



References on the Administration of Agents to Neonatal Rats Using ALZET® Osmotic Pumps

Q7001: A. Rahman, *et al.* Intraventricular infusion of quinolinic acid impairs spatial learning and memory in young rats: a novel mechanism of lead-induced neurotoxicity. *J Neuroinflammation* 2018;15(1):263

ALZET Comments: Quinolinic acid; Saline; CSF/CNS (right lateral ventricle); Rat (neonate); 1007D; 7 days; Dose (9 mM); Controls received mp w/ vehicle; animal info (21-day old Wistar rat pups); behavioral testing (Spatial learning and memory test); ALZET brain infusion kit used; Brain coordinates (anteroposterior—3 mm behind bregma; lateral—3.6 mm from midline; and depth—3.8 mm from skull surface);.

Q6297: B. H. Kim, *et al.* Age-Dependent Effects of ALK5 Inhibition and Mechanism of Neuroprotection in Neonatal Hypoxic-Ischemic Brain Injury. *Dev Neurosci* 2017;39(1-4):338-351

ALZET Comments: SB505124; Sodium citrate; DMSO; SC; Rat (neonate); 1007D; 7 days; 30% DMSO used; Controls received mp w/ vehicle; animal info (Wistar rat pups); behavioral testing (sensorimotor testing, Morris water maze); SB505124 is a ALK5 receptor antagonist; Therapeutic indication (hypoxic-ischemic brain injury);.

Q5737: M. Ishido, *et al.* Neonatal rotenone lesions cause onset of hyperactivity during juvenile and adulthood in the rat. *Toxicol Lett* 2017;266(42-48)

ALZET Comments: Rotenone; SMSO, PEG 300; SC; Rat (neonate); Controls received mp w/ vehicle; animal info (5-14 days); 50% DMSO: 50% PEG 300 used; Therapeutic indication (Hyperactivity disorder); Dose (3.0 mg/kg/day);.

Q6394: M. Guardia Clausi, *et al.* Delayed ALK5 inhibition improves functional recovery in neonatal brain injury. *J Cereb Blood Flow Metab* 2017;37(3):787-800

ALZET Comments: SB505124; SC; Rat (neonate); 1007D; 7 days; Dose (5 mg/h); Controls received mp w/ vehicle; animal info (Wistar pups); behavioral testing (Cylinder rearing test, sticky label test, beam walking test); SB505124 is an antagonist of the type 1 TGFβ1 receptor ALK5; Therapeutic indication (hypoxia-ischemia);.

Q5149: J. D. Frost, Jr., *et al.* Vigabatrin therapy implicates neocortical high frequency oscillations in an animal model of infantile spasms. *Neurobiol Dis* 2015;82(1-11)

ALZET Comments: Tetrodotoxin; PBS; CSF/CNS (somatosensory cortex); Rat (neonate); 2004; 28 days; Controls received mp w/ vehicle; animal info: 11 or 12 day-old male rat pups; functionality of mp verified by EEG; dose-response (pg 3); Plastics One cannula used; Dose: 200 μL of 12 μM tetrodotoxin; Brain coordinates; AP: 2.2, ML: 2.0 from bregma and 0.8 mm below the surface of cortex.

Q3774: B. L. Callaghan, *et al.* Early Emergence of Adult-Like Fear Renewal in the Developing Rat After Chronic Corticosterone Treatment of the Dam or the Pups. *Behavioral Neuroscience* 2014;128(594-602)

ALZET Comments: Corticosterone; Water, deionized; SC; Rat (neonate); 1007D; 7 days; Control animals received mp w/ vehicle; animal info (naive, Sprague Dawley, P7). no stress pg 595-596. "The entire surgery took less than 5 min and the rats recovered well. The dorsal placement of the micropump was chosen because it does not interfere with the feeding position of pups." pg 595. "...dams in the current studies tolerated the pups well after both surgeries and there were no instances of cannibalism or obvious abuse (e.g., bite marks)" pg 596; pumps removed after 1 week;.

Q3166: J. Qiu, *et al.* Neuroprotective Effects of MicroRNA-210 on Hypoxic-Ischemic Encephalopathy. *BIOMED RESEARCH INTERNATIONAL* 2013;;(1):U1-U5

ALZET Comments: Oligonucleotide, miR-210 mimic; inhibitor, miR-210; Saline; CSF/CNS; Rat (neonate); 1007D; 72 hours; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, P7); ischemia (hypoxic-ischemic encephalopathy); gene therapy;.

Q3243: T. Miki, *et al.* Activity-Dependent Neurotrophin Signaling Underlies Developmental Switch of Ca²⁺ Channel Subtypes Mediating Neurotransmitter Release. *Journal of Neuroscience* 2013;33(48):18755-18763

ALZET Comments: Tetrodotoxin; K252a; Saline; CSF/CNS (cerebellum); Rat (neonate); 1007D; 7 days; Controls received mp w/ vehicle; animal info (Wistar/ST, Postnatal day 6); ALZET brain infusion kit 1 used; tissue perfusion (cerebellum);.



teratology; good methods(pg. 18757); Pump implantation shown figure 6A pg.P18761. K252a is a CaM kinase and phosphorylase inhibitor;

Q1485: J. L. Wilkinson-Berka, *et al.* Aliskiren reduces vascular pathology in diabetic retinopathy and oxygen-induced retinopathy in the transgenic (mRen-2)27 rat. *Diabetologia* 2011;54(10):2724-2735

ALZET Comments: Aliskiren; lisonopril; SC; Rat; Rat (neonate); 2ML4; 1007D; 16 weeks; Controls received sham surgery; animal info (Sprague-Dawley, transgenic (mRen-2)27, postnatal days 12-18, female, 180-210 g, STZ-induced diabetes); pumps replaced every 4 weeks; long-term study; diabetes; enzyme inhibitor (renin);

P9368: J. L. W. Berka, *et al.* Identification of a Retinal Aldosterone System and the Protective Effects of Mineralocorticoid Receptor Antagonism on Retinal Vascular Pathology. *Circulation Research* 2009;104(1):124-U309

ALZET Comments: Aldosterone; DMSO; saline; SC; Rat (neonate); 1007D; 7 days; Animal info (Sprague Dawley, OIR); 2% DMSO used.

P8303: M. H. Zissen, *et al.* Tolerance, opioid-induced allodynia and withdrawal associated allodynia in infant and young rats. *Neuroscience* 2007;144(1):247-262

ALZET Comments: Morphine; Saline; SC; Rat (neonate); 1003D; 72 hours; Controls received mp w/ vehicle; dose-response (p. 250); comparison of acute or intermittently injections vs. mp; vs. pellet; good methods (p. 249); tolerance; post op. care (IP penicillin, fluid therapy); animal info (Sprague-Dawley); morphine withdrawal; behavioral testing; "Using the pellet in P7 rats produced a high rate of mortality from respiratory depression following pellet implantation and precluded parallel studies in the younger rats." (p. 254); Vetbond tissue adhesive was used.

P8494: D. C. Stoller, *et al.* Role of kappa and delta opioid receptors in mediating morphine-induced antinociception in morphine-tolerant infant rats. *Brain Research* 2007;1142(28-36

ALZET Comments: Morphine; SC; Rat (neonate); 1003D; 72 hours; Controls received mp w/ vehicle; tolerance; post op. care (10% povidone iodine swab); animal info (P14, 30 g); Vetbond tissue adhesive used to close incision.

P8623: O. H. Khan, *et al.* Calcium antagonism in neonatal rats with kaolin-induced hydrocephalus. *Journal of Child Neurology* 2007;22(10):1161-1166

ALZET Comments: Magnesium chloride; magnesium sulfate; SC; Rat (neonate); 2002; 2004; 14 days; Controls received mp w/ saline, equimolar; dose-response (table 1); comparison of SC injections vs. mp; stress/adverse reaction : (see pg 1162) high magnesium sulfate concentrations led to necrosis and skin sloughing at implant site; animal info (Sprague-Dawley, P7); skin was closed with staples (wound clips used).

P7934: M. H. Zissen, *et al.* Acute and chronic morphine alters formalin pain in neonatal rats. *Neuroscience Letters* 2006;400(1-2):154-157

ALZET Comments: Morphine; Saline; Rat (neonate); 1003D; 72 hours; Controls received mp w/ vehicle; post op. care (penicillin, ringer's solution); animal info (male and female Sprague-Dawley); Vetbond tissue used.

P7827: S. Thyssen, *et al.* Ontogeny of regeneration of beta-cells in the neonatal rat after treatment with streptozotocin. *Endocrinology* 2006;147(5):2346-2356

ALZET Comments: Glucagon-like polypeptide-1(9-39); Saline; SC; Rat (neonate); 1002; 2 weeks; Controls received mp w/ vehicle; no stress (see pg. 2352); peptides; animal info (Wistar, PD5, STZ-treated); GLP-1 receptor antagonist; "GLP-1-(9-39) treatment did not alter weight gain in these animals or have any visible deleterious effect.";

P7924: A. Suryawan, *et al.* Expression of the TGF-beta family of ligands is developmentally regulated in skeletal muscle of neonatal rats. *PEDIATRIC RESEARCH* 2006;59(2):175-179

ALZET Comments: Follistatin; PBS; SC; Rat (neonate); 11 days; Peptides; animal info (10 days old).

P7020: D. C. Stoller, *et al.* Buprenorphine blocks withdrawal in morphine-dependent rat pups. *PEDIATRIC ANESTHESIA* 2004;14(8):642-649



ALZET Comments: Morphine sulphate; Water, distilled; SC; Rat (neonate); 1003D; 72 hours; Controls received mp w/ isotonic saline; dependence; Vetbond tissue used.

P6448: Y. Abreu-Villaca, *et al.* Prenatal nicotine exposure alters the response to nicotine administration in adolescence: Effects on cholinergic systems during exposure and withdrawal. *Neuropsychopharmacology* 2004;29(5):879-890

ALZET Comments: Nicotine; Water, sterile; SC; Rat (neonate); 1002; 2ML2; 2 weeks; Controls received mp w/ vehicle; teratology; 1002's used in neonatal rats and 2ML2 pumps were used in adult rats; incision was closed with wound clips.

P6038: S. Sarlos, *et al.* Retinal angiogenesis is mediated by an interaction between the angiotensin type 2 receptor, VEGF, and angiopoietin. *American Journal of Pathology* 2003;163(3):879-887

ALZET Comments: PD123319; IP; Rat (neonate); 2004; Controls received mp w/ vehicle; animal info (11 days old); insertion wound was then closed with a small stitch.

P5134: C. I. Thompson, *et al.* Plasma constituents and mortality in rat pups given chronic insulin via injection, pellet, or osmotic minipump. *Can. J Physiol Pharmacol* 2002;80(180-192)

ALZET Comments: Insulin, bovine; Saline; SC; Rat (neonate); 1002; 10 days; Animal info (neonates, 9 days old), controls received mp w/ vehicle; functionality of mp verified by plasma insulin levels and residual aspiration; comparison of pellet vs. sc injections vs. mp; no stress (see p. 186); "The minipumps appeared to be well tolerated and caused no obvious difficulty with nursing" (p. 186); teratology; peptides; "...pups tolerate insulin more readily from a minipump than from a pellet..." (p. 190) "pellets caused high mortality within 24 h" (abstract); "Hypothermia is safe, and it has been shown to be an effective technique for inducing anesthesia in neonatal and preweaning rats. We therefore used moderate hypothermia to subcutaneously implant the osmotic minipumps..." p. 186; "It took approximately 1.5 minutes to implant the minipump in each pup..." p. 186; "The present studies indicate that subcutaneous insulin pellets are not suitable for this purpose (chronic insulin delivery in rat pups), since rat pups do not tolerate them well." p. 191.

P5341: D. C. Stoller, *et al.* Loss of antinociceptive efficacy in rat pups infused with morphine from osmotic minipumps. *Pharmacology* 2002;66(1):11-18

ALZET Comments: Morphine sulfate; Saline, isotonic; SC; Rat (neonate); 1003D; 72 hours; Controls received mp w/ saline; toxicology; teratology; tolerance; dependence; 6-day and 14-day old rat pups implanted; incision closed w/ vetbond tissue adhesive.

P5789: G. Santoni, *et al.* Expression of substance P and its neurokinin-1 receptor on thymocytes: Functional relevance in the regulation of thymocyte apoptosis and proliferation. *NEUROIMMUNOMODULATION* 2002;10(4):232-246

ALZET Comments: Substance P; SR140333; Water, distilled; DMSO; SC; Rat (neonate); 2001; 7 days; Controls received mp w/ one of two vehicles; functionality of mp verified by plasma levels of (sp); dose-response (p.241); peptides; SR140333 (A NK-1R antagonist) was diluted in 1% DMSO distilled water, alone, or in combination with (sp); pups were 28 days old.

P6604: M. J. Marino, *et al.* Haloperidol-induced alteration in the physiological actions of group I mGlu in the subthalamic nucleus and the substantia nigra pars reticulata. *Neuropharmacology* 2002;43(2):147-159

ALZET Comments: Haloperidol; Lactic acid; NaOH; saline; SC; Rat (neonate); 2001; 16 hours; Cyanoacrylate adhesive applied over sutures; animal info (15-18 days old, 20-37 grams).

P5382: E. Margotti, *et al.* TRKB signalling controls the expression of N-methyl-D-aspartate receptors in the visual cortex. *European Journal of Neuroscience* 2002;16(6):1067-1074

ALZET Comments: Immunoglobulin G, TrkB; Saline; CSF/CNS (occipital cortex); Rat (neonate); 16 days; Controls received mp w/ vehicle; functionality of mp verified by TrkB-IgG immunohistochemistry in visual cortex; immunology; TrkB-IgG consists of the soluble form of the tyrosine Kinase receptor engineered as an immunoadhesin by fusing it to the Fc portion of an IgG; 20-21 day old rats used; Fig. 2A (graphic of infusion site).

P5628: S. Eiden, *et al.* Developmental and food-access-dependent changes in effector systems activated by leptin. *PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY* 2002;445(3):366-374



ALZET Comments: Leptin; PBS; SC; Rat (neonate); 10 days; Controls received mp w/ vehicle; comparison of injections v. mp; peptides; 14 day and 25 day old rat pups used.

P4822: H. Sameshima, *et al.* Long-term magnesium sulfate treatment as protection against hypoxic-ischemic brain injury in seven-day-old rats. *American Journal of Obstetrics and Gynecology* 2001;184(185-190)

ALZET Comments: Magnesium sulfate;; SC;; Rat (neonate);; 1003D;; 3 days;; Controls received mp w/ saline; functionality of mp verified by measuring magnesium ion concentrations; teratology; seven-day old rat pups weighed on average 13.9 ± 2.5 grams; neuroprotection; ischemia (cerebral).

P5008: S. E. Robinson, *et al.* Effect of perinatal buprenorphine exposure on development in the rat. *Journal of Pharmacology and Experimental Therapeutics* 2001;298(2):797-804

ALZET Comments: Buprenorphine; Methadone; Water; SC; Rat (pregnant); Rat (neonate); 14, 28 days; controls received mp w/ vehicle; replacement therapy (enterectomy); dose-response (graphs p. 802); teratology; toxicology; dependence; no stress (see pg. 258-259); 28-day pumps implanted in pregnant rats; 14-day pumps implanted in 10-day old rat pups.

P4632: A. B. Lohmann, *et al.* Buprenorphine substitution ameliorates spontaneous withdrawal in fentanyl-dependent rat pups. *Pediatr. Res* 2001;49(1):50-55

ALZET Comments: Fentanyl citrate; Saline, isotonic; SC; Rat (neonate); 1003D; 72 hours; Controls received mp w/ vehicle; teratology; tolerance; dependence; the surgical incision was closed with Vetbond Tissue Adhesive; pumps implanted in 14-day old rat pups.

P5021: S. Eiden, *et al.* Leptin responsiveness of juvenile rats: proof of leptin function within the physiological range. *JOURNAL OF PHYSIOLOGY-LONDON* 2001;530(131-139)

ALZET Comments: Leptin, recombinant mouse; PBS; SC; Rat (neonate); 1002; 2002; 9 days; controls received mp w/ vehicle; functionality of mp verified by plasma leptin levels; dose-response (page 135); peptides; 1002 pumps used in 15-day old pups, 2002 used in 24-day old pups; His6-tagged murine leptin used.

P4328: S. R. Thornton, *et al.* Fentanyl self-administration in juvenile rats that were tolerant and dependent to fentanyl as infants. *Pharmacology Biochemistry and Behavior* 2000;65(3):563-570

ALZET Comments: Fentanyl HCl; Saline, pyrogen-free isotonic; SC; Rat (neonate); 1003D; 3-5 days; Controls received mp with saline; tolerance; dependence; pain.

P4553: T. A. Doucette, *et al.* Use of osmotic minipumps for sustained drug delivery in rat pups: effects on physical and neurobehavioural development. *Physiology and Behavior* 2000;71(207-212)

ALZET Comments: Saline; SC; Rat (neonate); 1007D; 9 days; Controls received sham surgery; no stress (p. 211-212); good surgical methods (p. 208-209); teratology.

P4722: C. H. Choe, *et al.* Sedative tolerance accompanies tolerance to the analgesic effects of fentanyl in infant rats. *Pediatr. Res* 2000;47(6):727-735

ALZET Comments: Fentanyl; Saline; Rat (neonate); 1003D; 3 days; Controls received mp w/ vehicle; functionality of mp verified by plasma fentanyl levels; dose-response (table p. 729 / graph p. 730); tolerance; dependence; pumps implanted in 14 day old rat pups; surgical incision was closed with Vetbond tissue adhesive (3M animal care products);

P8482: J. A. Trauth, *et al.* Adolescent nicotine exposure causes persistent upregulation of nicotinic cholinergic receptors in rat brain regions. *Brain Res* 1999;851(1-2):9-19

ALZET Comments: Nicotine; SC; Rat (neonate); Rat; 1002; 2ML2; 17 days; No stress (see pg. 10); animal info (P30-P47, Sprague-Dawley, male, 120 g, female 100 g); anesthetized with ether; adult animal info (90 days old, 350 g, Sprague-Dawley); incision was closed with wound clips.

P4308: S. R. Thornton, *et al.* Long-term alterations in opiate antinociception resulting from infant fentanyl tolerance and dependence. *European Journal of Pharmacology* 1998;363(113-119)



ALZET Comments: Fentanyl HCl;; Saline;; SC;; Rat (neonate);; 1003D;; 3-5 days;; controls received mp w/ vehicle; tolerance; dependence;.

P4180: S. R. Thornton, *et al.* Characterization of neonatal rat morphine tolerance and dependence. *Eur. J. Pharmacol* 1997;340(161-167)

ALZET Comments: Morphine sulfate; Saline, sterile isotonic; SC; Rat (neonate); 1003D; 3 days; controls received mp w/saline; pumps implanted in 14 day old rat pups; "osmotic minipumps may provide a reliable method of examining the tolerance and dependence liability of many opioids in neonatal rats" (p. 165); toxicology; teratology; tolerance; dependence; good surgical methods (p.102).

P3449: S. R. Thornton, *et al.* Characterization of neonatal rat fentanyl tolerance and dependence. *J. Pharmacol. Exp. Ther* 1997;281(1):514-521

ALZET Comments: Fentanyl; SC; Rat (neonate); 1003D; no duration posted; controls received mp w/ saline; excellent methodology for working with neonates; animals were given penicillin G prophylactically, along with .5 ml saline to prevent hypovolemia; pumps were implanted 1.5 cm from the base of the tail to obviate problems w/ nursing; tolerance; dependence; teratology.

P3542: C.-B. Steeb, *et al.* Systemic infusion of IGF-I or LR(3)IGF-I stimulates visceral organ growth and proliferation of gut tissues in suckling rats. *Am. J. Physiol. (Gastrointest. Liver Physiol. 35)* 1997;272(G522-G533)

ALZET Comments: Insulin-like growth factor I; Insulin-like growth factor I, LR3-; SC; Rat (neonate); 1007D; 6.5 days; controls received mp w/ vehicle; peptides; teratology; neonates were 6 or 12 days old; recomb. human IGF-I and human LR3IGF-I used; good surgical methodology (see pg G523).

P3889: W. J. Brooks, *et al.* Effect of chronic administration of NMDA antagonists on synaptic development. *Synapse* 1997;26(104-113)

ALZET Comments: APV; Saline; CSF/CNS (occipital cortex); Rat (neonate); 2002; 14 days; controls received mp w/vehicle; animal info (15-day old); ALZET brain infusion kit used; APV is 2-amino-5-phosphonovaleric acid.

P1950: G. F. Glasscock, *et al.* Effects of continuous infusion of insulin-like growth factor I and II, alone and in combination with thyroxine or growth hormone, on the neonatal, hypophysectomized rat. *Endocrinology* 1992;130(1):203-210

ALZET Comments: Insulin-like growth factor I; Insulin-like growth factor II; Acetic acid; PBS; SC; Rat (neonate); 1003D; 9 days; peptides; teratology; pumps implanted in 10-day old rat pups; pumps replaced on postnatal days 13 and 16; functionality of mp verified by IGF serum levels assayed by RIA; wound clips used.

P0594: N. Bouby, *et al.* Stimulation of tubular reabsorption of magnesium and calcium by antidiuretic hormone in conscious rats: study in Brattleboro rats with hereditary hypothalamic diabetes insipidus. *Pflugers Arch* 1984;402(458-464)

ALZET Comments: Vasopressin, 1-desamino-8-D arginine; Saline; IP; Rat (neonate); 2002; 2+ weeks; no stress p. 463 - refers to value of exp. with non-stressed animals; prior to implant w/ mp, neonate rats received daily sc admin. of Vasopressin, 1-desamino-8-D arginine; peptides; teratology.