References on the Administration of Agents in Neonatal Animals

Using ALZET® Osmotic Pumps


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).

Q6526: A. Vivekanandarajah, et al. Intermittent hypercapnic hypoxia effects on the nicotinic acetylcholine receptors in the developing piglet hippocampus and brainstem. Neurotoxicology 2017;60(23-33

ALZET Comments: Nicotine Hydrogen Tartate Salt; Water (sterile); IP; Pig (neonate); 2ML2; 14 days; Dose (2.0 mg/kg/day); animal info (mixed-breed miniature piglets); comparison of patch vs mp; Resultant plasma level (serum cotinine: 23.1 +17.3 ng/mL); "The use of an osmotic minipump as opposed to a skin patch was chosen as the method of nicotine delivery given it provides a steady state, same dose, infusion over our 14 day study whereas patches result in sudden spikes in plasma levels and require replacement of patches every 1–2 days dependent on chosen patch ” pg. 2 ;.


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).


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).


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 TGFß1 receptor ALK5; Therapeutic indication (hypoxia-ischemia).


ALZET Comments: Clozapine-N-oxide; Saline; SC; Mice (neonate); 1007D; 7 days; Controls received mp w/ vehicle; animal info (11-14 days); clozapine-N-oxide (CNO) Therapeutic indication (learning and memory); Dose (1 mg/kg).


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.


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."

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;.

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;.

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);.

ALZET Comments: Noggin, human, recomb.; CSF/CNS; Rabbit (neonatal); 1003D; 2001; 3, 7 days; Controls received mp w/ vehicle; animal info (New Zealand, 24 hours old); ALZET brain infusion kit used.

ALZET Comments: Fluoxetine; Saline; SC; Mice (neonate); 1007D; 7 days; Controls received mp w/ vehicle; dose-response (Fig. 1); no stress (see pg. 2197); pump implantation/removal did not alter overall behavior in the novelty-induced hypophagia (NIH) test; behavioral testing (elevated plus maze, open-field, NIH tests, forced swim test; Dose: 2, 3, and 4 mg/kg/day.

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

ALZET Comments: Diazepam; DMSO; propylene glycol; SC; Mice; mice (neonate); 1002; 2002; 14 days; Controls received mp w/ vehicle; dose-response (Fig. 1); no stress (see pg. 193); post op. care (flumazenil); animal info (C57BL/6 x 129/SvJ, male, 14 days old, 60 days old); 50% DMSO used; behavioral testing (maze); wound clips used; 50% propylene glycol used.

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.

**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.

**P8483**: M. Say, *et al.* Changes in serotoninergic receptors 1A and 2A in the piglet brainstem after intermittent hypercapnic hypoxia (IHH) and nicotine. Brain Res 2007;1152:17-26  
**ALZET Comments**: Nicotine; Water, sterile; IP; Pig (neonate); 2ML2; 2 weeks; Controls received mp w/ vehicle; SIDS; animal info (mini-piglet; 0-2 days old).

**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).

**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.

**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, PDS, 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.";

**ALZET Comments**: Hepatocyte growth factor, recomb. human; PBS; SC; Rat (neonate); 7 days; Controls received mp w/ vehicle; no stress (see pg. 577); animal info (C57BL/6, 0-2 days old).

**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).

**P8207**: R. Machaalani, *et al.* Postnatal nicotine and/or intermittent hypercapnic hypoxia effects on apoptotic markers in the developing piglet brainstem medulla. Neuroscience 2006;142(1):107-117  
**ALZET Comments**: Nicotine hydrogen tartrate salt; Water, sterile; IP; Pig (neonate); 2ML2; 11-13 days; Controls received mp w/ vehicle; functionality of mp verified by serum cotinine; no stress (see p.109); animal info (mixed-breed miniature piglet, 2 days old, male, female, 1.2 kg).

**ALZET Comments**: Candesartan; Saline, physiological; SC; Pig (neonate); 7 days; Controls received mp w/ vehicle; no stress (see pg. F923); animal info (female, Danish Landrace; 2, 23 days old); congenital urinary tract obstruction model.
**ALZET Comments:** Nicotine hydrogen tartrate salt; water, sterile; IP; Pig (neonate); 2ML2; 2 weeks; Controls received mp w/ vehicle; functionality of mp verified by cotinine levels in serum and urine; no stress (see pg. 326); post op. care (cephalexin).

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

**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.

**ALZET Comments:** Nicotine tartrate; Saline; SC; Sheep (lamb, neonate); 2ML4; 4 weeks; Controls received mp w/ vehicle; functionality of mp verified by nicotine plasma levels (HPLC method); cardiovascular; teratology; postnatal lambs (1 day old).

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.

**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.

**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.

**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.

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).

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).

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.

ALZET Comments: Insulin-like growth factor I; Insulin-like growth factor I, LR3-; Acetic acid; SC; Pig (neonate); 2001; 8,9 or 18 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; pumps replaced after 8 or 9 days; peptides;.

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).

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.,

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. Thornt0n, 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.

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).

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.

ALZET Comments: Growth hormone, recomb. human;; PBS;; IP;; pig (neonate);; 2ML1;; 7 days;; controls received mp w/vehicle; peptides.

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

ALZET Comments: Calcitonin gene-related peptide; scrotal; pig (neonate); 2002; 2 weeks; controls received mp w/PBS; tissue perfusion (undescended testes); replacement therapy (cryptorchidism); dose-response; peptides; "Injection of excess CGRP into the scrotum may delay descent...the pig model has overcome some of these difficulties as the o.

ALZET Comments: Epidermal growth factor; Devazepide; DMSO; Ringer’s solution, lactated; SC; Guinea pig (neonate); 1003D; 2002; 4,15 days; peptides.

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).

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).

ALZET Comments: Insulin-like growth factor I; Saline; Acetic acid; SC; pig (neonate); 2001; 7 days; controls received mp w/ saline; functionality of mp verified by plasma assays; peptides; recomb. human IGF-I used.

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.

ALZET Comments: APV; Saline; CSF/CNS (thalamus); ferret (neonate); 2001; 1 week; controls received mp w/vehicle.

ALZET Comments: MK-329; DMSO; Saline; SC; Guinea pig (neonate); Guinea pig (pregnant); 2002; 2ML4; 1003D; 4,15 days; Animal info (female, pregnant, or neonate 1-3 hours old); cholecystokinin receptor antagonist; controls received mp w/vehicle; teratology; peptides.

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.

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.