



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

**Chlorpromazine**

**P2717:** P. N. M. Konings, *et al.* Chronic haloperidol and chlorpromazine treatment alters in vitro B-endorphin metabolism in rat brain. *European Journal of Pharmacology* 1990;191(115-128

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

**ALZET Comments:** controls received mp w/ vehicle

**P1348:** T. N. Myschuk, *et al.* Long term (1 week) tranquilization of mice using Alzet(R) mini-osmotic pumps. *Can. Lab Anim. Sci. News* 1987;20(1):18-20

**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

**P1137:** T. P. Davis, *et al.* Neuroleptic drug treatment alters in vitro central neurotensin metabolism. *Psychoneuroendocrinology* 1987;12(4):253-260

**Agents:** Chlorpromazine; Haloperidol **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **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

**P0908:** P. Frey. Changes in cholecystokinin content in rat brain after subchronic treatment with neuroleptics. *Annals of the New York Academy of Sciences* 1985;448(601-603

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

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

**P0447:** T. P. Davis, *et al.* Centrally acting drugs alter in vitro B-endorphin processing in the rat. *European Journal of Pharmacology* 1984;100(249-251

**Agents:** Chlorpromazine; haloperidol; Phenobarbital; Promethazine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2001; **Duration:** 8 days;

**ALZET Comments:** Comparison of agents effects

**P0385:** P. Frey. Cholecystokinin octapeptide levels in rat brain are changed after subchronic neuroleptic treatment. *European Journal of Pharmacology* 1983;95(87-92

**Agents:** Chlorpromazine; Clozapine; Haloperidol **Vehicle:** HCl; Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 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)**

**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; **Strain:** DAT-cre; iCre-DAT; DAT-cre-ribotag; iCre-DAT-ribotag; **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);



**Q7989:** D. Esen-Sehir, *et al.* Establishing an effective dose for chronic intracerebroventricular administration of clozapine in mice. *Acta Neuropsychiatr* 2019;31(6):305-315

**Agents:** Clozapine **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricles); **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2006; **Duration:** 3 weeks;

**ALZET Comments:** Dose (0,12.5,25, or 50 ug/day); Controls received mp w/ vehicle; ALZET brain infusion kit 3 used; Brain coordinates (AP -0.5 mm, ML ± 1.4mm and DV 3mm from the skull surface); neurodegenerative ( );

**Q7925:** N. D. Jayaraj, *et al.* Reducing CXCR4-mediated nociceptor hyperexcitability reverses painful diabetic neuropathy. *Journal of Clinical Investigation* 2018;128(6):2205-2225

**Agents:** Clozapine-N-Oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Nav1.8-Cre;RC::L-hM3 Dq; **Pump:** Not Stated; **Duration:** 4 weeks;

**ALZET Comments:** Dose (10 mg/kg/day); Controls received mp w/ vehicle; Clozapine-N-oxide aka CNO; diabetes;

**Q11254:** M. D. M. Cajiao-Manrique, *et al.* A male mouse model of WIN 55,212-2 self-administration to study cannabinoid addiction. *Frontiers in Pharmacology* 2023;14(1143365)

**Agents:** Clozapine-N-oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Pump:** 2004; **Duration:** 15 days;

**ALZET Comments:** 0.9% saline used; Controls received mp w/ vehicle; animal info (Male; 8 weeks old); behavioral testing (Motivation; Persistence of response; Compulsivity); dependence;

**Q5793:** F. Donato, *et al.* Stellate cells drive maturation of the entorhinal-hippocampal circuit. *Science* 2017;355(6330):

**Agents:** Clozapine-N-oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice (neonate); **Strain:** C57/Bl6; **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; **Strain:** C57BL/6J; **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;

## Fluphenazine

**P0908:** P. Frey. Changes in cholecystokinin content in rat brain after subchronic treatment with neuroleptics. *Annals of the New York Academy of Sciences* 1985;448(601-603)

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

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

## Haloperidol (2021-Present)

**Q10966:** K. Nagaoka, *et al.* Acetaminophen improves tardive akathisia induced by dopamine D(2) receptor antagonists. *Journal of Pharmacological Sciences* 2023;151(1):9-16

**Agents:** Haloperidol **Vehicle:** Cyclodextrin, hydroxypropyl-b; **Route:** Not Stated; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML4; **Duration:** 21 days;

**ALZET Comments:** Dose: (1 mg/kg/day); animal info (Male, 9 weeks old, 200-250 g); pumps replaced: removed on the 21st day and new pumps were implanted in the same manner; behavioral testing (open field test.); akathisia



**Q10608:** E. Montalban, *et al.* Translational Profiling of Mouse Dopaminergic Neurons Reveals Region-Specific Gene Expression, Exon Usage, and Striatal Prostaglandin E2 Modulatory Effects. *Molecular Psychiatry* 2022;27(4):2068-2079

**Agents:** Misoprostol; Haloperidol **Vehicle:** PBS; Saline; **Route:** IP; CSF/CNS (intracerebral); **Species:** Mice; **Strain:** Wild-type; **Pump:** 1004; 2004; **Duration:** Not Stated

**ALZET Comments:** animal info (D2-TRAP; C57BL/6 mice Male; Female; Transgenic); behavioral testing (rotarod/food-cued Y maze); bilateral cannula used; neurodegenerative (Parkinson's; Addiction; Schizophrenia); Therapeutic indication (Neuromodulators);

**Q9516:** T. C. Uzuneser, *et al.* Presynaptic vesicular accumulation is required for antipsychotic efficacy in psychotic-like rats. *Journal of Psychopharmacology* 2021;35(1):65-77

**Agents:** Haloperidol; Haloperidol, analog compound **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2001; **Duration:** 7 days;

**ALZET Comments:** Dose (); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male rats, 300-350 g); behavioral testing (locomotion test); d-amphetamine sulfate aka AMPH; ALZET brain infusion kit 2 used; Brain coordinates (0.8 mm posterior, 1.4 mm lateral, 4.5 mm ventral from the bregma); cyanoacrylate adhesive;

**Q10327:** A. Servonnet, *et al.* Dopaminergic mechanisms underlying the expression of antipsychotic-induced dopamine supersensitivity in rats. *Neuropharmacology* 2021;197(108747)

**Agents:** Haloperidol **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML2; **Duration:** 17 days;

**ALZET Comments:** Dose: (0.5 mg/kg/day); Controls received mp w/o vehicle; (sham surgery)animal info: Male rats (200-275 g); dependence;

**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; **Strain:** Wistar; **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 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; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** 14 days;

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

**Q10575:** M. Kimura, *et al.* Upregulation of Heat-Shock Protein HSP-70 and Glutamate Transporter-1/Glutamine Synthetase in the Striatum and Hippocampus in Haloperidol-Induced Dopamine-Supersensitivity-State Rats. *Pharmacology, Biochemistry and Behavior* 2021;211(173288)

**Agents:** Haloperidol **Vehicle:** Acetic acid; H2O; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML2; **Duration:** 14 days;

**ALZET Comments:** Dose (0.75 mg/kg/day); 2% glacial acetic acid/H2O used; Controls received mp w/ vehicle; animal info (Male; 11 weeks old; Weigh 240-270 g); neurodegenerative (Schizophrenia);

**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; **Strain:** Sprague-Dawley; **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 rats, 220-270 g, 6-10 weeks old); Haloperidol aka HAL, Olanzapine aka OLZ, Lithium Chloride aka Li; neurodegenerative (Schizophrenia);



### Olanzapine (2017-Present)

**Q11343:** K. L. Kooij, *et al.* Intranasal administration of olanzapine has beneficial outcome in a rat activity-based anorexia model. *European Neuropsychopharmacology* 2023;71(65-74

**Agents:** Olanzapine **Vehicle:** Acetic acid, glacial; saline; **Route:** SC; **Species:** Rat; **Strain:** WU; **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** Dose-response: (1, 2.75, 7.5 mg/kg); animal info (Female outbred 50 & 175 g); post op. care (Carprofen); comparison of intranasal administration vs mp; "To establish constant plasma levels in the chronic experiment, we used osmotic minipumps." p. 67

**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:** 28d **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);

**Q8854:** R. H. Isaacson, *et al.* Olanzapine-induced liver injury in mice: aggravation by high-fat diet and protection with sulforaphane. *Journal of Nutritional Biochemistry* 2020;81(108399

**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;

**Q7450:** J. Cunningham, *et al.* F160. Samidorphan, an Opioid Receptor Antagonist, Mitigates Olanzapine-Induced Metabolic Dysfunction in Female Rats. *Biological Psychiatry* 2019;85(10):

**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;

**Q7821:** D. Groos, *et al.* Chronic antipsychotic treatment targets GIRK current suppression, loss of long-term synaptic depression and behavioural sensitization in a mouse model of amphetamine psychosis. *J Psychopharmacol* 2018;269881118812235

**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); "



**Q7793:** E. Courty, *et al.* Antenatal antipsychotic exposure induces multigenerational and gender-specific programming of adiposity and glucose tolerance in adult mouse offspring. *Diabetes & Metabolism* 2018;44(3):281-291

**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); dependence; 42.5% DMSO, 42.5% propylene glycol and 15% ethanol used;

**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)

**Agents:** Haloperidol, olanzapine **Vehicle:** Cyclodextrin, **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;

**Q5988:** A. Stefanidis, *et al.* Prevention of the adverse effects of olanzapine on lipid metabolism with the antiepileptic zonisamide. *Neuropharmacology* 2017;123(55-66)

**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 **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; "...mp serve some preferable aspect such as to reduce stress to the animals, minimize unwanted experimental variables, and hold the drug concentration constant"

**Q5063:** N. Ito, *et al.* Contribution of protein binding, lipid partitioning, and asymmetrical transport to drug transfer into milk in mouse versus human. *Pharm Res* 2013;30(9):2410-22

**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.

**P5912:** F. I. Tarazi, *et al.* Long-term effects of olanzapine, risperidone, and quetiapine on ionotropic glutamate receptor types: Implications for antipsychotic drug treatment. *Journal of Pharmacology and Experimental Therapeutics* 2003;306(3):1145-1151

**Agents:** Olanzapine; risperidone; quetiapine fumerate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Duration:** 28 days; **ALZET Comments:** Functionality of mp verified by residual volume; antipsychotic drugs

**P6169:** S. Kapur, *et al.* Antipsychotic Dosing in Preclinical Models is Often Unrepresentative of the Clinical Condition: A Suggested Solution Based on in Vivo Occupancy. *Journal of Pharmacology and Experimental Therapeutics* 2003;305(2):625-631

**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



**P5866:** F. I. Tarazi, *et al.* Long-term effects of newer antipsychotic drugs on neuronal nitric oxide synthase in rat brain. NITRIC OXIDE-BIOLOGY AND CHEMISTRY 2002;7(4):297-300

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

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

**P5122:** F. I. Tarazi, *et al.* Long-term effects of olanzapine, risperidone, and quetiapine on serotonin 1A, 2A and 2C receptors in rat forebrain regions. Psychopharmacology 2002;161(263-270

**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

**P2736:** J. Georgieva, *et al.* Neurochemical effects of prolonged treatment with remoxipride as assessed by intracerebral microdialysis in freely moving rats. Prog. Neuro-Psychopharmacol. Biol. Psychiat 1994;18(1187-1201

**Agents:** Remoxipride HCl **Vehicle:** Sodium chloride; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley, albino; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** animal info: albino, male, 250-280 g; 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

**P2204:** H. Ericson, *et al.* Subchronic treatment of rats with remoxipride fails to modify sigma binding sites in the brain. European Journal of Pharmacology 1992;226(157-161

**Agents:** Remoxipride HCl; Haloperidol **Vehicle:** Water; Acetic acid; **Route:** SC; **Species:** Rat; **Strain:** Not Stated; **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);

**Q8159:** N. Amada, *et al.* Brexpiprazole has a low risk of dopamine D2 receptor sensitization and inhibits rebound phenomena related to D2 and serotonin 5-HT2A receptors in rats. Neuropsychopharmacol Rep 2019;39(4):279-288

**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:** 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);

**Q1929:** E. C. Muly, *et al.* Relationship between Dose, Drug Levels, and D2 Receptor Occupancy for the Atypical Antipsychotics Risperidone and Paliperidone. *Journal of Pharmacology and Experimental Therapeutics* 2012;341(1):81-89

**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

### Spiiperone

**P1288:** T. S. Shippenberg, *et al.* Motivational effects of opioids; influence of D-1 versus D-2 receptors antagonists. *European Journal of Pharmacology* 1988;151(233-242)

**Agents:** Spiiperone; SCH-23390 **Vehicle:** DMSO; Water; **Route:** SC; **Species:** Rat; **Strain:** Not Stated; **Pump:** 2001; 2ML1; **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

**P1444:** H. Ueda. Time course study of changes in the activity of rats during intraventricular infusion of 6-hydroxydopamine, haloperidol and sulpiride: a study of the relationship between an origin of the negative symptoms in schizophrenia and catecholamines. *J. Iwate Med. Assoc* 1988;40(3):385-398

**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

**P0630:** B. Costall, *et al.* The continuity of dopamine receptor antagonism can dictate the long-term behavioural consequences of a mesolimbic infusion of dopamine. *Neuropharmacology* 1985;2(3):193-197

**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 injection vs. mp infusion; 2 mp/rat - bilateral infusion; mp primed overnight; vehicles listed used w/DOP; concomitant Sulp admin. ip

### Trifluoperazine

**P0144:** G. G. Dougherty Jr, *et al.* Amphetamine behavioral toxicity: rotational behavior after chronic intrastriatal infusion. *Biological Psychiatry* 1981;16(5):479-488

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