Recent References on the Administration of Antipsychotics Using ALZET® Osmotic Pumps

Chlorpromazine


Agents: Haloperidol; Chlorpromazine Vehicle: Saline, sterile; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 8 days;

ALZET Comments: controls received mp w/ vehicle


Agents: Chlorpromazine HCl Vehicle: Not Stated; Route: IP; SC; Species: Mice; Pump: 2002; Duration: 7, 10 days;

ALZET Comments: Complications with sc delivery; no stress/stress


Agents: Chlorpromazine; Haloperidol Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 8 days;

ALZET Comments: controls received sham op; concomitant infusion of agents; comparison of agents effects; functionality of mp verified by gravimetric analyses


Agents: Flupenthixol, cis-; Flupenthixol, trans-; Amitriptyline; Amphetamine; Atropine; Chlorpromazine; Clozapine; Fluphenazine; Haloperidol; Morphine; Prazosin Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 2 weeks;

ALZET Comments: mp model not stated; comparison of sc injections vs. mp infusion; antihypertensive


Agents: Chlorpromazine; Haloperidol Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 8 days;

ALZET Comments: Comparison of agents effects


Agents: Chlorpromazine; Clozapine; Haloperidol Vehicle: HCl; Saline; Route: SC; Species: Rat; Pump: 2001; 2ML2; 2ML4; Duration: 2, 4 weeks;

ALZET Comments: 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

Clozapine (2017-Present)


Agents: Clozapine-N-oxide Vehicle: Saline; Route: Abdomen; Species: Mice; Pump: Not Stated; Duration: 6 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (10-week old male NaV1.8-Pdi C57BL/6 mice); Clozapine-N-oxide aka CNO; immunology;


Agents: Clozapine-N-Oxide Vehicle: DMSO; Route: CSF/CNS; Species: Mice; Pump: 2006; Duration: 6 weeks;

ALZET Comments: Dose (1 mg/kg/day); 0.05% DMSO used; Clozapine-N-Oxide aka CNO; neurodegenerative (Alzheimer's Disease);

**Agents:** Clozapine-N-Oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** Not Stated;

**ALZET Comments:** Dose (2 mg/kg/day); Controls received mp w/ vehicle; animal info (Ten- to twelve-week- old-male mice); Clozapine-N-oxide aka CNO; cardiovascular;


**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;

Q9077: B. Stutz, et al. Dopamine neuronal protection in the mouse Substantia nigra by GHSR is independent of electric activity. Molecular Metabolism 2019;24(120-138

**Agents:** Clozapine-N-oxide; Salvinorin B **Vehicle:** DMSO; Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Dose (CNO- 0.3 mg/kg or Salvinorin B- 5 mg/kg); Controls received mp w/ vehicle; animal info (); Clozapine-N-oxide aka CNO, excitatory DREADD agonist, Salvinorin B aka inhibitory DREADD agonist ; neurodegenerative (Parkinson’s Disease);


**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 inhibitor); dependence;


**Agents:** Clozapine **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricles); **Species:** Mice; **Pump:** 2006; **Duration:** 3 weeks;

**ALZET Comments:** Dose (0.125, 0.25, 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 ();


**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);

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;
ALZET® Bibliography

Fluphenazine

Agents: Flupenthixol, cis-; Flupenthixol, trans-; Amitriptyline; Amphetamine; Atropine; Chlorpromazine; Clozapine; Fluphenazine; Haloperidol; Morphine; Prazosin

Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 2 weeks;

ALZET Comments: mp model not stated; comparison of sc injections vs. mp infusion; antihypertensive

Haloperidol (2016-Present)

Q9312: M. Kimura, et al. Effects of repeated electroconvulsive shocks on dopamine supersensitivity psychosis model rats. Schizophrenia Research 2021;228(1-6)

Agents: Haloperidol

Vehicle: Glacial acetic acid; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;

ALZET Comments: Dose (0.75 mg/kg/day); 2% Glacial Acetic Acid used; Controls received mp w/ vehicle; animal info (twelve-week-old male Wistar rats, 240-270 g); Haloperidol aka HAL; ischemia (Schizophrenia);

Q9311: M. Kimura, et al. Reduction of dopamine and glycogen synthase kinase-3 signaling in rat striatum after continuous administration of haloperidol. Pharmacology, Biochemistry and Behavior 2021;202(173114)

Agents: Haloperidol

Vehicle: Glacial acetic acid; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;

ALZET Comments: Dose (0.75 mg/kg/day); Controls received mp w/ vehicle; animal info (twelve-week-old male Wistar rats, 240-260 g); Haloperidol aka HAL; neurodegenerative (Schizophrenia);


Agents: Haloperidol; Lithium Chloride; Olanzapine

Vehicle: Cyclodextrin, 2-Hydroxypropyl-B; Route: SC; Species: Rat; Pump: 2ML4; Duration: 28 days;

ALZET Comments: Dose (0.5 mg/kg/day Haloperidol; 2 mmol/L/kg/day Lithium Chloride; 7.5 mg/kg/day Olanzapine); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, 220-270 g, 6-10 weeks old); Haloperidol aka HAL, Olanzapine aka OLZ, Lithium Chloride aka Li; neurodegenerative (Schizophrenia);

Q8921: E. C. Onwordi, et al. Synaptic density marker SV2A is reduced in schizophrenia patients and unaffected by antipsychotics in rats. Nature Communications 2020;11(1):246

Agents: Haloperidol; Olanzapine

Vehicle: Cyclodextrin, B-Hydroxypropyl; Route: SC; Species: Rat; Pump: 2ML4; Duration: 28 days;

ALZET Comments: Dose (0.5 or 2 mg/kg/day ; 7.5 mg/kg/day); 20% B-Hydroxypropylcyclodextrin used; Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, body weight 240–270 g, 6–10 weeks of age); Haloperidol aka HAL; Olanzapine aka OLZ; neurodegenerative (Schizophrenia);

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: 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)." pg.75 ; Vehicle control used but identity not stated. Brain concentration of agents include ((Hal 3.42 ± 0.42 ng/g), (Ola 26.32 ± 1.78 ng/g)); Therapeutic indication (chronic Hal- and Ola-treatments were able to at least partially reverse the AMPH-induced psychotic state by reversing the effects of amphetamines on reducing surface expression of GIRK channels); "


**Agents:** Haloperidol, olanzapine  
**Vehicle:** Cyclodextrin, 2-Hydroxypropyl-;  
**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:** Haloperidol Vehicle: Acetic acid, water  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML2  
**Duration:** Not Stated;

**ALZET Comments:** 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);


**Agents:** Haloperidol-Hcl  
**Vehicle:** Saline;  
**Route:** SC  
**Species:** Mice  
**Pump:** 2004  
**Duration:** 14 days;

**ALZET Comments:** 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);


**Agents:** Haloperidol Vehicle: Acetic acid, glacial; Water  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML2  
**Duration:** 14 days;

**ALZET Comments:** Dose (0.75 mg/kg/day); 2% glacial acetic acid/H2O solution (pH adjusted to 3.8 with NaOH); Controls received mp w/ vehicle; animal info (Eleven-week-old male Wistar rats weighing 240–270 g); Therapeutic indication (dopamine supersensitivity psychosis);
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;


**Agents:** Haloperidol  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 14 days;  
**ALZET Comments:** Controls received mp w/ vehicle; Animal info (female Sprague-Dawley rats); behavioral testing (Locomotor activity boxes); Haloperidol aka HAL;


**Agents:** Haloperidol  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 14 days;  
**ALZET Comments:** Controls received mp w/ vehicle; Animal info (OVX Sprague Dawley rats, 200-250 g, 2 months old); post op. care (Anafen analgesic 0.1 mL/rat, and local antibiotic ointment); replacement therapy (estrogen replacement); MRI compatible PEEK tubing used; Dose (0.25 mg/kg/day); Therapeutic indication (Schizophrenia);


**Agents:** Haloperidol, Olanzapine  
**Vehicle:** Cyclodextrin, hydroxypropyl-β-; Ascorbic acid;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 28 days;  
**ALZET Comments:** Controls received mp w/ vehicle; Animal info (Male Sprague-Dawley rats, body weight 240–270 g, 6–10 weeks old); Haloperidol aka HAL, Olanzapine aka OLZ, Lithium Chloride aka Li; neurodegenerative (Schizophrenia);

**Olanzapine (2017-Present)**

Q9257: E. F. Halff, et al. Effects of chronic exposure to haloperidol, olanzapine or lithium on SV2A and NLGN synaptic puncta in the rat frontal cortex. *Behavioural Brain Research* 2021;405(113203

**Agents:** Haloperidol; Lithium Chloride; Olanzapine  
**Vehicle:** Cyclodextrin, 2-Hydroxypropyl-B-;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 28 days;  
**ALZET Comments:** Dose (0.5 mg/kg/day Haloperidol; 2 mmol/L/kg/day Lithium Chloride; 7.5 mg/kg/day Olanzapine); Controls received mp w/ vehicle; Animal info (Male Sprague-Dawley rats, 220-270 g, 6-10 weeks old); Haloperidol aka HAL, Olanzapine aka OLZ, Lithium Chloride aka Li; neurodegenerative (Schizophrenia);

Q8921: E. C. Onwordi, et al. Synaptic density marker SV2A is reduced in schizophrenia patients and unaffected by antipsychotics in rats. *Nature Communications* 2020;11(1):246

**Agents:** Haloperidol; Olanzapine  
**Vehicle:** Cyclodextrin, B-Hydroxypropyl;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 28 days;  
**ALZET Comments:** Dose (0.5 or 2 mg/kg/day; 7.5 mg/kg/day); 20% B-Hydroxypropylcyclohexane used; Controls received mp w/ vehicle; Animal info (Male Sprague-Dawley rats, body weight 240-270 g, 6–10 weeks of age); Haloperidol aka HAL, Olanzapine aka OLZ, neurodegenerative (Schizophrenia);


**Agents:** Olanzapine  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 4 weeks;  
**ALZET Comments:** Dose (8 mg/kg/d); Controls received mp w/ vehicle; Animal info (Female C57BL/6 J mice (8 weeks old)); pumps replaced every 2 weeks; dependence;
**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).” pg.75 ; Vehicle control used but identity not stated. Brain concentration of agents include ((Hal 3.4 ± 0.42 ng/g), (Ola 26.32 ± 1.78 ng/g)); Therapeutic indication (chronic Hal- and Ola-treatments were able to at least partially reverse the AMPH-induced psychotic state by reversing the effects of amphetamines on reducing surface expression of GIRK channels);

**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-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;

**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);

Quetiapine
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;
Bibliography


**Agents:** 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, cephapirin 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. **Vehicle:** DMSO; water; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** Not Stated;

**ALZET Comments:** 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.


**Agents:** Olanzapine; risperidone; quetiapine fumerate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

**ALZET Comments:** Functionality of mp verified by residual volume; antipsychotic drugs


**Agents:** Haloperidol; olanzapine; risperidone; quetiapine; clozapine **Vehicle:** Water; acetic acid, glacial; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7 days;

**ALZET Comments:** 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


**Agents:** Olanzapine; risperidone; quetiapine fumarate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; antipsychotic agents


**Agents:** Olanzapine; Risperidone; Quetiapine fumarate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

**ALZET Comments:** controls received mp w/ vehicle; functionality of mp verified by residual volume; antipsychotic agents

Remoxipride


**Agents:** Remoxipride HCl **Vehicle:** Sodium chloride; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** 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


**Agents:** Remoxipride HCl; Haloperidol **Vehicle:** Water; Acetic acid; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3,14 days;

**ALZET Comments:** controls received sham operations
Risperidone (2010-Present)

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. Neuropharmacology 2016;105(61-71

**Agents:** Risperidone  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 21 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (C58/J); 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


**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


**Agents:** Risperidone  **Vehicle:** Cyclodextrin, hydroxypropyl beta;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 28 days;

**ALZET Comments:** 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% cyclodextrin 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

Spiperone


**Agents:** Spiperone; SCH-23390  **Vehicle:** DMSO;  **Route:** SC;  **Species:** Rat;  **Pump:** 2001;  **Duration:** 7 days;

**ALZET Comments:** functionality of mp verified after delivery; dopamine antagonist
**Sulpiride**

**P2115:** L.-W. Zhou, et al. Triazolam blocks the initial rotational effects of quinpirole but permits the later developing reduction of dopamine D2-mediated rotational behavior and dopamine D2 receptors. European Journal of Pharmacology 1992;218(219-227)

**Agents:** Quinpirole HCl; Sulpiride; Triazolam  
**Vehicle:** Ascorbic acid; DMSO;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 2001;  
**Duration:** 6 days;  
**ALZET Comments:** Quinpirole is a dopamine agonist; antidepressant; stability verified in vitro for 7 days


**Agents:** Dopamine, 6-hydroxy-; Haloperidol; Sulpiride  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 8 days;  
**ALZET Comments:** Japanese, English abstract


**Agents:** Dopamine HCl; Sulpiride  
**Vehicle:** Nitrogen; Sodium metabisulfite;  
**Route:** CSF/CNS (nucleus accumbens); IP;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 13 days;  
**ALZET Comments:** 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

**Trifluoperazine**


**Agents:** Trifluoperazine; Amphetamine sulfate, d-  
**Vehicle:** Saline;  
**Route:** CSF/CNS (corpus striatum);  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 7 days;  
**ALZET Comments:** caudate putamen