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.

2. Clozapine

Agents: Clozapine-N-oxide Vehicle: DMSO; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Dose (0.3 mg/kg); 2.75% DMSO used; Controls received mp w/ vehicle; animal info (Transgenic mice (C57Bl6/J), 2 weeks old); Clozapine-N-oxide aka CNO; dependence;

Q7611: A. Obeidat, et al. Nociceptive neuroplasticity of the murine knee joint precedes severe structural joint damage in a surgical model of OA. Osteoarthritis and Cartilage 2019;27/Agents: Clozapine N-oxide Vehicle: Vehicle; Route: SC; Species: Mice; Pump: Not Stated; Duration: 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (10 weeks old, Male ); behavioral testing (Pressure Application Measurement, Up-Down staircase Test); Clozapine N-Oxide aka CNO; enzyme inhibitor (Nociceptor inhibtor); dependence;

Agents: Clozapine Vehicle: Saline; Route: CSF/CNS (lateral ventricles); Species: Mice; Pump: 2006; Duration: 3 weeks;
ALZET Comments: Dose (0,12.5,25, or 50 ug/day); Controls received mp w/ vehicle; animal info (C57BL/6J); ALZET brain infusion kit 3 used; Brain coordinates (AP −0.5 mm, ML ± 1.4mmand DV 3mm from the skull surface); neurodegenerative ();
ALZET Bibliography

Agents: Clozapine-N-Oxide Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 4 weeks;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; Clozapine-N-oxide aka CNO; diabetes;

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

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

Q8240: T. A. Lanz, et al. Postmortem transcriptional profiling reveals widespread increase in inflammation in schizophrenia: a comparison of prefrontal cortex, striatum, and hippocampus among matched tetrad s of controls with subjects diagnosed with schizophrenia, bipolar or major depressive disorder. Transl Psychiatry 2019;9(1):151
Agents: Haloperidol or Risperidone Vehicle: Acetic Acid; Route: CSF/CNS; Species: Rat; Pump: Not stated; Duration: 21 days;
ALZET Comments: Dose (haloperidol-0.25 mg/kg/day or risperidone-5 mg/kg/day); 1% Acetic Acid used; Controls received mp w/ vehicle; animal info (2 months old, Sprague Dawley, Male); neurodegenerative (Psychiatric Disorder);

Agents: haloperidol Vehicle: water, distilled, ascorbic acid and cyclodextrin buffered; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Dose (0.05, 0.5 mg/kg/day); distilled water containing 0.3% ascorbic acid / 10% cyclodextrin used; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 330-380 g); behavioral testing (AMPH-induced locomotion, within-session habituation, acoustic startle response, novel object recognition); HAL is an antipsychotic drug that targets the postsynaptic D2 receptors; schizophrenia induced by amphetamine-sensitization-induced psychosis model;

Agents: Haloperidol; PG-01037 dihydrochloride Vehicle: Acetic Acid, glacial; NaOH; Tween 80 Buffered; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Dose ((haloperidol 0.75 mg/kg/day), PG-01037 (0.6 mg/kg/day)); 2% glacial acetic acid/H2O solution (pH 3.6 w/ NaOH) with 0.5% Tween 80 used; Controls received mp w/ vehicle; animal info (7 weeks, male, Wistar); post op. care (antibiotic treatment; identity not stated); behavioral testing (Quinpirole-induced hyperlocomotion); comparison of oral administration of haloperidol vs mp; PG-01037 is a selective dopamine D3 antagonist; minipumps were removed 14 days after implantation. “In this study, we were unable to use an osmotic pump for continuous administration of blonanserin due to poor solubility in the vehicle used for haloperidol.” p.31;

Agents: haloperidol; olanzapine. **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
**ALZET Comments:** "Dose ((Hal 0.5 mg/kg/d), (Ola 10 mg/kg/d)); Controls received mp w/ vehicle; animal info (6-12 weeks, male, C57BL/6 or homo- and heterozygous C57BL6-D2eGFP); behavioral testing (TruScan open field); Resultant plasma level ((Hal 5.85 ± 0.27 ng/mL), (Ola 45.93 ± 5.72 ng/mL)); haloperidol (Hal) and olanzapine (Ola) are antipsychotic drugs;
"Furthermore, in animal studies, APDs were often administered with regimens that fail to achieve the high D2R occupancy (>70%) required to yield therapeutic benefits (Farde et al., 1988; Kapur and Mamo, 2003; Kapur et al., 2003). To overcome such limitations, we delivered haloperidol or olanzapine via implanted osmotic mini-pumps, which offers a reliable method to obtain clinically meaningful levels of D2R blockade (Amato et al., 2011; Amato et al., 2018; Samaha et al., 2007, 2008)."

**Agents:** Haloperidol, olanzapine. **Vehicle:** Cyclodextrin, 2-Hydroxypropyl-B-; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 8 weeks;
**ALZET Comments:** Dose (Haloperidol- 2mg/ kg/ day, Olanzapine-10 mg/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;

5. Olanzapine

**Agents:** Olanzapine, Samidorphan. **Vehicle:** Not stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 days;
**ALZET Comments:** animal info (Female,); Olanzapine aka OLZ, Samidorphan aka SAM; dependence;

**Agents:** haloperidol; olanzapine. **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
**ALZET Comments:** "Dose ((Hal 0.5 mg/kg/d), (Ola 10 mg/kg/d)); Controls received mp w/ vehicle; animal info (6-12 weeks, male, C57BL/6 or homo- and heterozygous C57BL6-D2eGFP); behavioral testing (TruScan open field); Resultant plasma level ((Hal 5.85 ± 0.27 ng/mL), (Ola 45.93 ± 5.72 ng/mL)); haloperidol (Hal) and olanzapine (Ola) are antipsychotic drugs;
"Furthermore, in animal studies, APDs were often administered with regimens that fail to achieve the high D2R occupancy (>70%) required to yield therapeutic benefits (Farde et al., 1988; Kapur and Mamo, 2003; Kapur et al., 2003). To overcome such limitations, we delivered haloperidol or olanzapine via implanted osmotic mini-pumps, which offers a reliable method to obtain clinically meaningful levels of D2R blockade (Amato et al., 2011; Amato et al., 2018; Samaha et al., 2007, 2008)."

**Agents:** Olanzapine. **Vehicle:** DMSO; Ethanol; Propylene Glycol; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks;
**ALZET Comments:** Dose (4 mg/kg/day); Controls received mp w/ vehicle; animal info (Female, Pregnant); Olanzapine aka OLZ; dependence; 42.5% DMSO, 42.5% propylene glycol and 15% ethanol used;

Agents: Haloperidol, olanzapine  
Vehicle: Cyclodextrin, 2-Hydroxypropyl-β-;  
Route: SC;  
Species: Rat;  
Pump: 2ML4;  
Duration: 8 weeks;  

ALZET Comments: Dose (Haloperidol- 2mg/ kg/ day, Olanzapine-10 mg/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;


Agents: Olanzapine  
Vehicle: Lactic acid;  
Route: SC;  
Species: Rat;  
Pump: 2ML2;  
Duration: Not Stated;  

ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague Dawley , female); half-life (2.5 hours) ; Therapeutic indication (Antipsychotic drugs); Dose (6 mg/kg/day);

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, anhydryus caffeine, cefotaxime sodium salt, cepahpirin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, 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: Haloperidol; 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[injectons]) can provide clinical-like occupancies for haloperidol, olanzapine, and risperidone." p. 630.


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

Q8240: T. A. Lanz, et al. Postmortem transcriptional profiling reveals widespread increase in inflammation in schizophrenia: a comparison of prefrontal cortex, striatum, and hippocampus among matched tetrads of controls with subjects diagnosed with schizophrenia, bipolar or major depressive disorder. Transl Psychiatry 2019;9(1):151
Agents: Haloperidol or Risperidone Vehicle: Acetic Acid; Route: CSF/CNS; Species: Rat; Pump: Not stated; Duration: 21 days;
ALZET Comments: Dose (haloperidol-0.25 mg/kg/day or risperidone-5 mg/kg/day); 1% Acetic Acid used; Controls received mp w/ vehicle; animal info (2 months old, Sprague Dawley, Male); neurodegenerative (Psychiatric Disorder);

Agents: Risperidone Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML4; Duration: 22 days;
ALZET Comments: Dose (1.5 mg/kg/d); animal info (male Wistar rats, 7 weeks old); neurodegenerative (schizophrenia thought to be caused by dopamine D2 receptor sensitization);

Q6104: K. Chikama, et al. Chronic atypical antipsychotics, but not haloperidol, increase neurogenesis in the hippocampus of adult mouse. Brain Research 2017;1676(77-82
Agents: Haloperidol; quetiapine; aripiprazole; clozapine; olanzapine; risperidone Vehicle: Not Stated; Route: IP; Species: Mice; Pump: 1004; Duration: 21 days;
ALZET Comments: 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;

Q5070: B. L. Teng, et al. Reversal of social deficits by subchronic oxytocin in two autism mouse models. Neuropsychopharmacology 2016;105(61-71
Agents: Risperidone Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; 1007D; Duration: 21 days;
ALZET Comments: 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);

Agents: Risperidone; paliperidone  Vehicle: Not Stated;  Route: Intragastric;  Species: Monkey (macaca mulata);  Pump: Not Stated;  Duration: 2 weeks;
ALZET Comments: 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

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.