid; SC; Rat; 2ML2; 21 days; Controls received mp w/ vehicle; pumps replaced after 2 weeks; animal info (male, Sprague-Dawley, 280-330 grams).

6. Quetiapine

**Q6104:** K. Chikama, et al. Chronic atypical antipsychotics, but not haloperidol, increase neurogenesis in the hippocampus of adult mouse. Brain Res 2017;1676(77-82

**ALZET Comments:** Haloperidol; quetiapine; aripiprazole; clozapine; olanzapine; risperidone; IP; Mice; 1004; 21 days; Dose (haloperidol 1 mg/kg/d, quetiapine 20 mg/kg/d, aripiprazole 3 mg/kg/d, clozapine 20 mg/kg/d, olanzapine 2 mg/kg/d, risperidone 0.5 mg/kg/d); Controls received mp w/ vehicle; “It is known that osmotic pumps serve some preferable aspect such as to reduce stress to the animals, minimize unwanted experimental variables, and hold the drug concentration constant” pg. 80;.

ALZET Comments: acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labetalol hydrochloride, nitrofurantoin + propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cepaparin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide; DMSO; water; IP; mice; 1003D; animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.


ALZET Comments: Olanzapine; risperidone; quetiapine fumarate; SC; Rat; 28 days; Functionality of mp verified by residual volume; antipsychotic drugs.


ALZET Comments: Haloperidol; olanzapine; risperidone; quetiapine; clozapine; Water; acetic acid, glacial; SC; Rat; 2ML2; 7 days; Plasma levels taken; dose-response (p. 629); comparison of daily injections vs. chronic mp; half-life (p. 626) 2-4 hours; haloperidol and risperidone were dissolved in distilled water; olanzapine, quetiapine and clozapine were dissolved in 1% to 2% acetic acid; great dose information; "we propose that only administration by pump (or administration more than four times a day[injections]) can provide clinical-like occupancies for haloperidol, olanzapine, and risperidone." p. 630.


ALZET Comments: Olanzapine; risperidone; quetiapine fumarate; SC; Rat; 28 days; Controls received mp w/ vehicle; antipsychotic agents.


ALZET Comments: Olanzapine; Risperidone; Quetiapine fumarate; SC; Rat; 4 weeks; controls received mp w/ vehicle; functionality of mp verified by residual volume; antipsychotic agents.

7. Remoxipride


ALZET Comments: Remoxipride HCl; Sodium chloride; SC; Rat; 2002; 14 days; controls received sodium chloride; functionality of mp verified by checking blood levels of drug and determining residual drug amount; comparison of sc injections vs mp; remoxipride is an antipsychotic drug.


ALZET Comments: Remoxipride HCl; Haloperidol; Water; Acetic acid; SC; Rat; 3,14 days; controls received sham operations.

8. Risperidone
Q6104: K. Chikama, et al. Chronic atypical antipsychotics, but not haloperidol, increase neurogenesis in the hippocampus of adult mouse. Brain Res 2017;1676(77-82)

**ALZET Comments:** Haloperidol; quetiapine; aripiprazole; clozapine; olanzapine; risperidone; IP; Mice; 1004; 21 days; Dose (haloperidol 1 mg/kg/d, quetiapine 20 mg/kg/d, aripiprazole 3 mg/kg/d, clozapine 20 mg/kg/d, olanzapine 2 mg/kg/d, risperidone 0.5 mg/kg/d); Controls received mp w/ vehicle; “It is known that osmotic pumps serve some preferable aspect such as to reduce stress to the animals, minimize unwanted experimental variables, and hold the drug concentration constant” pg. 80;.


**ALZET Comments:** Risperidone; SC; Mice; 1002; 1007D; 21 days; Controls received mp w/ vehicle; animal info (C58/J); pumps replaced every 14 days; behavioral testing (chamber choice task; acoustic startle test; marble burying assay); “This pump replacement allowed dosage to be adjusted for increased body weight during the chronic risperidone treatment.” pg 62-63; Dose (2 mg/kg/day); used clozapine slow-release pellets because of drug solubility for osmotic minipumps (pg.62);.


**ALZET Comments:** Risperidone; paliperidone; Intragastric; Monkey (macaca mulata); 2 weeks; Animal info (male, Rhesus, 4.2-6.3 years old); pumps replaced; 2-week pump replaced with 4-week pump containing saline for a washout period. 4-week pump was then replaced with 2-week pump to continue dosing.


**ALZET Comments:** Risperidone; Cycloheximide, hydroxypropyl beta; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 180-200 g); post op. care (Baytril); stress/adverse reaction: "infections" (see pg. 156); 20% cycloheximide used; "We chose to administer risperidone through osmotic minipumps to ensure steady-state plasma levels and avoid plasma fluctuations observed with drug injections." pg 156.


**ALZET Comments:** Risperidone; Water, sterile; acetic acid; sodium hydroxide; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (Sprague-Dawley, male, 357 grams; 11 weeks old); behavioral study.


**ALZET Comments:** Haloperidol; risperidone; Acetic acid; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; no stress (see pg. 1131); half-life (p. 1131) 4-6 times shorter in rodents than in humans; post op. care (bupivicaine); animal info (male, Sprague-Dawley, 9-10 weeks old, 280-430 grams); "This dosing regimen also takes into consideration the reported 4-6 times shorter half-life of antipsychotic drugs in rodents than humans and highlights the advantage of using minipumps in the present study for continuous drug administration to achieve receptor occupancies comparable to clinical use in humans." (p. 1131).


**ALZET Comments:** Olanzapine; risperidone; quetiapine fumerate; SC; Rat; 28 days; Functionality of mp verified by residual volume; antipsychotic drugs.

ALZET Comments: Haloperidol; olanzapine; risperidone; quetiapine; clozapine; Water; acetic acid, glacial; SC; Rat; 2ML2; 7 days; Plasma levels taken; dose-response (p. 629); comparison of daily injections vs. chronic mp; half-life (p. 626) 2-4 hours; haloperidol and risperidone were dissolved in distilled water; olanzapine, quetiapine and clozapine were dissolved in 1% to 2% acetic acid; great dose information; "we propose that only administration by pump (or administration more than four times a day[injections]) can provide clinical-like occupancies for haloperidol, olanzapine, and risperidone." p. 630.

ALZET Comments: Olanzapine; risperidone; quetiapine fumerate; SC; Rat; 28 days; Controls received mp w/ vehicle; antipsychotic agents.

ALZET Comments: Olanzapine; Risperidone; Quetiapine fumarate; SC; Rat; 4 weeks; controls received mp w/ vehicle; functionality of mp verified by residual volume; antipsychotic agents.

9. Spiperone

ALZET Comments: Spiperone; SCH-23390; DMSO; Water; SC; Rat; 2001; 2ML1; 7 days; functionality of mp verified after delivery; dopamine antagonist.

10. Sulpiride

ALZET Comments: Quinpirole HCl; Sulpiride; Triazolam; Ascorbic acid; DMSO; SC; mice; 2001; 6 days; Quinpirole is a dopamine agonist; antidepressant; stability verified in vitro for 7 days.

ALZET Comments: Dopamine, 6-hydroxy-; Haloperidol; Sulpiride; CSF/CNS; Rat; 8 days; Japanese, English abstract.

ALZET Comments: Dopamine HCl; Sulpiride; Nitrogen; Sodium metabisulfite; CSF/CNS (nucleus accumbens); IP; Rat; 13 days; mp model not stated; comparison of SULP ip injec vs. mp infusion; 2 mp/rat - bilateral infusion; mp primed overnight; vehicles listed used w/DOP; concomitant SULP admin. ip.

11. Trifluoperazine

ALZET Comments: Trifluoperazine; Amphetamine sulfate, d-; Saline; CSF/CNS (corpus striatum); Rat; 7 days; caudate putamen.