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

1. Adamantane

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

2. AP5, AP6, AP7

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
ALZET Comments: AP5, D-; Saline; CSF/CNS (paraflocculus); Rat; 2002; 2 weeks; 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.

P5795: T. C. Foster*, et al.* Receptor blockade reveals a correspondence between hippocampal-dependent behavior and experience-dependent synaptic enhancement. Brain Res 2000;871(1):39-43
ALZET Comments: AP5, DL-; Saline; CSF/CNS; Rat; 2002; 2 weeks; Controls received mp w/ vehicle; (D-APS) or D-2-Amino-5-phosphonpentanoic acid is an NMDA-receptor antagonist; Behavioral testing (Y-maze).

P2017: D. L. Somers*, et al.* N-methyl-D-aspartate receptor antagonism alters substance P and Met-enkephalin biosynthesis in neurons of the rat striatum. J. Pharmacol. Exp. Ther 1992;262(2):823-833
ALZET Comments: AP5; CPP; CSF, artificial; CSF/CNS; Rat; 2002; 7 days; dose-response; NMDA antagonists; both D- and L-enantiomers of AP5 infused.

P1611: J. T. Schmidt. Long-term potentiation and activity-dependent retinotopic sharpening in the regenerating retinotectal projection of goldfish: common sensitive period and sensitivity to NMDA blockers. J. Neurosci 1990;10(1):233-246
ALZET Comments: AP6; AP7; AP5; CSF/CNS (tectal ventricle); fish; 2002; 12-24 days; functionality of mp verified by recovery of remaining drug soltn. at end of study; good methods for infusion to tectal ventricle; pumping in 20 degrees celsius environment, discusses dilution of drug in fluids of fish's brain; NMDA antagonists.

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
ALZET Comments: MK-801; AP5, D-, NBQX; CNQX; CSF, artificial; CSF/CNS (intrathecal); Rat; 2002; 2 weeks; Glutamate receptor antagonists; MK-801 & AP5 are NMDA recept. antag.; NBQX & CNQX are AMPA recept. antag.

P4708: S. M. Allan*, et al.* Cortical death caused by striatal administration of AMPA and interleukin-1 is mediated by activation of cortical NMDA receptors. Journal of Cerebral Blood Flow and Metabolism 2000;20(1409-1413
ALZET Comments: NPQX; AP5, D-;; Saline, sterile; Serum albumin;; CSF/CNS (cortex);; Rat;; Comparison of striatal injections vs. mp; "because of less reflux of the injected solution, more reproducible lesions were obtained in the cortex when an infusion pump was used, whereas no obvious difference in the striatal lesions between the two methods was found." P. 1410. D-AP5 is an NMDA-receptor antagonist.

P1406: J. Tonkiss*, et al.* Intra-ventricular infusion of the NMDA antagonist AP5 impairs performance on a non-spatial operant DRL task in the rat. Exp. Brain Research 1988;73(181-188
ALZET Comments: Phosphopentanoic acid, 2-amino; AP5; CSF, artificial; Sodium hydroxide; CSF/CNS; Rat; 2002; 14 days; NMDA antagonist.

3. ARL 15896AR

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
ALZET Comments: ARL 15896AR;; PBS;; SC;; Rat;; 7 days;; 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).

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
ALZET Comments: Clomethiazole; AR-R15896AR; NXY-059; SC; Monkey; 2001D; 48 hours; 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); AR-R15896AR is a low affinity uncompetetive NMDA antagonist; NXY-059 is a nitrone-derived free radical trapping agent; ischemia (cerebral).

4. Caroverine

P9015: M. L. Duan*, et al.* Low-dose, long-term caroverine administration attenuates impulse noise-induced hearing loss in the rat. Acta Oto-laryngologica 2006;126(11):1140-1147
ALZET Comments: Caroverine; Saline, physiological; SC; Rat; 1003D; 12 hours; 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).

5. CGX-1007

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
ALZET Comments: CGX-1007; CSF, artificial; CSF/CNS (amygdala); Rat; 9 days; Controls received mp w/ vehicle; comparison of ICV injections vs. mp; peptides; CGX-1007 is a polypeptide NMDA receptor antagonist.

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
ALZET Comments: CGX-1007; Saline; CSF/CNS (intrathecal, cisterna magna); Rat; 2001D; 16 hours; Controls received mp w/ vehicle; dose-response (fig. 1); no stress (see pg. 203); dose-dependent paralysis and mortality; peptides; ischemia (cerebral); animal info (male, Sprague-Dawley, 275-350 g); agent also known as Conantokin-G; NMDA receptor antagonist; middle cerebral artery occlusion; stretched PE-10 tubing to a PE-60 connection piece.

6. 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
ALZET Comments: CP-101; 606-27; Saline; DMSO; SC; Rat; 2001D; 24 hours; Controls received mp/ w vehicle; dose-response; ischemia (cerebral); 606-27 is a NMDA antagonist.

7. 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
ALZET Comments: LY274614; Saline; SC; Rat; 2ML1; 1 week; LY274614 is an NMDA receptor antagonist.

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
ALZET Comments: LY-274614; Saline; SC; mice; 7 days; comparison of ip injections vs. mp; tolerance; LY-274614 is a competitive NMDA receptor antagonist.

8. Memantine

P2745: E. Eisenberg*, et al.* The clinically tested N-methyl-D-aspartate receptor antagonist memantine blocks and reverses thermal hyperalgesia in a rat model of painful mono-neuropathy. Neurosci. Lett 1995;187(17-20
ALZET Comments: Memantine; IP; Rat; 2ML1; 7 days; controls received mp w/ saline or no sciatic ligation; comparison of ip injections vs. mp; memantine is 1-amino-3,5-dimethyl-amandate, an NMDA receptor antagonist; multiple pumps per animal (2).

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
ALZET Comments: Memantine; DMSO; saline; SC; Mice; 1003D; 3 days; 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;.

P4234: W. A. Lagreze*, et al.* Memantine is neuroprotective in a rat model of pressure-induced retinal ischemia. Invest. Ophthalmol. Vis. Sci 1998;39(6):1063-1066
ALZET Comments: Memantine HCl; Water; SC; Rat; 2ML2; 14 days; controls received mp w/saline; functionality of pump verified by residual volume; NMDA antagonist; "the pumps reached a steady state plasma level after approximately 12 hours (p. 1064); ischemia (retinal).

P3479: M. Misztal*, et al.* Learning deficits induced by chronic intraventricular infusion of quinolinic acid - protection by MK-801 and memantine. Eur. J. Pharmacol 1996;296(1-8
ALZET Comments: Quinolinic acid; Memantine; MK-801; Saline; SC; CSF/CNS; Rat; 2002; 2ML2; 2 weeks; ALZET brain infusion kit used; animals were given ICV quinolinic acid concurrently w/ subcutaneous NMDA antagonists.

9. MK-801

Q6825: M. F. Davies*, et al.* Sedative but Not Analgesic a2 Agonist Tolerance Is Blocked by NMDA Receptor and Nitric Oxide Synthase Inhibitors. Anesthesiology 2001;95(184-191):
ALZET Comments: Dexmedetomidine; MK-801; Saline; SC; Rat; 1007D; 2002; 7 days; 14 days; Dose (Dexmedetomidine (5 mg/kg/h or 10 mg/kg/h); MK-801 (9.6mg/ml); NO2-arginine (6 mg/ml); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats (B&K, Fremont, CA) weighing 250–350 g); NO2-Arginine is a NOS inhibitor; MK-801 is a NMDA antagonist.

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
ALZET Comments: KN93; KN92; MK-801; DMSO; saline; CSF/CNS (intrathecal); Rat; 1003D; 2001; 2002; 3,7,14 days; 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.

P5327: C. L. Jordan*, et al.* Evidence that androgen acts through NMDA receptors to affect motoneurons in the rat spinal nucleus of the bulbocavernosus. Journal of Neuroscience 2002;22(21):9567-9572
ALZET Comments: MK-801; Saline; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; NMDA receptor antagonist.

P2514: G. R. Lewin*, et al.* NMDA receptors and activity-dependent tuning of the receptive fields of spinal cord neurons. Nature 1994;369(482-485
ALZET Comments: MK-801; Saline; SC; Rat; 4 weeks; NMDA receptor antagonist.

P4859: S. Oh*, et al.* Modulation of the levels of NMDA receptor subunit mRNA and the bindings of [H-3]MK-801 in rat brain by chronic infusion of subtoxic dose of MK-801. Neurochemical Research 2001;26(5):559-565
ALZET Comments: MK-801; Saline; CSF/CNS; Rat; 2001; 7 days; controls received mp w/ vehicle; MK-801 is an NMDA-receptor antagonist; 1 week recovery period after surgery.

P4036: K. R. Powell*, et al.* Lack of NMDA receptor involvement in caffeine-induced locomotor stimulation and tolerance in rats. Pharmacol. Biochem. Behav 1998;59(2):433-438
ALZET Comments: MK-801; Water, distilled; SC; Rat; 2ML1; 7 days; MK-801 is NMDA receptor antagonist dizocilpine; controls received sham pumps; tolerance.

P3005: R. X. Zhang*, et al.* Pre-emptive intrathecal Mk-801, a non-competitive N-methyl-D-aspartate receptor antagonist, inhibits the up-regulation of spinal dynorphin mRNA and hyperalgesia in a rat model of chronic inflammation. Neurosci Lett 1998;241(1):57-60
ALZET Comments: MK-801; Saline; CSF/CNS (intrathecal); Rat; 2001; 3 days; Controls received mp w/ vehicle; NMDA receptor antagonist.

P4746: H. S. Kim*, et al.* Changes of $GABA_A$ receptor binding and subunit mRNA level in rat brain by infusion of subtoxic dose of MK-801. Brain Research 2000;880(28-37
ALZET Comments: MK-801;; Saline;; CSF/CNS;; Rat;; 2ML1;; 7 days;; Controls received mp w/ vehicle; 1-week recovery period; MK-801 an NMDA antagonist; dummy cannula used before pump implantation;.

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
ALZET Comments: MK-801; AP5, D-, NBQX; CNQX; CSF, artificial; CSF/CNS (intrathecal); Rat; 2002; 2 weeks; Glutamate receptor antagonists; MK-801 & AP5 are NMDA recept. antag.; NBQX & CNQX are AMPA recept. antag.

P4738: C. Ikonomidou*, et al.* Neuronal death enhanced by *N*-methyl-$_D$-aspartate antagonists. PNAS 2000;97(23):12885-12890
ALZET Comments: MK-801; CPP; NBQX; Memantine; MPQX; 3-nitro-propionate;; SC;; Rat;; 28 days;; Controls received mp w/ vehicle; MK-801 also called Dizocilpine; Neuroprotection; 3-nitro-propionate also called 3NP; glutamate (NMDA) antagonists;.

P3706: A. S. Basile*, et al.* N-Methyl-D-aspartate antagonists limit aminoglycoside antibiotic-induced hearing loss. Nature Medicine 1996;2(12):1338-1343
ALZET Comments: MK-801; Ifenprodil tartrate; DMSO; Water, deionized; Alkamuls EL620; SC; Guinea pig; 2002; no duration posted; long-term study, pumps replaced after 14 days; agents NMDA antagonists; 40% DMSO used; dizocilpine maleate used.

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
ALZET Comments: MK-801; memantine hydrochloride; Saline; NaCl; DMSO; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Wistar, 220-270 g.); 10% DMSO used; MK-801 is an NMDA receptor antagonist.

P3461: S. Dunbar*, et al.* Concurrent spinal infusion of MK801 blocks spinal tolerance and dependence induced by chronic intrathecal morphine in the rat. Anesthesiology 1996;84(1177-1188
ALZET Comments: MK-801; Morphine; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; controls received saline infusion; good methods p. 1178; tolerance; dependence; NMDA receptor antagonist.

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
ALZET Comments: MK-801; phencyclidine hydrochloride; Sodium chloride; SC; Rat; 2ML2; 6 days; Controls received mp w/ vehicle; dose-response; comparison of SC injections vs. mp; post op. care (wound plast); NMDA antagonists.

P3479: M. Misztal*, et al.* Learning deficits induced by chronic intraventricular infusion of quinolinic acid - protection by MK-801 and memantine. Eur. J. Pharmacol 1996;296(1-8
ALZET Comments: Quinolinic acid; Memantine; MK-801; Saline; SC; CSF/CNS; Rat; 2002; 2ML2; 2 weeks; ALZET brain infusion kit used; animals were given ICV quinolinic acid concurrently w/ subcutaneous NMDA antagonists.

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
ALZET Comments: Morphine; MK-801; CSF/CNS (intrathecal); Rat; 2001; 5 days; Controls received mp w/ saline; tolerance; animal info (male, Wistar, 350-375g); NMDA receptor antagonist.

10. 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
ALZET Comments: Morphine HCl; Mrz 2/579; Saline; SC; Rat; 2ML1; 72 hours; 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
ALZET Comments: MRZ 2/579; Water, sterile; Rat; 2ML1; 2ML2; 7 days; 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
ALZET Comments: MRZ 2/579; SC; Rat; 2ML1; 1 week; 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.

11. Phencyclidine HCl

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
ALZET Comments: Phencyclidine HCl; Saline; SC; Rat; 2ML4; 2 weeks; Controls received mp w/ vehicle; functionality of mp verified by PCP serum levels; NMDA antagonist.

12. 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
ALZET Comments: Phosphonovaleric acid, 2-amino-5-; CSF/CNS (prefrontal cortex); Rat; 2002; 1, 2 weeks; 1 day; 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.

P1406: J. Tonkiss*, et al.* Intra-ventricular infusion of the NMDA antagonist AP5 impairs performance on a non-spatial operant DRL task in the rat. Exp. Brain Research 1988;73(181-188
ALZET Comments: Phosphopentanoic acid, 2-amino; AP5; CSF, artificial; Sodium hydroxide; CSF/CNS; Rat; 2002; 14 days; NMDA antagonist.

13. 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
ALZET Comments: Physostigmine salicytate; procyclidine hydrochloride; Propylene glycol; acetic acid, glacial; ethanol; water; SC; Rat; 2001; 3 days; Functionality of mp verified by plasma levels; dose-response (table 1); enzyme inhibitor (cholinesterase); procyclidine is an NMDA antagonist.