**Recent References on the Administration of NMDA (N-Methyl-D-Aspartate) Antagonists Using ALZET® Osmotic Pumps**

## Adamantane

**P3920:** L. Stitz, *et al.* Lack of antiviral effect of amantadine in borna disease virus infection. Med Microbiol Immunol 1998;186(195-200
**Agents:** Adamantane, 1-amino- **Vehicle:** Water, sterile distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** functionality of mp verified by serum levels; comparison of oral doses vs. mp; immunology; agent is NMDA antagonist also called amantadine or 1-adamantanamide

## AP5, AP6, AP7 (2002-Present)

**Q4996:** X. F. Li, *et al.* The Posterodorsal Medial Amygdala Regulates the Timing of Puberty Onset in Female Rats. Endocrinology 2015;156(10):3725-36
**Agents:** Bicuculline; AP5, D-; **Route:** CSF/CNS (posterodorsal subnucleus); **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (female, Sprague Dawley, late pregnant); bilateral cannula used; behavioral testing (social interaction; play fighting behavior); Cannula placement verified via histological analysis; bilateral infusion with Plastics One cannula;

**Q4743:** K. Shinohara, *et al.* Post-acquisition hippocampal NMDA receptor blockade sustains retention of spatial reference memory in Morris water maze. Behavioural Brain Research 2014;259(;):261-267
**Agents:** AP5, D- **Vehicle:** CSF, artificial; **Route:** CSF/CNS (hippocampus); **Species:** Rat; **Pump:** 1007D; **Duration:** 7, 14 days;
**ALZET Comments:** Animal info (male, albino Wistar); pumps replaced every 7 days; Plastics One bilateral cannula used; Multiple pumps per animal (2); behavioral testing (Morris water maze, probe test); tissue perfusion (hippocampus); Cannula placement verified via histological analysis; pumps primed for 24 hours in 37C saline; bilateral infusion;

**Q2592:** R. G. M. Morris, *et al.* N-methyl-d-aspartate receptors, learning and memory: chronic intraventricular infusion of the NMDA receptor antagonist d-AP5 interacts directly with the neural mechanisms of spatial learning. European Journal of Neuroscience 2013;37(5):700-717
**Agents:** AP5, D- **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (male, Lister hooded); behavioral testing (water maze, place task, cue task);

**Q2588:** J. Inglis, *et al.* Upstairs/downstairs revisited: spatial pretraining-induced rescue of normal spatial learning during selective blockade of hippocampal N-methyl-d-aspartate receptors. European Journal of Neuroscience 2013;37(5):718-727
**Agents:** AP5, D- **Vehicle:** CSF, artificial; **Route:** CSF/CNS (dorsal hippocampus); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (Lister-Hooded); bilateral cannula used; behavioral testing (water maze); bilateral infusion;

**Q3056:** T. J. Brozoski, *et al.* Local NMDA Receptor Blockade Attenuates Chronic Tinnitus and Associated Brain Activity in an Animal Model. PLoS One 2013;8(10):U388-U398
**Agents:** AP5, D- **Vehicle:** Saline; **Route:** CSF/CNS (paraflocculus); **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
**ALZET Comments:** Controls received mp w/ methylene dye; animal info (male, Long-Evans, 60 days old); functionality of mp verified by residual volume; tissue perfusion (paraflocculus); brain tissue distribution; Used PE-50 tubing. D-AP5 is an NMDA antagonist. Pumps anchored to muscle/connective tissue via nylon suture

**Q0288:** C. S. Wong, *et al.* N-Methyl-D-aspartate receptor antagonist D-AP5 prevents pertussis toxin-induced alterations in rat spinal cords by inhibiting increase in concentrations of spinal CSF excitatory amino acids and downregulation of glutamate transporters. Brain Research Bulletin 2009;80(1-2):69-74
**Agents:** AP5, D- **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;
**ALZET Comments:** Controls received mp w/ saline; animal info (Male, Wistar, 400-420 g); two intrathecal catheters inserted; behavioral testing (tail flick latency)

**P9792:** T. Uekita, *et al.* Pretraining Does Not Ameliorate Spatial Learning Deficits Induced by Intrahippocampal Infusion of AP5. Behavioral Neuroscience 2009;123(3):520-526
**Agents:** AP5 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (hippocampus); **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; multiple pumps per animal (2); animal info (male, albino, Wistar, 2 months old); Plastics One cannula used; silicon rubber used

**P7585:** M. Day, *et al.* Post-training N-methyl-D-aspartate receptor blockade offers protection from retrograde interference but does not affect consolidation of weak or strong memory traces in the water maze. Neuroscience 2006;137(1):19-28
**Agents:** AP5, D- **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 7, 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; pumps replaced after 7 days; post op. care (carpofen); animal info (male, Lister-hooded 230-280 g); electrophysiology

**P7462:** M. Sakai, *et al.* Characteristics of sound discrimination enhancement after sound exposure in adult rats. Behavioral Neuroscience 2005;119(4):961-973
**Agents:** Ap5, D- **Vehicle:** Saline; **Route:** CSF/CNS (auditory cortex); **Species:** Rat; **Pump:** 1003D; **Duration:** 60 hours;
**ALZET Comments:** Controls received mp w/ vehicle; no stress (see pg. 970); post op. care (ampicillin, fradiomycin); animal info (male, Wistar); cannula placement verified via fast blue dye; external pump application

**P5616:** Z. H. Wen, *et al.* D-2-amino-5-phosphonopentanoic acid inhibits intrathecal pertussis toxin-induced thermal hyperalgesia and protein kinase C gamma up-regulation. Brain Research 2003;963(1-2):1-7
**Agents:** AP5, D- **Vehicle:** Saline; **Route:** CSF/CNS (Intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;
**ALZET Comments:** (D-AP5) is D-2-Amino-5-phosphonopentanoic acid.

**P5652:** I. Nagano, *et al.* Ventral root avulsion leads to downregulation of GluR2 subunit in spinal motoneurons in adult rats. Neuroscience 2003;117(1):139-146
**Agents:** MK-801; AP5, D-, NBQX; CNQX **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2002;
**Duration:** 2 weeks;
**ALZET Comments:** Glutamate receptor antagonists; MK-801 & AP5 are NMDA recept. antag.;

**R0199:** R. G. M. Morris, *et al.* Elements of a neurobiological theory of the hippocampus: the role of activity-dependent synaptic plasticity in memory. PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON SERIES B-BIO LOGICAL SCIENCES 2003;358(1432):773-786
**Agents:** AP5, D-; LY326325 **Vehicle:** CSF, artificial **Route:** CSF/CNS (dorsal hippocampus); **Species:** Rat, Mice **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle

**R0179:** S. J. Martin, *et al.* New life in an old idea: The synaptic plasticity and memory hypothesis revisited. Hippocampus 2002;12(5):609-636
**Agents:** AP5, D- **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; Mice; **Pump:** Not Stated; **Duration:** Not Stated;
**ALZET Comments:** Brief mention of pump use on p. 622

## ARL 15896AR

**P6348:** J. W. B. Marshall, *et al.* Assessment of cognitive and motor deficits in a marmoset model of stroke. ILAR JOURNAL 2003;44(2):153-160
**Agents:** Clomethiazole; AR-R15896AR; NXY-059 **Vehicle:** Saline; **Route:** SC; **Species:** Monkey (marmoset); **Pump:** 2001D;
**Duration:** 48 hours;
**ALZET Comments:** Controls received mp w/ vehicle; pumps replaced every 24 hours; post op. care (incubator);

**P6197:** J. W. B. Marshall, *et al.* Comparison of the neuroprotective effect of clomethiazole, AR-R15896AR and NXY-059 in a primate model of stroke using histological and behavioural measures. Brain Research 2003;972(1-2):119-126
**Agents:** Clomethiazole; AR-R15896AR; NXY-059; **Route:** SC; **Species:** Monkey; **Pump:** 2001D; **Duration:** 48 hours;
**ALZET Comments:** Controls received mp w/ saline; functionality of mp verified by plasma drug concentration at 24 hours; pumps replaced after 24 hours; multiple pumps per animal (2 for NXY-059 exp); post-op care (incubator 3-5 days);

**P4405:** E. F. Cregan, *et al.* [(S)-Alpha-phenyl-2-pyridine-ethanamine dihydrochloride], a low affinity uncompetitive N-methyl-D-aspartic acid antagonist, is effective in rodent models of global and focal ischemia. Journal of Pharmacology and Experimental Therapeutics 1997;283(1412-1424
**Agents:** ARL 15896AR **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
**ALZET Comments:** Controls received mp with vehicle; functionality of mp verified by blood levels; comparison of twice daily injections vs. mp; ARL 15896AR is [(S)-alpha-phenyl-2-pyridine-ethanamine dihydrochloride, a low affinity non-competitive NMDA receptor antagonist; ischemia (cerebral)

## Caroverine

**R0266:** E. E. L. Swan, *et al.* Inner ear drug delivery for auditory applications. Advanced Drug Delivery Reviews 2008;60(15):1583-1599
**Agents:** Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNKI-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisone; Caroverine; Methionine, D-; Thiourea; Liposome, cationic; Neomycin **Route:** SC; Ear (round window membrane); Ear (cochlea); Ear (scala tympani); Ear; **Species:** Guinea pig; **Duration:** 3, 7, 14, 28 days;
**ALZET Comments:** Gene therapy; peptides; no stress; enzyme inhibitor (peroxidase); stress/adverse reaction (see pg 1593) "Ref #161 found local trauma and inflammatory responses"; tissue perfusion (scala tympani, cochlea, round window membrane); comparison of middle ear injections vs. mp; Review, see pgs. 1587 - 1589, 1591, 1593 - 1595, refs #49, 50, 60, 63, 72, 75, 102, 104,180, 181, 194-201

**P9015:** M. L. Duan, *et al.* Low-dose, long-term caroverine administration attenuates impulse noise-induced hearing loss in the rat. Acta Otolaryngologica 2006;126(11):1140-1147
**Agents:** Caroverine **Vehicle:** Saline, physiological; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** 12 hours;
**ALZET Comments:** Controls received mp w/ vehicle; no stress (see pg. 1144); animal info (male, Sprague Dawley, 250-300 g.); AMPA and NMDA receptor antagonist; agent also known as spasmium; "administration of caroverine through a subcutaneous micro-osmotic pump was shown to be a simple and effective method for the delivery of caroverine into the inner ear. More importantly, this kind of drug delivery can avoid severe side effects induced by caroverine injected by high-dose but short-term administration." (p. 1144)

## CGX-1007

**P7560:** X. C. M. Lu, *et al.* Effects of delayed intrathecal infusion of an NMDA receptor antagonist on ischemic injury and peri-infarct depolarizations. Brain Research 2005;1056(2):200-208
**Agents:** CGX-1007 **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal, cisterna magna); **Species:** Rat; **Pump:** 2001D; **Duration:** 16 hours;
**ALZET Comments:** Controls received mp w/ vehicle; dose-response (fig. 1); dose-dependent paralysis and mortality; peptides; ischemia (cerebral); animal info (male, Sprague-Dawley, 275-350 g); middle cerebral artery occlusion; stretched PE-10 tubing to a PE-60 connection piece

**P6635:** M. E. Barton, *et al.* The effect of CGX-1007 and CI-1041, novel NMDA receptor antagonists, on kindling acquisition and expression. Epilepsy Research 2004;59(1):1-12
**Agents:** CGX-1007 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (amygdala); **Species:** Rat; **Pump:** Not Stated; **Duration:** 9 days;
**ALZET Comments:** Controls received mp w/ vehicle; comparison of ICV injections vs. mp; peptides;

## CP 606-27

**P5604:** Y. Yang, *et al.* Reduced brain infarct volume and improved neurological outcome by inhibition of the NR2B subunit of NMDA receptors by using CP101,606-27 alone and in combination with rt-PA in a thromboembolic stroke model in rats. Journal of Neurosurgery 2003;98(2):397-403
**Agents:** CP-101; 606-27 **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;
**ALZET Comments:** Controls received mp/ w vehicle; dose-response; ischemia (cerebral); 606-27 is a NMDA antagonist

## Ketamine

**Q8801:** A. J. Peters*, et al.* Ketamine Alters Hippocampal Cell Proliferation and Improves Learning in Mice after Traumatic Brain Injury. Anesthesiology 2018;129(2):278-295
**Agents:** Ketamine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;
**ALZET Comments:** Dose (30 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL/6J, 8 to 12 weeks old); neurodegenerative (Brain Injury);

**Q6361:** J. L. Marcos*, et al.* Role of the spinal TrkB-NMDA receptor link in the BDNF-induced long-lasting mechanical hyperalgesia in the rat: A behavioural study. European Journal of Pain 2017;21(10):1688-1696
**Agents:** Ketamine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;
**ALZET Comments:** Dose (1.2 mg/day/rat); animal info (Adult male Sprague–Dawley rats weighing 250–350 g);

**Q6466:** J. P. Hamm*, et al.* Altered Cortical Ensembles in Mouse Models of Schizophrenia. Neuron 2017;94(1):153-167 e8
**Agents:** Ketamine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 1 week;
**ALZET Comments:** Dose (60 mg/kg/day); animal info (Mutant Df(16)A+/− mice); Therapeutic indication (schizophrenia);

**Q5038:** Plato Mak*, et al.* Long-Term Antihyperalgesic and Opioid-Sparing Effects of 5-Day Ketamine and Morphine Infusion ("Burst Ketamine") in Diabetic Neuropathic Rats. PAIN MEDICINE 2015;16(1781-1793
**Agents:** Ketamine; morphine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 5 days;
**ALZET Comments:** Controls received dummy implant; animal info (male, Wistar); post op. care (carpofen IP injection); behavioral testing (nociception, rotarod, open field); diabetes; pumps removed after 5 days; Dose (20 mg/kg/day);

**Q5280:** M. S. Maral Tajerian, Ph.D., , *et al.* Differential Efficacy of Ketamine in the Acute versus Chronic Stages of Complex Regional Pain Syndrome in Mice. Anesthesiology 2015;123(6):1435-1447
**Agents:** Ketamine **Vehicle:** Saline, sterile; **Route:** SC; **Species:** mice; **Pump:** 1007D; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Male C57/B6J mice aged 12 to 14 weeks); good methods (pg 1436); behavioral testing (pg 1437); Limb fracture; pumps removed 8 days after implantation; Dose (2 mg/kg/day);

**Q0005:** M. K. Boettger*, et al.* Spinally applied ketamine or morphine attenuate peripheral inflammation and hyperalgesia in acute and chronic phases of experimental arthritis. Brain, Behavior; Immunity 2010;24(3):474-485
**Agents:** Ketamine; Morphine **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2ML4; **Duration:** 21 days;
**ALZET Comments:** Controls received mp w/ vehicle; tolerance; ALZET brain infusion kit used; half-life pg 477 (2.5 hrs in CSF (ketamine); 2.1 hrs (morphine)); animal info (Female, Lewis, 6-8 wks old, 160-180 g); dorsal laminectomy; behavioral testing (pain related behavior)

**P8855:** F. Haugan*, et al.* Ketamine blocks enhancement of spinal long-term potentiation in chronic opioid treated rats. Acta Anaesthesiologica Scandinavica 2008;52(5):681-687
**Agents:** Morphine; Ketamine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ saline or no treatment; no stress (see pg. 683); tolerance; animal info (female, Sprague Dawley, 210-320); "No behavioral differences could be observed between groups, suggesting that the animals were not suffering significant distress due to the implantations + treatment." (p. 683); pain

**P6777:** Y. Shiga*, et al.* The inhibition of aortic smooth muscle cell proliferation by the intravenous anesthetic ketamine. Anesthesia & Analgesia 2004;99(5):1408-1412
**Agents:** Ketamine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7,9 days;
**ALZET Comments:** Controls received mp w/ saline; cardiovascular

**P5337:** L. A. B. Slot, *et al.* Experimental conditions for the continuous subcutaneous infusion of four central analgesics in rats. Pharmacology Biochemistry and Behavior 2002;72(4):943-951
**Agents:** Morphine HCl; Ketamine HCl; Imipramine HCl; gabapentin **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
**ALZET Comments:** Controls received mp w/ saline; no stress (see pg. 947); 14 day stability verified by HPLC on all agents; the site of pump placement was massaged daily to avoid tissue adherance; opioid and non-opioid analgesics; body weight gain information provided

**P6585:** F. C. Colpaert, *et al.* Large-amplitude 5-$HT_{1A}$ receptor activation: a new mechanism of profound, central analgesia. Neuropharmacology 2002;43(6):945-958
**Agents:** F13640; morphine HCL; imipramine HCl; ketamine HCl; gabapentin **Vehicle:** Water, double distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ saline; dose-response (fig. 3); comparison of IP & SC injections vs. mp; tolerance; dependence; "Continuous F 13640 infusion uniquely produced profound analgesia in this model of severe, chronic pain." (p. 955)

## LY274614

**P6076:** H. B. Zhu, *et al.* Region-specific changes in NMDA receptor mRNA induced by chronic morphine treatment are prevented by the co-administration of the competitive NMDA receptor antagonist LY274614. MOLECULAR BRAIN RESEARCH 2003;114(2):154-162
**Agents:** LY274614 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1 week;
**ALZET Comments:** LY274614 is an NMDA receptor antagonist

**P2707:** P. J. Tiseo, *et al.* Modulation of morphine tolerance by the competitive N-methyl-D-aspartate receptor antagonist LY274614: assessment of opioid receptor changes. J. Pharmacol. Exp. Ther 1994;268(1):195-201
**Agents:** LY-274614 **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 8 days;
**ALZET Comments:** controls received mp w/ saline; "The use of the osmotic pump allows pharmacokinetic differences (ie. elimination rates) among coadministered drugs to be minimized." (pg. 199); tolerance

**P2697:** K. Elliott, *et al.* The NMDA receptor antagonists, LY274614 and MK-801, and the nitric oxide synthase inhibitor, NG-nitro-L-arginine, attenuate analgesic tolerance to the mu-opioid morphine but not to kappa opioids. Pain 1994;56(69-75
**Agents:** LY-274614 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;
**ALZET Comments:** Comparison of ip injections vs. mp; tolerance; LY-274614 is a competitive NMDA receptor antagonist

**P3127:** P. J. Tiseo, *et al.* Attenuation and reversal of morphine tolerance by the competitive N-methyl-D-aspartate receptor antagonist, LY274614. J. Pharmacol. Exp. Ther 1993;264(3):1090-1096
**Agents:** LY-274614; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** controls received mp with saline; tolerance; drugs pH'ed to 7.0; pumps used because inj . of Lilly compound caused sedation, and because inj. could cue subsequent morphine administration

## Memantine (2007-Present)

**Q10577:** C. Kondak, *et al.* Hydromethylthionine Enhancement of Central Cholinergic Signalling is Blocked by Rivastigmine and Memantine. Journal of Neurochemistry 2021;160(2):172-184
**Agents:** Rivastigmine; Memantine **Vehicle:** Aqua ad injectabilia; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
**ALZET Comments:** Dose (Rivastigmine 0.5 mg/kg/d; Memantine 1 mg/kg/d); dose-response (see p. 174); animal info (60 of each species so 120 mice total; Female; 6-8 months old; NMRI); enzyme inhibitor (Rivastigmine); wound clips used; neurodegenerative (Alzheimer's Disease);

**Q6534:** Y. C. Wang*, et al.* Post-acute delivery of memantine promotes post-ischemic neurological recovery, peri-infarct tissue remodeling, and contralesional brain plasticity. J Cereb Blood Flow Metab 2017;37(3):980-993
**Agents:** Memantine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
**ALZET Comments:** Dose (4 or 20 mg/kg/d); animal info (8-12 week old C57BL6/j male mice weighing 23-28g); ischemia (cerebral); "...we decided to use a subcutaneous delivery strategy for memantine in this study using miniosmotic pumps, given that miniosmotic pumps allowed to achieve most stable plasma memantine levels " pg.981 ; Therapeutic indication (stroke);

**Q6653:** H. R. E. Y. Kim*, et al.* NMDA Receptors as Potential Therapeutic Targets in Diabetic Nephropathy: Increased Renal NMDA Receptor Subunit Expression in Akita Mice and Reduced Nephropathy Following Sustained Treatment With Memantine or MK-801. Diabetes 2016;65(3139–3150
**Agents:** Memantine HCl; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
**ALZET Comments:** Dose (Memantine (2 mg/kg/day); dizocilpine (0.5 mg/kg/day)); 0.9% Saline used; Controls received mp w/ vehicle; animal info (10-week-old DBA/2J mice); Dizocilpine AKA (MK-801); diabetes

**Q4623:** M. Trotman*, et al.* The dichotomy of memantine treatment for ischemic stroke: dose-dependent protective and detrimental effects. JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM 2015;35(230-239
**Agents:** Memantine **Vehicle:** DMSO; saline; **Route:** SC; **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, C57BL6, 22-32g); 10% DMSO used; dose-response (237); ischemia (cerebral); memantine is a NMDA Glur antagonist;

**Q4352:** M. T. Castaneda*, et al.* Neuroprotection of medial septal cholinergic neurons by memantine after intralateral septal injection of Abeta(1-40). NEUROREPORT 2015;26(450-454
**Agents:** Memantine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 8 days;
**ALZET Comments:** Animal info (male, Sprague Dawley, 300-400g); neurodegenerative (Alzheimer's disease); brain tissue distribution;

**Q2903:** L. V. Colom*, et al.* Memantine protects cholinergic and glutamatergic septal neurons from Abeta(1-40)-induced toxicity. Neuroscience Letters 2013;541(;):54-57
**Agents:** Memantine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 8 days;
**ALZET Comments:** Animal info (Sprague Dawley, 300-400g); neurodegenerative (Alzheimer's disease, dementia)

**Q0286:** S. Rosi*, et al.* Accuracy of hippocampal network activity is disrupted by neuroinflammation: rescue by memantine. Brain 2009;132(2464-2477
**Agents:** Endotoxin, LPS; Memantine **Vehicle:** Not Stated; **Route:** CSF/CNS (fourth ventricle); SC; **Species:** Rat; **Pump:** 2004; 2ML4; **Duration:** 4 weeks;
**ALZET Comments:** Controls received mp w/ aCSF; animal info (3-month-old, male, F-344, Sprague Dawley); multiple pumps per animal (2); no stress (see pg 2468) "No adverse neurological signs were observed..."; behavioral testing (exploration)

**P9835:** P. Nasr*, et al.* N-Methyl-d-aspartate Receptor Antagonists Have Variable Affect in 3-Nitropropionic Acid Toxicity. Neurochemical Research 2009;34(3):490-498
**Agents:** Ifenpradil; memantine; MK-801 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated;
**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague Dawley)

**Q0464:** S. R. Chen*, et al.* Antinociceptive effects of chronic administration of uncompetitive NMDA receptor antagonists in a rat model of diabetic neuropathic pain. Neuropharmacology 2009;57(2):121-126
**Agents:** Neramexane mesylate; Memantine; Gabapentin **Vehicle:** Saline, sterile; Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, 225-250 g, STZ induced diabetes); functionality of mp verified by plasma drug levels; post op. care (penicillin); wound clips used; neuropathic pain

**P9208:** C. J. Dong, *et al.* alpha-2 adrenergic modulation of NMDA receptor function as a major mechanism of RGC protection in experimental glaucoma and retinal excitotoxicity. Investigative Ophthalmology & Visual Science 2008;49(10):4515-4522
**Agents:** Brimonidine; Memantine; Atipamezole **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Duration:** 2 weeks;
**ALZET Comments:** Enzyme inhibitor (PDE-4); animal info (male, Sprague Dawley, 350-400 g.);

**P9043:** O. Cauli, *et al.* Acute liver failure-induced death of rats is delayed or prevented by blocking NMDA receptors in brain. American Journal of Physiology Gastrointestinal and Liver Physiology 2008;295(3):G503-G511
**Agents:** MK-801; Memantine hydrochloride **Vehicle:** Saline; NaCl; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Wistar, 220-270 g.); 10% DMSO used;

**R0245:** C. G. Parsons, *et al.* Memantine: a NMDA receptor antagonist that improves memory by restoration of homeostasis in the glutarnatergic system - too little activation is bad, too much is even worse. Neuropharmacology 2007;53(6):699-723
**Agents:** Memantine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 1 week;
**ALZET Comments:** Functionality of mp verified by plasma levels; learning; memory; review p. 703

**P8713:** J. Kusari, *et al.* Effect of memantine on neuroretinal function and retinal vascular changes of streptozotocin-induced diabetic rats. Investigative Ophthalmology & Visual Science 2007;48(11):5152-5159
**Agents:** Memantine **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 3,4 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by plasma MEM levels; pumps replaced after 2 weeks; animal info (male, Brown Norway, 250-300g); diabetes

## MK-801 (2005-Present)

**Q6653:** H. R. E. Y. Kim, *et al.* NMDA Receptors as Potential Therapeutic Targets in Diabetic Nephropathy: Increased Renal NMDA Receptor Subunit Expression in Akita Mice and Reduced Nephropathy Following Sustained Treatment With Memantine or MK-801. Diabetes 2016;65(3139–3150
**Agents:** Memantine HCl; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
**ALZET Comments:** Dose (Memantine (2 mg/kg/day); dizocilpine (0.5 mg/kg/day)); 0.9% Saline used; Controls received mp w/ vehicle; animal info (10-week-old DBA/2J mice); Dizocilpine AKA (MK-801); diabetes

**Q4029:** O. Cauli, *et al.* Blocking NMDA Receptors Delays Death in Rats with Acute Liver Failure by Dual Protective Mechanisms in Kidney and Brain. NEUROMOLECULAR MEDICINE 2014;16(360-375
**Agents:** MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Wister, 220-270g); MK-801 is an NMDA receptor blocker;

**Q2629:** P. Sokoloff, *et al.* Direct and indirect interactions of the dopamine D(3) receptor with glutamate pathways: implications for the treatment of schizophrenia. NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY 2013;386(2):107-124
**Agents:** MK-801 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
**ALZET Comments:** Control animals received mp w/ saline; wound clips used; post op. care (Vetedine, Negrol spray)

**Q3552:** I. Lundgaard, *et al.* Neuregulin and BDNF Induce a Switch to NMDA Receptor-Dependent Myelination by Oligodendrocytes. PLOS BIOLOGY 2013;11(12):U147-U164
**Agents:** MK-801 **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1004; **Duration:** 18 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Female, Sprague Dawley, 9-12 weeks old, 200-225g); cyanoacrylate adhesive; used anchoring screws and dental cement; used Plastics one cannula 30g; delayed delivery for 3 days; MK-801 is a NMDA receptor channel blocker;

**Q2554:** G. Grasselli, *et al.* Abnormal NMDA receptor function exacerbates experimental autoimmune encephalomyelitis. British Journal of Pharmacology 2013;168(2):502-517
**Agents:** MK-801 **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (6-8 wks old); ALZET brain infusion kit 3 used;

**Q9030:** N. Wegener, *et al.* Evaluation of brain pharmacokinetics of (+)MK-801 in relation to behaviour. Neuroscience Letters 2011;503(1):68-72
**Agents:** MK-801 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (caduate putamen); **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** Dose (4.5 ul/h); animal info (Naive adult male Sprague–Dawley rats, 240–360g); behavioral testing (Water Maze); MK-801 aka non-competitive NMDA receptor antagonist (+)-5-methyl-10,11-dihydro-5H-dibenzocyclohepten-5,10-imine maleate; Brain coordinates (AP: +0.1, LM: ±2.6, DV: −3.2 mm relative to bregma; −3.3 mm interaural);

**Q2381:** A. L. Spieles-Engemann, *et al.* Subthalamic Nucleus Stimulation Increases Brain Derived Neurotrophic Factor in the Nigrostriatal System and Primary Motor Cortex. JOURNAL OF PARKINSONS DISEASE 2011;1(1):123-136
**Agents:** MK-801 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;
**ALZET Comments:** Control animals received mp w/ saline; animal info (Sprague Dawley, male, 200-250 g)

**Q0779:** R. Sarkis, *et al.* Chronic dizocilpine or apomorphine and development of neuropathy in two rat models I: Behavioral effects and role of nucleus accumbens. Experimental Neurology 2011;228(1):19-29
**Agents:** MK-801; apomorphine HCL hemihydrate **Vehicle:** Saline; Ascorbic acid; **Route:** CSF/CNS (nucleus accumbens);
**Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (adult, female, Sprague Dawley, 200-300 g); post op. care (dexamethasone injections to prevent brain edema); behavioral testing (mechanical allodynia, Paw withdrawal latency, cold allodynia, hotplate test, spontaneous motor activity); cannula placement verified by picomicrograph of brain section; CCI, chronic constriction injury; SNI, spared nerve injury

**Q1291:** A. J. Ramsey, *et al.* Impaired NMDA receptor transmission alters striatal synapses and DISC1 protein in an age-dependent manner. Proceedings of the National Academy of Sciences of the United states of America 2011;108(14):5795-5800
**Agents:** MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; Animal info (NR1-KD)

**Q0272:** E. L. A. van Dorp, *et al.* Morphine-6 beta-glucuronide Rapidly increases Pain Sensitivity Independently of Opioid Receptor Activity in Mice and Humans. Anesthesiology 2009;110(6):1356-1363
**Agents:** Morphine-6 beta-glucuronide; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;
**ALZET Comments:** Animal info (adult, male, CD-1, TrKO, B6129F1); "Osmotic pumps afford continuous opioid infusions and control for hyperalgesia associated with withdrawal in opioid-dependent subjects that potentially confounds experiments in which chronic opioid treatment is accomplished via repeated acute injections." pg 1357

**P9835:** P. Nasr, *et al.* N-Methyl-d-aspartate Receptor Antagonists Have Variable Affect in 3-Nitropropionic Acid Toxicity. Neurochemical Research 2009;34(3):490-498
**Agents:** Ifenpradil; memantine; MK-801 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated;
**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague Dawley)

**P9865:** J. Kocerha, *et al.* MicroRNA-219 modulates NMDA receptor-mediated neurobehavioral dysfunction. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2009;106(9):3507-3512
**Agents:** MK-801; oligonucleotide, antisense **Vehicle:** Not Stated; **Route:** SC; CSF/CNS; **Species:** Mice; **Pump:** 1002; 2002;
**Duration:** 5, 7 days;
**ALZET Comments:** Controls received mp w/ saline; antisense (LNA-antimiR-219); animal info (12 wks old, 25 g.); tygon tubing used; MK-801 also known as dizocilpine

**P9370:** R. E. De Bittencourt-Navarrete, *et al.* NMDA receptor blockade alters the intracellular distribution of neuronal nitric oxide synthase in the superficial layers of the rat superior colliculus. Brazilian Journal of Medical and Biological Research 2009;42(2):189-196
**Agents:** MK-801 **Vehicle:** Saline; **Route:** CSF/CNS (superior collicus); **Species:** Rat; **Pump:** 2002; **Duration:** 10,12 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (adult, male Lister); cyanoacrylate adhesive

**P8755:** Z. H. Wen, *et al.* N-Methyl-D-aspartate receptor antagonist MK-801 attenuates morphine tolerance and associated glial fibrillary acid protein up-regulation: a proteomic approach. Acta Anaesthesiologica Scandinavica 2008;52(4):499-508
**Agents:** Morphine; MK-801 **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
**ALZET Comments:** Controls received mp w/ saline; tolerance; animal info (male, Wistar, 350-375g); NMDA receptor antagonist

**P8881:** A. H. Rezvani, *et al.* Chronic nicotine and dizocilpine effects on nicotinic and NMDA glutamatergic receptor regulation: Interactions with clozapine actions and attentional performance in rats. Progress in Neuro-Psychopharmacology & Biological Psychiatry 2008;32(4):1030-1040
**Agents:** Nicotine; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (adult, female, Sprague Dawley); MK-801 is also known as dizocilpine; schizophrenia

**P8848:** G. Klein, *et al.* Acute and chronic heroin dependence in mice: Contribution of opioid and excitatory amino acid receptors. European Journal of Pharmacology 2008;586(1-3):179-188
**Agents:** MK-801; LY293558 **Vehicle:** Saline, physiological; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;
**ALZET Comments:** Controls received vehicle; comparison of SC injections vs. mp; dependence; animal info (male, CD-1, adult); "only MK-801 infusion was effective in reducing the subsequent withdrawal jumping." (p. 186); "We observed that LY293558 delivery by continuous infusion-but not acute bolus dose injection-prior to acute heroin injection reduced naloxone-precipitated withdrawal jumping" (p. 186)

**P9043:** O. Cauli, *et al.* Acute liver failure-induced death of rats is delayed or prevented by blocking NMDA receptors in brain. American Journal of Physiology Gastrointestinal and Liver Physiology 2008;295(3):G503-G511
**Agents:** MK-801; Memantine hydrochloride **Vehicle:** Saline; NaCl; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Wistar, 220-270 g.); 10% DMSO used; MK-801 is an NMDA receptor antagonist

**P8079:** S. Nakamura, *et al.* Cognitive dysfunction induced by sequential injection of amyloid-beta and ibotenate into the bilateral hippocampus; protection by memantine and MK-801. European Journal of Pharmacology 2006;548(1-3):115-122
**Agents:** Memantine; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 6 weeks; 11 days;
**ALZET Comments:** Controls received mp w/ vehicle; dose-response (fig.2); long-term study; pumps replaced every 2 weeks; animal info (male, F344/DuCrj, 10 wk old, 220-250g.); neurodegenerative (Alzheimer's disease)

**P7782:** I. Glezer, *et al.* Innate immunity triggers oligodendrocyte progenitor reactivity and confines damages to brain injuries. FASEB Journal 2006;20(2):U405-U430
**Agents:** Endotoxin, LPS; MK-801 **Vehicle:** Saline, sterile; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 3, 7 days;
**ALZET Comments:** Controls received mp w/ vehicle; immunology; animal info (male, Sprague-Dawley, 250g.)

**P7826:** J. E. Garrett, *et al.* Effect of N-methyl-D-aspartate receptor blockade on plasticity of frontal cortex after cholinergic deafferentation in rat. Neuroscience 2006;140(1):57-66
**Agents:** MK-801 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
**ALZET Comments:** Controls received mp w/ PBS; animal info (male, fischer 344, 3 month old, NBM lesions)

**P7891:** M. T. Armentero, *et al.* Prolonged blockade of NMDA or mGluR5 glutamate receptors reduces nigrostriatal degeneration while inducing selective metabolic changes in the basal ganglia circuitry in a rodent model of Parkinson's disease. NEUROBIOLOGY OF DISEASE 2006;22(1):1-9
**Agents:** MK-801; pyridine, 2-methyl-6-(phenylethynyl)- **Vehicle:** Saline; water; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
**ALZET Comments:** Controls received mp w/ saline; dose-response (fig. 1); multiple pumps per animal (2); neurodegenerative (Parkinson's disease) animal info (male, Sprague-Dawley, 250-280grams.); MPEP; 6-OHDA induced striatal lesion

**P7288:** J. Scholz, *et al.* Blocking caspase activity prevents transsynaptic neuronal apoptosis and the loss of inhibition in lamina II of the dorsal horn after peripheral nerve injury. Journal of Neuroscience 2005;25(32):7317-7323
**Agents:** zVAD; MK-801 **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks; 7, 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; comparison of intrathecal injections vs. mp; enzyme inhibitor (caspase); peptides; MK-801also known as dizocilpine; catheter tip location confirmed at end of infusion

**P7258:** E. D. Levin, *et al.* Chronic nicotine and dizocilpine effects on regionally specific nicotinic and NMDA glutamate receptor binding. Brain Research 2005;1041(2):132-142
**Agents:** Nicotine ditartrate; MK-801 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
**ALZET Comments:** Controls received mp w/ vehicle; MK-801 is also known as dizocilpine

**P7285:** Y. Dai, *et al.* $Ca^{2+}$/calmodulin-dependent protein kinase II in the spinal cord contributes to neuropathic pain in a rat model of mononeuropathy. European Journal of Neuroscience 2005;21(9):2467-2474
**Agents:** KN93; KN92; MK-801 **Vehicle:** DMSO; Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 1003D; 2001; 2002; **Duration:** 3,7,14 days;
**ALZET Comments:** Controls received mp w/ vehicle, or KN92 control peptide; no stress (see pg. 2472); enzyme inhibitor (Ca/Calmodulin - dependent protein Kinase II); peptides; 10% DMSO; cannula tip location verified by dissection; NMDA receptor antagonist

## MRZ 2/579

**P4910:** A. K. Houghton, *et al.* Mrz 2/579, a fast kinetic NMDA channel blocker, reduces the development of morphine tolerance in awake rats. Pain 2001;91(201-207
**Agents:** Morphine HCl; Mrz 2/579 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 72 hours;
**ALZET Comments:** controls received mp w/ vehicle; half-life (p. 202) Mrz 2/579 plasma of 140-180 minutes; Mrz 2/579 is an NMDA channel blocker (antagonist); one group received morphine alone, other group received multiple pumps per animal (2), one containing morphine, one containing Mrz 2/579;

**P4933:** P. Bienkowski, *et al.* Effects of a novel uncompetitive NMDA receptor antagonist, MRZ 2/579 on ethanol self-administration and ethanol withdrawal seizures in the rat. European Journal of Pharmacology 2001;413(81-89
**Agents:** MRZ 2/579 **Vehicle:** Water, sterile; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML1; 2ML2; **Duration:** 7 days;
**ALZET Comments:** controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose response (p. 86 text); comparison of IP injections vs. mp; MRZ 2/579 is an uncompetitive NMDA receptor antagonist; 2 different models used to evaluate plasma level differences;

**P4710:** S. M. Holter, *et al.* Novel uncompetitive *N*-Methyl-$_D$-Aspartate (NMDA)-receptor antagonist MRZ 2/579 suppresses ethanol intake in long-term ethanol-experienced rats and generalizes to ethanol cue in drug discrimination procedure. The Journal of Pharmacology and Experimental Therapeutics 2000;292(2):545-552
**Agents:** MRZ 2/579 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1 week;
**ALZET Comments:** Controls received mp w/ vehicle; peptides; dependence; MRZ 2/579 is (1-amino-1,3,3,5,5-pentamethyl-cyclohexane hydrochloride) an NMDA-receptor antagonist.

## Phencyclidine (2001-Present)

**Q9018:** S. Takahashi, *et al.* ASP2905, a specific inhibitor of the potassium channel Kv12.2 encoded by the Kcnh3 gene, is psychoactive in mice. Behavioural Brain Research 2020;378(112315
**Agents:** Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
**ALZET Comments:** Dose (1.2 mg/day/mouse); Controls received mp w/ vehicle; animal info (male ddY mice aged 4–5 weeks); behavioral testing (Forced Swim Test; Water-Finding Task); Phencyclidine aka PCP; neurodegenerative (Schizophrenia);

**Q9086:** S. Thomson, *et al.* Reduced expression of synapsin II in a chronic phencyclidine preclinical rat model of schizophrenia. Synapse 2019;73(5):e22084
**Agents:** Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** Dose (5 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 250-300 g, 3 months old); Phencyclidine aka PCP; gene therapy;

**Q10106:** M. D. Berquist, *et al.* Phencyclidine-like in vivo effects of methoxetamine in mice and rats. Neuropharmacology 2018;134(Pt A):158-166
**Agents:** Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 11 days;
**ALZET Comments:** Dose (3.0 mg/kg/day); 0.9% Saline used; animal info: Male rats (Harlan Sprague-Dawley weighing 220-240 g); weighing 20-25 g; behavioral testing (Substitution testing); Phencyclidine aka (PCP)

**Q2590:** A. Balla, *et al.* Effects of novel, high affinity glycine transport inhibitors on frontostriatal dopamine release in a rodent model of schizophrenia. European Neuropsychopharmacology 2012;22(12):902-910
**Agents:** Phencyclidine hydrochloride **Vehicle:** Saline, sterile, physiological; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, wks old, 160-200 g, 280-320 g)

**Q0375:** C. S. Pedersen, *et al.* Chronic infusion of PCP via osmotic mini-pumps: A new rodent model of cognitive deficit in schizophrenia characterized by impaired attentional set-shifting (ID/ED) performance. Journal of Neuroscience Methods 2009;185(1):66-69
**Agents:** Phencyclidine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/saline; animal info (Lister hooded, male); post op. care (Baitril, Rimadyl); "Using PCP mini-pump infusion instead of the well described intraperitoneal dosing bears the advantage of reducing the animal's stress levels, bypasses the risk of potential mis-dosing that could arise from multiple dosing events and consequently may reduce the number of animals needed." pg 69

**P7825:** G. Pitas, *et al.* Anti-phencyclidine monoclonal antibody binding capacity is not the only determinant of effectiveness, disproving the concept that antibody capacity is easily surmounted. Drug Metabolism and Disposition 2006;34(6):906-912
**Agents:** Phencyclidine HCL **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 4 days;
**ALZET Comments:** Functionality of mp verified by serum PCP concentrations; half-life (pg. 907) 3.9 hours in rats; tolerance; animal info (male, Sprague-Dawley, 270-300g.)

**P6979:** F. Sams-Dodd. (+) MK-801 and phencyclidine induced neurotoxicity do not cause enduring behaviours resembling the positive and negative symptoms of schizophrenia in the rat. Basic & Clinical Pharmacology & Toxicology 2004;95(5):241-246
**Agents:** MK-801; phencyclidine hydrochloride **Vehicle:** NaCl; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 6 days;
**ALZET Comments:** Controls received mp w/ vehicle; dose-response; comparison of SC injections vs. mp; post op. care (wound plast); NMDA antagonists

**P5913:** E. M. Laurenzana, *et al.* Treatment of adverse effects of excessive phencyclidine exposure in rats with a minimal dose of monoclonal antibody. The Journal of Pharmacology and Experimental Therapeutics 2003;306(3):1092-1098
**Agents:** Phencyclidine; phencyclidine HCL; **Vehicle:** Saline; sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; serum levels taken; good methods p. 1093; half-life (p. 1093) =3.9 h in rats; dependence; behavioral study

**P6200:** A. Balla, *et al.* Subchronic continuous phencyclidine administration potentiates amphetamine-induced frontal cortex dopamine release. Neuropsychopharmacology 2003;28(1):34-44
**Agents:** Phencyclidine, HCL **Vehicle:** Saline, sterile physiological; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 3,14 days;
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by serum PCP levels



**P5135:** A. K. Jebelli, *et al.* Prenatal phencyclidine induces heightened neurodegeneration in rats in some brain regions, especially during 2nd trimester, but possible anti-apoptotic effects in others. Pharmacol Toxicol 2002;90(20-25
**Agents:** Phencyclidine **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML1; **Duration:** 5 days;
**ALZET Comments:** controls received a saline pellet as a "sham minipump"; teratology

**P4816:** S. V. Kyosseva, *et al.* Differential and region-specific activation of mitogen-activated protein kinases following chronic administration of phencyclidine in rat brain. Neuropsychopharmacology 2001;24(267-277
**Agents:** Phencyclidine HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 3,10, 20 days;
**ALZET Comments:** Controls received mp w/ vehicle; dose-response p. 270-271

**P4936:** A. Balla, *et al.* Continuous phencyclidine treatment induces schizophrenia-like hyperreactivity of striatal dopamine release. Neuropsychopharmacology 2001;25(2):157-164
**Agents:** Phencyclidine HCl **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 2,3 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by serum PCP levels; dose response (graphs p. 160); schizophrenia

**P5180:** A. Balla, *et al.* Phencyclidine-induced dysregulation of dopamine response to amphetamine in prefrontal cortex and striatum. Neurochem. Res 2001;26(8-9):1001-1006
**Agents:** Phencyclidine HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 2 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by PCP serum levels; NMDA antagonist

## Phosphonovaleric Acid

**P7792:** K. Takehara-Nishiuchi, *et al.* Systems consolidation requires postlearning activation of NMDA receptors in the medial prefrontal cortex in trace eyeblink conditioning. Journal of Neuroscience 2006;26(19):5049-5058
**Agents:** Phosphonovaleric acid, 2-amino-5- **Vehicle:** Not Stated; **Route:** CSF/CNS (prefrontal cortex); **Species:** Rat; **Pump:** 2002; **Duration:** 1, 2 weeks; 1 day;
**ALZET Comments:** Controls received mp w/ a CSF; ALZET brain infusion kit 1 used; animal info (male, Wistar, 210-270g., 9 wk. old); NMDA receptor antagonist; cannula placement verified by Nissl-staining

**P8242:** J. O. Hahm, *et al.* Disruption of retinogeniculate afferent segregation by antagonists to NMDA receptors. Letters to Nature 1991;351(6327):568-570
**Agents:** MK-801; Phosphonovaleric acid, D-2 amino-5-; Phosphonovaleric acid, L-2 amino-5- **Vehicle:** Saline; **Route:** CSF/CNS; SC; **Species:** Ferret; **Pump:** 2001; **Duration:** 1 week;
**ALZET Comments:** Controls received mp w/ vehicle or inactive isomer; dose-response (fig. 1); cyanoacrylate adhesive used; animal info (2-3 weeks old)

**P1597:** M. F. Bear, *et al.* Disruption of experience-dependent synaptic modifications in striate cortex by infusion of an NMDA receptor antagonist. J. Neurosci 1990;10(3):909-925
**Agents:** Phosphonovaleric acid, 2-amino-5- **Vehicle:** Saline, sterile; **Route:** CSF/CNS (striate cortex); **Species:** Cat; **Pump:** 2001; **Duration:** 7 days;
**ALZET Comments:** Stability verified in vitro at 38 degrees for 7 days; discussion of spatial distribution via brain infusion, good methods

**P1642:** Q. Gu, *et al.* Blockade of NMDA-receptors prevents ocularity changes in kitten visual cortex after reversed monocular deprivation. Brain Research 1989;47(281-288
**Agents:** Phosphonovaleric acid, 2-amino-5- **Vehicle:** Saline; **Route:** CSF/CNS (visual cortex); **Species:** Cat; **Pump:** 2001; **Duration:** Not Stated;
**ALZET Comments:** stress/adverse reaction: necrosis around cannula (see pg. 283-284); 2 pumps implanted per animal for bilateral infusion

**P1180:** A. Kleinschmidt*, et al.* Blockade of 'NMDA' receptors disrupts experience-dependent plasticity of kitten striate cortex. Science 1987;238(355-358
**Agents:** Phosphonovaleric acid, 2-amino-5- **Vehicle:** Not Stated; **Route:** CSF/CNS (visual cortex); **Species:** Cat (kitten); **Pump:** Not Stated; **Duration:** 7 days;
**ALZET Comments:** Pump model not stated; controls left untreated; mp connected to cannula; multiple pumps per animal (2); agent infused in 1st pump, 2nd pump infused saline in opposite hemisphere; 2 doses of agent infused

### Procyclidine HCl

**P6802:** E. K. Choi*, et al.* Protection by sustained release of physostigmine and procyclidine of soman poisoning in rats. European Journal of Pharmacology 2004;505(1-3):83-91
**Agents:** Physostigmine salicytate; procyclidine hydrochloride **Vehicle:** Propylene glycol; acetic acid, glacial; ethanol; water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 3 days;
**ALZET Comments:** Functionality of mp verified by plasma levels; dose-response (table 1); enzyme inhibitor (cholinesterase); procyclidine is an NMDA antagonist