References on the Administration of NMDA Agonists Using ALZET® Osmotic Pumps

Aspartic Acid


**Agents:** Oligonucleotide, antisense; Oligonucleotide sense; Kainate, dihydro-; Aspartic acid, DL-threo-B-benzyloro-  **Vehicle:** Saline, sterile;  **Route:** CSF/CNS (optic nerve);  **Species:** Rabbit;  **Pump:** 1003D;  **Duration:** 3 days;

**ALZET Comments:** Controls received mp w/ vehicle, or contralateral nerves; antisense (glutamate transporters GLAST + GLT-1); animal info (adult, male, white New Zealand)


**Agents:** Aspartic acid, dl-threo-B-hydroxy; spermine, 1-naphthyl acetyl  **Vehicle:** Not Stated;  **Route:** CSF/CNS (intrathecal, subarachnoid space);  **Species:** Rat;  **Pump:** 1007D;  **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ saline; enzyme inhibitors (GLT-1, GluR2)


**Agents:** (aspartic acid-glutamic acid-valine-aspartic acid)-CHO  **Vehicle:** Not Stated;  **Route:** IP;  **Species:** Rat;  **Pump:** 2001;  **Duration:** 1 hour; 24 hours; 240 hours;

**ALZET Comments:** Dose (5nM DEVD-CHO); animal info (Male, 3month-old Sprague±Dawley rats); (aspartic acid-glutamic acid-valine-aspartic acid)-CHO aka DEVD-CHO; enzyme inhibitor (caspase 3); DEVD-CHO is a tetrapeptide aldehyde;

P3908: A. Hirata, et al. AMPA receptor-mediated slow neuronal death in the rat spinal cord induced by long-term blockade of glutamate transporters with THA. Brain Research 1997;771(37-44

**Agents:** Aspartic acid, dl-threo-B-hydroxy; Glutamate, l-  **Vehicle:** CSF, artificial;;  **Route:** CSF/CNS (subarachnoid space, intrathecal);  **Species:** Rat;  **Pump:** 2ML1;  **Duration:** Not Stated;

**ALZET Comments:** Dose-response; cannula position verified


**Agents:** Aminobutyric acid, Y-; Aspartic acid, dl-threo-B-hydroxy; Aspartic acid, l-; Cysteine sulfinic acid; Glutamic acid, l-; Radio-isotopes  **Vehicle:** 3H tracer; Acetate; Saline;  **Route:** CSF/CNS (corpus striatum); CSF/CNS (hippocampus);  **Species:** Rat;  **Pump:** 2002;  **Duration:** 2 weeks;

**ALZET Comments:** comparison of injec. vs. mp infusion; amino acids infused separately & simultaneously

Cycloserine


**Agents:** Cycloserine, L-  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Mice (transgenic);  **Pump:** 2004;  **Duration:** 28 days;

**ALZET Comments:** Animal info (TgCRND8, male, female, 3 mo old)

Cysteinesulfinic Acid


**Agents:** Aminobutyric acid, Y-; Aspartic acid, dl-threo-B-hydroxy; Aspartic acid, l-; Cysteine sulfinic acid; Glutamic acid, l-; Radio-isotopes  **Vehicle:** 3H tracer; Acetate; Saline;  **Route:** CSF/CNS (corpus striatum); CSF/CNS (hippocampus);  **Species:** Rat;  **Pump:** 2002;  **Duration:** 2 weeks;

**ALZET Comments:** comparison of injec. vs. mp infusion; amino acids infused separately & simultaneously
Dehydroepiandrosterone


**Agents**: estrogen; progesterone; dehydroepiandrosterone  
**Vehicle**: DMSO;  
**Route**: SC;  
**Species**: Rat;  
**Pump**: Not Stated;  
**Duration**: Not Stated;  
**ALZET Comments**: animal info: Sprague-Dawley, bladder outlet obstruction model, ovariectomized model; functionality of mp verified by plasma measurement; mp used to infuse estrogen, progesterone, and DHEA to examine their effect on angiogenesis of the bladder detrusor; dose: E2 (0.1 mg/kg/day); P4 (1mg/kg/day); P4 and DHEA (300 ug/kg/day);


**Agents**: Dehydroepiandrosterone sulfate  
**Vehicle**: PBS;  
**Route**: CSF/CNS (ventral tegmental area); CSF/CNS (nucleus accumbens);  
**Species**: Rat;  
**Pump**: Not Stated;  
**Duration**: 14 days;  
**ALZET Comments**: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, FSL, 230-260 g.); cannula placement verified by microscopy; brain tissue distribution


**Agents**: Estradiol, 17B-; Testosterone; Progesterone; Pregnan-3, 20-dione, 5B--; Pregnan-3a-ol, 20-one, 5a--; Dehydroepiandrosterone; Testosterone, 5a-dihydroxy  
**Vehicle**: Ethanol; Water, distilled;  
**Route**: CSF/CNS;  
**Species**: Rat;  
**Pump**: 2ML1;  
**Duration**: 3, 7 days;  
**ALZET Comments**: Controls received mp w/ vehicle; ALZET brain infusion kit used; 3% ethanol; animal info (Sprague-Dawley, 250-325 g)


**Agents**: Angiotensin II; Dehydroepiandrosterone  
**Vehicle**: Not Stated;  
**Route**: SC; CSF/CNS;  
**Species**: Rat;  
**Pump**: Not Stated;  
**Duration**: 7, 14, 21 days;  
**ALZET Comments**: Controls received mp w/ vehicle, or saline; replacement therapy (ovariectomy); NE-100 is N,N-dipropyl-2-(4-methoxy-3-(2-phenylethoxy) phenyl)-ethylamine; allopregnanolone; DHP and THP metabolite stereoisomers


**Agents**: NE-100; Progesterone; Pregnenolone; Dehydroepiandrosterone; Pregnan-3, 20-dione, 5B--; Pregnan-3a-ol, 20-one, 5a--; Pregnan-3, 20-dione, 5a; Pregnan-5B-ol,20-one, 3a; Pregnan-3B-ol,20-one, 5B; Pregnan-3B-ol,20-one, 5a  
**Vehicle**: Water, distilled; Ethanol;  
**Route**: SC; CSF/CNS;  
**Species**: Rat;  
**Pump**: 2002;  
**Duration**: Not Stated;  
**ALZET Comments**: Controls received mp w/ vehicle, or saline; replacement therapy (ovariectomy); NE-100 is N,N-dipropyl-2-(4-methoxy-3-(2-phenylethoxy) phenyl)-ethylamine; allopregnanolone; DHP and THP metabolite stereoisomers


**Agents**: Testosterone; estradiol; dihydrotestosterone; dehydroepiandrosterone  
**Vehicle**: PEG 300;  
**Route**: SC;  
**Species**: Rabbit;  
**Pump**: 2002;  
**Duration**: 2 weeks;  
**ALZET Comments**: Controls received mp w/ vehicle, or saline; replacement therapy (ovariectomy); animal info (female, New Zealand, white, 4.5-5.0 kg, OVX (for some))


**Agents**: Pregnenolone; dehydroepiandrosterone  
**Vehicle**: Saline; fadrozole;  
**Route**: SC;  
**Species**: Rat;  
**Pump**: 2002;  
**Duration**: Not Stated;  
**ALZET Comments**: Controls received mp w/ vehicle; replacement therapy (gonadectomy); comparison of IP injections vs. chronic mp; dehydroepiandrosterone (DHEA) and pregnenolone are sex hormone precursors
ALZET Bibliography


**Agents:** Testosterone; dehydroepiandrosterone; dihydrotestosterone, 5-alpha-; androstenediol, delta 5-3B, 17B; estradiol; progesterone  
**Vehicle:** PEG;  
**Route:** SC;  
**Species:** Rabbit;  
**Pump:** 2002;  
**Duration:** 2 weeks;  
**ALZET Comments:** Controls received mp w/ vehicle; replacement therapy (ovariectomy); multiple pumps per animal (2)


**Agents:** Dehydroepiandrosterone  
**Vehicle:** Propylene glycol;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 2 weeks;  
**ALZET Comments:** controls received mp w/ vehicle; functionality of mp verified by plasma levels; replacement therapy (castration p. 1754); immunology; dehydroepiandrosterone is also known as DHEA.


**Agents:** Progesterone; Cortisol; Cortisone; Dehydroepiandrosterone; Androstenedione, 4-; Androstendiol, 5-; Testosterone; Nortestosterone, 19-; Estradiol, B-; Estrone; Estril; Deoxycorticosterone  
**Vehicle:** PEG 400;  
**Route:** IV (lower cava);  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 15 days;  
**ALZET Comments:** controls received mp with PEG; no stress (see pg. 351); pumps placed into peritoneal cavity and sutured to musculature; surgical wound sprinkled with sulphathiazol


**Agents:** Dehydroepiandrosterone sulfate  
**Vehicle:** Ethanol;  
**Route:** SC;  
**Species:** Monkey;  
**Pump:** 2ML2;  
**Duration:** 6 weeks;  
**ALZET Comments:** Functionality of mp verified by urine and serum DHEA levels; pumps replaced every 14 days; 70% ethanol used although not recommended by manufacturer; DHEA infused only 2 wks. but preceded and followed by 2 wks. of saline only


**Agents:** Androstenedione; Dehydroepiandrosterone; Dehydroepiandrosterone sulfate  
**Vehicle:** Not Stated;  
**Route:** Not Stated;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 15 days;  
**ALZET Comments:** no comment posted


**Agents:** Pregnenolone; Dehydroepiandrosterone  
**Vehicle:** Olive oil;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 2002;  
**Duration:** 15 days;  
**ALZET Comments:** comparison of sc injections vs. mp infusion; comparison of agents effects; 1/2 of male mice used were castrated

**Ibotenic Acid**


**Agents:** Amyloid protein, Beta (1-40); ibotenic acid  
**Vehicle:** Saline;  
**Route:** CSF/CNS (hippocampus);  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** Not Stated;  
**ALZET Comments:** Dose (B-amyloid (0.075, 0.15, or 0.224 µg/µl); ibotenic acid (0.01875, 0.15, or 0.0562 µg/µl)); Controls received mp w/ vehicle; animal info (Twenty male Albino Wistar rats weighing ~340 g); B-amyloid and ibotenic acid are neurotoxins; neurodegenerative (Alzheimer’s);
Agents: Ibotenic acid; Kainic acid; Quinolinic acid Vehicle: PBS; Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: controls received mp w/ vehicle

Agents: Ibotenic acid Vehicle: Not Stated; Route: CSF/CNS (middle temporal area); Species: Monkey; Pump: 2001; Duration: 3 days; 23 hours;
ALZET Comments: no comment posted

NMDA
Q8648: F. Mannara, et al. Allosteric modulation of NMDA receptors prevents the antibody effects of patients with anti-NMDAR encephalitis. Journal of Neurology 2020;143(9):2709-2720
Agents: NMDAR-CSF Vehicle: Not Stated; Route: CSF/CNS; Species: Mice; Pump: Not stated; Duration: 14 days;
ALZET Comments: Animal info (male C57BL/6J mice, 8-10 weeks old, 25-30 g); behavioral testing (Novel object location; locomotor activity); Brain coordinates (0.2 mm posterior and ± 1.00 mm lateral from bregma, depth 2.2 mm); dependence;

Agents: NMDAR-CSF Vehicle: CSF; Route: CNS/CSF (lateral ventricle); Species: Mice; Pump: Not stated; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male C57BL/6J mice, 8 to 10 weeks old (25–30g)); behavioral testing (prepulse inhibition of the acoustic startle reflex; novel object location; general locomotor activity); Multiple pumps per animal (2 pumps); NMDAR aka Anti-N-methyl-D-aspartate receptor; dependence;

Agents: NMDAR-CSF Vehicle: Saline; Route: CSF/CNS (left lateral ventricle); Species: Mice; Pump: 1004; Duration: 18 days;
ALZET Comments: Controls received mp w/ vehicle; animal info: C57BL/6 male mice (age: 8 weeks; weight: 22-24 g); functionality of mp verified by behavioral tests; neurodegenerative (anti-NMDAR encephalitis); behavioral testing (spontaneous locomotor activity, open field test, NOR test, Morris Water maze); Immunology, immunotherapy; brain tissue distribution; cyanoacrylate adhesive; “The diffusion of methylene blue in all ventricles was confirmed in all mice examined” pg 331; Cannula placement verified via methylene blue or thionine solution injection into brain; NMDAR-CSF aka Anti-N-methyl-D-aspartate receptor-CSF; CSF collected from patients with anti-NMDAR encephalitis; Brain coordinates; 0.4 mm posterior to bregma, 1.0 mm lateral to the lambda point, and 2.0 mm deep from the dural surface

Agents: NMDA; Magnesium sulfate Vehicle: PBS; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2002; Duration: 4-8 weeks;
ALZET Comments: controls received mp with PBS; long-term study, pumps replaced every 2 weeks; NMDA given with MgS04

Agents: NMDA; Glycine; Magnesium sulfate; APV Vehicle: PBS; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not Stated; Duration: 1, 2, or 4 weeks;
ALZET Comments: controls received no agent or mp w/. IMPBS alone or w/.15M glycine in .IMPS; 0.2 and 0.5M NMDA for 1-2 weeks poorly tolerated; .15M for 2 & 4 weeks better; NMDA and other agents infused in pairs
**Pregnolone**

**Q3194:** A. Gonzalez-Usano, *et al.* Pregnenolone Sulfate Restores the Glutamate-Nitric-Oxide-cGMP Pathway and Extracellular GABA in Cerebellum and Learning and Motor Coordination in Hyperammonemic Rats. *ACS Chemical Neuroscience* 2014;5(2):100-105

**Agents:** Pregnenolone sulfate  
**Vehicle:** DMSO; saline, sterile;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** 2004;  
**Duration:** 28 days;  
**ALZET Comments:** Control animals received mp w/vehicle; animal info (male, Wistar, 140-160 g); ALZET brain infusion kit 2 used; 10% DMSO used; "PregS is administered intracerebrally because it does not cross the blood-brain barrier." pg 104; behavioral testing (Y-Maze)

**P8283:** J. L. W. Yau, *et al.* Central administration of a cytochrome P450-7 alpha product 7 alpha-hydroxypregnenolone improves spatial memory retention in cognitively impaired aged rats. *Journal of Neuroscience* 2006;26(43):11034-11040

**Agents:** Pregnenolone; Dehydroepiandrosterone  
**Vehicle:** CSF, artificial; Cyclodextrin, hydroxypropyl, beta;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 2 weeks;  
**ALZET Comments:** Controls received mp w/ vehicle; ALZET brain infusion kit used; animal info (male, Lister hooded, 29 months, 500-600 grams); dental cement used to secure cannula; behavioral study; 10% cyclodextrin used; aging


**Agents:** NE-100; Progesterone; Pregnenolone; Dehydroepiandrosterone; Pregnane -3,20-dione, 5B; Pregnane -3-ol,20-one, 5a; Pregnane -3B-ol,20-one, 5a  
**Vehicle:** Water, distilled; Ethanol;  
**Route:** SC; CSF/CNS;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 7, 14, 21 days;  
**ALZET Comments:** Controls received mp w/ vehicle, or saline; replacement therapy (ovariectomy); NE-100 is N,N-dipropyl-2-(4-methoxy-3-(2-phenylethoxy) phenyl)-ethylamine; allopregnanolone; DHP and THP metabolite stereoisomers

**P6016:** S. Veiga, *et al.* Neuroprotection by the steroids pregnenolone and dehydroepiandrosterone is mediated by the enzyme aromatase. *Journal of Neurobiology* 2003;56(4):398-406

**Agents:** Pregnenolone; dehydroepiandrosterone  
**Vehicle:** Saline; fadrozole;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** Not Stated;  
**ALZET Comments:** Controls received mp w/ vehicle; replacement therapy (gonadectomy); comparison of IP injections vs. chronic mp; dehydroepiandrosterone (DHEA) and pregnenolone are sex hormone precursors

**Quinolinic Acid**


**Agents:** Quinolinic acid  
**Vehicle:** Saline;  
**Route:** CSF/CNS (right lateral ventricle);  
**Species:** Rat (neonate);  
**Pump:** 1007D;  
**Duration:** 7 days;  
**ALZET Comments:** 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)

**Q5843:** B. Kalaska, *et al.* Serum metabolic fingerprinting after exposure of rats to quinolinic acid. *Journal of Pharm Biomed Anal* 2016;131(175-182

**Agents:** Quinolinic acid  
**Vehicle:** DMSO;  
**Route:** IP;  
**Species:** Rat;  
**Pump:** 2006;  
**Duration:** 28 days;  
**ALZET Comments:** Controls received mp w/ vehicle; replacement therapy (ovariectomy); NE-100 is N,N-dipropyl-2-(4-methoxy-3-(2-phenylethoxy) phenyl)-ethylamine; allopregnanolone; DHP and THP metabolite stereoisomers


**Agents:** Quinolinic acid, 1H-Cy;  
**Vehicle:** Saline, physiological;  
**Route:** IP;  
**Species:** Guinea pig;  
**Pump:** 1007D;  
**Duration:** 5 days;  
**ALZET Comments:** Brain tissue distribution; animal info (female, Hartley, adult, 300-480 g); lateral compression of the spinal cord (spinal cord injury; SCI); nephrology; behavioral testing (motor testing, CTM reflex/sensory testing)
R0207: T. W. Stone. Kynurenines in the CNS: from endogenous obscurity to therapeutic importance. Progress in Neurobiology 2001;64(185-218

Agents: Quinolinic acid Vehicle: Not Stated; Route: CSF/CNS; Species: Rat; Pump: Not Stated; Duration: 14 days;
ALZET Comments:


Agents: Quinolinic acid Vehicle: Saline; 3H tracer; Radio-isotopes; Route: SC; Species: Gerbil; Pump: 1007D;
ALZET Comments: no comment posted


Agents: Quinolinic acid Vehicle: PBS; Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: controls received mp w/ saline; comparison of ICV injections vs. mp; no stress (see pg. 305); stress/adverse reaction only in animals receiving ICV injections (pg.305)


Agents: Quinolinic acid Vehicle: Saline; 13C tracer; Radio-isotopes; Route: SC; Species: Gerbil; Pump: 1007D; Duration: 7 days;
ALZET Comments: Controls received saline; functionality of mp verified by in vitro assay, in vivo assays on blood and tissue samples; 13C-QUIN (labeled) used; analyzed fluid & tissue distribution of labeled quinolinic acid

P3492: T. Bazzett, et al. The neuronal NOS inhibitor L-MIN, but not 7-NINA, reduces neurotoxic effects of chronic intrastratal administration of quinolinic acid. Brain Research 1997;775(229-232

Agents: Quinolinic acid; Nitroindazole, 7-, sodium salt; thiocitrulline dihydrochloride, methyl- Vehicle: PBS; Route: CSF/CNS (striatum); Species: Rat; Pump: 2002; Duration: Not Stated;
ALZET Comments: Dose-response; microdialysis; quinolinic acid administered alone or w/ 1 other agent in same pump; enzyme inhibitor; nitric oxide synthase inhibitor;


Agents: Quinolinic acid Vehicle: Not Stated; Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 3, 14 days;
ALZET Comments: ALZET BIK; pumps removed after 3 or 14 days, infusion tubing sealed and left in place, behavioral testing


Agents: Quinolinic acid; Memantine; MK-801 Vehicle: Saline; Route: SC; CSF/CNS; Species: Rat; Pump: 2002; 2ML2; Duration: 2 weeks;
ALZET Comments: ALZET brain infusion kit used; animals were given ICV quinolinic acid concurrently w/ subcutaneous NMDA antagonists


Agents: Ibotenic acid; Kainic acid; Quinolinic acid Vehicle: PBS; Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: controls received mp w/ vehicle


Agents: Quinolinic acid; Picolinic acid Vehicle: Saline; Route: CSF/CNS (striatum); Species: Rat; Pump: 2002; Duration: 1,7 days, 7 days;
ALZET Comments: Controls received mp w/ saline; agents infused alone or concommittantly
Agents: Quinolinic acid  Vehicle: PBS,  Route: CSF/CNS (striatum); Species: Rat; Pump: 2002; Duration: 18 days;
ALZET Comments: controls received mp w/phosphate buffered saline; microdialysis; pump attached to dialysis probe anchored via guide cannula; stylet maintained patency of 8 mm cannula

Agents: Quinolinic acid  Vehicle: Not Stated;  Route: CSF/CNS (striatum); Species: Rat; Pump: 2002; Duration: 14-17 days;
ALZET Comments: functionality of mp verified in vitro for 22 days; detailed methods; excitotoxin; pumps used in a microdialysis infusion apparatus; detailed schematic on p. 2

Agents: Quinolinic acid  Vehicle: PBS,  Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 7,14,21 days;
ALZET Comments: controls received mp with vehicle; comparison of striatal injections vs. mp

Agents: Quinolinic acid; Nicotinic acid; AP7; Kynurenic acid  Vehicle: Radio-isotopes; 3H tracer; NaOH; PBS; HCl; Route: CSF/CNS (striatum); CSF/CNS (hippocampus); Species: Rat; Pump: 2002; Duration: 15 hours; 2 weeks;
ALZET Comments: Controls received mp with nicotinic acid; functionality of mp verified by measurement of radioactivity; dose response;