Published in final edited form as:
Peptides. 2007 December ; 28(12): 2435–2513. doi:10.1016/j.peptides.2007.09.002.

Endogenous Opiates and Behavior: 2006

Richard J. Bodnar*
Department of Psychology and Neuropsychology Doctoral Sub-Program, Queens College, City University of New York, Flushing, NY 11367

Abstract

This paper is the twenty-ninth consecutive installment of the annual review of research concerning the endogenous opioid system, now spanning thirty years of research. It summarizes papers published during 2006 that studied the behavioral effects of molecular, pharmacological and genetic manipulation of opioid peptides, opioid receptors, opioid agonists and opioid antagonists. The particular topics that continue to be covered include the molecular-biochemical effects and neurochemical localization studies of endogenous opioids and their receptors related to behavior (Section 2), and the roles of these opioid peptides and receptors in pain and analgesia (Section 3); stress and social status (Section 4); tolerance and dependence (Section 5); learning and memory (Section 6); eating and drinking (Section 7); alcohol and drugs of abuse (Section 8); sexual activity and hormones, pregnancy, development and endocrinology (Section 9); mental illness and mood (Section 10); seizures and neurological disorders (Section 11); electrical-related activity and neurophysiology (Section 12); general activity and locomotion (Section 13); gastrointestinal, renal and hepatic functions (Section 14); cardiovascular responses (Section 15); respiration and thermoregulation (Section 16); and immunological responses (Section 17).

1. Introduction

This twenty-ninth installment of the annual review of research concerning the endogenous opioid system summarizes published papers during 2006 that studied the behavioral effects of molecular, pharmacological and genetic manipulation of opioid peptides, opioid receptors, opioid agonists and opioid antagonists. This review continues the excellent tradition initiated by Drs. Abba Kastin, Gayle Olson, Richard Olson, David Coy and Anthony Vaccarino in the reviews spanning from 1978 through 2000. As begun in the summaries of papers published over the past five years (2001–2005 papers), two major sections of the review have been added because of the rapid and large expansion of the field. The first is the molecular-biochemical effects and neurochemical localization studies of endogenous opioids and their receptors especially as they may eventually relate to behavior (Section 2). The second is the examination of the roles of these opioid peptides and receptors in their most studied aspect, pain and analgesia (Section 3). As with the previous reviews, subsequent sections will cover the roles of opioid peptides and receptors in the areas of stress and social status (Section 4); tolerance and dependence (Section 5); learning and memory (Section 6); eating and drinking (Section 7); alcohol and drugs of abuse (Section 8); sexual activity and hormones, pregnancy, development and endocrinology(Section 9); mental illness and mood (Section 10); seizures

*Corresponding Author: Dr. R.J. Bodnar, Department of Psychology, Queens College, CUNY, 65-30 Kissena Blvd., Flushing, NY 11367; Telephone: 718-997-3543; FAX: 178-997-3257; e-mail: E-mail: richard.bodnar@qc.cuny.edu.

and neurological disorders (Section 11); electrical-related activity and neurophysiology (Section 12); general activity and locomotion (Section 13); gastrointestinal, renal and hepatic functions (Section 14); cardiovascular responses (Section 15); respiration and thermoregulation (Section 16); and immunological responses (Section 17). To accommodate these additional large sections, only published articles are covered in this review; published abstracts from scientific meetings are not covered, but will be added as they are published in the scientific literature. Given the scope of this review, a paper may be inadvertently overlooked. If this is the case, please accept my apologies, and send the citation and abstract to richard.bodnar@qc.cuny.edu, and I will include it in the next yearly review.

2. Endogenous Opioids and Receptors

2a. Molecular-biochemical effects

This sub-section will review current developments in the molecular and biochemical characteristics of opioid peptides and receptors by subtypes: mu agonists and receptors (2a-i), delta agonists and receptors (2a-ii), kappa agonists and receptors (2a-iii), and OFQ/N and the ORL-1 receptor (2a-iv).

2a-i. Mu agonists and receptors—Endocytosis of the MOR-1D splice variant as well as DOR and the CB1 receptor is mediated by an agonist-independent and constitutive PLD2 activation (604). Separation of MOR desensitization and internalization effects was demonstrated with endogenous receptors in primary neuronal LC cultures (40). Exons 11 and 1 promoters of the MOR gene were characterized in transgenic mice (1249). The splice variants of MOR, SV1 and SV2 do not exhibit binding to [3H] diprenorphine (212). Five single nucleotide polymorphisms were identified for the MOR promoter, and no differences in construct activity were found in control and morphine-treated animals (297). MOR-effector coupling and trafficking occurred in DRG neurons with DAMGO producing greater internalization in MOR/partial differential opioid receptors (1180). MOR-DOR functional interactions occur through receptor-G (i1) alpha fusion (1051). The poly C binding protein 1 is a regulator of the proximal promoter of the mouse MOR gene (716). There is interplay between Sps and poly C binding protein 1 on MOR gene expression (960). The neuron-restrictive silencer factor interacts with Sp3 to synergistically repress the MOR gene (577). Mitochondrial damage decreases MOR, but not DOR function in neuronal SK-N-SH cells (941). Diffusion of MOR at the surface of human neuroblastoma SH-SY5Y cells is restricted to permeable domains (990). Differences in the intracisternal A-particle element in the 3′ noncoding region of the MOR gene in CXBK mice appear to cause this relatively insensitive phenotype (446). Although 14-methoxymetopon displayed similar binding affinities for multiple splice variants of the MOR gene, its potency varied widely for the same splice variants (713). MOR activation of ERK ½ is GRK3 and arrestin dependent in striatal neurons (712). Introduction of a hydroxyl group in position 2 of the cyclohexyl residue of spiropiperidine decreased the binding affinity of mu receptors and OFQ/N (177). Morphine displays PKC-dependent and DAMGO displays GRK2-dependent mechanisms of MOR desensitization in human embryonic kidney 293 cells (529). Null and operational models of mu opioid binding in the mouse vase deferens revealed that DAMGO and DALDA were full agonists while morphine and endomorphin derivatives acted as partial agonists (967). There is direct nose-to-brain transfer of morphine after nasal administration to rats (1216). Transport is not rate-limiting in morphine glucuronidation in the single-pass perfused liver preparation (291). Greater in vitro inhibition of M6G relative to M3G formation from morphine occurred following treatment with (R)- and (S)-methadone and structurally related opioids (804). M6G was identified in chromaffin cell secretory granules (411). Mu opioid receptors are activated by Vitex agnus-castus methanol extracts (1204). Binding of [(35) S] GTPgammaS is stimulated by endomorphin-2 and morphiceptin analogs (343). An aequorin luminescence-based calcium

assay gives pharmacologically-relevant data for mu and delta opioid agonists without involving radioactivity or animal tissues (344). The latter assay also indicated that D-1-Nal or D-2-Nal substitutions in position 4 of endomorphin-2 produced mu receptor antagonists, whereas substitution in position 3 produced partial agonists (346). The tripeptides, Tyr-Pro-Ala-NH2 and Tyr-Pro-Ala-OH, which do not bind to mu receptors, are potent inhibitors of endomorphin degrading enzymes in the brain (345). A partial agonistic effect of 9-hydroxycorynatheidine was observed on MOR in the guinea pig ileum (747). Synthesis, radio labeling and receptor binding was accomplished for [3H] [(1S, 2R) ACPC2] endomorphin-2 (569). MOR, DOR and KOR binding properties were observed for 8-[N-(4′-phenyl)-phenethyl) carboxyamido] analogues of cyclazocine and ethylketocyclazocine (1214). Pharmacokinetics of morphine was slower in flounder than in trout (837). A direct and sensitive analysis of morphine, codeine and other bioactive drugs in human urine was performed by cation-selective exhaustive injection and sweeping micellar electrokinetic chromatography (671). Alkyl chain length altered mu opioid activity of 3, 6-bis {H-Tyr/H-Dmt-NH (CH2) m, n]-2(1H) pyrazinone derivatives (1031). Determination of human urinary opiates occurred with application of poly (methacrylic acid-ethylene gycol dimethacrylate) monolith micro extraction coupled with capillary zone electrophoresis (1207). Urinary excretion of morphine and codeine occurred following the administration of single and multiple doses of opium preparations prescribed in Taiwan as “brown mixture” (680). There are natural heroin impurities derived from tetrahydrobenzylisoquinoline alkaloids (1128). [Sar2] endomorphin-2 was almost equipotent to the parent peptide in mu opioid receptor binding, and was highly resistant to enzymatic degradation (512). Morphine-3-O-propionyl-6-O-sulfate had four times greater affinity than morphine at the MOR (248). Mu opioid binding can be detected in a competitive displacement assay using a beta-imager (916). Identification of potent phenyl imidazoles such as 4-aminocarbonyl-2, 6-dimethyl-Phe as opioid receptor agonists was completed (133). A class of 4-substituted-8-(2-phenyl-cyclohexyl)-2-8-diaza-spiro[4,5]decan-1-one inhibitors was designed achieving antagonist selectivity against the mu opioid and ORL1 receptors (15) that show improved metabolic stability (16) and superior pharmacological and pharmacokinetic properties (17). Chimeric peptides containing a mu opioid receptor ligand and an ORL-1 receptor ligand, Ac-RYYRIK-amide were synthesized (560). Derivatives of 14-aminomorphinones with substitution in the aromatic ring of cinnamoylaminomorphinones and codeinones produced potent mu agonists (844). A novel mu opioid antagonist was created by replacement of the N-terminal tyrosine residue in opioid peptides containing 3-(2, 6-dimethyl-4-carbamoylphenyl) propanoic acid (Dcp) results in a novel mu opioid antagonist (701). Lysine at the C-terminus of the Dmt-Tic opioid pharmacophore produced new lead compounds in the formation of opioid peptidomimetics (57). Multiple ligands from Dmt-Tic and morphinan pharmacophores produced agonists with MOR, KOR and DOR properties (836). Whereas maximal stimulation of [35S]GTPgammaS binding decreased in canine thalamic and spinal cord homogenates for mu > ORL1 > kappa > delta opioid compounds, cortical homogenates showed an affinity order of kappa > ORL1 > delta > mu (650). Morphine increased 5HT, Na (+), K (+)-ATPase activity differentially as a function of adulthood and adolescence (432), and reduced human 5-HT3A receptors in an ondansetron assay (1225). Bivalent ligands containing homo- and heterodimeric pharmacophores at mu, delta and kappa opioid receptors were developed and synthesized in an in vitro assay (895). Potent and highly selective chiral tri-amine and tetra-amine MOR ligands were identified by lead optimization using mixture-based libraries (831). Opioid and CCK receptors also have overlapping pharmacophores required for binding affinity and biological activity (8). QSAR studies were performed upon 4-phenylpiperidine derivatives as mu opioid agonists by a neural network method (1194). A HPLC assay for morphine was developed in small plasma samples (293). Morphine concentrations in bone marrow paralleled plasma morphine concentration for up to 14 days after death in rabbits (178). Unbound concentrations of oxycodone were three times higher in brain than in blood, indicating active influx at the blood-brain barrier (118). An implantable buprenorphine delivery system was characterized using in vitro and in vivo

techniques (594). Capillary electrophoresis contributed to the identification of HMOR-3O-glucide and N-oxides in hydromorphone metabolism in humans (58). STW 5 (Iberoglast) binds to intestinal 5-HT, muscarinic M3 and opioid receptors (1038). A member of the heat shock protein 40 family, hlj1, binds to the carboxyl tail of the human MOR (31).

Pre-POMC cDNA from the ostrich pituitary gland was sequenced revealing the positions for gamma-MSH, ACTH, AMSH, gamma-LPH, beta-MSH and BEND (824). PC1/3 and PC/2 gene expression and post-translational endoproteolytic POMC processing is regulated by photoperiod in the seasonal Siberian hamster (465). BEND analysis in the hypothalamus or PAG is not affected by diurnal variation (348). BEND is present in the stallion testis, but appears to be derived from POMC gene expression in the pituitary (1057). Three POMC subtype genes and subsequent peptides were identified in the pars distalis and intermedia of the barfin flounder pituitary (1101). TAN-821 and TAN-1014 have been developed respectively as agonists and antagonists of the putative epsilon receptor (368).

Histamine was released during constant rate infusion of morphine in dogs (423). Cholinergic nicotinic stimulation of endogenous morphine release occurs from lobster nerve cord (1327). Dextrorotatory morphinans inhibited alpha3beta4 nicotinic Ach receptor subunit cRNAs-induced inward currents in the presence of Ach in Xenopus oocytes (639). Myristoylated G proteins (Galphai1 and GalphaoA) were maximally activated by DAMGO, Menk and Lenk, whereas endomorphin-1 and –2 as well as BEND produced strong, but not maximal responses. Morphine, methadone, fentanyl and buprenorphine produced statistically significant activation (983). 3-aminopropionyl substituted fentanyl analogs were synthesized and displayed opioid activity (906). New hybrid derivatives of fentanyl were found to be active at the MOR and I2-imidazoline binding sites (261). Buprenorphine and norbuprenorphine display in vivo glucuronidation as determined by liquid chromatography-electrospray ionization-tandem mass spectrometry (488). An immunalysis microplate ELISA was validated for the detection of buprenorphine and its metabolite norbuprenorphine in urine (778). Opioid disposition occurs in human sweat after controlled oral codeine administration (1003). CYP2D6-dependent formation of morphine does not exclusively explain the central effects of codeine; codeine-6-glucuronide is an additional active moiety (696). Pharmacokinetic modeling of oxycodone in sheep displayed delayed equilibration between brain and blood levels that would be affected by changes in both cerebral blood flow and blood brain barrier permeability (1164). The principal metabolic pathway of oxycodone in humans is CYP3A-mediated N-demethylation, but circulating oxidative and reductive metabolites provide a negligible contribution to central opioid effects (627). The use of PTX-insensitive Galpha mutants revealed that the potency for mu agonists was highest for cells expressing Galpha (i3) and Galpha (o) and lowest with Galpha (i1) and Galpha (i2) (228). NalBzOH displays agonist activity at MOR, DOR and KOR, but not ORL-1 receptors expressed either in a heterologous cell system or in a native environment (862). FK33–824, a mu opioid agonist decreases enzymatic activity of PKC, adenylate cyclase and PKA in porcine granulosa cells (546). The anti-opioid actions of NPVF, a NPFF agonist was observed in a decrease to opioids to voltage-gated (N-type Ca2+ currents and enhancement of muscarinic-induced intracellular Ca2+ release in SH-SY5Y cells as they do in neurons (570).

Naltrexone increased PKCepsilon, ERK and integrin alpha 7 in SH-SY5Y neuroblastoma cells (857). Long-acting naltrexone had a 1-month pharmacokinetic activity in plasma that was proportional to dose and number of treatments (302). The dissociation of [3H] naloxone was four times faster under displacement than under infinite dilution conditions, demonstrating the retention effect of receptors confined in space (1061). Naltrexone release from biodegradable microspheres produced constant rates of release culminating in 80% over 2 months (691). Two novel tripartite codrugs of naltrexone and 6beta-naltrexol with hydroxybupropion were synthesized as potential alcohol abuse and smoking cessation agents (440). Transdermal

delivery of 6-beta-naltrexol was enhanced by a codrug linked to hydroxybupropion (588). MOR antagonists were synthesized and evaluated from novel octahydro-1H-pyrido [1, 2-a] pyrazine (633) and from N-substituted trans-3, 4-dimethyl-4-(3-hydroxyphenyl) piperadine (634). The permeation of nalmefene hydrochloride was better across the middle turbinate, posterior septum and superior turbinate mucosa (301).

2a-ii. Delta agonists and receptors—Knock-in mice expressing fluorescent DOR uncovered G protein-coupled receptor dynamics in vivo (996). Simultaneous activation of DOR and the sensory neuron-specific receptor-4 hetero-oligomer by the mixed bivalent agonist BAM-22 activates the latter, but inhibits the former (132). Morphine and pain-related stimuli enhance cell surface availability of somatic DOR in rat dorsal root ganglia (393). Delta and mu opioid receptors were cloned, heterologously expressed and pharmacologically characterized from the brain of a urodele amphibian, the rough-skinned newt, Taricha granulosa (127). Adenosine A1 and A2 receptor agonists increase c-fos in striatal GABAergic Enk, but not GABAergic DYN striatal neurons as well as increasing striatal PreEnk (553). The enrichment by 18-fold with FACS robustly increased beta-arrestin-1-GFP expression associated with strong human DOR desensitization (10). A new duplicate DOR in zebra fish was characterized (911). Enk and SP are found in reduced concentrations in primary culture striatal neurons relative to adult preparations (330). The mGluRI antagonists, LY367385 and MPEP reduce NMDA-induced expression of the Pro-Enk gene in neocortex, yet enhance AMPA-induced expression of the neocortical Pro-Enk gene (674). Pro-enk was identified in the hypothalamus and striatum using a method allowing selective isolation of neuropeptides of murine brains lacking carboxypeptidase E (268). ProEnk A 119–159 is a stable ProEnk A precursor fragment identified in human circulation (323). Only the C-terminus glucose conjugate of Lenk showed transport by glucose transporters and hPepT1 (1237). Whereas only a few samples of adherent human fetal chromaffin cells expressed Menk early in vitro, almost all of the neurosphere-like colonies appearing later expressed Menk (1321). Human Menk binds to anionic phosphatidylserine in high preference to zwitterionic phosphatidylchlorine in large unilamellar vesicles (586). Lenk binds in a turn confirmation to DOR, but it is not a (1–4) beta-turn (108). Nasal administration of Lenk is facilitated by a thiolated polycarbophil that slows Lenk degradation (82), and reversible lipidization is preferable for the oral delivery of Lenk (1185). 6-N, N-dimethylamino-2, 3-napthalimide was identified as a new environment-sensitive probe in delta- and mu-selective opioid peptides (1149). The novel, orally active, DOR agonist, RWJ-394674 is biotransformed to the potent MOR agonist RWJ-413216 (229). Highly potent and selective phenylmorphan-based inverse agonists of the DOR were developed (1117). AUF-1 is expressed in the developing brain, binds to AT-rich double-stranded DNA, and regulates Enk gene expression (287). Design and synthesis were completed of novel hydrazide-linked bifunctional peptides as delta/mu opioid receptor agonists and CCK1/CCK2 receptor antagonists (641). Three types of latex nanoparticles carrying NTI derivatives were identified as possessing high DOR affinity (453). A new method using HPLC with electrochemical detection was developed allowing for the simultaneous measurement of Menk, Lenk, endomorphin-1 and endomorphin-2 (677).

Selective alkylation of delta-2 opioid receptors occurred following NAC 5′Nti-isothiocyanate in the NAC and ventral caudate; beta-chlornaltrexamine was nonselective for MOR and DOR in the same site (734). Distinct subcellular localization for constitutive and agonist-modulated palmitoylation of the human DOR was described (900). Pertussis-toxin abolished DPDPE-induced inhibition of forskolin-stimulated intracellular cAMP production that was rescued by Galpha (i2), but not Galpha (i3) or Galpha (o) mutants; the former, but not latter mutants co-precipitated with DOR. Long-term DPDPE treatment allowed pertussis toxin-induced elimination of naloxone-induced superactivation of adenylyl cyclase activity, an effect again rescued by Galpha (i2) mutants (1311). DPDPE, acting through Gi-coupled DOR receptors mediate phosphorylation of CPI-17 and MLC20 through preferential activation of the PI3K/

ILK pathway (486). Down-regulation of the glutamate transporter EAAC1 occurred following expression and activation of the DOR and its agonist, DPDPE (1240). Genetically-engineered human mesenchymal stem cells produce Menk at augmented higher levels in vitro (1078). Lenk caused membrane currents across lipid membranes through adsorption, transportation and desorption, effects confirmed using fluorescence spectrometry and confocal laser scanning microscopy (687). DADL induces a reversible hibernation-like state in HeLa cells (1152). DADL molecules enter the cytoplasm and nucleus of LNCap cells that are devoid of opioid receptors, and binds to perichromatin fibrils where transcription and early splicing of pre-mRNAs and pre-rMRNAs occur, thereby resulting in decreased transcription and proliferation without apoptosis (59). AVP enhances PAG synthesis and secretion of Enk and BEND, but not DYN (1263).

2a-iii. Kappa agonists and receptors—KOR activation of p38 MAPK is GRK3- and arrestin-dependent in neurons and astrocytes (141). Netrin-1 signaling regulates de novo protein synthesis of KOR by facilitating polysomal partition of its mRNA (1133). Naloxone and NBNI, but not selective mu or delta antagonists increased, whereas DYN decreased the cell surface level of the human KOR by activation-induced down-regulation and pharmacological chaperone-mediated enhancement (200). KOR affinity in a human embryonic kidney cell system indicated a rank order of cyclazocine, naltrexone, SKF10047, xorphanol, WIN44441, nalorphine, butorphanol, nalbuphine, lofentanil, dezocine, metazocine, morphine, hydromorphone and fentanyl (399). A cDNA encoding KOR in zebra fish has been cloned and characterized (27). GEC1 interacts with the kappa opioid receptor and enhances its expression (188). Big DYN, a 32-amino acid Pro-DYN peptide consisting of DYN A and DYN B showed similar selectivity for human KOR as DYN A, was less selective than DYN A for human MOR, DOR and ORL1, but activated G proteins more potently than DYN A; DYN B was less potent and selective (771). Big DYN and DYN A, but not DYN B causes leakage effects in large unilamellar phospholipid vesicles thereby causing perturbations in the lipid bilayer (490). DYN A inserts its N-terminus into the bilayer of the bicelle, whereas DYN B resides on the surface of the bilayer (673). Bikunin was identified as an endogenous inhibitor of DYN convertase in human cerebrospinal fluid (1077). Although selective opioid agonists developed for mammalian opioid receptors did not fully recognize opioid binding sites in zebra fish brain, DYN A showed good affinities in the nanomolar range (409). Pro-DYN cDNA's were cloned in eels and tilapia (24). NalBzOH binding is abolished in triple MOR/KOR/DOR mice, and in vivo changes reflect that of a nonselective opiate drug (235). N-substituted 4beta-methyl-5-(3-hydroxyphenyl)-7alpha-amidomorphans are potent, selective kappa opioid receptor antagonists (171). New C (4)-modified salvinorin A analogues were synthesized as KOR agonists (636). Salvinorin A analogues were also synthesized following effects of configuration at C (2) and substitution at C (18) (73) along with those isolated from Salvia divinorum (1120). Salvinorin A, a selective KOR agonist was used in a combined ligand-based and target-based drug design approach for G-protein coupled receptors (1041). A unique binding epitope was found for salvinorin A, a non-nitrogenous KOR agonist (548). Bioisosteric modification of the C-2 thioacetate isoester of salvinorin A produced a potent and selective KOR agonist (1070). The substitution of a tert-butyl with a cyclobutyl moiety in buprenorphine created a highly selective KOR agonist with low addictive potential and dependence liability (877). 3D-QSAR studies were performed upon orvinol analogs as kappa-opioid agonists (656). The extraction fraction for NAC DA in the mouse is increased following NBNI treatment (186). The application of Schild-analysis to the antagonism of U50488H by NBNI provides pharmacological evidence for KOR in Planaria (934).

2a-iv. OFQ/N and ORL-1 receptor—OFQ/N binding to ORL-1 receptors triggers internalization of these components into vesicular compartments that is dependent on PKC and occurs selectively for N-type calcium channels (25). OFQ/N, but not partial agonists induce

concentration-dependent endocytosis and recycling of the human ORL1 receptor, enhancing up regulation of adenylyl cyclase activity (1059). OFQ/N differentially activates ERK, p38 and JNK MAPK to contribute to potentiations of prostaglandin vasoconstriction after fluid percussion brain injury (38). The induction of Pro-OFQ/N mRNA by cAMP appears to be mediated by a cAMP-response element, histone acetylation and through CREB (1301). The ORL-1 receptor utilizes both G (oA) and G (oB) for signal transduction (1136). OFQ/N and its agonist, Ro64-6198 display great regional similarities in binding assays using [(35) S]-GTPgammaS binding (390). OFQ/N and DYN A analogues with Dmp substituted for N-terminal aromatic residues show ORL-1 and opioid receptor preferences (989). A novel D-proline amide class of spiropiperidines was developed as an effective ORL-1 antagonist (410). OFQ/N (1–13) NH2 analogues modified in the 9 and/or 13 positions were synthesized and showed biological activity (828). An enzymatically-resistant OFQ/N peptide containing a carbamic acid residue was synthesized (665). Indole derivatives were designed, synthesized and biologically evaluated as novel OFQ/N receptor antagonists (1079). Potential ORL-1 ligands were synthesized from spiro-[piperidine-4,2′(1′H)-quinazolin]-4′ (3′H)-ones and spiro-[piperidine-4,5′ (6′H)-[1,2,4]triazolo[1,5-c]quinazolines] (809). Trap-101, an achiral analogue of J-113397 was identified as a potent ORL-1 antagonist (1132). Both 3-(4-Piperidinyl) indoles and 3-(4-piperidinyl) pyrrolo-[2, 3-b] pyridines are ligands for the ORL-1 receptor (96). A series of hexapeptides with a general formula of Ac-RYY-R/K-W/I-R/K-NH (2) were identified as novel partial agonists for the ORL-1 receptor (428).

BDNF induced expression of Pro-OFQ/N mRNA's that in turn induced expression of immediate early genes in hippocampal cultures. OFQ/N, but not nocistatin increased both neurite length and number in hippocampal cultures (954). Mature OFQ/N and nocistatin were identified in human brain and CSF (534).

2b. Neuroanatomical localization

This sub-section will review current neuroanatomical studies indicating localization of opioid peptides and receptors by subtypes: mu agonists and receptors (2b-i), delta agonists and receptors (2b-ii), kappa agonists and receptors (2b-iii), OFQ/N and ORL-1 receptor (2b-iv), and opioid-related neuroanatomy (2b-v).

2b-i. Mu agonists and receptors—Immunohistochemical labeling of the MOR carboxy terminal splice variant mMOR-1B4 was observed in the olfactory bulb, cerebral cortex, BNST, hippocampus, habenula, amygdala, thalamus, hypothalamus, median eminence, SN, VTA, oculomotor nucleus, red nucleus raphe nuclei, PAG, LC, trigeminal nucleus reticular formation, area postrema and Purkinje and deep cerebellar nuclei (1314). Whereas acute morphine decreased MOR gene expression in the PAG, chronic morphine decreased PAG and striatal MOR and KOR gene expression in female rats (1113). MOR, KOR and DOR receptors were found in disc-shaped and stellate cells of the inferior colliculus with MOR and GABA receptors co-localized in the central nucleus, dorsal cortex and external cortex of the inferior colliculus. BEND and GABA neurons were in close proximity to each other (1126). MOR is extensively co-localized with parvalbumin, but not somatostatin, in the hippocampal dentate gyrus (299). There is a distinct distribution of DA D1 receptor and MOR-1 receptor immunoreactivities in the amygdala and interstitial nucleus of the posterior limb of the anterior commissure (508). Reciprocal connections of endomorphin-1- and endomorphin-2-containing neurons were observed between the tubural and lateral hypothalamus on the one hand, and the medial, commissural, lateral and gelatinous parts of the NTS on the other (492). Mu opioid receptors were found in nerve fibers within the bovine pineal gland, whereas delta opioid receptors were observed on nerve fibers in the pineal perivascular space and intraparenchema. DOR, MOR and Lenk were co localized in some nerve fibers (908). Whereas BEND and TH immunoreactive axon terminals of MPOA cells that project to the SFO were predominantly

axo-somatic, NPY terminals were more axo-dendritic (559). POMC co-localizes with CRF in axon terminals of the noradrenergic LC (948). Fluoxetine increased mu opioid receptor expression in obese Zucker rat C/P, dentate gyrus, lateral septum, amygdala, and frontal, parietal and piriform cortices (222). MOR possessed little overlap with preprotachykinin B in the dorsal horn of the spinal cord (917). The seizure-resistant rodents, Proechimys guyannesis, display high DAMGO binding in the medial amygdala, dorsal dentate gyrus and PAG, and decreased DAMGO binding in the anterior olfactory tubercule, cingulate cortex, thalamus, basolateral amygdala, SN and dorsal hippocampus (963). Whereas lower medial septal, but not MPOA MOR densities were lower in older reproductively senescent male Japanese quail than females or young males, DOR densities in both the medial septum and MPOA were lower in this group (871).

Heroin decreased NPFF-immunoreactivity in the NTS and reduced NPFF fibers in the median eminence, pituitary stalk and neurohypophysis, but increased NPY neurons and fibers in the thalamic PVN and BNST (279). Both morphine and methadone increased c-Fos expression in the striatum and NAC (1111). Morphine produced up-regulation of the functional expression of neurokinin-1 receptors in cortical neurons (1181). Morphine respectively reduced and increased ascorbic acid release in the striatum and NAC of rats (421). Morphine increased fMRI signals in the NAC, extended amygdala, orbitofrontal cortex, hippocampus, PAG and hypothalamus and decreased fMRI signals in the anterior cingulated gyrus in the brains of healthy volunteers (70).

2b-ii. Delta agonists and receptors—Enk afferents from the posterior BNST and the basomedial and cortical amygdaloid nuclei innervate the medial amygdaloid nuclei whereas Enk afferents from the anterolateral BNST as well as the cortical, medial and basomedial amygdaloid nuclei innervate the central amygdaloid nucleus (920). Striatal dendrites display co-localization of DOR and dopamine D1 receptor immunoreactivity (29). Striatal projection neurons to the SN mostly possess Enk-only and SP-only cells; Enk/SP co localized neurons primarily projecting to the SN do not appear confined to striosomes (1183). Enk is found in overlapping distributions with VP, VIP, CRF, gastrin releasing peptide, calbindin and calcretin in both mouse and rat (801). SP was more robust than Enk in their broad distribution in song control nuclei of 11 different oscine species (653). Four different Enks, but not DYN is found in synovium, bone marrow, periosteum and juxta-articular bone in rat joints (79). DOR immunoreactivity was evenly distributed throughout the neuropil of the feline reticular formation, and was very dense in the ventral and central areas of cytoplasm and medium to large dendrites of the parabrachial nuclei and LC (28). L-enk and the DOR were found most predominantly in the inner spiral bundle of the guinea pig cochlea, whereas DYN and KOR were found in both the inner and outer spiral bundles (533). Menk is found in small diameter and diffusely localized neurons throughout the superficial grey and stratum opticum of the superior colliculus of the camel (767). Enk is localized in the dorsolateral septal nucleus of the fire-bellied toad, Bombina orientalis (318).

2b-iii. Kappa agonists and receptors—Although KOR was often co-localized with MOR, small ovoid KOR-containing cells were observed in close apposition with larger MOR-containing cells in medial thalamus, PAG and brainstem (415). KOR and GAD67 immunoreactivity have been found in OFF and NEUTRAL cells in the RVM (1222). Axonal mRNA transport and localized translational regulation of KOR occur in primary neurons of the DRG (90). KORS have been localized in the lipid rafts which are micro domains of plasma membranes rich in cholesterol and sphingolipids (1250). Unprocessed DYN was much greater than co-existent DYN peptides in the axon terminals of Pro-DYN neurons projecting to the CA3 region of the hippocampus and in the striatal projections to the VTA (1253). DYN and neurokinin B are co expressed in hypothalamic arcuate neurons extending to the ME and periventricular zone with these fibers projecting to the PVN, anterior hypothalamus, MPOA,

median preoptic nucleus, anteroventral periventricular nucleus and BNST (152). DYN and neurokinin B immunoreactivity are co localized in the arcuate nucleus and median eminence of the sheep (352). Dopamine D1 receptors have subcellular distributions that are conducive to interactions with Pro-DYN in the NAC shell (449). Moreover, CART is co localized with pro-DYN and DA D1 receptors in the NAC (489). Pro-DYN mRNA labeling is in the mouse olfactory tubercule, lateral septum, C/P, central amygdala, PVN, SON, LHA, VMH, lateral reticular nucleus and NTS; it is also co-localized with NPY mRNA in the arcuate nucleus (669). Long-day exposure produces greater DYN A1–17 expression in the hypothalamo-pituitary axis, ependymal cells, subcomissural organ and lateral and third brain ventricle choroid plexus in the Siberian hamster than short-day exposure (776).

2b-iv. OFQ/N and the ORL-1 receptor—OFQ/N was immunolocalized in the rat cochlea in tunnel fibers as well as inner and outer hair cells (571). The slow rate of divergence in the amino acid of OFQ/N precursor sequences in lungfish was analyzed (638).

2b-v. Opioid-related neuroanatomy

3. Pain and Analgesia

This section has four major parts examining recent advances in: a) pain responses especially as they may relate to opioid function, b) opioid analgesia organized as a function of receptor subtypes, c) sex, age and genetic differences in opioid analgesic responses, and d) opioid mediation of other analgesic responses.

3a. Pain responses

The following sub-sections examine work done on spinal (3a-i) and supraspinal (3a-ii) circuits respectively.

3a-i. Spinal circuits—Nociceptive behaviors (8–24 h) outlasted spinal c-Fos increases (2 h) following skin-muscle incisions, and after 24 h, surgically-treated animals were no different from controls in c-Fos-induced increases induced by thermal stimulation. Morphine was more effective in blocking nociceptive behaviors relative to c-Fos-induced increases (1325). Hindlimb and abdominal stretches occurred during labor, and were increased by systemic oxytocin. Morphine decreased oxytocin-induced stretching responses without altering labor duration, and decreased labor-induced c-Fos elevations in lumbosacral spinal segments (175). Although MOR mechanisms are not essential in the processing of acute noxious mechanical and electrical stimuli by WDR neurons, they may play an important role in endogenous inhibitory mechanisms that regulate the development of spinal neuronal sensitization during windup (422). Absence of Reelin results in significant reductions in mechanical sensitivity and a pronounced thermal hyperalgesia and aberrant neuronal positioning of Dab-1 immunoreactivity in the dorsal spinal cord (1163). Chronic constriction injury of the saphenous nerve in rats produce significant allodynia and hyperalgesia that is sensitive to morphine gabapentin, amitryptaline and WIN55212-2 administration, that increases c-Fos as well as MOR and CB-1 receptor expression in the spinal cord, and that leads to decreased functional receptive fields downstream to the injury accompanied by A-fiber ectopic discharges (1174). Spinalized rats laminectomized in the lumbo-sacral region displayed increased multi-unit efferent discharges from the ventral root following mechanical von Frey hair mechanical stimulation of the hindpaw. During discharges and after discharges were reduced by resiniferatoxin, a potent capsaicin analogue, whereas only after-discharges were reduced by morphine, ketamine and ezlopitant (1255). Partial injury of tail-innervating nerves creates both mechanical allodynia and non-allodynia in different subgroups of rats; the former group shows greater losses of spinal MOR, whereas the latter group displays more augmented mechanical allodynia following peripheral naloxone and spinal CTOP (49).

3a-ii. Supraspinal circuits—A rodent pain model of gynecologic surgery involving laparotomy with tonic distension of the cervix and lower uterine segment was shown to be sensitive to systemic and intrathecal morphine (1125). There are strong pharmacological correlation between the formalin test and the neuropathic pain behavior in different species with chronic constriction injury (1166). An animal model of chronic inflammatory pain using large volumes of adjuvant to the intra-articular space of the rat knee showed sensitivity to morphine, dexamethasone and ibuprofen, but different temporal sensitivity from acute models (1221). Experimental pancreatitis produced visceral pain and increased thoracic DYN content with lidocaine injections into the RVM or nucleus gracilis or spinal DYN antisera reversing its effects (1154). Transgenic mice with early-stage pancreatic cancer displayed visceral pain that was enhanced by centrally-acting, but not peripherally-acting opioid antagonists (1008). An abdominal withdrawal reflex model of visceral pain due to colorectal distension was established in a behavioral assessment in rats (1264). NRM on cells excited by colorectal distension facilitate responses to colorectal distension itself, which in turn augments excitation of NRM off cells that then act to suppress cutaneous nociception (134). Anterior cruciate ligament transaction produced experimental osteoarthritis and joint pain accompanied by increased nitrite and inducible NO synthase, effects reduced by morphine, L-NAME, indomethacin and meloxicam (174). One can differentiate between capsaicin-induced allodynia and hyperalgesia using a thermal operant assay; both effects were blocked by morphine (835). The orofacial formalin test in the mouse appears to be a strong behavioral model for studying physiology and modulation of trigeminal nociception; morphine inhibits formalin responses in both phases (702). Formalin injection directly into the knee joints of rats produced the characteristic two phases of nociception; morphine blocked both phases in a naloxone-reversible manner, whereas diclofenac and midazolam reduced only the second phase, whereas meclizine and loratadine increased the second phase (735). Experimental pain-related responses are induced by a scorpion Buthus martensi Karsch sting (52). Zymosan applied to the tibial-tarsal joint produces hypernociception elicited by articular dorsal flexion movement, an effect blocked by morphine and indomethacin (430). Animals with chronic constriction injury had free access to a light: dark chamber, and chose the less-preferred light part of the chamber following stimulation of the injured paw in the more-preferred dark chamber. Whereas morphine, gabapentin, duloxetine and 8-OH-DPAT reinstated preferences for the dark side of the chamber, gaboxadol and WIN55,212–2 did not (890). The use of calibrated forceps are a reliable tool for pain, morphine analgesia and morphine tolerance (706). Ultrasonic vocalizations occur primarily during the interphase of the formalin test, and are suppressed by morphine in a naloxone-reversible manner (863). Hairless mice fed a special diet develop atoplic-like dry skin inducing prolonged scratching that is dose-dependently blocked by naloxone, but not H1 or 5HT(1/2) antagonists (369). Administration of 2,4,6-Trinitrochlorobenzene to hairless mice produced a naltrexone- and L-NAME-reversible itch response (1138).

3b. Opioid analgesia

The following sub-sections examine advances in our understanding of opioid-mediated analgesia in the past year especially as they pertain to the opioid receptor subtypes and their genes: i) mu agonists and receptors, ii) delta agonists and receptors, iii) kappa agonists and receptors, and iv) OFQ/N and the ORL-1 receptor. A large number of studies examine either knockout or knockdown techniques to indicate roles of the receptors, and potential splice variants in opioid analgesic function. Separate paragraphs are devoted to studies in which other transmitter and peptide systems affect opioid analgesia; the effects of opioid manipulations upon analgesia induced by other peptides and transmitters are covered in Section 3d. Finally, human studies related to opioid and particularly mu receptor-mediated analgesia is covered at the end of Section 3b-v.

3b-i. Mu agonists and receptors

Morphine: A rank-order analgesic potency of morphine was observed on the paw pressure, hot-plate and tail-withdrawal tests with the lowest on the formalin test, effects independent of stimulus intensity on all tests. A within-subject cumulative dosing procedure resulted in lower ED50 values than a between-subject procedure, and the ED50 of morphine progressively increased when the cut-off value was adjusted from 4 to 5, 6, 7 and 8 standard deviations above the mean (796). Nociceptive stimulus modality-related differences occurred in pharmacokinetic-pharmacodynamic modeling of morphine in the rat such that drug effects were more effective for mechanical relative to thermal stimuli (1015). Sub-analgesic doses of DAMGO or fentanyl enhanced morphine analgesia through induction of MOR endocytosis (454). Opiate receptor-dependent analgesia is associated with several compounds bound to Gbetagamma subunits (110). The analgesic, tolerant, dependent, rewarding and sensitizing effects of morphine, but not kappa agonists were lost in mice lacking adenylyl cyclase type 5 that is highly enriched in striatum (582). Mice lacking phospholipase Cbeta1 displayed hypersensitivity to pain and reduced morphine analgesia and tolerance formation (685). Morphine administered systemically or directly into the ACC produced a naloxone-sensitive reduction in pain affect, as demonstrated by decreased aversiveness of noxious cutaneous stimulation in nerve-damaged animals with no concomitant alteration of response to mechanical stimulation (623). NAC morphine-induced increases in thermal and mechanical hindpaw latencies were blocked by naloxone, BFNA and NBNI, but not NTI (1244). Morphine in the thalamic nucleus submedius reduced the second phase of formalin-induced evoked spinal dorsal horn nociceptive responses in a naloxone-reversible manner (1317). Microinjections into the thalamic nucleus submedius of morphine, endomorphin-1 or DADL, but not the kappa agonist, spiradoline, dose-dependently inhibited mechanical and cold allodynia induced by spinal nerve ligation, effects blocked by general and mu, but not delta antagonism (1187). Similarly, microinjections into the ventrolateral orbital cortex of morphine, endomorphin-1 or DADL, but not the kappa agonist, U-62066, dose-dependently inhibited mechanical and cold allodynia induced by spinal nerve ligation, effects blocked by general and mu, but not delta antagonism (1318). Morphine, gabapentin and lamotrigine produced analgesia of similar potencies in attenuating capsaicin and nerve-injury-induced mechanical hypersensitivity (535). Morphine modulated potentiation of capsaicin-evoked TRPV1 responses through a cyclic AMP-dependent PKA pathway (1160). Intrathecal naloxone or CTAP blocked systemic morphine- and fentanyl-induced analgesia on mechanical measures of nociception as well as thermal responses to the hindpaw, but not forepaw (198). However, noncompetitive interactions between the opioid antagonists, CTAP and naltrexone were observed in the rat tail-withdrawal assay (1175). Morphine-associated pruritus occurred after a single extradural injection in a horse (150). Two studies independently demonstrated that morphine-induced decreases in intraocular pressure and pupil diameter in rabbits was blocked by naloxone and partially reversed by L-NAME or L-glutathione, indicating NO involvement (111,296). Low-dose morphine-induced hyperalgesia was blocked by PLC inhibitors (U73122) and blockers (calphostin C), also by ketamine and MK-801, and finally by AS against PLCbeta3 (378). Acute and chronic morphine increases Phase II pain-associated behaviors on the formalin test in neonatal rats after four days of abstinence (1332).

Mu Opioid Agonists: Human opiorphin, a physiological inhibitor of Enk-inactivating zinc endopeptidases produced potent analgesia in chemical and mechanical pain models (1223). Peripherally-mediated antinociception of the mu-opioid receptor agonist 2-[(4,5alpha-epoxy-3-hydroxy-14beta-methoxy-17-methylmorphinan-6beta-yl)amino]acetic acid (HS-731) occurred after subcutaneous and oral administration in rats with carrageenan-induced hindpaw inflammation (100).

Mu Opiate Agonists: L-methadone, but not D-methadone produced stronger anti-allodynic effects in the spinal nerve ligation model relative to morphine, oxycodone and methadone itself (646). 6-acetyl-codeine analgesia was blocked by AS probes targeting Exons 1 and 2 of the MOR gene (780). The ability of buprenorphine to increase tail-flick latencies correlated with the extent and duration of reduced numbers of mu opioid receptor binding; however, residual analgesia after 8 h was not accompanied by mu binding changes (320). Ventricular and intrathecal buprenorphine analgesia on the formalin test was blocked by ventricular and intrathecal naloxone and the ORL-1 antagonist, J113397. Methadone and morphine were more effective than buprenorphine in increasing thermal and pressure thresholds in cats (1067). Systemic buprenorphine analgesia was blocked by systemic or intrathecal, but not ventricular naloxone, and was enhanced by systemic or ventricular J113397. Systemic, but not ventricular or intrathecal buprenorphine decreased formalin-induced Fos activity in the lumbar dorsal horn (1257). Thienorphine produced a similar analgesic duration as buprenorphine, but was longer than the latter in antagonizing morphine-induced lethality (1279). The analgesic efficacy of such partial opioid agonists as buprenorphine or tramadol was increased in mice with targeted inactivation of the alpha2A-adrenoceptor gene or in wild-type mice treated with atipamezole and yohimbine (874). Tramadol produced analgesia in MOR KO mice that was blocked by alpha-2 adrenergic antagonists alone or with naloxone, but not by methysergide (499). Isobolographic analysis revealed dual-site synergism in the systemic and intraplantar antinociceptive response of tramadol in the formalin test in rats (921). Oral and intrathecal, but not ventricular oxycodone, but not morphine produced analgesia in diabetic mice. Whereas, mu but not kappa or delta antagonism blocked oxycodone analgesia in non-diabetic mice, kappa, but not mu or delta antagonists blocked oxycodone analgesia in diabetic mice (852). Whereas subcutaneous oxycodone and oxymorphone produced potent analgesia in the hot-plate and paw pressure tests, intrathecal oxymorphone produced far more potent effects than intrathecal oxycodone (645). Liposome-encapsulated hydromorphone provided extended analgesia in a rat model of neuropathic pain (1047). Analgesic effects were observed after epidural administration of hydromorphone in horses (822), and similar effects were observed following subarachnoid hyperbaric morphine, buprenorphine and methadone (823). Systemic and intrathecal remifentanil produced naltrexone-reversible analgesia on the acetic acid test in Rana pipiens (792). Gabapentin activated the NO-cyclic GMP-K+ channels pathway in inhibiting formalin-induced pain (869). Spinal alpha-2 adrenergic and muscarinic receptors as well as the NO release cascade mediated the supraspinally-produced effectiveness of gabapentin in decreasing mechanical hypersensitivity in mice after partial nerve injury (1103).

Endomorphins: Intrathecal endomorphin-2, but not endomorphin-1 or DAMGO analgesia was prevented by antisera directed against DYN A(1–17), but not DYN B(1–13); this effect was reversed by pretreatment with ultra-low doses of BFNA or naloxonazine that were ineffective at mu opioid receptors (788). Endomorphin-1 and endomorphin-2 produced analgesia when injected directly into an inflamed hindpaw, effects blocked by mu, but not kappa antagonists, and with delta antagonism blocking the latter but not former effect. Antibodies raised against BEND, Lenk or Menk failed to affect endomorphin-induced analgesia (622). Endomorphin-1 produced longer-lasting analgesia when injected in nanoparticles coated with polysorbate 80 (679). The analogues, guanidine-[d-Ala(2), pCl-Phe (4)] endomorphin-1, the four D-Ala-containing tetrapeptides and a chloro-halogenated d-Pro-Gly-containing pentatpetides of endormorphin-1 showed potent and prolonged analgesic activity (681). Strong opioid receptor binding and analgesic activity were found with analogues of endomorphin-2 and morphiceptin with phenylalanine mimics in position 3 or 4 (384). The novel analogue, [Dmt1]endomorphin-1 produced spinal and supraspinal analgesia that was blocked by naloxone and BFNA, but not naloxonazine, indicating mu-2 action (527). Tyr-Pro produced naloxone-reversible analgesia on the tail-flick test, and [3H]-Tyr-Pro could be found in endomorphin-related tetra- and tri-peptides in brain (968). The modulation of

endomorphin-1 and –2 analgesia by L-NAME was inhibited and reversed by L-Arg and naloxone respectively (204).

BEND: A BEND anti-serum blocks thermal analgesia noted at the initial stages of a murine osteosarcoma (47). Intraplantar BEND respectively suppressed and potentiated concanavalin A-induced paw edema at high and low doses in delta- and kappa-selective antagonist fashion in two inbred strains that differed in BEND-induced modulation of phagocytosis and NO production (1065).

Manipulations affecting Mu Analgesia: Dextro- and levo-naloxone each reversed the attenuation of morphine analgesia induced by lipopolysaccharides in the mouse spinal cord through a non-opioid mechanism (1233). Bicuculline or picrotoxin administered into the ventrolateral orbital cortex enhanced the ability of morphine to inhibit tail-flick latencies in this region, whereas muscimol and THIP attenuated the morphine-induced response (930). Gabapentin enhances the analgesic response to morphine in an acute model of pain in male rats (775). SB203580, a p38 MAPK inhibitor reversed antianalgesia induced by dextro-morphine or morphine in the mouse spinal cord (1234). Endothelin ETA receptor blockade potentiates morphine analgesia but does not affect gastrointestinal transit in mice (748). Mice lacking P-glycoprotein displayed enhanced analgesic effects to morphine and fentanyl, but not meperidine. Morphine and fentanyl stimulated P-glycoprotein ATPase activity as well (439). Mice lacking one allele of glial cell line-derived neurotrophic factor displayed enhanced morphine analgesia and enhanced NAC DA output (11). Enhancement and restoration of the analgesic efficacy of codeine and morphine occurred following delta9-THC (1219). Systemic morphine produced antinociception mediated by spinal 5-HT7, but not 5-HT1A and 5-HT2 receptors (290). The I2-imidazoline binding site ligand, phenyzoline enhanced morphine analgesia on the tail-flick and hot-plate tests, whereas its ortho-phenyl derivative decreased this response (394). Synergistic analgesia occurs between the phosphodiesterase inhibitor, zaprinast and morphine in the spinal cord of rats on the formalin test (1276), whereas riboflavin enhanced this measure as well (84). Blockers of the gap junction channel, carbenoxolone and Gap27 reduced morphine analgesia after intrathecal administration (1090). Co-administration of the non-competitive NMDA antagonist, MK-801 and morphine attenuated neuropathic pain (441). [Ser1]-histogranin, a peptide NMDA receptor antagonist enhanced morphine analgesia in the formalin test (438). Naloxone pretreatment and post treatment blocked the morphine-induced and dipyrone-induced analgesic potentiation in the tail-flick test in rats (467). Hemokinin-1, a mammalian tachykinin peptide, markedly potentiated the antinociceptive effects of morphine administered at the peripheral and supraspinal level (364). Enhanced antinociceptive effects of morphine were noted in histamine H2 receptor gene KO mice (790). Lithium potentiated morphine analgesia in a time-sensitive manner near the end of the light phase of the light:dark cycle (549). Ketamine enhanced the analgesic, cataleptic and hypoactive effects of morphine in a naloxone-reversible manner, with the first effect reduced by yohimbine, but not glibenclamide (163). BIBP3226, a NPY Y1 receptor antagonist, prevented the ability of neuropeptide FF to reduce morphine analgesia on the tail-flick test (331). Rats over expressing beta-arrestin 2 in the PAG display decreased morphine analgesia (522). The analgesic effects of the CB2 receptor agonist AM1241, but not morphine were absent in CB2 KO mice (497). Animals allowed wheel-running activity displayed significantly less morphine- and M6G-induced analgesia elicited from the vlPAG than inactive rats (744). Both GABA-B and GABA-A agonists reduced morphine-induced Straub tail responses in mice (1295). Resiniferatoxin, a potent capsaicin analogue decreased individual, but not combined immunoreactivities of mu opioid receptors and transient receptor potential vanilloid type-1 neurons in the DRG and dorsal horn. This was accompanied by enhancements in the analgesic magnitude and duration following intrathecal DAMGO and morphine as well as systemic morphine; the number, but not affinity of spinal [^{3}H-DAMGO] binding was also decreased (197). The methanolic extract of Polygala telephiodes antagonized morphine analgesia on the

hot-plate test, improved morphine-induced memory impairments on the elevated plus maze, and suppressed naloxone-precipitated jumping behaviors in morphine-dependent mice (309).

Mu receptors: The 3′ non-coding region of MOR is important is morphine analgesia, and appears to be the reason for a disrupted response in CXBK mice (555). MOR KO mice displayed spinal morphine analgesia at higher doses that was blocked by naloxone and NBNI, but not NTI. Spinal U50488H, but not DPDPE analgesia was observed in MOR KO mice (1254).

3b-ii. Delta agonists and receptors—There is a crucial role of delivery and trafficking of DOR in opioid analgesia and tolerance (1313). Chronic pain-induced emotional dysfunction is associated with astrogliosis due to cortical DOR dysfunction (815). Protease activated receptor 2 agonists activate trigeminal nociceptors and induce functional competence in DOR (885). Dextro- and levo-morphine attenuated delta and kappa opioid-mediated analgesia in MOR KO mice (1235). The mechanical and thermal allodynic as well as the thermal hyperalgesic effects of neuropathic pain were enhanced in DOR KO mice (810). The peripheral delta agonist, [dVal(L)2,Ala(L)5]Enk produced naloxone-reversible and NTI-reversible analgesia induced by osteosarcoma cells injected into mouse femur with greater potency than morphine (131). Dmt-Tic-CH2-Bid, a potent DOR receptor agonist produced NTI-reversible analgesia and reduced immobility during forced swimming (1155). Chimeric glycosylated peptides of Menk and FMRFamide, like [O-Glu-Ser5]Yfa, display increased levels of analgesia and increased bioavailability (737).

3b-iii. Kappa agonists and receptors—The antinociceptive and hypothermic effects of the KOR agonist, Salvinorin A are abolished in a novel strain of KOR-1 KO mice, indicating an effect mediated by KOR-1 and not KOR-2 receptors (33). The antinociceptive effects of salvinorin A in mice were blocked by NBNI, but not by BFNA or Nti (528). Elevated levels of DYN through the activation of bradykinin receptors contribute to the maintenance of neuropathic pain, an effect blocked by bradykinin B1 and B2 receptors only when elevated DYN is present (626; comment by (26)). Spinal cord DYN expression increases, but does not drive microglial prostaglandin production or mechanical hypersensitivity after incisional surgery in rats (1329). U50488H administered into the contralateral hindpaw of animals exposed to unilateral arthritis induction reduced hindpaw oedema, ankle joint inflammation, pain behaviors, inflammatory severity in both hind paws and decreased cartilage oligomeric matrix protein, effects reversed by the peripheral opioid antagonist, naloxone methiodide (99). Whereas morphine was effective in treatment of herpetic pain, the KOR agonist, nalfurafine, suppressed herpetic and post-herpetic pain to similar degrees following intrathecal administration. Spinal MOR was down regulated in the post-herpetic period (1103). Whereas stimulation of MOR and DOR induced hyperalgesia, stimulation of KOR induced analgesia in the hot-plate test in the naked mole-rat (1129). DYN A protein levels, increased in peripheral nerves and footpads of STZ diabetic mice, produces analgesia with activation of KOR and hyperalgesia with activation of NMDA receptors in these mice (531). Salvinorin A produced short-lived (10 min) analgesia on the tail-flick, hot-plate and acetic acid writhing tests, effects blocked by NBNI (755). Nalfurafine, a KOR agonist, inhibited scratching behavior secondary to cholestasis induced by chronic ethynylestradiol injections in rats (502). KT-95, an agonist binding to mu, delta and kappa receptors induced analgesia on the acetic acid writhing test that was blocked by NBNI, but not naloxone. KT-95-induced amelioration of scopolamine-induced memory impairments was unaffected by NBNI, but blocked by sigma antagonism (473).

3b-iv. OFQ/N and ORL-1 receptor—OFQ/N continues to present a complex picture concerning its role in pain responses producing both “pro-nociceptive” and “anti-nociceptive”

actions depending on such factors as site of administration, dose and time course. This section therefore presents these data separately.

Pro-nociceptive actions: Administration of the ORL-1 antagonist, UFP-101 produced analgesia on the formalin test following ventricular administration and hyperalgesia following intrathecal administration. Mice receiving systemic administration of the ORL-1 antagonist, J-113397 or ORL-1 KO mice displayed increased nociceptive behaviors on the formalin test (961). OFQ/N administered into the vicinity of the knee caused a shift in weight bearing to the contralateral leg in rats, and reduced paw withdrawal thresholds and latencies to the affected foot, effects independent of mast cell activation (756). OFQ/N and PGE2 induced allodynia that was blocked by the ORL-1 antagonist, JTC-801 and that was absent in Pro-OFQ/N KO mice. OFQ/N-induced allodynia was unaffected by inhibition of PG production by indomethacin, and the PGE receptor agonist, AE1-329 stimulated OFQ/N from spinal slices and induced allodynia (860). Both partial sciatic nerve transaction and administration of CFA up regulated OFQ/N and the ORL-1 receptor in the dorsal root ganglion; these effects were accompanied by increases in activating transcription factor 3, a neuronal marker of nerve injury (202). Hyperalgesia induced by OFQ/N was blocked by melatonin that in turn produced analgesia that was blocked by naloxone and the melatonin receptor antagonist, luzindole (1188). Two novel ORL-1 peptide analogues, Peptide-1 and –2 produced pro- and anti-nociceptive effects respectively with the latter block the effects of the former. Peptide-1 produced greater decreases in MAP than OFQ/N, and the latter's hypotensive effect was blocked by Peptide-2 (896). The OFQ/N agonist Ac-RYYRIK-ol produced hyperalgesia following supraspinal administration and analgesia following intrathecal administration as well as producing decreased locomotion and increased food intake (427).

Antinociceptive actions: Intrathecal OFQ/N produced analgesia in monkeys that was blocked by the ORL-1 antagonist, (+)J-113397, but not naltrexone with its metabolite OFQ/N(2–17) present at 1.5 but not 4.5 hours later (599). Intrathecal OFQ/N as well as electro acupuncture attenuated in an ORL-1-sensitive manner the hyperalgesia induced by CFA with greater effects observed when OFQ/N and electro acupuncture were combined (365).

3b-v. Human studies

Volunteers: The high-estrogen state was associated with regional increases in baseline MOR availability in women and a greater activation of endogenous opioid neurotransmission during the pain stressor (1050). Using [18F]-fluorodiprenorphine PET in healthy volunteers, it was found that heat pain stimulation reduced diprenorphine binding in limbic and paralimbic areas including the NAC and insula (1062). The 118A>G single nucleotide polymorphism of the MOR appears important in morphine- and M6G-induced pain control in healthy human volunteers (695) as well as reducing alfentanil-induced analgesia and respiratory depression (856). Endogenous pain-inhibitory systems activated by spatial summation are opioid-mediated given naloxone's effectiveness in volunteer male and female subjects (538). Pain thresholds and tolerance were higher in men at high risk for hypertension, with greater ratings of pain and salivary cortisol following naltrexone treatment (13). Oxycodone was more effective than morphine in a multimodal, tissue-differentiated experimental pain model (1064). CRF increased tolerance to pressure, but not heat pain in a naloxone-insensitive manner; the CRF-induced increases in plasma BEND and BLPH did not correlate with the pain tolerance thresholds (743). Both alfentanil and morphine reduced human experimental muscle pain (1002). Transdermal fentanyl was better tolerated than transdermal buprenorphine in terms of skin irritation as measured by erythema (997).

Dental Pain: Both BEND and somatostatin levels were higher in exposed and inflamed dental pulps than in uninjured pulps (806).

Chronic Pain: A meta-analysis (373) revealed that weak and strong opioids outperformed placebo for pain and function in chronic noncancer pain patients. Withholding of opioid therapy should not be a consequence of concern of hastening death in a large hospice population (919). The frequency of the minor allele of the functional A118G polymorphism of the human MOR gene was lower in patients with acute and chronic pain (514). Parental history of chronic pain appears to be correlated with impairments in endogenous opioid analgesic systems (142). Intrathecal morphine produced greater pain relief in patients with non-cancerous chronic back pain, an effect accompanied by increased pruritus, nausea and vomiting (937). Intrathecal fentanyl and sufentanil for the treatment of chronic pain was found to be potent and efficacious (1173). Intravenous morphine was effective in acute pain without much incidence of nausea or vomiting (128), but was marginally better than placebo treatment for acute abdominal pain (381). Chronic pain patients administered oral morphine for one month became hyperalgesic and tolerant on the cold presser, but not a heat model of pain (217). Chronic pain patients administered intrathecal morphine displayed significantly less OFQ/N in cerebrospinal fluid that controls (938). Effective treatment of chronic moderate-to-severe non-malignant pain was observed with polymer-coated extended-release morphine sulfate capsules (840). Ganglionic local opioid application (GLOA) was effective for treatment of chronic headache and facial pain (451). Use of morphine and other opiates was associated with greater risk of fracture due to falls related to dizziness (1158). Opioid switching from oral slow release morphine to oral methadone improves pain control in chronic non-malignant pain over a nine-month follow-up study (359). Administration of naloxone following long-term morphine treatment produced withdrawal and reinstatement of lower morphine doses to produce analgesia in a selected group of chronic pain patients (693). CJC-1008, a long-acting parenteral opioid analgesic was effective in the treatment of postherpetic neuralgia (1177). Hydrocodone produced greater amounts of abuse liability than NSAIDs or tramadol in a female group of patients treated for chronic non-cancer pain (6). Intrathecal hydromorphone reduced intractable nonmalignant pain (304), and was shown to be safe and efficacious in acute emergency-related pain (180). Hydromorphone can be produced as a minor metabolite of morphine within minutes in chronic pain patients (234). Daily-extended release hydromorphone was effective in patients with persistent moderate to severe chronic pain (1211). Oxytrex, a combination of oxycodone and an ultra-low naltrexone dose, minimized physical dependence while providing effective analgesia in patients with low back pain (1205). Extended release oxymorphone appeared effective in pain relief for osteoarthritis of the hip or knee (593), and was more effective and less costly than an oxycodone-acetaminophen combination for osteoarthritis pain of the hip or knee (732). A weight-based dose of oxycodone without adjustment for age between 6 months and 7 years is valuable for evaluating dosing schedules and routes (316). Although rofecoxib was more effective in ameliorating chronic osteoarthritis pain in the knee than acetaminophen, the latter reduced plasma BEND levels (1025). The analgesic effect of pamidronate is not caused by the elevation of BEND level in Paget's disease (77). Serum BEND and IgE are useful biomarkers for itch and disease severity in patients with atopic dermatitis (635). Electro acupuncture was effective in the treatment of postthoracotomy pain (1226). Opioid expenditures and utilization increased in the Medicaid system between 1998 and 2003, particularly for morphine derivatives (135).

Cancer Pain: The use of low morphine doses in opioid-naïve cancer patients with pain appeared to be a reliable method in pain treatment (769). Epidural morphine produced greater analgesia than intravenous morphine for oral cancer surgery with pectoralis major myocutaneous flap reconstruction (1042). Oxycodone was as efficacious and tolerable as morphine for cancer pain treatment (945). Three-cycle fentanyl patch system significantly improves pain control in gynecologic cancer (547). Even though oral morphine is not contra-indicated, there is a trend to use a fentanyl patch as the first-choice strong opioid in cancer patients undergoing titration, in the presence of intractable pain and in the absence of dysphagia (956). S-methadone had a shorter half-life and shorter population pharmacokinetics than R-

methadone in hospice patients with cancer pain (45). There was a beneficial effect of low-dose Ketamine addition to epidural administration of morphine-bupivacaine mixture for cancer pain (1007). Midazolam was an effective adjunct therapy to morphine in the alleviation of severe dyspnea perception in patients with advanced cancer (827).

Surgical Pain: The A118G single nucleotide polymorphism of MOR appears to moderate, but does not mediate the effects of the anger-out trait on postoperative pain responses (144). Age and the prior use of psychotropic agents before surgery were positively associated with a higher rate of postoperative morphine consumption (240). Intrathecal morphine was similar to epidural morphine during liver resection surgery for postoperative pain relief (276), but improved pain relief after abdominal aortic surgery (105), and is effective in treating elderly patients in a regular post surgical ward (667). Intrathecal morphine combined with bupivacaine reduced pain scores following dorsal rhizotomy in children (469). Morphine and Entonox were not very effective analgesics in children undergoing chest drain removal (140). Rectal morphine administered in solution or gel form administered as premedications were effective analgesics (707). Following laparoscopic cholecystectomy surgery, children with sickle-cell disease consume twice as much morphine, report more pain and have longer hospital stays than non-sickle cell children (246). No adverse events in pediatric ketamine sedations occurred with morphine pretreatment (1200). There was an association of MOR gene polymorphism (A118G) with increased morphine consumption for analgesia after total knee arthroplasty (214). Both perioperative and PCA morphine were effective analgesics for total knee arthroplasty (1153). DepoDur, an epidural extended-release morphine formulation produced extended pain relief after knee arthroplasty (452), and high doses of oral morphine were effective after total hip arthroplasty (720). Addition of morphine and ketolorac to ropivacine enhanced pain levels in patients with arthroscopic knee surgery (838). The level of post-operative pain after hip or knee arthroplasty correlated with plasma levels of ACTH, BLPH and BEND (741). Moreover, there was an inverse correlation between the level of post-operative pain and pre-operative levels of CSF BLPH, but not ACTH or BEND (742).

Intraoperative administration of tramadol for postoperative nurse-controlled analgesia resulted in earlier awakening and less sedation than morphine in children after cardiac surgery (218). Tramadol is comparable to morphine during adenotonsillectomy for obstructive sleep apnea in children (494). Tramadol with lornoxicam had the least immunity depression during postoperative analgesia relative to morphine or tramadol alone (1196). Postoperative cognitive function and pain relief was more effective with tramadol as compared to fentanyl patient-controlled analgesia (839). Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery (23), but a meta-analysis still finds its clinical significance undetermined (1005). Acute opioid tolerance developed during infusion of remifentanil for pediatric scoliosis surgery (245). A combination of low ropivacine and morphine doses was not more effective than a higher ropivacaine dose in post-operative analgesia for arterial bypass surgery of the lower extremities (354), and ropivacaine had opiate sparing effects following total knee arthroplasty (1004). The use of continuous epidural infusion or PCA of levobupivacaine produced comparable analgesia in terms of postoperative morphine consumption (278). Caudal bupivacine into the sacral hiatus was more effective than morphine in attenuating intraoperative and postoperative pain and stress responses in children undergoing abdominal surgery (1116). Oxycodone absorption is similar after buccal and sublingual instillation during surgery in children (605). Hydrocodone and acetaminophen combinations produced similar pain relief to rofecoxib in functional endoscopic sinus surgery (221), whereas acetaminophen and ketoprofen produced pain relief in children after soft tissue or orthopedic surgery (471). Remifentanil is a reasonable alternative to fentanyl when using a target controlled propofol infusion in patients undergoing craniotomy for supratentorial lesions (271). Rofecoxib decreased pain scores and morphine consumption after orthopedic, breast and spine surgery (951). Propofol prevented post-operative pruritus induced by epidural

morphine with ropivacaine (607). Intravenous bolus of ultra-low-dose naloxone added to morphine does not enhance analgesia in emergency department patients (97). Preoperative flurbiprofen axetil reduced postoperative pain and morphine needs for spinal fusion surgery (1258). Intraoperative infusion of dexmedetomidine reduces postoperative analgesic requirements (429), and can substitute for fentanyl for bariatric surgery (340).

Caesarean Pain: Oral morphine was better than intravenous morphine PCA in controlling pain after cesarean delivery (264). Chloroprocaine failed to affect epidural morphine for post cesarean delivery analgesia (468). Droperidol, allzapride and propofol, but not promethazine had prophylactic effects on spinal morphine-induced pruritus following caesarean section (480). However, ondansetron and tropisetron did not prevent intraspinal morphine- and fentanyl-induced pruritus in elective cesarean delivery (988). Sufentanil and morphine added to hyperbaric bupivacaine in supraspinal anesthesia for caesarean section improved pain relief (551). Naloxone is rarely used to reverse opiate effects in newborn infants, and its use can be curtailed further without increasing respiratory morbidity (121).

Pre-operative intrathecal morphine enhanced the quality of postoperative analgesia for total abdominal hysterectomy (552). Human opioid receptor A118G polymorphism increased intravenous PCA morphine consumption after total abdominal hysterectomy (213). Intrathecal bupivacaine, clonidine and morphine were more effective than general anesthesia for pain relief and functional status after vaginal hysterectomy (1063). Lornoxicam and ketoprofen reduced post-operative pain and morphine consumption following hysterectomy (550). Women undergoing hysterectomy with a genetic polymorphism of the interleukin IL-1Ra receptor, but not polymorphisms in interleukin-1 displayed greater variability in post-operative morphine consumption for pain (85). Gabapentin attenuated late, but not acute pain after abdominal hysterectomy (335). Intrathecal adenosine was not efficacious for postoperative pain relief following abdominal hysterectomy (1023).

3c. Sex, age and genetic differences

So-called organismic variables play vital roles in the mediation of opioid analgesic responses, and continue to attract a great deal of attention. The first variable is the sex or gender of the animal, and opioid receptor subtypes appear to play important roles in whether there is a sex differences in analgesia and whether it is mediated by circulating gonadal hormones. Test-specific and route-specific variables also come into play that not only informs us about sex differences in opioid analgesic function, but other functions covered in other parts of the review. Aging factors, and especially genetic factors from both inbred and transgenic models continue to play a vital role in our understanding of opioid analgesic function.

3c-i. Sex—Female rats have more PAG-RVM output neurons than males, but males have more activated PAG-RVM cells than females during inflammatory pain. Systemic morphine significantly suppressed CFA-induced Fos in males only (700). Testosterone produces anti-hyperalgesic effects during development in male animals that is maintained during adulthood. Morphine analgesia inhibits inflammation-induced pain in adult gonadectomized, but not neonatally-gonadectomized animals (114). Male rodents and nonhuman primates display greater analgesic responses than females following mu and kappa opioids, particularly those that display low efficacy such that they appear to act as full agonists in males, but antagonists in females. These effects interact with drug history, genotype and the modality, duration and intensity of the nociceptive stimulus (67). Whereas estrogen attenuates OFQ/N analgesia elicited from the spinal cord in the female, testosterone is required for OFQ/N analgesia in the male rat (227). Male rats displayed greater analgesic and antihyperalgesic effects of morphine than females on CFA-induced pain over a 3-week time course (1192). Male rats displayed greater analgesia on a visceromotor pain test following systemic loperamide and inventricular,

but not intrathecal morphine than female rats (521). Female rats, and particularly ovariectomized females displayed more marked leftward shifts in morphine's dose-response curve following the barbiturate, pentobarbital (243). Testosterone levels that affected male sexual behavior and reproductive physiology did not similarly alter basal nociception or morphine analgesia (1085). Chronic sucrose intake reduced the antagonist effect of BFNA on morphine-induced analgesia in female, but not male rats (241). Whereas female Fischer rats showed greater enhancements of contact hypersensitivity following spiradoline, but not SNC80, both sexes showed comparable analgesic and antidiuretic effects following both compounds (314). Neurokinin-1 receptor antagonism decreased mu and kappa opioid-induced enhancement of contact hypersensitivity in females but not males (315). Female rats displayed greater analgesia following oxycodone and U50488H than males, and male rats showed greater hyperalgesia following low oxycodone and U50488H doses (477).

Gender differences in sensitivity to short duration cold pain were associated with variations in the genes for transient receptor potential A subtype 1, catecol-O-methyltransferase and fatty acid amide hydroxylase (579). Placebo analgesia occurred in males with female experimenters, suggesting the importance of the social context in which the pain is recorded (350). Women undergoing dental procedures displayed greater nalbuphine analgesia than men with men displaying a late onset anti-analgesia following nalbuphine. Pretreatment with chlorpromazine or haloperidol enhanced nalbuphine analgesia eliminating any sex difference, and abolished the male anti-analgesia (389).

3c-ii. Aging—Morphine analgesia did not differ between young and aged rats using tail-flick latencies, but older animals showed a decreased analgesic response using a method measuring tail-flick thresholds as well as escape thresholds from electrical stimulation of the mesencephalic reticular formation (249).

3c-iii. Genetic differences—Opioid-induced hyperalgesia that occurs after repeated morphine was strongly strain-dependent in 15 inbred groups of mice with genetic analysis identifying a genetic locus near the beta-2 adrenergic receptor gene. The selective beta2-adrenergic antagonist, butoxamine blocked opioid-induced hyperalgesia (662). Low doses of naltrexone enhanced morphine analgesia and attenuated the development of morphine tolerance in Sprague-Dawley and Long-Evans rat strains, but not in F344 or Lewis rat strains (1115). Fischer rats displayed greater carrageenan-induced swelling and pain as well as lower circulating levels of TNF-alpha and higher levels of IL-6 as compared to Lewis rats. Although morphine reduced carrageenan-induced behaviors in both strains, low morphine doses produced a mechanical allodynia and hyperalgesia in the noninflamed paw of Fischer, but not Lewis rats (337). Lewis rats displayed lower thresholds for CRF-induced analgesia, and higher doses of the CRF antagonist, astressin to produce hyperalgesia that was blocked by morphine pretreatment (1167).

3d. Opioid mediation of other analgesic responses

This section summarizes studies that indicate that analgesia elicited by a wide range of peptides and transmitters can alternatively and respectively be sensitive (3d-i) or insensitive (3d-ii) to opioid manipulations using agonists, antagonists and transgenic knockouts.

3d-i. Opioid-sensitive analgesic responses—Central galanin-induced analgesia was reduced in morphine-tolerant rats, and these animals displayed an up-regulation of galanin-like immunoreactivity in the hypothalamic arcuate nucleus (1238). The neurotensin agonist NT1 displayed analgesia and tolerance on the hot-plate test that was not cross-tolerant with morphine, but was sensitive to naloxone on the jumping, but not licking response. The neurotensin-2 receptor antagonist blocked neurotensin, but not morphine analgesia on the hot-

plate test (130). Intrathecal naloxone inhibited but was less effective than an Oxy antagonist in blocking the ability of Oxy or PVN stimulation to reduce the withdrawal responses to mechanical and cold stimuli in sciatic nerve-ligated rats (782). KOR and DOR antagonists block the antinociceptive effect of Oxy in formalin-induced pain responses in mice (945). VP-induced analgesia elicited from the PAG was blocked by naloxone and V2, but not V1 receptor antagonists (1260). Ghrelin inhibited inflammatory pain induced by carrageenan that was reversed by naloxone (1037). The COX-2 inhibitor, SC236 produced hypoalgesic effects in carrageenan-treated rats that were blocked by naltrexone and absent in morphine-tolerant animals (357). The PKC inhibitor, chelerythrine blocked basic spinal c-Fos expression to formalin pain as well as the naloxone-induced increases in spinal c-Fos expression to formalin pain (842). The analgesic effects of fatty acid amide hydrolase inhibition with URB597 in a rat model of neuropathic pain were blocked by naloxone and CB-1 antagonism (520). Intraplantar injection of CXCL2/3, but not CXCL12 elicited naloxone-reversible mechanical and thermal analgesia that was abolished by systemic polymorphonuclear cell depletion (958). Central melatonin produced antihyperalgesic, but antiallodynic actions in sciatic nerve-injured mice, effects blocked by naloxone and L-arginine (1140), and naloxone blocked melatonin-induced analgesia (723). The SSRI, fluvoxamine produced analgesia that was blocked by intrathecal and systemic administration of general, mu and delta, but not kappa antagonists in sciatic nerve-injured mice (851). Fluoxetine-induced analgesia on the tail immersion and hot-plate assays was significantly less potent in STZ-induced diabetic mice, and reversed by opioid and muscarinic, but not alpha-2 adrenergic antagonists (32). Inhibition of the jaw opening reflex and single neurons in the trigeminal subnucleus caudalis by activation of striatal D2 dopamine receptors was suppressed by striatal quinpirole and reversed by systemic naloxone (991). Desimiprimine and trimipramine-induced analgesia were blocked by Nti, but only by high doses of naltrexone (875). A chlorinated chimeric peptide of Menk and FMRFa, [p-Cl Phe(4)], produced a naloxone-reversible analgesia (447). Analgesia induced by AMPA receptor antagonism in the spinal cord was blocked by mu and delta opioid antagonists (606). L-arginine and a NO donor each produced analgesia that were blocked by naloxone and NBNI, and that was more greatly reduced by antisera directed against DYN(1–13) than against Menk (219). Nitrous oxide produced analgesia on the acetic acid writhing test that was markedly reduced in mice lacking the ORL-1 receptor; acetic acid induced greater increases in plasma ACTH in this KO mice (472). Ketamine produced analgesia in the electrical stimulation test in singly-housed, but not group-housed rats. Whereas ketamine decreased mu opioid binging in the hippocampus in group-housed animals, it increased mu opioid binding in the frontal cortex and hippocampus of singly-housed animals (72). Transfer of CD4+ T-cell lymphocytes blocked visceral hyperalgesia in mice that was reversed by naloxone methiodide (1156). Intrathecal Tyr-d-Arg-Phe-Sar produced analgesia that was blocked by BFNA, naloxonazine and NBNI, but not Nti as well as by an antiserum directed against DYN B, but not DYN A, alpha-neo-endorphin, Menk or Lenk. Pro-DYN KO mice also showed a lesser analgesic response as well (786). Intrathecal Tyr-d-Arg-Phe-Sar produced analgesia that was blocked by selective mu-1, but not mu-2 opioid peptide antagonists (787). Inhibition of fatty acid amide hydrolase produced naloxone-reversible analgesia on the spinal nerve ligation and mild thermal injury tests (181). Naloxone-sensitive analgesia on the acetic acid and formalin tests was observed following (+/−)-cis-(6-ethyl-tetrahydropyran-2-yl)-formic acid (728). Analgesic effects induced by automatically controlled rotating acupuncture in rats were blocked by naloxone (583). Acupuncture inhibited in a naloxone-reversible manner the ability of noxious tooth pulp stimulation to induce Fos expression in the trigeminal nucleus subcaudalis, the transitional region between the subnucleus caudalis and subnucleus interpolaris, the inferior olivary nucleus, the ventrolateral and centrolateral thalamic nuclei, SON, PVN, NTS and rostral ventrolateral medulla (539). Analgesia, but not freezing behaviors elicited by electrical stimulation of the ventrolateral PAG was blocked by naltrexone, whereas midazolam blocked both behaviors (272). The NE and 5HT reuptake inhibitor, venlafaxine produced analgesia that was blocked by high naloxone doses, but not by N-omega-nitro-L-

arginine (426). Mu, but not delta and kappa opioid receptor antagonists block interferon-alpha-induced analgesia from the thalamic nucleus submedius (1186). Tolerance to nicotine-induced analgesia occurred faster in MOR KO mice, nicotine-induced tolerance decreased MOR in C/P and the core and shell of the NAC, but not the spinal cord (377). The visceral analgesic effects of the anti-viral drug, ribavirin were partially blocked by naloxone, enhanced by D2 receptor antagonists, and unaffected by alpha-2 NE or Ach antagonism (1). Whereas carrageenan produced hyperalgesia in control animals, this procedure produced naloxone-reversible analgesia in rats deficient in polyamine (325). NSAID drugs produce analgesia in sheep that are blocked by intrathecal naloxone or atipamezole (692). Artemin reduces herpes-related pain responses in mice inoculated with herpes simplex, an effect associated with decreased spinal DYN, but not BEND (41). Analgine, ketrolac and xefocam each produced analgesia that developed tolerance and cross-tolerance with morphine, but was not blocked by naloxone (1135). The pyrazolyl-thiazole derivative (B50) produced naloxone-sensitive analgesia on the writhing, but not tail immersion test with removal of the methyl group or substitution of a bromo group resulting in loss of analgesia (924). Moderate hypercapnia reduced nociceptive behaviors on the formalin test in a naloxone-reversible manner, but failed to alter arcuate BEND (372). Exposure to an extremely low frequency magnetic field for four days produced analgesia and increased hypothalamic BEND and SP as well as brainstem 5HT (62).

Mu opioid antagonism is observed for the analgesic and GI transit inhibition induced by 7-hydroxymitragynine, isolated from Thai herbal medicine Mitragyna speciosa (746). Analgesia induced by the ethanolic extract from the flowers of Combretum leprosum was observed on formalin-, capsaicin- and glutamate-induced pain tests, effects reversed by naloxone, 5HT1A and 5HT2A antagonists, but not by NO precursors or 5HT3 antagonism (909). The antinociceptive effects of Thymus broussonetli Boiss extracts on the formalin test in mice and rats were blocked by naloxone (310). GDHCF, the active ingredient of the stem bark of Hintonia standleyana increases hot-plate latencies and decreases acetic acid-induced writhing, effects blocked by naloxone, L-NAME and glibenclamide (270). Analgesia on the formalin and hot-plate tests induced by an extract of echium amonenum Fisch & C.A. Mey was blocked by naloxone (460). The tonic and phasic analgesic, anti-depressant and hypothermic effects of the aqueous root extract of Securidaca longepedunculata were blocked by naloxone pretreatment (7). The antinociceptive effect of Hyptis pectinata leaves extract was blocked by naloxone (676). Attenuation of visceral nociception by alpha- and beta-amyrin, a triterpenoid mixture isolated from the resin of Protium heptaphyllum produced naloxone-reversible actions in mice (668). Further, oleanolic acid, a pentacyclic triterpene attenuated mustard oil-induced colonic nociception, an effect blocked by naloxone, but not yohimbine (714). Mechanical allodynia and thermal hyperalgesia caused by chronic constriction injury were blocked by processed Aconiti tuber in a NBNI-sensitive, but naloxone-insensitive manner (1247). A recombinant herpes simplex vector encoding human Pro-Enk to macaque feet induced Enk peptide production in the application area that resulted in a long-acting anti-hyperalgesic and analgesic response to C-fiber stimulation of the application area (1271). Irradiation of osteolytic sarcoma cells improved pain-related behaviors in a manner similar to ketorolac; decreases in spinal pain mediators including DYN and COX-2 were noted (1168).

3d-ii. Opioid-insensitive analgesic responses—Intrathecal, but not ventricular administration of neuropeptide W-23 or Neuropeptide B, endogenous ligands of GPR7 reduced mechanical allodynia induced by sciatic nerve ligation in a naloxone-insensitive manner (1256). Intrathecal CART (55–102) attenuated hyperalgesia and allodynia in as mouse model of neuropathic, but not inflammatory pain in a naloxone-independent manner (259). Intrathecal sensory neuron-specific receptor agonists, bovine adrenal medulla 8–22 and (Tyr6)-gamma2-MSH-6-12, inhibit formalin-induced nociception and neuronal Fos-like immunoreactivity in the spinal cord in a naloxone-insensitive manner (199). Whereas mGlu1 and mGlu5 antagonist co treatment enhanced inhibition of formalin-induced pain, neither antagonist paired with

morphine showed enhanced effects on this measure (1009). L-glutamate sodium in the PVN enhanced acupuncture analgesia, an effect abolished by VP antisera, but only mildly affected by naloxone. PVN L-glutamate sodium increased VP, but not OXY, Lenk, BEND or DYN A (1–13) concentrations (1262). Analgesic activity of a non-peptide imidazolidinedione somatostatin agonist was not reversed by naloxone (521). Although morphine and the 5HT3 agonist, m-CPBG, each reduced phase 1 and phase 2 nociceptive responses on the formalin test, the former was unaffected by intrathecal 5HT3 antagonism, and the latter was unaffected by intrathecal naloxone (1275). The 5HT1A receptor antagonist, WAY-100635 administered systemically or in the RVM attenuated mechanical hypersensitivity in rats with spinal nerve injury in a 5HT-1A antagonist sensitive, but not naloxone-sensitive manner (1208). The SSRI, fluvoxamine produced stronger analgesic effects than fluoxetine or citalopram, but all were naloxone-insensitive (1000). The antinociceptive activity of chemical congeners of improgan optimizing side chain length was nonpioid (484). Delta9-THC and R-methanandamide produced analgesia on the phenyl-p-quinone stretch test in mice that was not blocked by opioid antagonism (437). Analgesia mediated by the TRPM8 cold receptor in chronic neuropathic pain is mediated by Group II/III metabotropic glutamate, but not opioid receptors (925). Vinpocetine and piracetam exerted antinociceptive effects in visceral pain that was potentiated by naloxone (2). The antinociceptive effects of the flavenoid myricitrin following glutamate, phorbol myriusate acetate, bradykinin and acetic acid, but not epinephrine or prostaglandin E (2), were blocked by the NO precursor, L-arginine, but not naloxone (768). A nonpioid pharmacological profile was observed for the novel analgesic M58996 in rat models of persistent and neuropathic pain (12). The antinociceptive effect of thalidomide on zymosan-induced experimental articular incapacitation was insensitive to naloxone antagonism (1142). Mice deficient in CD26, a multifunctional cell surface glycoprotein showed decreases in endopeptidase activity, increased SP, normal endomorphin-2, and short nociceptive latencies that were normalized by a SP NK1 antagonist or dipeptidyl-peptidase activity (424). A long-form alpha-neurotoxin from cobra venom produced potent opioid-independent analgesia (203). Analgesia induced by crotoxin isolated from crotalus durissus terrificus venom was opiate- and Ach-independent (1305). 12-acetyoxyhawtriwaic acid lactone, a diterpene from Egletes viscose, attenuated capsaicin-induced ear edema and hindpaw nociception in mice through a naloxone-independent response (764). The anti-inflammatory and analgesic effects of bee venom acupuncture were blocked by yohimbine, but not naloxone (50). Two compounds derived from bis selenide increased pain thresholds in the acetic acid, capsaicin and tail-flick tests in a naloxone-insensitive manner (993).

4. Stress and Social Status

In comparison with previous years, the amount of studies investigating the role of stressors in analgesic responses has dramatically declined as the use of selective opioid agonists and antagonists as well as the use of animals with knockouts of opioid receptor genes in analgesic processes has dramatically increased. This prompted us to include Section 3b in the present review. This section will continue to examine the phenomenon of stress-induced analgesia (4a), emotional responses in opioid-mediated behaviors (4b), and opioid involvement in stress response regulation (4c).

4a. Stress-induced analgesia

One major theme of stress-induced analgesia is to examine its role vis a vis the opioid system. Ecologically relevant, parametric and sex/age variables continue to play an important role in the neurobiological substrates mediating these responses. Female rats placed on an exercise schedule on running wheels displayed decreased sensitivity to analgesia elicited by morphine, levorphanol, buprenorphine and butorphanol with the sensitivity restored upon return to sedentary conditions (1048). Mice placed on a restricted feeding schedule displayed more

potent analgesic effects to morphine during that time in the light:dark schedule in which feeding was entrained; this effect was not observed in adrenalectomized mice, suggesting a role for endogenous glucocorticoid secretion (1277).

Increased opioid mediated warm water swim analgesia, but no changes in CWS analgesia were observed in mice lacking the proneuropeptide convertase PC2 (247). CWS, but not fentanyl analgesia was blocked by an anti-neural-cell-adhesion molecule that in cultured DRG neurons, was reduced by BEND in a naloxone-reversible manner (485). Immobility induced by clamping the neck of mice produced a naloxone-reversible analgesia on a tonic pain test, the acetic acid writhing test (781). Rats repeatedly exposed to swim stress developed thermal hyperalgesia that was blocked by naloxone and naloxonazine, but not NTI or NBNI only if the antagonist was administered before each forced swimming episode (1075). Chronic restraint stress induced increased responsiveness in formalin-induced pain in the temporomandibular joint and decreases in the effectiveness of morphine analgesia. In contrast, fluoxetine produced greater analgesic effects in the stressed group (382). Swim stress-induced analgesia on the hot-plate test observed in wild-type male and female mice was reversed in MOR-KOR-DOR KO mice and in MOR-DOR KO females. Swim stress-induced analgesia delayed front- and hindpaw behaviors on the hot plate test, increased tail-flick latencies and increased ACTH and corticosterone levels in both wild-type and KO females (236).

4b. Emotional responses in opioid-mediated behaviors

Anxiogenic responses were elicited by CFA or sciatic nerve ligation as well as by ventricular administration of mu or delta antagonists or DYN. CFA or neuropathic pain decreased [35S] GTPgammaS binding induced by DAMGO or SNC80 in amygdala neurons, but increased this response following kappa agonists in the amygdala (812). Ventricular morphine produced anxiolytic effects on the elevated plus maze that was mediated by vasopressinergic system and nitric oxide pathways (544). Prenatal exposure to unpredictable shock enhanced subsequent morphine-induced CPP and greater depressive behaviors on the forced swim test; these behaviors were blocked by postnatal exposure to an enriched environment (1261). Morphine and naloxone administered into the inferior colliculus respectively decreased and increased defensive attention, immobility and escape behavior thresholds. Whereas morphine stimulated bicuculline-induced increases in fear thresholds when administered into the inferior colliculus, naloxone reduced those thresholds (161). Lateral, but not medial septal injections of morphine produced naloxonazine-sensitive reductions in open-arm exploration in the plus maze, and reduced head-dipping frequency in the hole board, effects associated with decreased Fos in ventral septum, dorsal hippocampus and anterior hypothalamus (647). Morphine, U50488H and SNC80 decreased rearing and climbing activity in the staircase paradigm with naloxone blocking the first and second, but not third agonist. Morphine produced analgesia on the hot-plate test, but failed to alter anxiety-related behaviors on the four-plate test. In contrast, alprazolam and diazepam reduced anxiogenesis, but failed to alter hot-plate latencies (957). CRF produced anxiogenesis, locomotion and grooming behaviors that were reduced by low doses of chronic morphine and increased by high doses of chronic morphine (104). Naltrexone microinjections into the central, but not the basolateral amygdala blocked the anxiolytic effects of diazepam in the plus maze (151). There was an atypical anxiolytic-like response to naloxone, but not selective opioid receptor subtype antagonists in benzodiazepine-resistant 129S2/SvHsd mice relative to C57BL/6JOlaHsd mice (965). Whereas Nti attenuated diazepam-induced anxiolytic effects in rats over expressing Pro-Enk in the amygdala, neither Nti nor BFNA altered diazepam-induced anxiolytic effects in normal animals (923). Social defeat stress-induced behavioral responses were mediated by the endogenous kappa opioid system such that NBNI and lack of the pre-pro-DYN gene blocked this immobility and subsequent cocaine-induced preferences in stressed mice (759). OFQ/N produces anxiolytic-like effects in the elevated plus maze and in the conditioned defensive burying test in rats that was blocked by

the ORL-1 antagonist, UFP-101 (1169). Coupling of ORL-1 receptors to G proteins was decreased in the NAC of anxious relative to non-anxious mice (644). The anxiogenic, hyperactive and impairments in spontaneous alternation induced by buprenorphine were impaired by high doses of clorazepate; buprenorphine-induced memory impairments were unaffected (643). Combinations of nalorphine and naloxone reduced climbing and rearing as well (779). SNC80 produced anxiolytic effects that were blocked by NTI, whereas Nti produced anxiogenic behaviors (898). Aged mice displayed increased anxiety-related behaviors on the light-dark and elevated plus-maze tests that were accompanied by increased astrocytes in the cingulated cortex due to dysfunction of DOR systems (816). Naltrexone reduced the reinforcing effects of ultraviolet preference in subjects who were frequent tanners (558).

4c. Opioid involvement in stress response regulation

Centrally-administered OFQ/N activates the hypothalamic-pituitary axis through and ORL-1 receptor-mediated up-regulation of CRF and POMC mRNA and stimulation of corticosterone release in rats (642). Prenatal morphine exposure blocks prenatal stress-induced up-regulation of mineralcorticoid and glucocorticoid receptors in the hippocampus in male, but not female rats. However, prenatal morphine exposure blocks prenatal stress-induced decreases in mineralcorticoid binding in the hippocampus of diestrous females, and glucocorticoid binding in the hypothalamus of estrous females (953). Blood-brain barrier increases in protein tracers were observed by the second day of morphine withdrawal that was accompanied by stress symptoms, whereas acute methamphetamine produced extravasation of endogenous serum protein (1020); the former effect was blocked by the 5HT modulator, AP-267 (1021). Naloxone and CRF increased deoxycorticosterone levels in cynomogolus monkeys (918). Both in vivo restraint in carp and in vitro administration of carp interleukin-1beta stimulated AMSH and n-acetylated BEND from the pituitary (774). Graded exercise increased plasma BEND levels in both young and old horses, whereas it failed to alter plasma cortisol levels in old horses (717). Whereas baseline Enk and DYN levels in the hippocampal dentate gyrus were lower in the Flinders Sensitive relative to the Flinders Resistant line of mice, running failed to affect opioid levels in the former group, but decreased dentate DYN mRNA in the latter group (102). The increases in ProEnk mRNA in developing Syrian hamsters by glucocorticoids are dependent on age and adrenal versus brain tissue (358). Plasma BEND, ACTH and cortisol responses were all higher and similar for arm and leg exercises at two exercise intensities in untrained subjects (725). Human exercise increased plasma Pro-Enk peptide F immediately and 15 min later, with peptide content in white and red blood cell layers increased after 15 min (153). Naloxone enhanced the ability of heat to induce exhaustion during high intensity exercise, an effect accompanied by increased in plasma BEND and ACTH. In contrast, cold attenuated these naloxone-induced effects (39). A polymorphism in MOR at A118G enhanced increased cortisol responses to naloxone, but lowered increased cortisol responses to social stress in volunteer subjects (211).

Greater levels of basal cortisol, but not ACTH were found in healthy subjects with a 118G allele in exon 1 of the MOR gene (68). Male subjects had greater HPA axis responses to a psychological stressor, whereas female subjects had greater cortisol reactivity to a naloxone challenge (1139). Interference with pre-pro-orexin, but not co-localized pre-pro-DYN in the perifornical hypothalamus reduced rapid eye movement sleep (192). Basal release of opioids appears not to affect eNOS expression in normal in vitro culture conditions, but might do so under stress (1006). Preoperative extradural bupivacaine and morphine lowered the cortisol stress response in dogs undergoing femoral-tibial joint surgery (1036). The ability of methanolic, ethanolic and aqueous extracts of Spondias mombin L to reduce novelty-induced rearing behaviors was insensitive to naltrexone (46).

5. Tolerance and Dependence

The most-often studied variables in the functional analysis of opioid-mediated responses next to analgesic processes are the underlying neurobiological roles of tolerance and dependence. This has continued unabated through the years, and continues to be a focus in this review. Developments will be reviewed for animal models in tolerance (Section 5a), and animal models in dependence and withdrawal responses (Section 5b).

5a. Animal models in tolerance

This section will be divided into the following sub-sections: (i) cellular effects on morphine tolerance, (ii) organismic effects on morphine tolerance, (iii) opioid effects on morphine tolerance, (iv) peptide-transmitter effects on morphine tolerance, and (v) other forms of opioid tolerance.

5a-i. Cellular effects on morphine tolerance—A review (402) analyzes the post-opioid receptor adaptations to chronic morphine focusing on altered functionality and associations with signaling molecules. Another review (53) indicates a crucial role for PKC in MOR desensitization and morphine tolerance. Adenylyl cyclase superactivation induced by long-term morphine, etorphine or methadone is dependent on receptor localized within lipid rafts and is independent of receptor internalization (1315). A proteonomic analysis of rat cerebral cortex, hippocampus and striatum after pellet exposure to morphine revealed 26 distinct proteins that were differentially expressed (94). DeltaFosB over expression in the mouse NAC produced faster development of morphine tolerance and dependence, less morphine analgesia and increased sensitivity to morphine-induced reward through a DYN-sensitive system (1284). Chronic treatment with fentanyl produces a different pattern from morphine in altering internalization or resensitization of MORs in the spinal cord under a pain-like state (501). Whereas morphine and buprenorphine produce tolerance and locomotor sensitization with non-internalization of MOR, etonitazene, which produces rapid endocytosis of MOR shows weak tolerance and a lack of locomotor sensitization (416). Acute and chronic morphine respectively increased and decreased neuroglycan C levels in the NAC, striatum, hippocampus, VTA and amygdala (505). Increased phosphorylation of neurogranin, protein kinase C and Ca2+/calmodulin dependent protein kinase II occurs in opioid tolerance and dependence (1035). Chronic morphine treatment increased the expression of the neural cell adhesion molecule in the dorsal horn of the mouse spinal cord (1091). Chronic morphine-mediated adenylyl cyclase superactivation is attenuated by the Raf-1 inhibitor, GW5074 (1283). The Gbetagamma that interacts with adenylyl cyclase in morphine tolerance originated from a Gs protein (1184). Chronic morphine treatment also increased the expression of vesicular glutamate transporter 1 in the mouse spinal cord (1092). A subpopulation of dorsal horn neurons displays enhanced NMDA receptor function after chronic morphine exposure (1316). Chronic morphine, but not D-amphetamine or nicotine, elevated autoantibodies to the MOR-DOR receptor and to the AMPA Glu1, but not NMDA NR2 subunit receptors (414). Dexamethasone mimics the inhibitory effect of chronic pain on the development of tolerance to morphine analgesia and compensates for morphine induced changes in G protein gene expression (518). Long-term exposure of SH-SY5Y cells to morphine revealed variations in 45 proteins using a whole cell proteomic analysis (830). Inhibition of neuronal nitric oxide synthase antagonizes morphine antinociceptive tolerance by decreasing the activation of p38 MAPK in the spinal microglia (689). Chronic morphine decreased proDYN gene expression in the striatum, but not NAC or hippocampus, whereas chronic oxycodone-6-oxime increased proDYN gene expression in the striatum and hippocampus, but not NAC. Chronic 14-methoxymetopon increased proDYN gene expression in the NAC and hippocampus, but not striatum (589). Chronic morphine decreases MOR signaling and reduces Ca2+ current density in sensory neurons (530). Chronic morphine increased lactate and myo-inositol, but decreased glutamate in thalamus and

somatosensory cortex using nuclear magnetic resonance spectroscopy (1242). Intermittent, but chronic morphine alters protein expression in the NAC (654). Whereas chronic morphine inhibited spinal GABA release, recurrent morphine withdrawal reversed this effect and elevated spinal glutamate levels. In contrast, acute morphine withdrawal increased both spinal GABA and glutamate release (303). Whereas chronic etorphine, but not morphine increased spinal G-protein-coupled receptor kinase 2, dynamin II, beta-arrestin 2 and phosphorylated-conventional PKC, chronic morphine, but not etorphine increased spinal glial fibrillary acidic protein. Manipulations that modulate glial fibrillary protein altered morphine-induced, but not etorphine-induced analgesic tolerance (820). Whereas acute morphine increases adenylate cyclase II activity by Galphas or PKC stimulation regulated by Gbetagamma subunits, chronic morphine decreases adenylate cyclase II activity upon stimulation of the Galphas, but not PKC pathway (994). Down-regulation in dopamine transporter function in striatum occurred during acute morphine addiction and its abstinence in rhesus monkey (1243).

5a-ii. Organismic effects on morphine tolerance—Antinociceptive tolerance was observed following cumulative intracranial microinjections of morphine into the PAG in the rat (795). Morphine analgesic tolerance in 129P3/J and 129S6/SvEv mice was largely absent because of differences in tail-flick responsivity between these strains and C57BL/6J mice (148). Acute morphine tolerance was observed in proestrous, but not ovariectomized female rats; chronic estradiol in ovariectomized animals reinstated acute morphine tolerance. Both forms of tolerance were blocked by the NMDA antagonist, memantine (1024). Chronic morphine drinking establishes morphine tolerance, but not addiction in Wistar rats (101). PKC and PKA inhibitors reinstate morphine-induced behaviors in morphine tolerant mice (1045). Lithium chloride reduced the development and expression of morphine-induced tolerance, but only the development of morphine-induced dependence in isolated guinea pig ileum (18). Continuous naltrexone opioid receptor antagonism abolished continuous morphine analgesia and potentiated morphine hyperalgesia with the latter, but not former effect blocked by the NMDA antagonist, MK-801. After subsiding, morphine hyperalgesia could be reinstated by a low, but not high morphine dose as well as the morphine metabolite, M3G (541). The ability of processed Aconiti tuber to increase the duration of repeated morphine analgesia before inducing tolerance was prevented by both mu (C-CAM) and kappa (NBNI) opioid antagonists (1034).

5a-iii. Opioid effects on morphine tolerance—Chronic morphine pretreatment reduced subsequent morphine-induced, but not heroin-induced, overdose lethality, and failed to form toxic concentrations of M6G (1072). OFQ/N KO mice or normal mice treated with the ORL-1 antagonist J113397 fail to display morphine tolerance when morphine is administered at the same dose. Escalating doses of morphine produce tolerance but not withdrawal symptoms in OFQ/N KO mice (220). Pro-Enk KO mice displayed a blunted morphine analgesic tolerance, but not changes in morphine-induced CPP or morphine-induced motor sensitization (731). Morphine-tolerant rats displayed increased DOR levels in varicosities that appose the postsynaptic membrane and interact with increased GAD. Delta agonists reduced morphine tolerance and significantly inhibited presynaptic GABA release (710). Attenuation of morphine tolerance and withdrawal syndromes was observed by co administration of nalbuphine (513). Intrathecal administration of BAM 22 produced analgesia in both opiate-naïve and morphine-tolerant rats, resumed morphine analgesia in morphine-tolerant rats, but produced hyperalgesia following chronic administration (522).

5a-iv. Peptide-transmitter effects on morphine tolerance—Calmodulin-stimulated adenylyl cyclase gene deletion reduced morphine-induced tolerance and dependence, but not acute analgesia (655). Glycogen synthase kinase 3beta and cyclin-dependent kinase 5 inhibitors abolished morphine-induced tolerance, but not analgesia (880). NRM administration of

GABA-A receptor antagonists augmented the development of morphine tolerance, whereas NRM GABA-A agonists attenuated morphine tolerance development. The GABA-A receptor-mediated IPSC was significantly increased in morphine-tolerant animals, an effect blocked by PKA inhibition (709). Whereas co treatment with the 5HT1A agonist, 8-OH-DPAT in the dorsal, but not median raphe nucleus delayed morphine analgesic tolerance, the 5HT2 antagonist, ketanserin failed to exert effects in the same sites (829). The CCK-2 antagonist, LY225910 administered into the NAC blocked morphine-induced tolerance, but failed to affect the acute antinociceptive effect of morphine (1245). Neuropeptide SF facilitated spinal morphine analgesia in normal and morphine tolerant animals (519). Supraspinal agmatine prevented the development of supraspinal morphine analgesic tolerance (592). The tricyclic antidepressant amitryptaline prevented morphine tolerance during its development and following a subsequent morphine challenge, and up regulated the spinal glutamate transporters GLAST and GLT-1 expression (1099). The NMDA antagonists MK-801 and CPP attenuated morphine tolerance in male, but not intact or ovariectomized female mice. MK-801 also facilitated morphine-induced hyperalgesia in male, but not female mice (147). There was an additive effect of dextromethorphan on the inhibitory effect of anti-NT4 on morphine tolerance (455). The glycine site-specific NMDA antagonist, (+)-HA966 reversed morphine tolerance and enhanced morphine antinociception in morphine-tolerant rats (5). Opioid tolerance was attenuated by AS targeting the regulator of PKC and Ca2+/calmodulin-dependent protein kinase II (1108) as well as by the antagonist, KN93, but not KN92. KN93 also prevented morphine dependence (1109). Inactivation of p38MAPK in spinal microglia inhibits morphine analgesic tolerance (254). Nicotine and morphine produced analgesic cross-tolerance that was blocked by the Ca2+ channel antagonists, nimodipine, diltiazem and flunarizine, but not verapamil (94). The endothelin receptor antagonist, BMS182874 reinstated morphine-induced GTP stimulation in tolerant animals to acute levels, and reduced the EC50 value in tolerant cells to that like acute morphine (87). The induction of morphine hyperallodynia in infraorbital nerve-injured rats was blocked by the 5HT1A agonist, F13640 before or after allodynia induction; F13640 also blocked morphine CPP and naloxone-induced conditioned place aversion (230). Administration of combined calcium-magnesium gels, but not calcium alone attenuated the development of morphine tolerance, morphine dependence and morphine withdrawal (933).

5a-v. Other forms of opioid tolerance—Chronic morphine administration resulted in tolerance to delta opioid receptor-mediated antinociception induced by Delt (922). Intrathecal administration of (−)-oxymorphone, but not (+)-oxymorphone up regulated spinal DYN, produced thermal and tactile hypersensitivity, and produced analgesic tolerance (386).

5b. Animal models in dependence and withdrawal responses

This section will be divided into the following sub-sections: (i) cellular effects on morphine dependence and withdrawal, (ii) organismic effects on morphine dependence and withdrawal, (iii) opioid effects on morphine dependence and withdrawal, (iv) peptide-transmitter effects on morphine dependence and withdrawal, and (v) other forms of opioid dependence and withdrawal.

5b-i. Cellular effects on morphine dependence and withdrawal responses—Morphine dependence was associated with changes in cytoplasmic and mitochondrial enzymes including proteins belonging to GTPase and GST super families, ATPase, asparaginase or proteasome subunit p27 families (93). Genetic variants of the P-glycoprotein gene Abcb1b modulate opioid-induced hyperalgesia, tolerance and dependence (661). Inhibition of adenylyl cyclase II activity following chronic opioid agonist exposure and withdrawal is modulated by phosphorylation (995). Both adenosine and naloxone increased regional cerebral blood flow in morphine-dependent rats accompanied by elevated blood pressure and heart rate (572).

Altered periodicity and expression of circadian clock gene, mPer1, occurred in mouse brain and kidney under morphine dependence and withdrawal (1193). Heroin produced oxidative stress and exogenous antioxidant-alleviated withdrawal responses (1246). MOR and orexin/hypocretin mRNA levels in the LH and striatum are enhanced by morphine withdrawal (1323). Opiate withdrawal induces dynamic expressions of AMPA receptors and its regulatory molecule CaMKIIalpha in hippocampal synapses (1320). Although acute and withdrawal-induced morphine and nicotine increased central and peripheral concentrations of pregnenolone, progesterone and allopregnanolone that was abolished by either adrenalectomy or gonadectomy, a challenge dose of morphine or nicotine 24 h after withdrawal failed to induce effects (233). Agmatine decreased the calcium signal in morphine-dependent CHO cells by activation of IRAS, a candidate for imidazoline I1 receptor (1236). The non-competitive NMDA antagonist reversed the decreases in postsynaptic density proteins in the hippocampus of rat offspring of morphine-addicted mothers (1268). Naloxone-precipitated morphine withdrawal up regulated MOR labeling in NAC, C/P, medial-basal thalamus, basolateral and basomedial amygdala, and VTA in prepubertal male, but not female mice with the GABA B agonist, baclofen re-establishing MOR levels in the first three brain areas in males (281). Naloxone-precipitated, but not spontaneous withdrawal in morphine-dependent rats increased MAPK1/2 phosphorylation in cortex and striatum in a manner similar to acute sufentanil, morphine and SNC-80, but not U50488H; morphine tolerance did not change MAPK ½ activity (42). Consumption of low naltrexone doses in the drinking water of morphine-dependent rats decreased withdrawal signs and increased MOR mRNA expression in the NTS, but not the LC, VTA, frontal cortex, striatum or amygdala (1145). Pregnant females treated with morphine pellets had offspring with higher morphine-induced and endothelin-1-induced G-protein stimulation (927). Acute and chronic morphine treatment respectively stimulated and decreased Na+, K+-ATPase activity with the latter effect augmented by naloxone precipitated withdrawal; these effects were inversely correlated with cAMP accumulation, and were modulated by PKA inhibitors and protein phosphatase inhibitors (1239). There is a lack of cAMP-specific phosphodiesterase 4 activation during naloxone-precipitated morphine withdrawal in rats (585). Chronic morphine increased NR1 NMDA mRNA in the central amygdala, and NR1 and NR2B NMDA protein in the NAC (55). Persistent and reversible morphine withdrawal-induced morphological reductions in spine density were observed in the NAC shell, but not core (280). Enhanced Fos expression was observed in glutamic acid decarboxylase immunoreactive neurons of the mouse PAG during opioid withdrawal (433). Galanin attenuates CREB phosphorylation induced by chronic morphine and naloxone challenge in Cath.a cells and primary striatal cultures (457).

5b-ii. Organismic effects on morphine dependence and withdrawal responses —A requirement for protein synthesis was proposed in the modeling of the onset of drug dependence (536). By adding a transient early phase and a delay of the buildup of protein, a modified ‘Joyce model’ of opioid dependence and withdrawal shows excellent fit of data (936). Genetic differences were noted among 12 strains of inbred mice in the ability of CFA to lower the ED50 of morphine analgesia, enhance morphine tolerance and alter physical dependence signs precipitated by naloxone (660). Global opiate withdrawal scores were evident 56 h later in female relative to male mice, but males display earlier signs of opiate withdrawal using paw tremors and wet dog shakes (876). Maternal deprivation specifically enhanced vulnerability to opiate dependence in rats (1150). Brief early handling increased morphine dependence in adult rats without differences in pre-pro-Enk or MOR levels in the limbic system (1151). Heroin self-administration respectively lowered and elevated ICSS thresholds in naïve and dependent rats. Naloxone increased heroin consumption and reversed heroin-lowering of ICSS thresholds in naïve rats, and increased heroin consumption and elevated ICSS thresholds further in dependent rats (568). Conditioned withdrawal is readily established to discrete cues associated with naloxone-precipitated withdrawal from acute,

infrequent opioid exposure (30). Morphine withdrawal for 18 h and 4 days reduced subsequent morphine analgesia, but the latter response was restored 20 days after withdrawal; this effect was augmented by stress applied after 18 hours. RU38486, a glucocorticoid receptor antagonist increased morphine analgesia four days after withdrawal (294). Naloxone-precipitated withdrawal from morphine produced potentiated startle responses which on the first day were blocked by inactivation of the basolateral or central nuclei of the amygdala or BNST, but not NAC, and which on the second day were blocked by inactivation of the NAC, but not the basolateral or central nuclei of the amygdala or BNST (450). Although the major human metabolite, 6beta-naltrexol, was as potent as naltrexone in precipitating withdrawal in opiate-dependent monkeys, it was far less potent than naltrexone in MOR binding, shifting alfentanil-induced analgesia to the right, and blocking opiate-induced respiratory depression and itching/scratching responses (598).

5b-iii. Opioid effects on morphine dependence and withdrawal responses— Novel depots of buprenorphine suspended in sesame oil have long-acting ameliorating effects for the management of physical dependence to morphine in mice (684).

5b-iv. Peptide-transmitter effects on morphine dependence and withdrawal responses—Whereas over expression of CREBGFP in the LC aggravated morphine withdrawal behaviors and sensitized the cAMP-signaling pathway, dnCREBGFP in the LC attenuated morphine withdrawal behaviors and hyperpolarized LC neurons (442). Mice lacking calcium-calmodulin-dependent protein kinase IV displayed less morphine analgesic tolerance, but no changes in acute morphine analgesia or physical dependence (600). Spinal modulation of CGRP by endocannabinoids participates in the development of opioid physical dependence (1131). ATP-dependent K+ channel blockade decreased nicotine-induced inhibition of withdrawal in morphine-dependent rats (1299). Morphine withdrawal responses were enhanced by inhibition of spinal phosphoinositide 3-kinase (1266). The D1 receptor agonist, SKF82958 was rewarding in morphine-dependent rats, and blocked naloxone-induced conditioned place aversions and somatic signs of opioid withdrawal while increasing P-Glu-R1, but not P-CREB in the NAC. Naloxone reduced SKF 82958-mediated P-GluR1 induction in morphine-dependent rats (183). Yohimbine pretreatment potentiated the efficiency of clonidine to decrease naloxone-precipitated opioid withdrawal signs (1073). Scopolamine attenuated such naloxone-precipitated withdrawal signs as jumping, writhing, weight loss, genital grooming, teeth chattering, ptosis, diarrhea and irritability (1241). Lack of neuropeptide Y attenuates the somatic signs of opiate withdrawal (864). RF9, a neuropeptide FF receptor antagonist, prevented opioid-induced tolerance associated with hyperalgesia (1039). Cross-talk between NO and ERK1/2 signaling pathways in the spinal cord mediates naloxone-precipitated withdrawal in morphine-dependent rats (165). Conantoxins and variants derived from cone snail venom inhibit naloxone-induced withdrawal jumping in morphine-dependent mice (1209). The aqueous and methanolic, but not chloroform extracts of rhizome and aerial parts of Valeriana officinalis L reduced naloxone-induced jumping in morphine-dependent mice (1017). Withdrawal responses from morphine, DAMGO and U50488H as well as the induced Ach response are reduced by isoquinoline alkaloid derivatives from A. mexicana and A. constricta as well as papaverine (166).

5b-v. Other forms of opioid dependence and withdrawal responses—Elevations in ICSS reward thresholds and somatic withdrawal signs are noted following spontaneous and naloxone-precipitated withdrawal from fentanyl (145). Caffeine paired with naloxone produced a quasi-morphine withdrawal syndrome in wild-type, but not adenosine A(2A)R(−/−) KO mice, although both groups had similar levels of striatal mu opioid receptors (98). MOR and KOR agonists antagonize icilin-induced wet-dog shaking in rats (1215).

6. Learning and Memory

Learning and memory effects of endogenous opioid peptides, their receptors, their agonists and their antagonists, as well as genetically altered animals continue to be studied extensively. Recent developments will be reviewed for animal models in CPP (Section 6a), conditioned aversion paradigms (Section 6b), drug discrimination and spatial learning (Section 6c), as well as memory and amnesia (Section 6d).

6a. Opiates and conditioned place preferences (CPP)

The following sections examine opioid CPP, non-opioid effects upon opioid CPP, and opioid effects upon non-opioid CPP respectively.

6a-i. Opioid CPP—CPP can be induced by both morphine and its metabolite, M6G in mice (1165). Rats that displayed high levels of seeking for novelty displayed greater morphine-induced CPP and increased morphine self-consumption (894). Prenatal morphine exposure during the time of opiate receptor appearance does not alter adult morphine-induced CPP or self-administration (952). Restraint, tail-pinch and social defeat in an agonistic encounter each produce the reinstatement of morphine-induced CPP that had been extinguished (950). Involvement of endogenous ligands for mu-, delta- and kappa-opioid receptors was observed in modulating morphine-induced CPP expression in rats (663). Morphine-induced CPP was increased by combinations of methyl-6,7-dimethoxy-4-ethyl-beta-carboline-3-carboxylate and restraint stress in out bred Sprague-Dawley and inbred Fischer 344 rats, yet this treatment decreased morphine-induced CPP in inbred Lewis rats (412). Naloxone, but neither proglumide nor MK-801, altered effects of morphine pre exposure on morphine-induced taste aversions to saccharin (355). Artificial rearing produced a greater morphine-induced CPP as adults than maternal rearing (694). There were differential changes in CREB in rat hippocampus, prefrontal cortex and NAC during the three phases of morphine-induced CPP in rats (1322).

6a-ii. Non-opioid effects on Opioid CPP—Inhibition of the ERK pathway or protein synthesis during re-exposure to morphine or cocaine erases previously learned place preferences (1143). Administration of protein synthesis blockers such as anisomycin or cycloheximide into the hippocampus, amygdala, or NAC, but not the VTA after a conditioning session blocked a morphine-induced CPP which did not return after further conditioning (777). However, another study (1272) failed to observe any effect of the protein synthesis inhibitor, anisomycin in the basolateral amygdala following retrieval to impair expression of morphine CPP. Intrahippocampal inhibition of protein kinase A attenuates morphine-induced conditioned place preference (1018). Inhibition of the cyclooxygenase pathway attenuated morphine-induced conditioned place preference in mice (398). D1/D2 dopamine receptor antagonists and D3 dopamine receptor agonists block foot shock stress-induced enhancement of morphine conditioned place preference (257). Mice lacking dopamine beta-hydroxylase fail to show morphine-induced CPP or hyper locomotion with viral restoration of dopamine beta-hydroxylase in the NTS, but not LC restoring morphine-induced CPP; the enzyme in both sites partially restores hyper locomotion (865). CCK B receptors in the NAC are necessary for the expression of morphine conditioned place preference by acting through D2 dopamine receptors (783). Ultra-low doses of nicotine reduce the expression of morphine-induced conditioned place preference in mice that was reversed by hexamethonium (1013). Theophylline inhibits tolerance and sensitization induced by morphine in a conditioned place preference paradigm (981). The too few mutant zebra fish displays food-induced, but not morphine-induced CPP (630). Administration of l-threo-3,4-dihydroxyphenylserine or carbidopa restored morphine-induced CPP in DBH KO mice that was then blocked by NK1 receptor antagonism (517). Corticosterone suppression can affect in the absence of an inescapable stressor block a morphine-induced CPP and induced changes in NAC DA, indicating that corticosterone is

involved in the expression, but not the induction of stress-induced sensitization of morphine CPP (277). Microinjection of D1 (SCH39166) or D2 (L-sulpiride) antagonists into the NAC shell, and to a lesser degree, the NAC core impaired the acquisition, but not the expression of a single-trial morphine-induced CPP (342). Repeated administration of apomorphine, SKF38393, quinpirole and sulpiride into the NAC enhanced morphine-induced CPP, whereas repeated NAC SCH23390 reduced morphine-induced CPP (1293). Ifenprodil, a NR2B subunit of the NMDA receptor antagonist, blocked CPP induced by morphine, but not natural rewards or social interaction. CPP induced by morphine, but not natural rewards or social interaction augments NR2B NMDA expression in the NAC and hippocampus (711). Intra-ventral pallidal glutamate antagonists block expression of morphine-induced CPP (258). The glycine site/NMDA receptor antagonist, MRZ2/576, reduced the acquisition and expression of CPP and locomotor activity induced by morphine in mice (1330). Ventricular administration of a neuropeptide FF agonist blocked the acquisition of a morphine CPP (724). Agmatine enhanced CPP induced by low morphine doses, an effect augmented by L-arginine, a NO precursor and blocked by L-NAME and aminoguanidine, NOS inhibitors (574); this potentiation was also modulated by alpha2-adrenoceptors (1098). An inhibitory effect of paeonol on morphine-induced locomotor sensitization and conditioned place preference was observed in mice (328). Mice that either lacked the pre-pro-orexin gene or received the orexin antagonist, SB334867A into the VTA failed to display morphine CPP or locomotor sensitization while reducing morphine-induced increases in DA levels (819). Prenatal cocaine exposure blocked morphine CPP as well as increased threat, avoidance and fleeing during a social encounter after isolation (326). Post-training and post-reactivation administration of amphetamine enhances morphine CPP (103).

6a-iii. Opioid effects on non-opioid CPP—The kappa and partial mu opioid agonist, nalbuphine blocked morphine-induced CPP and increased NAC DA metabolites, but failed to affect morphine-induced locomotor sensitization (1110). Glycyl-glutamine, an inhibitory dipeptidyl synthesized from BEND(1–31) inhibited the acquisition and expression a nicotine CPP, and blocked acquisition of a conditioned place aversion induced by chronic nicotine paired with mecamylamine, but not one paired with the kappa agonist, U50488H (404).

6b. Opiates and conditioned aversion paradigms

Morphine administration 20 h prior to naloxone produced greater conditioned place aversion than naloxone alone and better than morphine-6-beta-naloxol pairing, implicating constitutively active mu receptors in this process (1032). The glutamate release inhibitor riluzole attenuated the formation of conditioned place aversion induced by naloxone in rats undergoing a single morphine exposure (525).

6c. Opiates and drug discrimination and spatial learning

The VTA and PAG appear more critical than the parabrachial nucleus in mediating antagonist-induced disruptions of the discriminative stimulus effects of systemic morphine for food reinforcement in both sexes of rats (613). Olfactory repeated discrimination reversal in rats was impaired by morphine but only at doses that affected performance of the well-learned performance discrimination (380). Discriminative-stimulus effects of methamphetamine and morphine are attenuated by cAMP-related compounds (1259). The NMDA antagonist, LY235959 produced additive and supra-additive effects on schedule-controlled responding when paired with butorphanol and nalbuphine, but only additive or sub-additive effects when paired with morphine or buprenorphine. LY235959 potentiated analgesia induced by all opioid agonists (349). Chlordiazepoxide and dizocilpine, but not morphine, selectively impair acquisition under a novel repeated-acquisition and performance task in rats (913). The NMDA antagonists, ketamine, phencyclidine and MK-801 generalized to the discriminative stimulus effects of U50488H, but not TRK-820 in rats. (800). Old mice lacking liver-derived IGF-I had

impairments in the acquisition of spatial memory that were accompanied by increased hippocampal Enk and DYN immunoreactivity but lower mRNA levels of the opioid peptides in the hippocampus (1094).

6d. Opiates and memory

Mu and kappa, but not delta opioid receptor agonists in the NAC regulate attentional learning in the blocking paradigm (504). Odor paired with tactile stroking in rat neonates produced odor preferences, and the acquisition and consolidation of this response was blocked by naltrexone (974). Odor-shock pairings in neonatal animals produce an odor preference that activates c-Fos in the granule cell layer of the olfactory bulb and the anterior piriform cortex. Post-training naltrexone treatment in the amygdala turned the odor preference into an aversion, blocked Fos expression in the piriform cortex, and activated Fos expression in the central nucleus of the amygdala (973). Beta-casomorphin-5, a mu-opioid agonist from bovine milk ameliorated scopolamine-induced impairments in spontaneous alternation behavior and passive avoidance in a mu- and mu1-antagonist sensitive manner (984). Morphine-induced state-dependent memory of passive avoidance was blocked by centrally-acting muscarinic and nicotinic antagonists, but not peripheral nicotinic antagonists. Centrally-acting, but not peripherally-acting anticholinesterase drugs enhanced morphine-induced retrieval (510). Morphine-induced amnesia in passive avoidance was decreased by L-arginine, whereas L-NAME and low morphine doses produced amnesia. Apomorphine inhibited morphine-induced amnesia, and the L-NAME-induced inhibition of morphine amnesia was blocked by DA D1 or D2 receptor antagonists (949). Morphine-induced deficits in passive avoidance learning were ameliorated in part by treadmill running exercise (14). Opioid receptor antagonism in the PAG prevented blocking of prediction errors during Pavlovian fear conditioning (762). Central, but not peripheral opioid receptor antagonism alleviated retrieval of infant fear memories in developing rats (1202). Big DYN increased step-through latencies on a passive avoidance task, increased locomotor activity and increased anxiolytic behaviors on the open field and elevated plus maze with all effects blocked by MK-801. In contrast, DYN A and DYN B increased memory through a NBNI-dependent mechanism, and failed to affect locomotor or anxiolytic responses (621). Mecamylamine-induced reductions in passive avoidance responses were blocked by DYN A (1–13) and DYN A (2–13) with the latter effect insensitive to NBNI antagonism. Mecamylamine-induced extracellular Ach decreases were also abolished by DYN A(2–13) in a kappa antagonist-insensitive manner (474). Ventricular administration of D1 and D2 agonists as well as D2 antagonists on a passive avoidance test day reversed morphine's pre-test amnestic effects, whereas central D1 antagonism prevented the restoration of passive avoidance responses by morphine administration on the test day (1294). Central L-glutamate and MK-801 administered prior to a passive avoidance test respectively reversed and enhanced amnesia induced by pretraining morphine, and respectively increased and decreased morphine state-dependent learning (1296). Morphine state-dependent learning sensitization was decreased by pretreatment with L-NAME and L-arginine (1292). The CB1 agonist, WIN55,212–2, mimicked the ability of pre-test morphine to restore passive avoidance learning, and enhanced morphine's ability as well; the CB1 antagonist AM-251 blocked morphine's and WIN55,212–2's memory-restorative effect (1297). Histamine administration prior to passive avoidance training decreased learning, whereas pre-test histamine reversed this amnestic effect. Mice sensitized with morphine or apomorphine exhibit reversals of histamine's pre-training amnestic effects with morphine's effects blocked by naloxone, SCH23390 or sulpiride (1298). Nicotine reversed morphine-induced amnesia and morphine-induced state-dependent learning, effects blocked by atropine (1300).

7. Eating and Drinking

This section will review ingestive effects as functions of opioid agonists (Section 7a), opioid antagonists (Section 7b), and the interaction of POMC-derived peptides (Section 7c).

7a. Opioid agonists and ingestive behavior

Whereas DAMGO in the NAC increased consumption of two types of flavored food pellets, intake of the preferred pellet in a choice test was respectively enhanced and reduced by DAMGO and naltrexone in the NAC; systemic naltrexone had no effect (1230). DAMGO-induced increases in high-fat feeding were blocked by naltrexone and muscarinic antagonism, but not by antagonists of DA, glutamate or nicotinic receptors (1218). Administration of morphine, but not DAMGO, Dyn or U50488H into the rostral lateral hypothalamus induced feeding, whereas naltrexone into the same site elicited c-Fos activation (652). Whereas bicuculline administered into the ventral pallidum increased saccharin, but not quinine or water in water-deprived rats, pallidal muscimol and SCH23390 reduced this response. Pallidal DAMGO initially suppressed, but then stimulated saccharin intake in water-deprived rats (1029). DAMGO increased fat preference and increased food intake in Osborne-Mendel fat-preferring rats, but only switched preference in S5B/PI fat-resistant rats. Osborne-Mendel rats also had increased MOR and MOR mRNA in the arcuate nucleus (65). Morphine time-dependently prevented acetic acid-induced writhing and the suppression of palatable food intake; haloperidol inhibited the former, but not latter response (1069). Mice with deletion of the DA transporter and thus elevated levels of DA enhances their tendency to work for a food reward without affects on Pavlovian or operant learning for that reward; increased DYN in the C/P and in the core, but not shell of the NAC were observed (156). Chronic infusion of OFQ/N increases food and ethanol intake in alcohol-preferring rats (224). Whereas OFQ/N prolongs feeding induced by food deprivation by decreasing activity of AMSH neurons involved in feeding termination, AMSH at doses capable of reducing deprivation-induced feeding, failed to affect OFQ/N-induced feeding (109). Novel ORL-1 agonists, OS-500 and OS-462 produced greater degrees of feeding than OFQ/N following ventricular, but not systemic administration, an effect blocked by the ORL-1 antagonist, UFP-101, but not NC-797 (308). The ability of the CRF2 receptor agonists, urocortin II and III to inhibit food intake was unaffected by OFQ/N (338). OFQ/N-induced feeding was respectively stimulated by muscimol and inhibited by bicuculline in cockerels (1100). BEND KO mice displayed increased systolic blood pressure, increased MPOA c-Fos activity and higher levels of urinary epinephrine secretion following a high-sodium diet relative to heterozygotes and controls (155). Preoperative epidural morphine together with postoperative transdermal fentanyl restored normal behavior and weight gain in pigs receiving abdominal surgery (715).

7b. Opioid antagonists and ingestive behavior

Increased body weight was observed in MOR KO mice, an effect accompanied by increased hypothalamic NPY mRNA (445). A diaryl ether derivative, (6-(4-{[(3-methylbutyl)amino] methyl}phenoxy)- nicotinamide, capable of displacing MOR, KOR and DOR agonists, suppressed food intake and weight gain in obese rats and mice, but failed to do so in MOR KO mice (1306). Naloxone decreased palatable food intake and increased latency to feed in sated, but not food-restricted rats without affecting food-anticipatory activity (63). Administration of BFNA or CTAP into the dorsal caudomedial shell of the NAC significantly reduced sucrose intake, but did not alter overall chow intake or body weight in rabbits, and also produced specific losses of MOR coupling to their G-proteins (1197). Chronic prevention of MOR G-protein coupling by BFNA in the pontine parabrachial nucleus persistently decreased consumption of standard but not palatable food (1198). CPPs induced by exposure to either high-sugar (Fruit Loops) or high-fat (Cheetos) snack foods were each dose-dependently suppressed by naltrexone (516). Food-induced behavioral sensitization that conditioned

activity was cross-sensitized with cocaine and morphine, and blocked by naltrexone and noncompetitive AMPA antagonism (648). Naloxone failed to reduce sucrose intake in mice with Enk deleted, with BEND and Enk deleted, and with DYN deleted, but showed normal inhibitory responses in mice with only BEND deleted (458). Naltrexone reduced sucrose intake, particularly in a group of rats exposed to a consummatory contrast paradigm and only for the relatively more valuable sucrose solution (1097). Naloxone reduced the ability of orexin and NPY to increase saccharin intake (374). Two studies by the same laboratory showed that central naloxone blocked the ability of central administration of interleukin-1beta to suppress water and salt intake in fluid-deprived and sodium-depleted rats induced by hypernatremia and hypovolemia; interleukin-1beta failed to affect saccharin intake (269,708).

7c. POMC-derived peptides and ingestion

Anticipation of ingestion of a corn oil emulsion increased hypothalamic POMC and orexin mRNA expression for up to 30 min of presentation and until ingestion (789). Mice lacking 11 beta-hydroxysteroid dehydrogenase type 1 show lower levels of arcuate CART and MC-4 receptors, but higher levels of melanin-concentrating hormone, and when on a high-fat diet display an up-regulation of AGRP concomitant with high-fat-induced hyperphagia (274). Starvation in Xenopus laevis produced significant reductions of immunopositive Menk, CART, Fos and urocortin-1 in the hypothalamic magnocellular nucleus accompanied by an increase in CRF (159).

Electroacupuncture produced greater decreases in weight loss and serum leptin levels, coupled with greater increases in serum BEND than diet restriction in female obese subjects (154).

8. Alcohol and Drugs of Abuse

The interaction between opiates and other drugs of abuse, particularly alcohol, continues to be a vigorous area of investigation. This section is organized into a consideration of how the opioid system works in the general area of drugs of abuse (Section 8a), in opiate self-administration (Section 8b) and in interactions with ethanol (Section 8c), THC (Section 8d), stimulants such as cocaine and amphetamine (Section 8e) and other abused drug classes (Section 8f).

8a. Opiates and drugs of abuse: reviews

New challenges and opportunities are reviewed in managing substance abuse in Malaysia (751).

8b. Opiates and self-administration studies

8b-i. Animal studies—Disrupting reconsolidation of conditioned withdrawal memories in the basolateral amygdala reduces suppression of heroin seeking in rats (463). A novel bivalent morphine/heroin vaccine prevented relapse to heroin addiction in rodents (34). Unlimited access to heroin increased daily self-administration across the circadian cycle with decreased levels of food intake occurring across the circadian cycle with daytime intake increasing meal frequency and nocturnal intake displaying smaller and briefer meals; this reduced body weight gain (196). Conditioned heroin-seeking, but not sucrose-seeking behaviors increased early gene expression of ania-3, MKP-1, c-fos and Nr4a3 in the medial frontal cortex, and of ania-3 in the orbitofrontal cortex and NAC (609). Destruction of dopamine neurons in the rostral linear nucleus and periaqueductal gray blocked the rewarding and sensitizing properties of heroin (351). Activation of group II metabotropic glutamate receptors in the NAC shell attenuates context-induced relapse to heroin seeking (117). Adenosine A2a blockade prevented the synergy between MOR and cannabinoid CB1 receptors and eliminated heroin-seeking behavior in addicted rats (1269). CRF antagonism, but not adrenalectomy blocked acute food-deprivation-induced reinstatement of heroin seeking in rats (1012). Nondependent monkeys

increased choice of heroin over food as the heroin dose increased with chronic naloxone and buprenorphine, but not methadone blocking this response. Heroin-dependent monkeys in withdrawal also showed increased heroin choice over food with methadone more effective than buprenorphine in blocking this latter effect (832). Whereas heroin and DAMGO reduced VTA GABA firing rats and internal capsule stimulation post-spike discharges, acquisition of heroin self-administration behavior increased the firing rate of VTA GABA neurons (1068). Prenatal heroin exposure disrupted the development of cholinergic-induced translocation and activation of PKC isoforms (493). Expression of NR1/NR2B N-methyl-D-aspartate receptors enhances heroin toxicity in HEK293 cells (292). 18-methoxycoronaridine acted in the medial habenula and interpedunuclar nucleus to decrease morphine self-administration in rats (403). Cardiovascular responses failed to change after naloxone administration in propofol-sedated piglets during opioid overdose (125). Although a CS previously paired with naltrexone-precipitated withdrawal suppressed heroin seeking in extinction, it elevated responding if rats had prior experience of heroin taking in the presence of the withdrawal CS (464).

8b-ii. Human studies—The prescribing of naloxone to actively-injecting heroin users in Chicago has been associated with a reversal in heroin-induced deaths between 2000 and 2003 (749). Diamorphine (heroin) prescriptions were a long-term commitment in the United Kingdom and were not associated with serious drug, health or social problems (773). The use of “take home naltrexone” for homeless drug users was evaluated for awareness and risk perception (1232). An intranasal diamorphine spray was effective as an alternative to injectable diamorphine for maintenance treatment (784). The incidence of heroin use in Zurich, Switzerland rose between 1975 and 1990, and then declined between 1990 and 2002 (850). There was an association between the availability of heroin and methadone and fatal poisoning in England and Wales between 1993 and 2004 (797). The greatest increases and then declines in methadone deaths happened on Saturdays (798). Heroin-using drivers displayed impairments that correlated with morphine and M6G blood levels (48). Massive decreases in Canadian heroin supply coincided with an Australian heroin shortage (1227). Malay subjects displayed a higher prevalence of current injection drug use, needle sharing and HIV infection than Chinese subjects (184). Methadone-induced overdose deaths were associated with testing positive for a tricyclic anti-depressant or benzodiazepine (179). Methadone maintenance patients are cross-tolerant to morphine analgesia at very high plasma morphine concentrations (44). Methadone-stabilized pregnant patients were safely transferred to buprenorphine using an immediate release morphine transition (532). S(+)-ketamine attenuated the increase in EEG activity and amplitude height of sensory-evoked potentials during rapid opioid detoxification (362). Nonketotic hyperglycemia coma occurred in toddlers after unintentional methadone ingestion (1122). Effective and ineffective methadone dosages overlap considerably for individual opioid-dependent patients (1130). Central morphine concentrations are on average twice as high as peripheral morphine concentrations in heroin overdose victims (244). Although most overdoses occur within 5 min after buying a drug and administering it alone, knowledge of dangers of mixing benzodiazepines with heroin actually increases the likelihood of such behaviors (284). Opioid-dependent individuals who had used heroin, had injected drugs, had witnessed a drug overdose or who had a history of one or more accidental overdoses were significantly more willing to treat with naloxone a companion who had overdosed (624). Opiate overdoses in Rhode Island were more likely in males under 54 in a private residence on weekends around 9 PM (770). Hydrocodone-related fatalities in Ontario typically occurred in the presence of another drug (1179). A strict correlation was not observed for the relationship between plasma cortisol levels, withdrawal symptoms and craving in abstinent and treated heroin addicts (825). Salvia divinorum, which contains the psychotropic, diterpene and the KOR agonist, salvinorin A is mostly smoked to achieve a short-lived but intense psychedelic experience in recreational users (408).

Post-mortum analyses of heroin abusers indicated that subjects with MOR A118G polymorphisms displayed exaggerated down-regulation of prepro-Enk, but also prepro-DYN especially in the NAC shell (300). The ability of levomethadone to reduce pupil size and miosis was attenuated in healthy human volunteers possessing the 118A>G single-nucleotide polymorphism of the MOR gene (697). However, a meta-analysis failed to find a relationship for a risk of substance dependence with the Asn40Asp (A118G) single nucleotide polymorphism of the human MOR (36). Sex, body weight, benzodiazepine use and creatinine clearance are not factors in prescription of heroin for heroin dependency (969). Subjective heroin effects were rated more positively in heroin inhaling than in injecting patients (970); mast cell mediator tryptase concentrations occurred in the latter, but not former treatment (971). Heroin addicts display increased polysialic neural cell adhesion molecule expression in the hippocampus (1203). 6-acetylmorphine assays are more accurate than morphine assays in detecting heroin use in urine samples (71). Analyses for papaverine metabolites were more sensitive for detecting illicit heroin use than analysis of 6-monacetylmorphine (884). DRI and CEDIA, but not REMEDi systems are best for preliminary tests of opiates in human urine (487). Pericardial fluid can be used in forensic assays of heroin and cocaine use (237). Straws used to inhaled heroin vapors contained heroin, its main metabolite, 6-acetylmorphine, caffeine and morphine (595); this was confirmed in an in vitro simulation of ‘chasing the dragon’ (596). The greater incidence of anesthesiologists to fentanyl abuse might be explained by second-hand exposure of fentanyl in air around the mouth of patients during surgery (406). Detoxified opioid-dependent individuals showed greater improvement on all assessment measures following implantation of naltrexone pellets relative to levomethadone treatment (420). Implants of 1.8–3.6 g of naltrexone in opioid dependent individuals maintained plasma levels of naltrexone above 1 nl/ml for 4 to 6 months respectively (1172). Sustained-release naltrexone treatment dose-dependently increased retention in treatment and increased the percentage of negative urine samples in opioid dependent individuals (231). Depot naltrexone was used in lieu of incarceration for coerced treatment for addicted offenders (730), and antagonized the reinforcing, subjective and physiological effects of heroin (1084). Judicially mandated naltrexone by opioid-dependent criminal offenders was analyzed (112,855), and provision of naloxone to injection drug users as an overdose prevention strategy in New York City proved efficacious (376,1231). Intranasal naloxone should be used earlier in a tiered-response emergency medical service unit (76). A minority of patients showed recurrent opioid toxicity within 12 h after pre-hospital care of presumed heroin overdose (124) with survival success greater when cardiac arrest is witnessed by emergency workers (123). Slow tapering from methadone maintenance in a program encouraging indefinite maintenance was generally ineffective in opioid-dependent individuals (160). Buprenorphine maintenance was more effective than tramadol detoxification in increasing outpatient treatment participation in opioid-dependent subjects (158). Naltrexone and buprenorphine was more effective than naltrexone alone in opioid dependent individuals in terms of retention (947) as well as lower positive urine samples for morphine and cocaine metabolites (397). Buprenorphine/naloxone doses greater than 8/2 mg provide minimal incremental value in terms of withdrawal suppression (238). Integrated buprenorphine and naloxone were effective for HIV clinical care in opioid-dependent individuals (1082), and its efficacy was maintained as a function of counseling sessions (347). Introduction of buprenorphine for treatment of substance abuse was robustly predicted by a facility’s prior use of naltrexone and medically-offered withdrawal programs (603). Earlier adoption of buprenorphine was found in private rather than public substance abuse treatment centers (597). Buprenorphine-based outpatient treatment was far more cost-effective than conventional outpatient and inpatient as well as anesthesia-induced detoxification procedures in Australian opiate-dependent individuals (1014), but adverse effects were observed in children after unintentional buprenorphine exposure (391). Slow-release buprenorphine or methadone was better than slow-release morphine in treating heroin addicts in terms of quality of life, symptoms and additional consumption (400). Interactions between buprenorphine and nonnucleoside reverse-transcriptase inhibitor and protease

inhibitor antiretrovirals were evaluated in opioid-dependent, buprenorphine/naloxone maintained HIV-negative volunteers (752,753). Oral slow release morphine over 6 months was safe and efficacious for maintenance treatment in heroin addicts (1148). Buprenorphine tablets were more effective than solutions in producing drug steady state in opiate-dependent individuals (232). Analgesia and sedation in the presence of a naltrexone implant presented a novel pharmacological challenge for emergency care (854). Naloxone and naltrexone, but not tramadol increased measures of opioid withdrawal in opioid-dependent patients (170). Although most patients in a Veterans Administration study successfully detoxified from opioid use following naltrexone treatment, a one-year follow-up revealed that very few remained engaged and stabilized in abstinence-oriented outpatient treatment (266). Predictors of retention in naltrexone maintenance for opioid dependence included methadone use and higher average bags per day of heroin (1083). Low-dose treatment with naltrexone may help reducing the manifestation of opioid withdrawal in dependent populations (719). Further, although behavioral naltrexone therapy improved retention in treatment for heroin-dependent patients, it generally achieved abstinence from opioids after three months, but only in 22% after six months (853). Naltrexone with fluoxetine prevented relapse to heroin addiction in Russian women (615). Anesthetic opioid detoxification did not differ from clonidine detoxification treatment when combined with psychosocial support in opioid dependent patients (336). Opioid demand in heroin-dependent individuals not in treatment is a function of drug supply, unit price and cocaine use (417). In two psychonautic studies, concomitant administration of naltrexone with codeine obviated opioid withdrawal syndrome in a single subject (870). Generic controlled release oxycodone approval was not followed by an increase in misuse or abuse (54). A patient genotyped as CYP2D6 PM could not metabolize oxycodone, but had better success with hydrocodone (1089). An automated DOI kit for urinary oxycodone was more reliable that a point-of-care assay (436).

8c. Opiates and ethanol

8c-i. Animal behavioral models—Enhanced morphine-induced ethanol drinking occurs in alcohol-preferring alko rats sensitized to morphine (859). Spontaneous opioid-mediated and withdrawal-associated CRF1-mediated ethanol drinking was observed in Sardinian alcohol-preferring rats (978). The Naples low-excitability rat line displayed greater alcohol intake and preferences as well as greater sensitivity to quinine and naltrexone than Naples high-excitability rats (892). The greater preferences for ethanol noted in C57BL/6J and hybrid C57BL/6J x CD-1 mice relative to CD-1 mice could not be linked to mesolimbic DA transporter neurochemistry and/or Enk levels, but rather with D2 receptor expression (1033). Whereas mu, but not delta opioid antagonism blocked ethanol-induced sensitization, this effect was not attributable to putative mu1 or mu3 opioid receptors (881). Both MOR and KOR antagonism blocked the reinforcing effects of ethanol on an artificial nipple administered to neonatal rats (846). GABAB receptor stimulation attenuates the locomotor effects of morphine in mice bred for extreme sensitivity to the stimulant effects of ethanol (476). KOR antagonism blocks Nac Da concentrations during operant ethanol, but not sucrose self-administration (298). Low and high doses of buprenorphine respectively increased and decreased ethanol consumption with the latter effect more effectively eliminated by the ORL-1 antagonist, UFP-101 relative to naltrexone (223). OFQ/N agonists reduce ethanol intake while increasing food intake in alcohol-preferring rats in a naloxone-sensitive manner (307). OFQ/N blocked ethanol-induced increases of GABA release, and decreased presynaptic GABA transmission in the central amygdala (962). Although Roman high avoidance strains consume more alcohol than Roman low avoidance strains, the latter show enhanced responsiveness on the hole board test following systemic ethanol. Whereas Roman high avoidance rats have higher Pro-DYN in the NAC shell and Pro-Enk in the cingulate, Roman low avoidance rats have higher Enk gene transcription in the dorsal striatum (425). Female, but not male mice lacking prepro-DYN show lower preferences and consumption of alcohol, but not changes in ethanol-induced loss of righting

reflexes, ethanol withdrawal, ethanol-induced CPP or conditioned taste aversions to ethanol (106). Estradiol valerate increased alcohol intake, decreased body weight and food intake, and reduced the number, but not content of arcuate BEND neurons (537). Losers in a social defeat test consumed more ethanol than winners, and thereby displayed lower anxiety levels. U50488H stimulated ethanol intake more in losers than winners, but only increased approach behaviors in losing mice not consuming ethanol (619). Antagonism of endogenous KOR systems potentiated the increased responsiveness of mesoaccumbal Da neurons to ethanol (1290). Naltrexone pretreatment blocked reinstatement behaviors on an operant ethanol lever induced by ethanol-associated context cues (149). Naltrexone reduced ethanol intake, but not craving behaviors in heavy- and light-drinking mice (329). Naltrexone was more effective in blocking the acquisition of alcohol intake in periadolescent relative to adult alcohol-preferring rats whereas greater tolerance to repeated naltrexone dosing was noted in adult relative to periadolescent rats (979). Both naltrexone and acamprosate reduced alcohol and water intake in a schedule-induced polydipsia task, and reduced head entries for food following the highest antagonist doses (324). Naloxone blocked analgesia induced by alcohol and nicotine alone as well as its synergistic combination (162).

8c-ii. Ethanol-induced changes in opioid systems—Whereas acute ethanol respectively decreased and increased Pro-Enk mRNA expression in the VTA and prefrontal cortex, chronic ethanol increased Pro-Enk mRNA in the core and shell of the NAC (765). Chronic ethanol decreased brain interstitial levels of Menk using in vivo microdialysis (1141). Intubated ethanol perinatally from Days 1–22 increased hypothalamic Menk levels in males and females, NAC Menk levels in females, and lowered Menk levels in the central nucleus of the amygdala in male and female animals (704). Alcohol administration increased extracellular levels of DYN A(1–8) in the rat NAC (727). Alcohol, nicotine and cocaine evoked release of endogenous morphine from the M.edulis pedal ganglia (1326). Chronic naltrexone prevented acute ethanol-induced increases in BEND plasma levels in Warsaw low-ethanol preferring, but not high-ethanol preferring rat strains (1289). Ethanol induces apoptotic death of developing fetal rat BEND neurons through suppression of cAMP production and activation of transforming growth factor-beta 1-linked apoptotic signaling (191). Ethanol suppression of hypothalamic POMC levels and splenic natural killer cell cytolytic activity is associated with a reduction in the expression of proinflammatory cytokines, but not anti-inflammatory cytokines in neuroendocrine and immune cells (189). Prenatal ethanol exposure altered the expression of period genes governing the circadian function of BEND neurons in the hypothalamic suprachiasmatic nucleus (190). Chronic ethanol inhibits natural killer cell function by suppressing the influences of BEND, CRF and the autonomic nervous system signals to the spleen (122). Rats exposed to ethanol through breast-feeding displayed decreased BEND in thymic cells whereas pre-natally ethanol-exposed rats displayed decreased 5HT content in immune cells (250).

8c-iii. Human studies—There are associations between the promoter and 3′ end of Pro-DYN as well as intron 2 of the human KOR with alcohol dependence in human individuals (1251). Acamprosate and naltrexone prevented decreases in ACTH and cortisol during alcohol abstinence, and this was associated with a reduced risk of relapse (575). Acamprosate increased BEND plasma concentrations in patients with high, but not low alcohol preference (576). Naltrexone was found to be superior to acamprosate in relapse prevention of alcoholism among individuals with low levels of clinical depression and alcohol dependence (803). Alcohol-dependent and PTSD subjects displayed significantly higher stress ratings and decreased ACTH responses on the cold pressor task response (129). Targeted naltrexone was better than daily naltrexone in affecting average daily drinking (466). Naltrexone's reduction in blood alcohol level following acute ethanol intoxication accounted for the changes in subjective and behavioral responses to alcohol but not the reduction in HR (902). Naltrexone appeared

effective in the treatment of alcohol dependence particularly with respect to heavy drinking (907). Cognitive behavioral therapy when combined with both naltrexone and acamprosate produced the greatest improvement in outcome measures in alcohol dependent individuals relative to each treatment alone (35, 339; but see (289)). Naltrexone produced strong positive associations between the number of positive social celebratory events and drinking although such events occurred on a minority of days (37). Although naltrexone failed to alter the Positive and Negative Syndrome Scale in alcoholic patients, it further augmented the dose-dependent effects of low, but not high doses of ketamine (616). G-hydroxybutyrate was more effective than naltrexone or disulfiram in reducing craving and altered biological markers of alcohol abuse (826). Although there was no clear advantage of naltrexone, disulfiram or their combination in the treatment of alcohol abuse in patients with psychotic spectrum disorders (903), they were effective in patients suffering from PTSD (904). Asp40 carriers acted as genetic moderators of naltrexone's effects on alcohol cue reactivity (757). Both the A118G polymorphism in the MOR gene and a polymorphism, G1510A, in the acetaldehyde dehydrogenase 2 gene were associated with alcohol dependence in a Japanese population (845). Intervention with morphine at the level of the neuroendocrine-immune axis decreased post-operative pneumonia rate in long-term alcoholics (1060). Nonalcoholic subjects with a family history of alcoholism exhibit lower plasma ACTH and BEND levels following stress and CRF stimulation conditions (1026).

8d. Opiates and THC

CB1 knockout mice display significant increases in striatal preproEnk and preproDYN as well as D4 DA receptor gene expression (396). Both morphine and the CB1 agonist HU210 inhibited Ach and GABA release in the NAC core that was blocked respectively by naloxone and the CB1 antagonist, SR141716 A. Co treatment of the two antagonists reversed their respective blockade of the agonist-induced inhibitory effects (999). MOR and CB1 receptors display reciprocal inhibition of receptor signaling and neuritogenesis (955), thereby failing to form hetero-oliogomers (215). Correspondingly, the acute and chronic suppression by the CB1 cannabinoid receptor inverse agonist AM251 on food intake and body weight was observed in both wild type and MOR KO mice (195). The CB-1 antagonist, SR 141716A blocked the ability of morphine to significantly reduce ventral pallidal GABA efflux, and blocked heroin, but not cocaine self-administration following administration into the NAC, but not the pallidum (157). Morphine in the PVN inhibited in a naloxone-sensitive manner the penile erections induced by PVN administration of the CB1 antagonist SR 141716A as well as the concomitant increases in PVN glutamic acid and NO (1076). Tolerance occurred to the reinforcing effects of morphine in delta9-tetrahydrocannibinol-treated mice (515). Cannabinoid type 2 agonists induce transcription of the MOR gene in Jurkat T cells (113). The acquisition of self-administration of the CB1 agonist WIN 55,212–2 was enhanced by both NBNI administered prior to the session in wild-type mice and in pro-DYN KO mice (766). Prenatal cannabis exposure was associated with increased MOR in the amygdala, reduced KOR mRNA in the mediodorsal thalamus and reduced Pro-Enk expression in the C/P. Prenatal alcohol exposure decreased KOR mRNA in the amygdala, claustrum, putamen and insula cortex (1191). Cannabidiol, a major constituent of cannabis, is an allosteric modulator at mu- and delta-opioid receptors (556). Whereas systemic naloxone and naltrexone prevented THC-induced release of Ach from prefrontal cortex and hippocampus, VTA administration of naloxonazine and the D1 DA receptor antagonist, SCH39,166 produced the same pattern of effects (912).

8e. Opiates and stimulants

8e-i. Animal behavioral studies—An AS to the MOR coding sequence 16–32 attenuated cocaine-induced behavioral sensitization and reward (495). Both contingent and non-contingent administration of cocaine increased Pro-DYN, but not Pro-Enk mRNA levels in the C/P, but not in the NAC or central nucleus of the amygdala (1331). Acute and chronic

administration of the selective delta opioid agonist SNC80 decreased both cocaine- and food-maintained responding in rhesus monkeys (288). Context-dependent extinction occurs for both cocaine- and morphine-induced floor preferences (878). Like repeated forced swim stress, prior activation of kappa opioid receptors with U50488H potentiates cocaine place preference conditioning (758). A combination of cocaine and heroin self-administered at a maximum of three infusions per hour was preferred to either drug alone, and continued during all hours of the light:dark schedule; increased fixed ratio schedules led to extinction (733). Discrete-trials heroin self-administration produced sensitization to the reinforcing effects of cocaine in rats (1199). Administration of estradiol valerate to 8-week old female rats destroyed arcuate BEND neurons and attenuated the acquisition of cocaine self-administration both with and without estrogen replacement therapy (975). The NK-1 receptor antagonist, GR82334 failed to affect cocaine self-administration or hyper locomotion, but attenuated morphine-induced locomotor activity while increasing heroin self-administration (914). Chronic buprenorphine enhanced acute cocaine-, but not acute heroin-induced locomotor increases early in buprenorphine treatment (1056). A combination of morphine and buprenorphine was more effective than U50488H in reducing self-injurious behavior induced by methamphetamine in mice (799). Sub-additive withdrawal occurs from cocaine and kappa opioid agonist combinations in Planaria (935).

8e-ii. Anatomical, molecular and neurochemical studies—MOR KO mice display reduced psycho stimulant effects on Da dynamics in the NAC (745). Cocaine-induced locomotor activity and Fos expression in enkephalinergic D2-type neurons in the NAC are sensitized for six months after repeated cocaine administration outside the home cage (478). Prenatal administration of morphine alone or in combination with cocaine significantly increased mu opioid receptor binding and MOR mRNA on post-natal days 1 and 7, but not 14 in the offspring, effects blocked by the D2 receptor antagonist, sulpiride (88). Prenatal cocaine and morphine respectively increase and decrease brain cyclin-dependent kinase (Cdk5) in rat pups (89). The mu antagonist, clocinnamox blocked cocaine- and methamphetamine-induced preDYN mRNA expression only in the rostral patch compartment of the dorsal striatum, attenuated zif/268 mRNA throughout the dorsal striatum, but did not alter regional psycho stimulant-induced Fos expression (479). DA D2 receptor antagonism in the arcuate nucleus attenuated cocaine-induced NAC BEND increases, and produced extinction behavior in cocaine self-administering rats (295).

DYN KO mice showed decreased NAC DA levels, but no changes in DA uptake under baseline and cocaine conditions, an effect enhanced by kappa agonists and blocked by antagonists. DYN KO mice showed less cocaine-induced locomotor activity, and NBNI failed to alter this response (185). In repeated cocaine-treated animals, CREB responses to DYN are mediated in opposite directions by drugs affecting the D1 and D3 DA receptors (1308). Mice lacking glucocorticoid receptors display decreased DYN and SP as well as D1 and D2 receptors in the dorsal striatum, but not NAC under baseline, but not following cocaine behavioral sensitization. In contrast, Enk mRNA levels are altered during cocaine use in glucocorticoid receptor KO mice (507). Increased striatal c-fos and SP, but not Enk gene expressions were noted in animals given access to running wheels and cocaine than either manipulation alone, an effect that peaked after two exposures (1220).

Methamphetamine-induced increases in striatal dopamine transmission were potentiated by morphine treatment (897). Amphetamine-induced increases in activity as well as striatal Pre-Enk and Pre-DYN mRNA and gene expression were blocked by SL327 and U0126, inhibitors of MAPK and ERK (1027). Chronic methamphetamine down-regulated MOR after 8 days, and after drug cessation, MOR levels returned to normal on Day 11 and then were up-regulated on Day 21 (210). L-methamphetamine and selective MAO inhibitors decrease morphine-reinforced and non-reinforced behavior in rats (459). Acute and chronic amphetamine

treatment decreased concanavalin A-lymphocyte proliferation together with increased Menk in the NAC, prefrontal cortex, spleen, thymus and splenic macrophages (43). The rewarding effects of morphine and methamphetamine were respectively aggravated and enhanced by administration of an astrocyte-conditioned medium into the NAC and cingulated cortex respectively. The glial modulator propentofylline suppressed both morphine's and methamphetamine's rewarding effects (818).

Ecstasy, 3,4-methylenedioxy-N-methylamphetamine, increased pro-DYN mRNA in the C/P following acute and chronic treatment, the prefrontal cortex following acute treatment, the NAC and hypothalamus following chronic treatment, but decreased gene expression in the VTA following acute and chronic treatment. Accordingly, DYN A levels were increased in the VTA following chronic Ecstasy treatment, and decreased in the NAC, prefrontal cortex and hypothalamus after acute Ecstasy treatment (282).

8e-iii. Human studies—Comparisons between heroin and heroin-cocaine polyabusers were made in terms of incidence of psychopathology (61). There was an association of DOR gene polymorphisms in methamphetamine dependence and psychosis (602). A 3- or 4-repeat allele of a 68-bp element in the promoter region of the Pro-DYN gene was found significantly more frequently in patients with methamphetamine dependence than in controls (849). Linkages between an IVS2+G691C single-nucleotide polymorphism and methamphetamine patients and transient psychosis were found (498). The Cocaine- and Heroin-Craving Questionnaires appear to predict dropout rates and in-treatment drug use by clients relative to visual analog scores (462).

8f. Opiates and other drug abuse classes

Three-marker haplotypes of the MOR gene were significant for smoking initiation, but were marginal for nicotine dependence (1309). Morphine increased locomotor activity to a greater degree in nicotine-withdrawn as compared to control mice, and effect accompanied by increased Da and 5HT in the striatum (1162). Beta2 nicotinic Ach receptor KO mice fail to display intra-VTA nicotine self-administration, but have normal morphine self-administration and normal nicotine withdrawal behaviors (86). Reinstatement of nicotine-induced place preferences was produced by nicotine or morphine, effects blocked by the calcium channel antagonists, nimodipine and flunarizine (91). Nicotine induced c-fos within CRF and Enk, but not DYN cells within the PVN (698). Norlaudanosoline and nicotine increase endogenous invertebrate ganglionic morphine (1328). Chronic swim stress increased nicotine's ability to increase plasma ACTH and BEND, but not corticosterone, whereas stress itself increased plasma corticosterone, but not ACTH or BEND (703). There was an association of the MOR A118G variant with reductions in the relative reinforcing value of nicotine in females, but not males (944). Naltrexone was efficacious in smoking cessation especially in females (587). A high dose of oral naltrexone appeared to augment the efficacy of the nicotine patch in producing smoking cessation after 4–6 weeks (866). Naltrexone and cognitive behavioral treatment based on the community reinforcement approach decreased craving in abstinent smokers (972). However, nicotine self-administration in rats was blocked by mecamylamine and hexamethonium, but not by naloxone (273).

9. Sexual Activity and Hormones, Pregnancy, Development and Endocrinology

This section will examine developments in the last year relating the endogenous opioid system to sexual activity (Section 9a), pregnancy (Section 9b), development (Section 9c), and general endocrinology (Section 9d).

9a. Sexual activity and hormones

Fentanyl and naloxone respectively decreased and increased sexually motivated song in male European starlings, a pattern opposite to Da (1001). MOR, DOR and KOR were expressed in human spermatozoa with MOR agonists and delta antagonists reducing motility (9). MOR is located on the acrosomal region and the neck region of human sperm (19). Plasma testosterone was respectively decreased and increased 4 and 24 h after morphine, fentanyl and buprenorphine, whereas plasma estradiol was decreased both 4 and 24 h after morphine, tramadol and buprenorphine in male rats (176). Insulin-like growth factor and growth factor-associated signal transduction pathways inhibited estradiol and progesterone facilitation of female reproductive behaviors as well as the behavioral effects of a DOR agonist (327). DYN A and B as well as Lenk-Arg(6) were more predominant in NAC, C/P and SN during estrus than during diestrus or proestrus, effects associated with cyclic fluctuations in the enzymatic cleavage of DYN (966). Estrogen in female rats suppressed 3H-DAMGO binding in rat cortical membranes in a manner similar to that of CCK-8 and a CCK-8 agonist, JMV-180 with the latter effects blocked by the CCK1 receptor antagonist, JMV-179 (931). Estrogen without progesterone increased ORL-1 mRNA expression in the anteroventral periventricular hypothalamus, MPOA and VMH and increased OFQ/N mRNA levels in the caudal part of the posterodorsal medial amygdala; estrogen and progesterone increased MPOA OFQ/N mRNA in the female rat (1040). LSN2120310, a selective estrogen receptor modulator for both ERalpha and ERbeta treats hot flushes in a morphine-dependent rat model (1178). Different progestins differentially modulate estradiol-induced BEND synthesis and release (915). The reproduction phase-related expression of BEND-like immunoreactivity in the nucleus lateralis tuberis of the female Indian major carp correlates with the number of leutinizing hormone cells and ovary during spawning (985). OFQ/N reduced tuberoinfindibular DA neurons just preceding its stimulation of the prolactin secretory response, effects blocked by ORL-1 antagonism that in turn inhibited the suckling-induced prolactin response (207). Naloxone acts as an antagonist of estrogen receptor activity in MCF-7 cells (334). DORs are found in a subpopulation of GnRH nerve terminals, primarily in the external layer of the ME. DPDPE-induced inhibition of cAMP accumulation and Go down regulation in a GnRH-secreting cell line is blocked by pertussis toxin (910). Estradiol valerate blocked ovariectomy-induced reductions in BEND and allopregnanolone, whereas progesterone increased plasma, hypothalamic and intermediate pituitary BEND. In contrast, medroxyprogesterone increased BEND only in hippocampus and intermediate pituitary (81). Oral tibolone maximally increased BEND in frontal lobe, hypothalamus and neurointermediate pituitary, also increased BEND in parietal lobe, anterior pituitary and plasma, but failed to alter hippocampal BEND in ovariectomized rats in parallel to allopregnanolone increases (392). Sexual dimorphism was observed in the organization of glutaminergic cells in the rat hypothalamic infindibular area for neurokinin B, but not for DYN (225). There was no role for endogenous opioid peptides in the reproductive suppression in subordinate female highveld mole-rats (1124).

Decreased BEND is found in serum and seminal plasma in infertile men (313). Exercise failed to elevate Pro-Enk peptide F during either follicular or luteal phases of the menstrual cycle in women (611). Both fluoxetine and clomipramine prevent premature ejaculation induced by naltrexone in opioid detoxification treatment (3). Normalization of hyperinsulinemia by chronic opioid receptor blockade occurred in hyperandrogenemic women (434).

9b. Pregnancy

Fetal morphine metabolism and clearance are constant during late gestation (387). Naloxone increased serum prolactin, but not the DOPAC/DA ratio in anti-progesterone-treated, but not control pregnant rats, and failed to affect mifepristone-induced decreases in TH immunoreactivity in the arcuate and periventricular hypothalamic nuclei (1052). Pro-Enk A mRNA in the luminal and glandular epithelium fell and GABA A receptor subunit in the

luminal epithelium and stromal cells fell during endometrial receptivity (932). Interleukin-1beta increased SON Oxy secretion and electrical activity in virgin, but not pregnant rats, whereas naloxone enhanced interleukin-1beta-induced SON Oxy secretion and electrical activity in pregnant, but not virgin rats (146). Caesarean section is associated with lower maternal concentrations of epinephrine, NE, ACTH, cortisol, prolactin and BEND compared with other modes of delivery (1171). Elevations in heat pain, but not cold pressor pain were not before and after parturition in pregnant women relative to non-pregnant women (172).

9c. Development

DAMGO and U69593, mu and kappa opioids, induced the differentiation of embryonic stem cells to neural progenitors (578). NMDA lesions placed in the rostral lateral PAG prevented morphine-induced inhibition of maternal behavior. Morphine-sensitized dams would choose to hunt insects rather than engage in maternal behavior, and lesions of the rostral lateral PAG restored the maternal response (1081). DYN induced a kappa receptor-sensitive immediate unconditioned increase in neonatal responsiveness to a surrogate nipple in newborn rats, but did not alter water intake through an intra-oral cannula. Pairing Dyn and suckling on a nipple increased responsiveness 1 day later, indicating conditioning (905). MOR and ORL-1 receptor binding are significantly and respectively increased in the NAC and VTA of two-day old rat pups relative to their dams, effects attributable to increased G-protein coupling which in turn showed greater effects in female relative to male pups in the NAC (483). Neonatally-handled male mice display greater body weights, increased plasma ACTH and corticosterone and decreased hypothalamic ACTH and CRF as adults, effects blocked by neonatal administration of AS directed against POMC (379). Neonatal treatment with naloxone increased the population of Sertoli cells and sperm production in adult rats (262). Facial expressions of pain, high activity levels, poor response to routine care and poor ventilator synchrony were associated with placebo versus morphine therapy, and could be used as markers for persistent pain in preterm infants (126).

9d. Endocrinology

Oxytocin increased ACTH, BEND, LH and prolactin secretion of cycling porcine pituitary cells, with oxytocin and CRF producing additive increases in pituitary BEND (608). The endocrine disruptor, bisphenol-A administered prenatally and postnatally led to an enhancement of the DA-dependent rewarding effect induced by morphine (785). DAMGO reversed the inhibitory effects of PGE1 upon Na,K-ATPase activity in SH SY5Y neuroblastoma cells; DAMGO increased this activity itself through a cyclosporine- and nifedipine-dependent Ca2+ channel system (1229).

10. Mental Illness and Mood

This section summarizes the few studies examining opioid involvement in mental illness (Section 10a) and mood (Section 10b).

10a. Mental Illness

Manipulations of Dyn, CREB, BDNF, MCH or Clock proteins in the NAC and VTA in rodents produce unique behavioral phenotypes directly relevant to depression (834). The kappa agonist, salvinorin A, induced two animal models of depression, namely increased immobility on the forced swim test and increased thresholds for ICSS without altering locomotor activity in an open field. These effects were accompanied by decreased DA, but not 5HT concentrations in the NAC (169). Delta agonists, including DPDPE and Delt II, decreased immobility in the forced swim test and increased frontal cortical BDNF mRNA expression in a NTI-sensitive manner, suggestive of anti-depressant actions (1127). The DOR agonist, (+)BW373U86

decreased immobility and increased BDNF mRNA in the frontal cortex, effects blocked by NTI, but not naltrexone or NBNI. Lenk and Menk produced similar patterns of effects, but up regulated BDNF mRNA in the hippocampus through DOR- and MOR-sensitive mechanisms. In contrast, BEND, endomorphin-1 and endomorphin-2 increased BDNF mRNA expression in frontal cortex, hippocampus and amygdala in a naltrexone-sensitive manner without affecting immobility (1304). The enkephalinase inhibitor, RB101 produced antidepressant and increased locomotor effects without inducing seizures, convulsions of alterations in BDNF mRNA expression (543). Whereas ORL-1 agonists produce anxiolytic-type effects on the elevated plus maze, light:dark aversion, operant conflict, startle, ultrasonic vocalizations and hole board tests, either ORL-1 antagonists and OFQ/N KO animals display anti-depressant effects on the forced swimming and tail suspension tests (388). The ORL-1 agonist, Ro64-6198, produced selective inhibition of marble burying in mice without affecting locomotor activity, thereby exhibiting anxiolytic and antidepressant actions (841).

Sustained sadness in depressed women was associated with decreased MOR binding potential in the left inferior temporal cortex, and in the anterior cingulate in those who did not respond to anti-depressants (567). Adherence to naltrexone in opioid-dependent patients produced less depression symptoms (267). Naltrexone reduced alcohol use and craving as well as symptoms measured by the Hamilton Rating Scale for Depression and Young Mania Rating Scale in patients with bipolar disorder and alcohol dependence (137). Nalmefene significantly improved scores on the Yale-Brown Obsessive-Compulsive Scale modified for Pathological Gambling markedly improving 59% of the subjects (413). Naltrexone rendered one-session exposure less effective for phobia treatment (610). Long-term use of high-dose oral naltrexone is safe using hepatic transaminase profiles in otherwise healthy patients with impulse-control disorders who restrict their intake of over-the-counter analgesics (584).

10b. Mood

People with high neuroticism displayed a graded cortisol, but not ACTH response to naloxone, whereas those with low neuroticism displayed a cortisol response that plateau (718). Reductions by naltrexone were observed on repressive coping and disclosure of emotional material (1278). Volunteers displayed less alertness, increased sedation and increased effort to perform a driving test following oxycodone/paracetamol relative to the NSAID, bromfenac (1157). Midgestational women who were battered showed higher levels of anxiety and depression than non-battered pregnant women, and plasma ACTH and BEND levels showed a significant linear relationship in battered, but not non-battered women (1105).

11. Seizures and Neurological Disorders

This section summarizes the research examining the role of the endogenous opioid system in the mediation of seizures (Section 11a) and neurological disorders (Section 11b).

11a. Seizures

Alfentanil enhanced the amplitude and number of hippocampal CA1 population spikes in control animals, but reduced in such spikes in pilocarpine-treated epileptic rats because of an increase in eliptiform population spikes; these effects were naloxone-reversible (986). Morphine enhanced pilocarpine-induced seizures and status epilepticus (360). The non-peptide delta agonists, SNC80 and (+)BW373U86 produced bilateral ictal and paroxysmal spike and discharges and brief changes in EEG recordings that were subject to quick tolerance and sensitivity to compounds used to treat absence seizures (542). A ketogenic diet decreased Pro-Enk gene expression induced by KA of the granular cells of the hippocampus as well as diminishing KA-induced AP-1 DNA-binding activity, Fos and Jun expression, and the phophorylated form of the three types of JNKs (848). EEG and convulsant effects were noted

following the delta opioid agonist SNC80 in one of four rhesus monkeys (260). Encephalitis induced by neurotrophic Borna disease virus induced seizures and DYN loss through hippocampal dentate cell loss. Kappa agonists prevented the seizure activity that was associated with an absence of DYN in dentate gyrus granule cells and an up regulation of Enk in CA1 interneurons (1054). Kappa agonists and antagonists respectively decreased and increased handling-induced convulsions in ethanol withdrawal-seizure prone, but not ethanol withdrawal-seizure resistant mice (69). HSV-1 infection caused loss of hippocampal DYN A reactivity, and the kappa agonist, U50488H blocked ictal activity (1055). Single nucleotide polymorphisms in the MOR subunit gene were not associated with idiopathic generalized epilepsy (66).

11b. Neurological disorders

Estradiol benzoate, but not tamoxifen was capable of blocking the methamphetamine-induced increase in striatal PPE mRNA levels as well as prevent loss of striatal dopamine transporter binding (263). In Parkinson Disease-related research, MPTP-treated monkeys displayed striatal DA denervation and dyskinesia accompanied by an increase in Pro-Enk-A mRNA levels in the rostral and lateral putamen and rostral caudate, effects blocked by pretreatment with the NR1A/2B NMDA antagonist, CI-1041, but not levodopa (802). Primates with Parkinsonian features with or without L-DOPA-induced dyskinesia displayed normal phenotypes of striatal medium spiny neurons, but showed axonal collateralization of striatofugal cells containing Dyn that project to the pars interna and externa of the globus pallidus (811). Naltrexone is one of eight nondopaminergic drugs in which the MPTP-lesioned promate correctly predicted phase II efficacy (356). Mice lacking preproOFQ/N gene expression display less loss of TH neurons in the SN and CP of MPTP-treated mice, but failed to show changes in methamphetamine-induced losses of DA in the CP (138). Aphakia mice that possess a naturally-occurring Pitx3 deficiency, display levo-dopa-sensitive locomotor deficits and such neuronal losses as DA transporter binding and DA receptor expression, Enk, DYN and neurotensin in a manner similar to adult animals receiving neurotoxin administration (1146). Hemiparkinsonian Nur77 KO mice showed exacerbated rotational responses to L-DOPA, and failed to show up-regulation of striatal Enk mRNA levels; DYN levels were unchanged (1071). SP induced toxic effects on SN DA neurons in a microglia-dependent manner in neuron-glial cultures, an effect reversed by DYN (107). The G-allele of the A118G single nucleotide coding region polymorphism of the MOR gene as well as a history of never smoking were independently associated with increased risk of earlier onset of levodopa-induced dyskinesia in Parkinson’s disease (1074).

R6/2 transgenic mice that display symptoms of Huntington’s disease display decreases in NR2A NMDA receptors in proportionally more striatal cells that contain Enk (20). Huntingtin inclusions do not down-regulate Pro-Enk genes in the R6/2 Huntington’s disease mouse (980). Endomorphin-2 protects against the beta-amyloid aggregate creator, Abeta1–42 in vitro and in vivo (1095). Perinatal 6-OHDA lesions decreased striatal DA and SP and increased striatal Menk, effects reversed by chronic perinatal administration of D1 (SKF-38393), but not D2 (quinpirole) agonists (1044). An adenosine A2A antagonist, CSC, but not U50488H produced a reversion of decreases in the duration of levo-dopa-induced rotations in 6-OHDA-treated rats that was accompanied by an increase in levo-dopa-induced preproDYN mRNA in the lesioned ventromedial striatum (120). Animals receiving traumatic brain injury displayed poor motor function for up to five days post-trauma when treated with morphine (1066). Oral exposure to manganese increased manganese levels and neuron injury in striatum and GP with apoptotic cells containing NOS, Enk and ChAT; these effects reduced locomotor activity and striatal DA content (690).

Decoy peptides that bind DYN noncovalently prevent NMDA receptor-mediated neurotoxicity in the spinal cord as well as DYN-induced paralysis and allodynia (1228). Mice bearing the G93A SOD1 mutation that leads to clinical symptoms of familial amyotrophic lateral sclerosis display prolonged survival with daily administration of morphine and taineptine (216). Intrathecal mu and delta, but not kappa agonists dose-dependently and opioid receptor-selectively induced spastic paraparesis in animals exposed to spinal ischemia (545). Intrathecal nicorandil and small-dose morphine can induce spastic paraparesis after a noninjurious interval of spinal cord ischemia in the rat (366). There was a transient loss of motor-evoked responses associated with caudal injection of morphine in a patient with spondylolisthesis undergoing spinal fusion (401). Unilateral labyrinthectomy causing vestibular behavioral deficits was accompanied by pre-pro-Enk up regulation and increased Fos activity in the medial vestibular nucleus. Blockade of this up regulation with naloxone or antisense probes increased the behavioral deficits (590). DYN anti-sera applied soon after spinal cord ischemia attenuated NOS up-regulation, and reduced both spinal edema and cell injury (1022). Endomorphin-1 and to a lesser extent endomorphin-2 inhibited Cu2+ and AAPH, a water-soluble initiator in inducing oxidation of low density lipoprotein, showing protection against free radical-induced neurodegenerative disorders (670). Naloxone failed to alter a postoperative coma in a patient with complete basilar syndrome after anterior cervical disectomy (1134). Neuroprotection by endogenous and exogenous PACAP following stroke was mediated in part by Enk (201).

12. Electrical-Related Activity and Neurophysiology

The following section will review neurophysiological effects described over the past year for mu (Section 12a), delta and kappa (Section 12 b) as well as ORL-1 (Section 12c) agonists and their receptors.

12a. Mu agonists and receptors

Morphine directly inhibited nociceptors in inflamed skin (1213). Morphine and DAMGO as well as the CB1 agonist, ACEA suppressed capsaicin-induced C-fiber-activated pERK expression in superficial dorsal horn neurons in normal animals. Whereas ACEA continued to suppress the smaller capsaicin-induced pERK expression in the dorsal horn after spinal nerve ligation, the opiates failed to exert suppression, and indeed enhanced the response at high concentrations (561). Spinal dorsal horn hyper excitability occurs following sustained morphine exposure (1093). Distinct populations of spinal cord lamina II interneurons expressed GIRK-dependent current responses to DAMGO (729). Primary afferent NMDA receptors increase dorsal horn excitation and mediate opiate tolerance in neonatal rats (1302). DAMGO inhibited an NMDA receptor-mediated large, low frequency, spontaneous excitatory postsynaptic current in neonatal rat spinal dorsal horn neurons (1118). Glutamate transporter inhibition increases EPSCs in the morphine naïve, but not morphine tolerant neonatal spinal cord slice (1119). Acidic pH increased the efficacy of BEND and morphine inhibition of Ca2 + transients in DRG neurons (1159). Local and systemic morphine produced a naloxone-reversible inhibition of the increase in excitatory amino acid release evoked by local application of capsaicin to the instep of the rat hindpaw (526). Gabapentin depresses C-fiber-evoked field potentials in rat spinal dorsal horn only after induction of long-term potentiation (1107). Endomorphin-2 was more potent than endomorphin-1 in competing for SP(1–7) binding in the dorsal horn of the spinal cord (119). Tramadol, but not its major metabolite, mono-O-demethyl tramadol, depressed compound action potentials in frog sciatic nerves (557). Blood oxygenation level-dependent visualization of synaptic relay stations of sensory pathways using fMRI along the axis - in response to graded sensory stimulation of a limb – produced morphine-induced and naloxone-reversible decreases in activity in the spinal cord (666).

DAMGO produced differential responsiveness in the three different types of spinally-projecting 5HT neurons in the RVM: Type 1 (irregular spontaneous activity, Type 2 (no

spontaneous activity) and Type 3 (repetitive activity without pause) (1310). Morphine inhibited the thermal hypersensitivity and increase in RVM 5HT induced by intraplantar prostaglandin E(2) and capsaicin (1049). BEND and GABA in the rostral ventrolateral medulla decreased specific favored pattern repetition rates (618). MOR agonists induced postsynaptic inhibitory potassium currents in a majority of central amygdala cells in the capsular, lateral and medial divisions, but more frequently inhibited bipolar/fusiform cells than triangular or multipolar neurons (208). DAMGO reduced the amplitude and frequency of polysynaptic inhibition between two neurons in organotypic hippocampal slices without the complication of epileptiform bursting in the preparation (448). Morphine stimulated ascorbic acid release in the NAC, but not the striatum (256). The maximal responses and EC50 values for glutamate-, NMDA-, GNSO-, and glutathione-induced [Ca2+]i increases and glutathione-induced glutamate release are similar in hippocampal neurons of control and morphine-addicted mothers (209).

DAMGO inhibited rat, but not human neocortical release of NE, whereas DPDPE and U50488H inhibited human, but not rat neocortical release of NE. DAMGO, U50488H and OFQ/N, but not DPDPE inhibited both rat and human neocortical release of 5HT (78). DAMGO inhibited sodium currents in prefrontal cortical neurons through PKA- and PKC-dependent mechanisms (1224). Short-term facilitation in the anterior cingulate gyrus occurred following stimulation of the medial thalamus in the rat, an effect reduced by morphine treatment in a naloxone-sensitive manner (1087). Intracortical circuits in rat anterior cingulate cortex are activated by nociceptive inputs mediated by the medial thalamus and are inhibited by morphine (1265). Chronic morphine exposure impaired short-term synaptic depression of the geniculo-cortical visual pathway (1182). Up-regulated L-type high voltage-gated Ca2+ channels cause an increase in diazepam binding inhibitor induced by sustained morphine exposure in mouse cerebrocortical neurons (1028). Whereas both endomorphin-1 and endomorphin-2 increased NAC DA efflux, the former, but not the latter effect was blocked by general, mu and mu-1 antagonists administered into the NAC (861). Whereas endomorphin-1 increased striatal DA release induced by electrical stimulation in a BFNA-sensitive, but naloxonazine-insensitive manner, endomorphin-2 increased striatal DA release induced by electrical stimulation only in the presence of diprotin A, but blocked by mu and mu-1 antagonism (51). Endomorphin-1 and endomorphin-2 inhibited SG neurons by producing an outward current, and reversing at a potential close to the equilibrium potential for K+. Both agonist effects were blocked by K+ channel inhibitors and the mu antagonist, CTAP. In contrast, dipeptidyl peptidase IV inhibition enhanced the effects of endomorphin-2, but not endopmorphin-1 (370).

Although acute morphine increased the firing rate of VTA DA neurons, morphine dependence increased the basal firing rate, but did not increase firing further. Naloxone-precipitated withdrawal returned VTA DA firing to naïve levels (395). DAMGO produced fast-firing inhibition in non-dopaminergic neurons in the SN and VTA of the zebra finch (375). DAMGO, OFQ/N and the CB-1 agonist, WIN55,122, inhibited I(Ba) in a patch clamp preparation in the neonatal rat NTS, effects eliminated by intracellular dialysis of a G(i)-protein antibody. Inhibitors of adenylate cyclase and PKA blocked the CB-1, but not opioid agonist responses (319). Tramadol inhibited LC activity, an effect reversed by alpha-2 adrenergic antagonism, potentiated by PCPA and 8-OH-DPAT, but unaffected by naloxone (83). Tramadol, fentanyl and sufentanil, but not morphine, blocks voltage-operated sodium channels in vitro in heterologously-expressed neurons (435).

12b. Delta and Kappa agonists and receptors

VTA DA neurons projecting to the baso-lateral amygdala displayed greater inhibition by Menk, whereas VTA DA neurons projecting to the NAC displayed greater inhibition by the kappa agonist, U69593. U69593, but not Menk, caused greater inhibition of DA IPSC's in the NAC

than in the amygdala (353). Following chronic vagal deafferentation, Menk inhibited the amplitude of evoked IPSC that was prevented by the group II mGluR-selective agonist, APDC. Mu opioid receptors were co localized on GABA profiles apposing dorsal motor nucleus of the vagus neurons following deafferentation, an effect decreased by APDC (139).

Kappa opioid receptor agonists inhibit VTA DA neurons projecting to the medial prefrontal cortex, but not NAC, and reduce DA levels in the former, but not latter structure (726). Repeated administration of the KOR agonist U-69593 increases stimulated Da extracellular levels in the Nac (367). U50488H inhibited the outwardly rectifying potassium channel in PC12 cells through a pertussis toxin-sensitive G-protein (659). Kappa opioid receptor antagonism enhanced the plateau potential amplitude to increase post spike excitability during spontaneous phasic activity in SON magnocellular neurons, ostensibly by eliminating the random element of burst termination without affecting burst initiation or the slow depolarization that follows burst termination (136). DYN and KOR antagonism inhibit hypothalamic hypocretin/orexin by direct postsynaptic actions by reducing excitatory synaptic tone, whereas electrical stimulation of hypothalamic hypocretin/orexin cells evoked DYN release (658).

12c. ORL-1 agonists and receptors

OFQ/N inhibited the phase delay and Fos expression of SCN neuronal activity induced by either glutamate and/or Compound B, an ORL-1 antagonist. OFQ/N also inhibited a light-induced phase delay of locomotor activity rhythms, an effect blocked by Compound B (1080).

13. General Activity and Locomotion

Female rats tested in the proestrous phase displayed the greatest locomotor sensitizing effects of morphine, whereas those tested in estrus showed the least. Gonadectomy in females treated with estradiol displayed locomotor activity similar to those in estrus (242). Morphine differentially increased activity in pig-tailed macaques depending on injection time with sustained increases when injected in the morning and decreases following increases when injected in the afternoon (1206). Whereas chronic clozapine and sulpiride reduced locomotor activity induced by morphine, sub chronic administration increased morphine-induced locomotor effects that were accompanied by increased D2 receptor mRNA expression (461). Morphine, but not U50488H or SNC80 respectively reduced and increased climbing behavior induced by high and low doses of apomorphine (506). Morphine-induced hyper locomotion, but not analgesia, was blocked by the MAO-A inhibitor, clorgyline (591). Morphine-induced hyper locomotion and reward was accompanied by activation of Src family kinase, and that its inhibitor, PP2 blocked morphine-induced hyper locomotion and reward (813). In contrast, neonatal exposure to bisphanol-A enhanced the rewarding and hyperlocomotor effects of morphine, and was accompanied by DA up-regulation in mouse limbic forebrain (817). Berberine exerted inhibitory effects against morphine-induced locomotor sensitization and analgesic tolerance in mice (1274). An extract of Papaver rhoeas reduced both the development and expression of morphine-induced sensitization of locomotor activity (982). Fentanyl-induced catalepsy was prolonged by both NG-nitro-L-arginine and 7-nitroindazole, effects blocked by L-arginine and naloxone, but not D-arginine (322). GNTI, a KOR antagonist, reduced MK-801-induced hyper locomotion and stereotypy in mice (928).

14. Gastrointestinal, Renal and Hepatic Functions

The following section will review opioid effects described over the past year for gastric function (Section 14a), intestinal function (Section 14b), nausea and emesis (Section 14c), and glucose function (Section 14d).

14a. Gastric Function

Naloxone or vagotomy does not influence centrally octreotide-induced inhibition of gastric acid secretion in rats. (383). Morphine and opium dependence reduced the severity of postoperative adhesions following abdominal gastric surgery (573).

14b. Intestinal Function

Morphine increased GI transit in horses over a 6 h period decreasing fecal weight and moisture as well as defecation frequency (115). The peripherally-acting opioid antagonist, N-methylnaltrexone reversed these effects (116). Morphine tolerance and dependence increased c-Kit expression in duodenum and ascending colon in a CTOP-sensitive manner (60). Morphine and WIN55212-2 each reduced GI transit, but CB1 antagonism or CB1 KO mice failed to affect morphine-induced inhibition. Similarly, neither naloxone nor naltrexone altered CB1 agonist-induced inhibition of GI transit (168). Morphine delivered by pellets produced far greater Salmonella infection in Peyer's patches, mesenteric lymph nodes and spleen than morphine delivered by minipump, an effect attributable to greater inhibition of GI transit. Whereas BEND relaxed rabbit jejunum contractility, naloxone respectively increased and decreased contractility at low and high concentrations respectively (239). Chemical coding of Type I myenteric neurons with different axonal projection patterns in the porcine ileum revealed 78% immunoreacted to Enk (540). Delt II, but not DPDPE or U50488H administered by minipump induced moderate Salmonella infection in the spleen, but did not affect GI transit (341). Both salvia divinorum and its active ingredient, Salvinorin A inhibited electrically-induced contractions of the guinea pig ileum, effects reduced by naloxone and NBNI, but not CTOP or NTI (167). Kappa and delta, but not mu opioid agonists enhanced the inhibition of plasma extravasation during chronic relative to acute intestinal inflammation; these effects were reversed by receptor-selective antagonists and NOS inhibitors. Chronic inflammation increased KOR and DOR protein levels in the whole jejunum and mucosa (524). Pro-Enk A mRNA expression is widely expressed in human GI tract, esophagus, pancreas and gallbladder (794). An inherent acceleratory effect of insulin on small intestinal transit could be observed in naloxone-induced inhibition of this response (889). Chronic desipramine treatment produced subsentivity to kappa agonist-induced inhibition of the peristaltic reflex, but supersensitivity to mu agonist-induced inhibition of propulsion velocity. Chronic desipramine treatment decreased both MOR and KOR in the myenteric plexus and colon of guinea pigs (164). The selective mu opioid receptor antagonist, alvimopan, improves delayed GI transit of postoperative ileus in rats (371). Long pulses of intestinal electrical stimulation inhibited canine intestinal motility in a naloxone-insensitive and NO-insensitive manner, but that was reversed by Ach and NE antagonists (686). Enteral naloxone was effective in treating opioid-induced constipation in a pediatric intensive care unit (1123). Low-dose naltrexone was effective for the treatment of irritable bowel syndrome (554).

14c. Nausea and Emesis

Ondansetron, but not droperidol was an effective prophylaxis of nausea and vomiting after intrathecal morphine in women undergoing caesarean section (891). Loperamide reduced kinetosis-induced nausea, and reduced the increases in ACTH and antidiuretic hormone induced by kinetosis in human volunteers (872).

14d. Glucose Function

DYN A(1–17) increased glucagon release from pancreatic islets with pancreatic beta cells treated with high glucose eliminating DREAM interactions with the Pro-DYN promoter downstream regulatory element, and thereby increasing Pro-DYN promoter activity. DREAM-KO beta cells show increased Pro-DYN activity as well (509). Metformin decreases plasma glucose in STZ-induced diabetic rats through an increase in adrenal BEND secretion to

stimulate mu opioid receptors that leads to an increase in GLUT-4 gene expression and a decrease of hepatic PEPCK gene expression (205). Metaformin also decreased fasting plasma glucose in healthy humans that was accompanied by an increase in plasma BEND and a decrease in serum cholesterol (873). The ginsenoside, Rh2 lowered plasma glucose and increased plasma BEND in a naloxone-sensitive manner in control, but not MOR KO STZ rats (625). Exocrine pancreatic secretion is inhibited by both OFQ/N and DOR agonists (672). The plasma glucose lowering action of Hei-Shug-Pian, the fire-processed product of the root of Aconitum was naloxone-reversible in STZ-induced diabetic rats (675). Myricetin lowered plasma glucose and increased plasma BEND in STZ-induced diabetic mice, effects eliminated by bilateral adrenalectomy, opioid receptor antagonists and by deletion of the MOR gene (682).

14e. Hepatic and Pancreatic Function

The analgesic effects of cholestasis induced by bile duct ligation were reduced by peripheral and direct intraplantar injections of naloxone and naloxone methiodide (833). Delta opioid agonists diminished the growth of the biliary tree in the development of cholestasis (736). Menk regulated oxidant-antioxidant status in the liver of CBA mice (1053). Chronic morphine produced pro-oxidant effects in hepatic glutathione concentrations and its synthesis pathway in a naltrexone-sensitive manner (887). Naltrexone and NOS inhibitors corrected the blunted chronotopic and inotropic responses to beta-adrenergic stimulation in cirrhotic rats (305). Naltrexone reduced development of hepatic fibrosis and cirrhosis, MMP2 activity, and decreased the number of hepatic stellate cells in bile duct ligated rats. Activation of hepatic stellate cells increased expressed delta-1 receptors and increased TIMP-1 expression following delta-1 and delta-2 agonists respectively (306). Monocytes and granulocytes from bile duct-ligated rats increased the percentage of opioid receptor labeling, but a decrease in opioid receptor expression on leukocytes due to cholestasis (793).

There is a low utility of plasma OFQ/N in patients with hepatocellular carcinoma (1058). Cholestatic patients with pruritus found limited relief in visual analogue scales for pruritus following naltrexone with virtually half showing withdrawal symptoms associated with the antagonist (721). Pro-Enk hypermethylation was enhanced in pure pancreatic juice compared with p53 mutation in the diagnosis of pancreatic carcinoma (858). A patient with pancreatic cancer with metastases to the liver has survived after four years of treatment with intravenous alpha-lipoic acid and naltrexone (80). Rifampin-mediated induction of oxycodone hepatic metabolism resulted in negative urine opioid screening (637). Naltrexone administration in alcoholic patients did not induce hepatic abnormalities and indeed alanine aminotrasferase and aspartate aminotransferase declined across the 12-week treatment (1270).

14f. Renal Function

PVN OFQ/N decreased RSNA, increased urine flow rate, decreased urinary sodium and potassium excretion, and increased free water clearance, effects that were blocked by renal denervation, [Arg8]VP and ORL-1 receptor antagonism. The ORL-1 antagonist, UFP-101 in the PVN increased RSNA and decreased urine flow (614). OFQ/N increased cystomanometric bladder capacity and voiding and decreased maximum bladder pressure and urine leakage in controlling neurogenic detrusor overactivity in patients (631). Naloxone abolished the recurrent inhibition of the bladder C fiber reflex in the cat (750). Renal failure and elevated creatinine kinase in a heroin addict was treated by fasciotomy and hyberbaric oxygen therapy (4).

15. Cardiovascular Responses

This section will review the work done in the last year on the role of opioids upon heart rate (Section 15a), cardioprotection and ischemic preconditioning (Section 15b) and blood pressure (Section 15c).

15a. Heart rate

Morphine stimulated vascular endothelial growth factor-like signaling in mouse retinal endothelial cells (187). U50488H increased HR, but decreased both MAP and renal blood flow in lambs aged 1 and 6 weeks (929). KOR is most abundant in the ventricular and atrial myocardium of the heart; DOR, but not MOR is found more in the atria than ventricles. Ligation of a renal artery increased Pro-Enk levels in ventricular myocardium, whereas isoprenaline administration decreased it (1210). Whereas the vagotonic influence of a Menk analogue was not dependent upon a sympatholytic influence, kappa stimulation with U50488H produced a sustained sympatholytic effect that was not easily reversed by NBNI (64). Mu receptor agonism with DAMGO and antagonism with BFNA respectively increased and decreased HR and systolic blood pressure in control rats, but not rats maintained on a high-fat diet despite the latter's baseline increases in systolic blood pressure (470). Activation of DOR through the opening of KATP channels reduces the severity of post resuscitation myocardial dysfunction (332). The monosialosyl ganglioside GM-1 reduces the vagolytic efficacy of delta2-opioid receptor stimulation (265). Repeated delta-1 opioid receptor stimulation reduces delta2-opioid receptor responses in the sinoarterial node (275). Bradycardia induced by D-Ala2, Leu5, Arg6-enkephalin (dalargin) is associated with activation of peripheral KOR (738). Negative inotropic and chronotropic effects of DOR antagonists are mediated through non-opioid receptors (739). Naloxone-precipitated morphine withdrawal induced PKC inhibitor-sensitive increases in Fos in right and left ventricles, and induced PKC inhibitor-insensitive increases in TH and NE in the heart (22). Baroreceptor activation by pressure in the carotid sinus or by electrical stimulation produced depressor and bradycardic responses that were attenuated by NTS administration of endomorphin-2, but not naloxone (1161). The opioid dipeptide, kytorphin inhibited isoprenaline-induced increases in twitch tension of cardiac muscle without affecting twitch tension itself; this effect was blocked by a kytorphin antagonist and naloxone (657). NO release from lobster heart was enhanced by morphine and decreased by naloxone and the NOS inhibitor, L-NAME (173). However, L-NAME, but not naltrexone exaggerated the hemodynamic response to clonidine in bile duct-ligated rats (1112). Naloxone reduced the immediate lethal response to severe shock in a canine model with a combination of hypertonic-hyperoncotic solutions (385). Administration of naloxone and butorphanol combined with exposure to electric foot shock increased heart and respiratory rate in the lizard, Uromastix hardwickii and the rooster, gallus domesticus (940). Buprenorphine and naloxone in combination with antiretroviral drugs increased the QT interval in HIV-negative and opioid-dependent subjects (56). Abrupt withdrawal from oxycontin decreased the left ventricular ejection fraction and produced new regional wall motion abnormalities (959). Increases in serum BEND by programmed exercise training were correlated with improvement of clinical symptoms and quality of life in female mitral valve prolapse patients (496).

15b. Cardioprotection and ischemic preconditioning

Chronic morphine was more effective than acute morphine in restoring diastolic and contractile function during cardioprotection; G(i) inhibition reduced affected both acute and chronic morphine effects. Whereas a G(s) inhibitor or PKA inhibitor blocked only chronic effects, a PKC inhibitor blocked only acute effects (888). Morphine attenuated hemorrhagic shock-induced hyper permeability (182). Morphine and naloxone respectively decreased and increased the rate of hemorrhage-induced hypovolemia in sheep (363). The JAK/STAT pathway is essential for opioid-induced cardioprotection with JAK2 acting as a mediator of

STAT3, Akt and GSK-beta (418). Morphine-induced neuroprotection of hippocampal neurons following oxygen-glucose deprivation was partially blocked by single and combined treatment with chelerythrine, a PKC blocker, epsilonv(1–2), a nPKCepsilon antagonist and MK-801 (333). Opioid preconditioning with Tan-67 induces opioid receptor-dependent neuroprotection against ischemia in rats (1319). Opioid receptor-independent protection of ischemic rat hepatocytes was observed following morphine (581). Central and peripheral opioid receptor antagonists block the cardioprotective effects of fentanyl (649). Myocardial ischemic tolerance occurs in the newborn rat and involves opioid receptors and mitochondrial K+ channels (807). Menk-Arg6-Phe7 produced cardioprotection in the ischemic preconditioning model (283). Activation of ERK and suppression of calcineurin interact in cardioprotection produced by DOR activation (500). The delta agonist, SNC-121 blunted the ischemic-induced increases in cardiac myocyte death produced by mineral oil layering to reduce gas exchange (882). Hypoxic preconditioning reduces glutamate-induced neuronal injury by increasing cortical DADL binding density without affecting DOR mRNA in a NTI-sensitive manner. In contrast, prolonged hypoxia causes severe neuronal injury and decreases DADL binding and DOR mRNA levels (1307). ARD-353, a nonpeptide delta agonist decreased infarct size following coronary artery occlusion that was blocked by a delta-1 antagonist (1201). Kappa agonists significantly reduced infarct size and plasma lactate dehydrogenase level by ischemia-reperfusion in a NBNI-sensitive manner (1312). Kappa-opioid receptor antagonism improved recovery from myocardial stunning in chronically instrumented dogs undergoing left anterior descending artery ischemia (419). Morphine and fentanyl respectively enhance and retard recovery of ventricular function after cardiopulmonary bypass (808).

15c. Blood pressure

Morphine exposure increased MAP and HR, and spontaneous morphine withdrawal produced a prolonged 72 h increase in MAP as measured by telemetry (761). BEND acts in limbic circuits as a depressor in regulation of arterial pressure as it relates to the development of essential hypertension (617). Blockade of endothelin-1 release contributes to the anti-angiogenic effect of POMC over expression in endothelial cells (628). Endomorphins restore the endothelium-dependent relaxation of the rabbit aorta rings exposed to high D-glucose through a NO-c-GMP pathway (683). Endomorphin2-ol was more potent than endomorphin2, but endomorphin1-ol was less potent than endomorphin1 in reducing systolic arterial pressure and heart rate with the former measure reversed by pretreatment with naloxone, atropine, L-NAME and bilateral vagotomy (1281). Morphine, meperidine, fentanyl and remifentanil all produced a concentration-dependent vasorelaxation of human artery rings that was insensitive to naloxone (431). Vasorelaxation induced by U50488H in the pulmonary artery was blocked by the K(V) channel blocker 4-AP, but not glibenclamide or TEA (1088). Arterial partial pressure of oxygen was significantly in horses receiving morphine during upper respiratory tract surgery (699). Stimulation of sensory neuropeptide release by OFQ/N leads to hyperaemia in acutely inflamed rat knees (1303). Remifentanil, sufentanil and fentanyl each induced a dose-dependent vasodepressor response in the cat pulmonary vascular bed that was attenuated by naloxone and diphenhydramine, but not glibenclamide (562,564,565). In contrast, meperidine induced a dose-dependent vasodilator response in the cat pulmonary vascular bed that was attenuated by naloxone and diphenhydramine, but not glibenclamide (563). The dextro-, but not levo-isomer of tramadol produces a concentration-dependent and naloxone-reversible relaxation of rodent aorta precontracted with phenylephrine (939). Tramadol stereoselectively attenuated endothelium-dependent relaxation in isolated rat aorta induced by Ach (1030). Spinal estrogen attenuates the exercise pressor reflex without changing gene expression of opiate receptors in the DRG (998). Hemorrhage induces c-Fos in arcuate POMC neurons and increases POMC mRNA in the MBH. Caudal arcuate administration of lidocaine inhibited hemorrhagic hypotension and bradycardia without affecting MAP or HR (405). Methylnaltrexone inhibits opiate and VEGF-induced angiogenesis through receptor transactivation (1043).

Transcutaneous magnetic stimulation of the Jianshi-Neiguan acupoints decreased the reflex pressor response, effects blocked by median nerve denervation or by pretreatment with general, kappa, delta, but not mu antagonists (1324). Naloxone blocked the ability of SP(1–7) to inhibit SP-induced vasodilation in a rodent model of inflammation of the hindpaw (1217).

Exaggerated opioid analgesia is observed in persons at enhanced risk for hypertension (754). Combined spinal-epidural anesthesia with intrathecal bupivacaine produced analgesia with lower incidence of maternal hypotension for cesarean delivery (1114). Low, but not high levels of trait anger in chronic low back pain sufferers were associated by naloxone-induced impairments in post-pain blood pressure (143). Formation clearance of morphine to M3G is reduced during the first 10 days in neonates undergoing venoarterial extra corporeal membrane oxygenation (901). Remifentanil attenuated hemodynamic changes after induction and tracheal intubation during cesarean delivery (566).

16. Respiration and Thermoregulation

16a. Respiration

DAMGO applied to the rostral ventrolateral medulla of newborn rats depressed fourth cervical ventral root inspiratory activity with facial nerve activity continuing to synchronize with pre-inspiratory bursts both in normal pups and pups receiving transverse sectioning between the pre-Botzinger complex and the parafacial respiratory group (867). DAMGO also depressed confocally imaged respiratory center neurons in on-line-calibrated newborn rat brainstem slices (977). Fentanyl-induced modulation of inspiration and expiration in juvenile rats was dissociated with caudal transactions at the level of the facila nerve blocked the latter response, but not the former response (511). Recurrent hypoxia in rats during development increases subsequent respiratory sensitivity to fentanyl (805). Morphine increases the transmesothelial resistance of the sheep parietal pleura in an in vitro preparation (1170). Morphine decreases gill ciliary activity through coupling to NO release in a bivalve mollusk (722). Optimal assessment of anesthesia associated with regular respiration, loss of blink, papillary and pedal withdrawal reflexes was obtained with intra-nasal doses of fentanyl, droperidol and medetomidine in mice (632). Both naloxone and peripherally-acting naloxone methiodide reversed the respiratory depression and analgesia induced by morphine, methadone and heroin, effects that did not appear to be sex-dependent in mice (651). Naloxone and epinephrine were equally effective for cardiopulmonary resuscitation in a rat asphyxia model (193,194). Naloxone reversed buprenorphine-induced respiratory depression (1147). Naloxone did not increase the minimum alveolar anesthetic concentration of sevoflurane in mice (664). Lenk decreased the burst frequency of the membrane potential of pre-Botzinger complex respiratory center neurons (503). OFQ/N reduced respiratory frequency in an apnea model of isolated brainstem-spinal cord newborn rat preparation, effects reversed by an ORL-1 antagonist, an activator of adenylyl cyclase and a phosphodiesterase-4 (but not 3 or 5) inhibitor (976). OFQ/N inhibited acid-invoked cough in guinea pigs by blocking acid-induced increases in Ca2+ in vagal jugular ganglionic neurons by inhibiting the sustained component of acid-induced inward current (640). Two analogues of OFQ/N, but not nocistatin reversed the inhibition by OFQ/N of electric field stimulation-induced excitatory nonadrenergic-non cholinergic and cholinergic constriction of the guinea pig isolated bronchus (1267). Endomorphin-1 and endomorphin-2 inhibited the response to electrical field stimulation in rat isolated bronchus at low, but not higher frequencies, and also inhibited cholinergic constriction in a naloxone-reversible manner, but had no effect upon the contractile response to exogenous Ach (1280); these effects were present in diabetic rats, but the endomorphin response was less marked (1282).

The acute agonal period during heroin overdose death is characterized by variations in respiratory distress (482). Heroin produced contact allergy and respiratory and mucosal complaints (475). Maximal buprenorphine-induced decreases in respiratory rate and pupil

diameter did not vary across doses in experienced opiate users, nor did subjective effects change (226). High doses of buprenorphine cause naloxone-insensitive respiratory depression, particularly in conjunction with benzodiazepine use (763). Whereas fentanyl produced dose-dependent decreases in respiratory rate in volunteers undergoing anesthesia, buprenorphine caused respiratory depression that leveled at 50% of baseline rates (255). Midazolam and morphine can produce harmful effects on cerebral oxygenation and hemodynamics in ventilated premature infants (1144). In neonates receiving central line placement for ventilation, combinations of morphine and tetracine provided superior analgesia with the former producing respiratory depression and the latter producing erythema (1096). Codeine was no more effective than placebo in an objective measurement of cough in chronic obstructive pulmonary disease (1046). There was no significant difference in the time to extubation after use of remifentanil and sufentanil in combination with propofol as anesthesia in adults undergoing nonemergency intracranial surgery (285).

16b. Thermoregulation

DAMGO administered into the NRM blocked noxious stimulation-evoked suppression of PGE2-induced BAT temperature increases (821). SNC80-induced hypothermia was attenuated by central L-NAME administration as well as by combined peripheral L-NAME and 7-NI administration (942). SNC80-induced produced hypothermia in a NTI-sensitive manner, an effect blocked by the 5HT1A antagonist, WAY100635, and enhanced by non-hypothermic doses of fluoxetine (943). Hydromorphone produced post anesthetic hyperthermia in cats (843). The ability of the GABA B agonist, baclofen in the pre-optic/anterior hypothalamus to decrease tonic activity and increase temperature sensitivity through membrane hyper polarization and decrease of input resistances was inhibited by the mu-opioid agonist, PL-017 (1252). Bile duct-ligated rats displayed hypothermia that was reversed by opioid antagonism and NOS inhibition (791). Naloxone restored heat stress-induced declines in GABA and glycine and prevented heat stress-induced increases in glutamate and aspartate (1019). The SSRI fluoxetine abated naloxone-induced increases in tail-skin temperature in ovariectomized rats (740). The 5HT2A antagonist mirtazapine increased tail temperatures following naloxone administration in morphine-dependent rats (886). Post-burn local hyperthermia in reducing burn injury was blocked by naloxone (1011). Intrathecal morphine intensified the intra-operative hypothermia induced by bupivacaine spinal anaesthesia for caesarean section (491).

17. Immunological Responses

Intrathecal chronic administration at the maximum tolerated doses of morphine hydromorphone, L-methadone, and naltrexone produced granulomas (21). POMC gene transfer, and particularly AMSH, reduced anchorage-dependent growth of melanoma cells in mice by reducing foci formation in lung attenuating their migratory and adhesive capabilities (678). Morphine decreased metalloproteinase activity through the NO-NOS system, implicating it in the treatment of fibrosarcoma (1016). Morphine stimulated CCL2 production by human neurons (964). Chronic, but not acute morphine induces apoptosis in neurons and astrocytes accompanied by up-regulation of FasL, Fas, Bad and active fragments of caspases-8 and –3 (317). Morphine promoted Jurkat cell apoptosis through pro-apoptotic FADD/P53 and anti-apoptotic PI3K/Akt/NF-kappaB pathways (1273). Morphine enhanced apoptosis of cultured human colonic cells in a NOS inhibitor-sensitive fashion, and produced a breach in the host defense barrier in a NOS inhibitor-insensitive fashion (361). Non-apoptotic cell death is induced by morphinone in human promyelocytic leukemia HL-60 cells (1104). Reduction of the brain apoptosis-related proteins, Fas, FasL, Bad and Bax occurred following naltrexone in mice (987). Morphine-induced suppression of natural killer cell activity was blocked by the NPY Y1 antagonist, BIBP3226 (992). Morphine reciprocally regulates IL-10 and IL-12

production by monocyte-derived human dendritic cells and enhances T cell activation (772). Morphine, DAMGO, DPDPE and U-69593 all produced neuroprotective effects against low-temperature-induced cell death in cultured hamster hippocampal neurons (1106). TPA increases expression and regulation of MOR in TPA-differentiated HL-60 promyelocytic leukemia cells (75). Interferon-gamma down-regulates transcription of the MOR gene in neuronal and immune cells (612). Morphine modulates the monocyte-macrophage conversion phase in an opiate antagonist-sensitive manner (456), and naloxone inhibits macrophage activation and atherosclerosis formation in mice (688). Acute morphine and morphine withdrawal inhibit phagocytosis through pertussis toxin-sensitive and –insensitive mechanisms respectively with the latter, but not former manipulation increasing cAMP levels (705). Over expression and blockade of cyclin-dependent kinase 5 respectively augmented and diminished DAMGO-induced neuroprotection from serum deprivation (1195). DAMGO induced up-regulation of annexin V apoptosis-inducing gene expression in PC12 cells stably transfected with MOR (1291). DAMGO inhibited ERK-1 and Akt signaling pathways activated by the chemokine receptor CXCL12 and abolished its neuroprotective effects during NMDA-induced neurotoxicity, effects reversed by general and mu antagonists (883). SNC, but not mu or kappa agonists promoted neural differentiation from multipotent stem cells through the activation of Trk-dependent tyrosine kinase (814). There is a requirement for Id1 in BEND opioid-induced oligodendrogensis in cultured adult rat hippocampal progenitors (899). Insulin decreased histamine and 5HT, but not BEND content in the thymus of in vitro preparations (251). The nucleus of rat peritoneal mast cells contained serotonin and histamine, but not BEND, insulin or triiodothyronine (252). EDAC fixation increases histamine, but not BEND, levels in such cells relative to paraformaldehyde (253).

Loperamide reversed the inhibition of insulin-stimulated 2DG uptake by tumor necrosis factor alpha in myoblast C2C12 cells (601). Chimeric DNA vaccine reverses morphine-induced immunosuppression and tumorigenesis (206). Morphine dependence diminished virus evolution in SHIV/SIV-infected rhesus macaques with an inverse relation between virus evolution and onset of clinical symptoms (1121). Chronic morphine exposure causes pronounced virus replication in the cerebral compartment and accelerated onset of AIDS in SIV/SHIV-infected Indian rhesus macaques (620). HIV-1 gp120 up-regulation of MOR occurred in TPA-differentiated HL-60 cells (74). Menk maintained the viability of SIV-infected cells through suppression of the expression of caspase-3 (1248). Delta opioid agonists attenuate HIV protein TAT(1–72)-induced oxidative stress in SK-N-SH cells (1176). The increased vulnerability of ApoE4 neurons to HIV proteins and opiates were provided protection by diosgenin and L-deprenyl (1137). HIV-1 Tat and opiate-induced changes in astrocytes promote chemotaxis of microglia through the expression of MCP-1 and alternative chemokines (312). CCR2 mediates the increases in glial activation by exposure to HIV-1 Tat and opiates (311). There was a correlation between SIV Tat evolution and AIDS progression in cerebrospinal fluid of morphine-dependent as compared to control macaques infected with SIV and SHIV (847). Naltrexone inhibits alcohol-mediated enhancement of HIV infection of T lymphocytes (1189). Further, an in vitro model of morphine withdrawal manifests the enhancing effect of HIV infection of human T lymphocytes through the induction of substance P (1190). Acupuncture reduced leukocyte migration into the mouse air pouch in a peripheral, but not spinal naloxone-reversible manner, but did not produce an anti-inflammatory effect (580).

Down-regulation of the opioid growth factor receptor is associated with progression of squamous cell carcinoma of the head and neck (760), yet the opioid growth factor receptor is unaltered with the progression of human pancreatic and colon cancers (1286). Regulation of corneal repair was effectuated by particle-mediated gene transfer of opioid growth factor receptor complementary DNA (1287) with corneal safety of topically applied naltrexone validated (1285). Adaptation of the homeostatic ocular surface epithelium occurred following

chronic treatment with naltrexone (1288). Pro-ENK KO mice developed less severe clinical signs of experimental autoimmune encephalomyelitis than wild-type mice that was accompanied by a reduction in MOG(35–55)-specific IFNgamma-producing cells (1212). Tumor-cell-targeted Menk analogues containing unnatural amino acids display in vitro antitumor activity (481). DADL stimulates Akt-dependent phosphorylation of c-jun in T cells (1010). DPDPE triggers monocyte adhesion even in pertussis toxin-treated cells, indicating involvement of G proteins other than Gi. This adhesion requires integrins, PI3Kgamma activation, and involves Src kinases, a guanine nucleotide exchange factor and a small GTPase (893). Chemotaxis of human and rat leukocytes is observed following the delta-selective non-peptidergic opioid SNC 80 (868). Deletion of the DOR in mice increases skin differentiation and delays wound healing (95). Kappa opioids induce a reversible inhibition of CFU-GM from CD133(+) cord blood cells (286). OFQ/N and ORL-1 KO respectively stimulate and reduce TNFalpha and IFNgamma transcripts in the spleen when challenged with staphylococcal enterotoxin A (407). Lipopolysaccharide induces ProEnk transcription in hypophysiotropic neurons of the rat periventricular hypothalamic nucleus suggesting a neuroendocrine role for Enk during immune stress (321). Interleukin-1 beta contributed to the up regulation of KOR mRNA in the DRG in response to peripheral inflammation (926). Lipopolysaccharide-induced interleukin-6 production in a mouse monocyte cell line is reduced by the kappa agonist, U50488H in a NBNI-sensitive manner (879). Lipopolysaccharide induced PC1/3 and PC2 substrate pro-Enk in the marginal zone of rat spleens (629). The expression of Pro-DYN gene is down-regulated by activation with lipopolysaccharide in U-937 macrophage cells (1086).

Abbreviations

ACC
anterior cingulate cortex

Ach
acetylcholine

ACTH
adrenocorticotrophic hormone

AMSH
alpha-melanocyte-stimulating hormone

AS
antisense

BEND
beta-endorphin

BAM 22
bovine adrenal medulla 22

BAT
brown adipose tissue

BDNF
brain derived neurotrophic factor

BFNA
beta-funaltrexamine

BLPH
beta-lipotropin

BNST
bed nucleus of the stria terminalis

Ca(2+)
calcium

cAMP
cyclic adenosine monophosphate

CART
cocaine and amphetamine-regulated transcript

CB
cannabinoid

CCK
cholecystokinin

cDNA
complementary deoxyribonucleic acid

CFA
complete Freund's adjuvant

CGRP
calcitonin gene-related peptide

ChAT
choline acetyltransferase

COX
cyclooxygenase

C/P
caudate/putamen

CPP
conditioned place preference

CREB
Ca(2+)/cAMP responsive element binding protein

CRF
corticotropin releasing factor

CS
conditioned stimulus

CSF
cerebrospinal fluid

CTAP
D-Phe-Cys-Tyr-D-Trp-Arg-Thr-Pen-Thr-NH2

CWS
cold-water swims

DA
dopamine

DADL
D-Ala(2), D-Leu(5)-enkephalin

DALDA
D-Arg-Phe-Lys-NH2

DAMGO
D-Ala(2), Nme(4), Gly-ol(5)-enkephalin

Delt
deltorphin

DOR
delta opioid receptor gene

DPDPE
D-Pen(2), D-Pen(5)-enkephalin

DREAM
downstream regulatory element antagonistic modulator

DRG
dorsal root ganglion

DRN
dorsal raphe nucleus

DYN
Dynorphin

Enk
enkephalin

EPSC
excitatory post-synaptic currents

ERK
extracellular regulated signal kinases

FMRI
functional magnetic resonance imaging

GI
gastrointestinal

GIRK
G-protein inwardly rectifying K+ channel subunit

GnRH
gonadotropin-releasing hormone

GP
globus pallidus

HIV
human immunodeficiency virus

HPLC
high performance liquid chromatography

HR
heart rate

ICSS
intracranial self-stimulation

IPSC
inhibitory post-synaptic currents

JNK
Jun N-terminal kinase

K(+)
potassium

KA
kainic acid

KO
knockout

KOR
kappa opioid receptor gene

LC
locus coeruleus

Lenk
leu-enkephalin

LH
leutinizing hormone

LHA
lateral hypothalamic area

LI
like immunoreactivity

LiCl
lithium chloride

L-NAME
N(omega)-nito-l-arginine methyl ester

M3G
morphine-3-glucuronide

M6G
morphine-6-glucuronide

MAP
mean arterial pressure

MAPK
mitogen-activated protein kinase

MBH
medial-basal hypothalamus

ME
median eminence

Menk
met-enkephalin

MOR
mu opioid receptor gene

MPOA
medial preoptic area

MPTP
1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine

MRI
magnetic resonance imaging

mRNA
messenger ribonucleic acid

NAC
nucleus accumbens

NalBzOH
naloxone benzoylhydrazone

NBNI
nor-binaltorphamine

NE
norepinephrine

NMDA
N-methyl-D-aspartate

NO
nitric oxide

NOS
nitric oxide synthase

NPY
neuropeptide Y

NRM
nucleus raphe magnus

NSAID
non-steroidal anti-inflammatory drug

NTI
naltrindole

NTS
nucleus tractus solitarius

OFQ/N
nociceptin

ORL-1
orphan receptor like receptor

Oxy
oxytocin

PAG
periaqueductal gray

PBN
parabrachial nucleus

PCPA
parachlorophenylalanine

PET
positron emission tomography

PGE
prostaglandin E

PKA
protein kinase A

PKC
protein kinase C

PLD2
phospholipase D2

POMC
pro-opiomelanocortin

PPE
Pre-pro-enkephalin

PTSD
post-traumatic stress disorder

PTX
pertussis toxin

PVN
paraventricular nucleus

RSNA
renal sympathetic nerve activity

RVM
rostral ventromedial medulla

SCN
suprachiasmatic nucleus

5HT
serotonin

SFO
sub-fornical organ

SG
substantia gelatinosa

SIV
simian immunodeficiency virus

SN
substantia nigra

SON
supraoptic nucleus

SP
substance P

SSRI
selective serotonin reuptake inhibitor

STZ
streptozotocin

TH
tyrosine hydroxylase

THC
tetrohydrocannibinol

VIP
vasoactive intestinal polypeptide

VMH
ventro-medial hypothalamic nucleus

VP
vasopressin

VTA
ventral tegmental area

WDR
wide dynamic range

References

1. Abdel-Salam OM. Antinociceptive and behavioral effects of ribavirin in mice. Pharmacol Biochem Behav 2006;83:230–238. [PubMed: 16563475]
2. Abdel-Salam OM. Vinpocetine and piracetam exert antinociceptive effect in visceral pain model in mice. Pharmacol Rep 2006;58:680–691. [PubMed: 17085860]
3. Abdollahian E, Javanbakht A, Javidi K, Samari AA, Shakiba M, Sargolzaee MR. Study of the efficacy of fluoxetine and clomipramine in the treatment of premature ejaculation after opioid detoxification. Am J Addict 2006;15:100–104. [PubMed: 16449099]
4. Abdullah MS, Al-Waili NS, Butler G, Babn NK. Hyperbaric oxygen as an adjunctive therapy for bilateral compartment syndrome, rhabdomyolysis and acute renal failure after heroin intake. Arch Med Res 2006;37:559–562. [PubMed: 16624660]
5. Adam F, Bonnet F, Le Bars D. Tolerance to morphine analgesia: evidence for stimulus intensity as a key factor and complete reversal by a glycine site-specific NMDA antagonist. Neuropharmacol 2006;51:191–202.

6. Adams EH, Breiner S, Cicero TJ, Geller A, Inciardi JA, Schnoll SH, Senay EC, Woody GE. A comparison of the abuse liability of tramadol, NSAIDs and hydrocodone in patients with chronic pain. J Pain Symptom Manage 2006;31:465–475. [PubMed: 16716877]
7. Adebiyi RA, Elsa AT, Agaie BM, Etuk EU. Antinociceptive and antidepressant like effects of Securidaca longepedunculata root extract in mice. J Ethnopharmacol 2006;107:234–239. [PubMed: 16647235]
8. Agnes RS, Lee YS, Davis P, Ma SW, Badghisi H, Porreca F, Lai J, Hruby VJ. Structure-activity relationships of bifunctional peptides based on overlapping pharmacophores at opioid and cholecystokinin receptors. J Med Chem 2006;49:2868–2875. [PubMed: 16686530]
9. Agirregoitia E, Valdivia A, Carracedo A, Casis L, Gil J, Subiran N, Ochoa C, Irazusta J. Expression and localization of delta-, kappa- and mu-opioid receptors in human spermatozoa and implications for sperm motility. J Clin Endocrinol Metab 2006;91:4969–4975. [PubMed: 16984994]
10. Aguila B, Roussel M, Jauzac P, Allouche S. High-purity selection and maintenance of gene expression in human neuroblastoma cells stably over-expressing GFP fusion protein. Application for opioid receptors desensitization. Brain Res 2006;1114:11–18. [PubMed: 16938287]
11. Airavaara M, Mijatovic J, Vihavainen T, Piepponen TP, Saarma M, Ahtee L. In heterozygous GDNF knockout mice the response of striatal dopaminergic system to acute morphine is altered. Synapse 2006;59:321–329. [PubMed: 16437537]
12. Akada Y, Mori R, Matsuura K, Suzuki K, Kato K, Kamiya M, Naba H, Kurokawa M, Ogihara T, Kato Y, Yamasaki F, Yamamoto I. Pharmacological profiles of the novel analgesic M58996 in rat models of persistent and neuropathic pain. J Pharmacol Sci 2006;102:205–212. [PubMed: 17031069]
13. al'Absi M, France C, Harju A, France J, Wittmers L. Adrenocortical and nociceptive responses to opioid blockade in hypertension-prone men and women. Psychosom Med 2006;68:292–298. [PubMed: 16554396]
14. Alaei H, Borjeian L, Azizi M, Orian S, Pourshanazari A, Hannien O. Treadmill running reverses retention deficit induced by morphine. Eur J Pharmacol 2006;536:138–141. [PubMed: 16549061]
15. Alberati D, Ceccarelli SM, Jolidon S, Krafft EA, Kurt A, Maier A, Pinard E, Stadler H, Studer D, Thomas AW, Zimmerli D. Design and synthesis of 4-substituted-8-(2-phenyl-cyclohexyl)-2–8-diaza-spiro[4,5]decan-1-one as a novel class of GlyT1 inhibitors: achieving selectivity against the mu opioid and nociceptin/orphanin FQ peptide (NOP) receptors. Bioorg Med Chem Lett 2006;16:4305–4310. [PubMed: 16762548]
16. Alberati D, Hainzl D, Jolidon S, Krafft EA, Kurt A, Maier A, Pinard E, Thomas AW, Zimmerli D. Discovery of 4-substituted-8-(2-phenyl-cyclohexyl)-2–8-diaza-spiro[4,5]decan-1-one as a novel class of GlyT1 inhibitors with improved metabolic stability. Bioorg Med Chem Lett 2006;16:4311–4315. [PubMed: 16757170]
17. Alberati D, Hainzl D, Jolidon S, Krafft EA, Kurt A, Pinard E, Thomas AW, Zimmerli D. 4-substituted-8-(2-phenyl-cyclohexyl)-2–8-diaza-spiro[4,5]decan-1-one as a novel class of GlyT1 inhibitors with superior pharmacological and pharmacokinetic parameters. Bioorg Med Chem Lett 2006;16:4321–4325. [PubMed: 16762550]
18. Alborzi A, Mehr SE, Rezania F, Badakhshan S, Mombeini T, Shafaroodi H, Moezi L, Ravan MN, Sharifian M, Dehpour AR. The effect of lithium chloride on morphine-induced tolerance and dependence in isolated guinea pig ileum. Eur J Pharmacol 2006;545:123–128. [PubMed: 16904101]
19. Albrizio M, Guaricci AC, Calamita G, Zarrilli A, Minoia P. Expression and immunolocalization of the mu-opioid receptor in human sperm cells. Fertil Steril 2006;86:1776–1779. [PubMed: 17007854]
20. Ali NJ, Levine MS. Changes in expression of N-methyl-D-aspartate receptor subunits occur early in the R6/2 mouse model of Huntington's disease. Dev Neurosci 2006;28:230–238. [PubMed: 16679770]
21. Allen JW, Horais KA, Tozier NA, Yaksh TL. Opiate pharmacology of intrathecal granulomas. Anesthesiol 2006;105:590–598.
22. Almela P, Cerezo M, Milanes MV, Laorden ML. Role of PKC in regulation of Fos and TH expression after naloxone induced morphine withdrawal in the heart. Naunyn Schmiedebergs Arch Pharmacol 2006;372:374–382. [PubMed: 16474935]

23. Al-Mujadi H, Al-Refai AR, Katzarov MG, Dehrab NA, Batra YK, Al-Qattan AR. Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Can J Anaesth 2006;53:268–273. [PubMed: 16527792]
24. Alrubaian J, Lecaude S, Barba S, Szynskie L, Jacobs N, Bauer D, Brown C, Kaminer I, Bagrosky B, Dores RM. Trends in the evolution of the prodynorphin gene in teleosts: cloning of eel and tilapia prodynorphin cDNAs. Peptides 2006;27:797–804. [PubMed: 16274850]
25. Altier C, Khosravani H, Evans RM, Hameed S, Peloquin JB, Vartian BA, Chen L, Beedle AM, Ferguson SS, Mezghrani A, Dubel SJ, Bourinet E, McRory JE, Zamponi GW. ORL1 receptor-mediated internalization of N-type calcium channels. Nat Neurosci 2006;9:8–10. [PubMed: 16378086]
26. Altier C, Zamponi GW. Opioid, cheating on its receptors, exacerbates pain. Nat Neurosci 2006;9:1465–1467. [PubMed: 17128281]
27. Alvarez FA, Rodriguez-Martin I, Gonzalez-Nunez V, de Velasco EM, Gonzalez Sarmiento R, Rodriguez RE. New kappa opioid receptor from zebrafish Danio rerio. Neurosci Lett 2006;405:94–99. [PubMed: 16842913]
28. Alvira-Botero MX, Garzon M. Cellular and subcellualr distributions of delta opioid receptor activation sites in the ventral oral pontine tegmentum of the cat. Brain Res 2006;1123:101–111. [PubMed: 17045971]
29. Ambrose LM, Gallagher SM, Unterwald EM, Van Bockstaele EJ. Dopamine D-1 and delta-opioid receptors co-exist in rat striatal neurons. Neurosci Lett 2006;399:191–196. [PubMed: 16517070]
30. Amitai N, Liu J, Schulteis G. Discrete cues with naloxone-precipitated withdrawal from acute morphine dependence elicit conditioned withdrawal responses. Behav Pharmacol 2006;17:213–222. [PubMed: 16571999]
31. Ancevska-Taneva N, Onoprishvili I, Andria ML, Hiller JM, Simon EJ. A member of the heat shock protein 40 family, hlj1, binds to the carboxyl tail of the human mu opioid receptor. Brain Res 2006;1081:28–33. [PubMed: 16542645]
32. Anjaneyulu M, Chopra K. Possible involvement of cholinergic and opioid receptor mechanisms in fluoxetine mediated antinociception response in streptozotocin-induced diabetic mice. Eur J Pharmacol 2006;538:80–84. [PubMed: 16650402]
33. Ansonoff MA, Zhang J, Czyzyk T, Rothman RB, Stewart J, Xu H, Zjwiony J, Siebert DJ, Yang F, Roth BL, Pintar JE. Antinociceptive and hypothermic effects of Salvinorin A are abolished in a novel strain of kappa-opioid receptor-1 knockout mice. J Pharmacol Exp Ther 2006;318:641–648. [PubMed: 16672569]
34. Anton B, Leff P. A novel bivalent morphine/heroin vaccine that prevents relapse to heroin addiction in rodents. Vaccine 2006;24:3232–3240. [PubMed: 16494974]
35. Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, Gastfriend DR, Hosking JD, Johnson BA, LoCastro JS, Longabaugh R, Mason BJ, Mattson ME, Miller WR, Pettinati HM, Randall CL, Swift R, Weiss RD, Williams LD, Zweben A. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized control trial. JAMA 2006;295:2003–2017. [PubMed: 16670409]
36. Arias A, Feinn R, Kranzler HR. Association of Asn40Asp (A118G) polymorphism in the mu-opioid receptor gene with substance dependence: a meta-analysis. Drug Alcohol Depend 2006;83:262–268. [PubMed: 16387451]
37. Armeli S, Feinn R, Tennen H, Kranzler HR. The effects of naltrexone on alcohol consumption and affect reactivity to daily interpersonal events among heavy drinkers. Exp Clin Psychopharmacol 2006;14:199–208. [PubMed: 16756424]
38. Armstead WM. Differential activation of ERK, p38 and JNK MAPK by nociceptin/orphanin FQ in the potentiation of prostaglandin cerebrovasoconstriction after brain injury. Eur J Pharmacol 2006;529:129–135. [PubMed: 16352304]
39. Armstrong DW 3rd, Hatfield BD. Hormonal responses to opioid receptor blockade: during rest and exercise in cold and hot environments. Eur J Appl Physiol 2006;97:43–51. [PubMed: 16468062]
40. Arttamangkul S, Torrecilla M, Kobayashi K, Okano H, Williams JT. Separation of mu-opioid receptor desensitization and internalization: endogenous receptors in primary neuronal cultures. J Neurosci 2006;26:4118–4125. [PubMed: 16611829]

41. Asano K, Asahina S, Sakai M, Matsuda T, Ou K, Maeda Y, Hisamitsu T. Attenuating effect of artemin on herpes-related pain responses in mice infected with herpes simplex. In Vivo 2006;20:533–537. [PubMed: 16900785]

42. Asensio VJ, Miralles A, Garcia-Sevilla JA. Stimulation of mitogen-activated protein kinase kinases (MEK1/2) by mu-, delta- and kappa-opioid receptor agonists in the rat brain: regulation by chronic morphine and opioid withdrawal. Eur J Pharmacol 2006;539:49–56. [PubMed: 16678156]

43. Assis MA, Collino C, Figuerola Mde L, Sotomayor C, Cancela LM. Amphtermine triggers an increase in met-enkephalin simultaneously in brain areas and immune cells. J Neuroimmunol 2006;178:62–75. [PubMed: 16904191]

44. Athanasos P, Smith CS, White JM, Somogyi AA, Bochner F, Ling W. Methadone maintenance patients are cross-tolerant to the antinociceptive effects of very high plasma morphine concentrations. Pain 2006;120:267–275. [PubMed: 16427197]

45. Auret K, Roger Gouke C, Ilett KF, Page-Sharp M, Boyd O, Oh TE. Pharmacokinetics and pharmacodynamics of methadone enantiomers in hospice patients with cancer pain. Ther Drug Monit 2006;28:359–366. [PubMed: 16778720]

46. Ayoka AO, Akomolafe RO, Iwalewa EO, Akanmu MA, Ukponmwan OE. Sedative, antiepileptic and antipsychotic effects of Spondias mombin L (Anacardiaceae) in mice and rats. J Ethnopharmacol 2006;103:166–175. [PubMed: 16188408]

47. Baamonde A, Lastra A, Juarez L, Garcia-Suarez O, Meana A, Hidalgo A, Menendez L. Endogenous beta-endorphin induces thermal analgesia at the initial stages of a murine osteosarcoma. Peptides 2006;27:2778–2785. [PubMed: 16930772]

48. Bachs L, Hoiseth G, Skurtveit S, Morlund J. Heroin-using drivers: importance of morphine and morphine-6-glucuronide on late clinical improvement. Eur J Clin Pharmacol 2006;62:905–912. [PubMed: 17021891]

49. Back SK, Lee J, Hong SK, Na HS. Loss of spinal mu-opioid receptor is associated with mechanical allodynia in a rat model of peripheral neuropathy. Pain 2006;123:117–126. [PubMed: 16564625]

50. Baek YH, Huh JE, Lee JD, Choi do Y, Park DS. Antinociceptive effect and the mechanism of bee venom acupuncture (Apipuncture) on inflammatory pain in the rat model of collagen-induced arthritis: mediation by alpha2-adrenoceptors. Brain Res 2006;1073–1074:305–310.

51. Bagosi Z, Jaszberenyi M, Bujdoso E, Szabo G, Telegdy G. The effects of endomorphins and diprotin A on striatal dopamine release induced by electrical stimulation- an in vitro superperfusion study in rats. Neurochem Int 2006;49:665–668. [PubMed: 16815593]

52. Bai ZT, Liu T, Chai ZF, Pang XY, Ji YH. Rat pain-related responses induced by experimental scorpion BmK sting. Eur J Pharmacol 2006;552:67–77. [PubMed: 17055482]

53. Bailey CP, Smith FL, Kelly E, Dewey WL, Henderson G. How important is protein kinase C in mu-opioid receptor desensitization and morphine tolerance? Trends Pharmacol Sci 2006;27:558–565. [PubMed: 17000011]

54. Bailey JE, Barton PL, Lezotte D, Lowenstein SR, Dart RC. The effect of FDA approval of a generic competitor to OxyContin (oxycodone HCl controlled-release) tablets on the abuse of oxycodone. Drug Alcohol Depend 2006;84:182–187. [PubMed: 16510252]

55. Bajo M, Crawford EF, Roberto M, Madamba SG, Siggins GR. Chronic morphine treatment alters expression of N-methyl-D-aspartate receptor subunits in the extended amygdala. J Neurosci Res 2006;83:532–537. [PubMed: 16453311]

56. Baker JR, Best AM, Pade PA, McCance-Katz EF. Effect of buprenorphine and antiretroviral agents on the QT interval in opioid-dependent patients. Ann Pharmacother 2006;40:392–396. [PubMed: 16507617]

57. Balboni G, Onnis V, Congiu C, Zotti M, Sasaki Y, Ambo A, Bryant SD, Jinsmaa Y, Lazarus LH, Trapella C, Salvadori S. Effect of lysine at C-terminus of the Dmt-Tic opioid pharmacophore. J Med Chem 2006;49:5610–5617. [PubMed: 16942034]

58. Baldacci A, Thormann W. Capillary electrophoresis contributions to the hydromorphone metabolism in man. Electrophoresis 2006;27:2444–2457. [PubMed: 16718649]

59. Baldelli B, Vecchio L, Bottone MG, Muzzonigro G, Biggiogera M, Malatesta M. The effect of the enkephalin DADLE on transcription does not depend on opioid receptors. Histochem Cell Biol 2006;126:189–197. [PubMed: 16416021]

60. Banach T, Zurowski D, Gil K, Weisbrodt NW, Rosenfeld G, Thor PJ. Peripheral mechanisms of intestinal dysmotility in the morphine teolerant and dependent rats. J Physiol Pharmacol 2006;57:73–82. [PubMed: 16601316]
61. Bandettini Di Poggio A, Fornai F, Paparelli A, Pacini M, Perugi G, Maremmani I. Comparison between heroin and heroin-cocaine polyabusers: a psychopathological study. Ann NY Acad Sci 2006;1074:438–445. [PubMed: 17105942]
62. Bao X, Shi Y, Huo X, Song T. A possible involvement of beta-endorphin, substance P and serotonin in rat analgesia induced by extremely low frequency magnetic field. Bioelectromagnetics 2006;27:467–472. [PubMed: 16622860]
63. Barbano MF, Cador M. Differetnail regulation of the consummatory, motivational and anticipatory aspects of feeding behavior by doapminergic and opioidergic drugs. Neuropsychopharmacol 2006;31:1371–1381.
64. Barlow MA, Deo S, Johnson S, Caffrey JL. Vagotonic effects of enkephalin are not mediated by sympatholytic mechanisms. Exp Biol Med 2006;231:387–395.
65. Barnes MJ, Holmes G, Primeaux SD, York DA, Bray GA. Increased expression of mu opioid receptors in animals susceptible to diet-induced obesity. Peptides 2006;27:3292–3298. [PubMed: 16996647]
66. Barratt C, Lai T, Nashef L, Valentin A, Fisniku L, Moran N, Asherson P, Makoff A. No association of single nucleotide polymorphisms in the mu-opioid receptor subunit gene with idiopathic generalized epilepsy. Epilepsia 2006;47:1728–1731. [PubMed: 17054695]
67. Barrett AC. Low efficacy opioids: implications for sex differences in opioid antinociception. Exp Clin Psychopharmacol 2006;14:1–11. [PubMed: 16503700]
68. Bart G, LaForge KS, Borg L, Lilly C, Ho A, Kreek MJ. Altered levels of basal cortisol in healthy subjects with a 118G allele in exon 1 of the MOR gene. Neuropsychopharmacol 2006;31:2313–2317.
69. Beadles-Bohling AS, Wiren KM. Anticonvulsive effects of kappa-opioid receptor modulation in an animal model of ethanol withdrawal. Genes Brain Behav 2006;5:483–496. [PubMed: 16923153]
70. Becerra L, Harter K, Gonzalez RG, Borsook D. Functional magnetic resonance imaging measures of the effects of morphine on central nervous system circuitry in opioid-naïve healthy volunteers. Anesth Analg 2006;103:208–216. [PubMed: 16790655]
71. Beck O, Bottcher M. Paradoxical results in urine drug testing for 6-acetylmorphine and total opiates: implications for best analytical strategy. J Anal Toxicol 2006;30:73–79. [PubMed: 16620535]
72. Becker A, Grecksch G, Schroder H. Pain sensitivity is altered in animals after subchronic ketamine treatment. Psychopharmacol 2006;189:237–247.
73. Beguin C, Richards MR, Li JG, Wang Y, Xu W, Liu-Chen LY, Carlezon WA, Cohen BM. Synthesis and in vitro evaluation of salvinorin A analogues: effect of configuration at C(2) and substitution at C(18). Bioorg Med Chem Lett 2006;16:4679–4685. [PubMed: 16777411]
74. Beltran JA, Pallur A, Chang SL. HIV-1 gp120 up-regulation of the mu-opioid receptor in TPA-differentiated HL-60 cells. Int Immunopharmacol 2006;6:1459–1467. [PubMed: 16846840]
75. Beltran JA, Peek J, Chang SL. Expression and regulation of the mu opioid peptide receptor in TPA-differentiated HL-60 promyelocytic leukemia cells. Int Immunopharmacol 2006;6:1331–1340. [PubMed: 16782547]
76. Belz D, Lieb J, Rea T, Eisenberg MS. Naloxone use in a tiered-response emergency medical services system. Prehosp Emerg Care 2006;10:468–471. [PubMed: 16997776]
77. Bender T, Donath J, Barna I, Gergely P Jr, poor G. The analgesic effect of pamidronate is not caused by the elevation of beta-endorphin level in Paget's disease – a controlled pilot study. Neuro Endocrinol Lett 2006;27:513–515. [PubMed: 16891991]
78. Berger B, Rothmaier AK, Wedekind F, Zentner J, Feuerstein TJ, Jackisch R. Presynaptic opioid receptors on noradrenergic and serotonergic neurons in the human as compared to the rat neocortex. Br J Pharmacol 2006;148:795–806. [PubMed: 16751796]
79. Bergstrom J, Ahmed M, Li J, Ahmad T, Kreicbergs A, Spetea M. Opioid peptides and receptors in joint tissues: study in the rat. J Orthop Res 2006;24:1193–1199. [PubMed: 16649179]
80. Berkson BM, Rubin DM, Berkson AJ. The long-term survival of a patient with pancreatic cancer with metastases to the liver after treatment with the intravenous alpha-lipoic acid/low-dose naltrexone protocol. Integr Cancer Ther 2006;5:83–89. [PubMed: 16484716]

81. Bernardi F, Pluchino N, Pieri M, Begliuomini S, Lenzi E, Puccetti S, Casarosa E, Luisi M, Genazzani AR. Progesterone and medroxyprogesterone acetate effects on central and peripheral allopregnanolone and beta-endorphin levels. Neuroendocrinology 2006;83:348–359. [PubMed: 16931878]

82. Bernkop-Schnurch A, Obermair K, Greimel A, Palmberger TF. In vitro evaluation of the potential of thiomers for the nasal administration of Leu-enkephalin. Amino Acids 2006;30:417–423. [PubMed: 16554973]

83. Berrocoso E, Mico JA, Ugedo L. In vivo effect of tramadol on locus coeruleus neurons is mediated by alpha2-adrenoceptors and modulated by serotonin. Neuropharm 2006;51:146–153.

84. Bertollo CM, Oliveira AC, Rocha LT, Costa KA, Nascimento EB, Coelho MM. Characterization of the antinociceptive and anti-inflammatory activities of riboflavin in different experimental models. Eur J Pharmacol 2006;547:184–191. [PubMed: 16962092]

85. Bessler H, Shavit Y, Mayburd E, Smirnov G, Beilen B. Postoperative pain, morphine consumption and genetic polymorphism of IL-1beta and IL-1 receptor antagonist. Neurosci Lett 2006;404:154–158. [PubMed: 16777324]

86. Besson M, David V, Suarez S, Cormier A, Cazala P, Changeux JP, Granon S. Genetic dissociation of two behaviors associated with nicotine addiction: beta-2 containing nicotinic receptors are involved in nicotine reinforcement but not in withdrawal syndrome. Psychopharmacol 2006;187:189–199.

87. Bhalla S, Ciaccio N, Wang ZJ, Gulati A. Involvement of endothelin in morphine tolerance in neuroblastoma (SH-SY5Y) cells. Exp Biol Med (Maywood) 2006;231:1152–1156. [PubMed: 16741067]

88. Bhat R, Chari G, Rao R. Effects of prenatal cocaine, morphine or both on postnatal opioid (mu) receptor development. Life Sci 2006;78:1478–1482. [PubMed: 16242731]

89. Bhat R, Chari G, Rao R, Wirtshafter D. Prenatal cocaine and morphine alter brain cyclin-dependent kinase (Cdk5) in rat pups. Neurotoxicol Teratol 28:625–628. [PubMed: 16962740]

90. Bi J, Tsai NP, Lin YP, Loh HH, Wei LN. Axonal mRNA transport and localized translational regulation of kappa-opioid receptor in primary neurons of the dorsal root ganglion. Proc Natl Acad Sci (USA) 2006;103:19919–19924. [PubMed: 17167054]

91. Biala G, Budzynska B. Reinstatement of nicotine-conditioned place preference by drug priming: effects of calcium channel antagonists. Eur J Pharmacol 2006;537:85–93. [PubMed: 16616917]

92. Biala G, Weglinska B. On the mechanism of cross-tolerance between morphine- and nicotine-induced antinociception: involvement of calcium channels. Prog Neuropsychopharmacol Biol Psychiat 2006;30:15–21.

93. Bierczynska-Krzysik A, Bonar E, Drabik A, Noga M, Suder P, Dylag T, Dubin A, Kotlinska J, Silberring J. Rat brain proteome in morphine dependence. Neurochem Int 2006;49:401–406. [PubMed: 16581157]

94. Bierczynska-Krzysik A, Pradeep John JP, Silberring J, Kotlinska J, Dylag T, Lubec G. Proteonomic analysis of rat cerebral cortex, hippocampus and striatum after exposure to morphine. Int J Mol Med 2006:775–784. [PubMed: 16964434]

95. Bigliardi-Qi M, Gaveriaux-Ruff C, Zhou H, Hell C, Bady P, Rufli T, Kieffer B, Bigliardi P. Deletion of delta-opioid receptor in mice alters skin differentiation and delays wound healing. Differentiation 2006;74:174–185. [PubMed: 16683988]

96. Bignan GC, Battista K, Connolly PJ, Orsini MJ, Liu J, Middleton SA, Reitz AB. 3-(4-Piperidinyl) indoles and 3-(4-piperidinyl)pyrrolo-[2,3-b]pyridines as ligands for the ORL-1 receptor. Biorg Med Chem Lett 2006;16:3524–3528.

97. Bijur PE, Schechter C, Esses D, Chang AK, Gallagher EJ. Intravenous bolus of ultra-low-dose naloxone added to morphine does not enhance analgesia in emergency department patients. J Pain 2006;7:75–81. [PubMed: 16459272]

98. Bilbao A, Cippitelli A, Martin AB, Granado N, Ortiz O, Bezard E, Chen JF, Navarro M, Rodriguez de Fonseca F, Moratalla R. Absence of quasi-morphine withdrawal syndrome in adenosine A2A receptor knockout mice. Psychopharamacol 2006;185:160–168.

99. Bileviciute-Ljungar I, Saxne T, Spetea M. Anti-inflammatory effects of contralateral administration of the kappa-opioid agonist U50,488H in rats with unilaterally induced adjuvant arthritis. Rheumatology (Oxford) 2006;45:295–302. [PubMed: 16249243]
100. Bileviciute-Ljungar I, Spetea M, Guo Y, Schutz J, Windisch P, Schildhammer H. Peripherally-mediated antinociception of the mu-opioid receptor agonist 2-[(4,5alpha-epoxy-3-hydroxy-14beta-methoxy-17-methylmorphinan-6beta-yl)amino]acetic acid (HS-731) after subcutaneous and oral administration in rats with carrageenan-induced hindpaw inflammation. J Pharmacol Exp Ther 2006;317:220–227. [PubMed: 16339394]
101. Binsack R, Zheng ML, Zhang ZS, Yang L, Zhu YP. Chronic morphine drinking establishes morephine tolerance, but not addiction in Wistar rats. J Zhejiang Univ Sci B 2006;7:892–898. [PubMed: 17048304]
102. Bjornebekk A, Mathe AA, Brene S. Running has differential effects on NPY, opiates and cell proliferation in an animal model of depression and controls. Neuropsychopharm 2006;31:256–264.
103. Blaiss CA, Janak PH. Post-training and post-reactivation administration of amphetamine enhances morphine CPP. Behav Brain Res 2006;171:329–337. [PubMed: 16698095]
104. Blatchford KE, Choi EA, McNally GP. Altered responsivity to central administrations of corticotrophin-releasing factor in rats with a history of opiate exposures. Behav Neurosci 2006;120:1169–1174. [PubMed: 17014268]
105. Blay M, Orban JC, Rami L, Gindre S, Chambeau R, Batt M, Grimaud D, Ichai C. Efficacy of low-dose intrathecal morphine for postoperative analgesia after abdominal aortic surgery: a double-blind randomized study. Reg Anesth Pain Med 2006;31:127–133. [PubMed: 16543098]
106. Blednov YA, Walker D, Martinez M, Harris RA. Reduced alcohol consumption in mice lacking preprodynorphin. Alcohol 2006;40:73–86. [PubMed: 17307643]
107. Block ML, Li G, Qin L, Wu X, Pei Z, Wang T, Wilson B, Yang J, Hong JS. Potent regulation of microglia-derived oxidative stress and dopaminergic neuron survival: substance P vs. dynorphin FASEB J 2006;20:251–258.
108. Blomberg D, Kreye P, Fowler C, Brickmann K, Kihlberg J. Synthesis and biological evaluation of leucine enkephalin turn mimetics. Org Biomol Chem 2006;4:416–423. [PubMed: 16446799]
109. Bomberg EM, Grace MK, Levine AS, Olszewski PK. Functional interaction between nociceptin/orphanin FQ and alpha-melanocyte-stimulating hormone in the regulation of feeding. Peptides 2006;27:1827–1834. [PubMed: 16584812]
110. Bonacci TM, Mathews JL, Yuan C, Lehmann DM, Malik S, Wu D, Font JL, Bidlack JM, Smrcka AV. Differential targeting of Gbetagamma-subunit signaling with small molecules. Science 2006;312:443–446. [PubMed: 16627746]
111. Bonfiglio V, Bucolo C, Camillieri G, Drago F. Possible involvement of nitric oxide in morphine-induced miosis and reduction of intraocular pressure in rabbits. Eur J Pharmacol 2006;534:227–232. [PubMed: 16516192]
112. Bonnie RJ. Judicially mandated naltrexone use by criminal offenders: a legal analysis. J Subst Abuse Treat 2006;31:121–127. [PubMed: 16919737]
113. Borner C, Hollt V, Kraus J. Cannabinoid type 2 agonists induce transcription of the MOR gene in Jurkat T cells. Mol Pharmacol 2006;69:1486–1491. [PubMed: 16434616]
114. Borzan J, Fuchs PN. Organizational and activational effects of testosterone on carrageenan-induced inflammatory pain and morphine analgesia. Neurosci 2006;143:885–893.
115. Boscan P, Van Hoogmoed LM, Farver TB, Snyder JR. Evaluation of the effects of the opioid agonist morphine on gastrointestinal tract function in horses. Am J Vet Res 2006;67:992–997. [PubMed: 16740092]
116. Boscan P, Van Hoogmoed LM, Pypendop BH, Farver TB, Snyder JR. Pharmacokinetics of the opioid antagonist N-methylnaltrexone and evaluation of its effects on gastrointestinal tract function in horses treated or not treated with morphine. Am J Vet Res 2006;67:998–1004. [PubMed: 16740093]
117. Bossert JM, Gray SM, Lu L, Shaham Y. Activation of group II metabrotrpic glutamate receptors in the nucleus accumbens shell attenuates context-induced relapse to heroin seeking. Neuropsychopharmacol 2006;31:2197–2209.

118. Bostrum E, Simonsson US, Hammarlund-Udenaes M. In vivo blood-brain barrier transport of oxycodone in the rat: indications for active influx and implications for pharmacokinetics/pharmacodynamics. Drug Metab Dispos 2006;34:1624–1631. [PubMed: 16763013]
119. Botros M, Hallberg M, Johansson T, Zhou Q, Lindeberg G, Frandberg PA, Tomboly C, Toth G, LeGreves P, Nyberg F. Endomorphin-1 and endomorphin-2 differentially interact with specific binding sites for substance P (SP) aminoterminal SP1–7 in the rat spinal cord. Peptides 2006;27:753–759. [PubMed: 16216386]
120. Bove J, Serrats J, Mengod G, Cortes R, Aguilar E, Marin C. Reversion of levodopa-induced fluctuations by the A2A antagonist CSC is associated with an increase in striatal preprodynorphin mRNA expression in 6-OHDA-lesioned rats. Synapse 2006;59:435–444. [PubMed: 16498608]
121. Box D, Cochran D. Safe reduction in administration of naloxone to newborn infants: an observational study. Acta Paediatr 2006;95:1083–1086. [PubMed: 16938754]
122. Boyadjieva N, Advis JP, Sarkar DK. Role of beta-endorphin, corticotrophin-releasing hormone, and autonomic nervous system in mediation of chronic ethanol on natural killer cell cytolitic activity. Alcohol Clin Exp Res 2006;30:1761–1767. [PubMed: 17010143]
123. Boyd JJ, Kuisma MJ, Alaspaa AO, Vuori E, Repo JV, Randell TT. Outcome after heroin overdose and cardiopulmonary resuscitation. Acta Anaesthesiol Scand 2006;50:1120–1124. [PubMed: 16987342]
124. Boyd JJ, Kuisma MJ, Alaspaa AO, Vuori E, Repo JV, Randell TT. Recurrent opioid toxicity after pre-hospital care of presumed heroin overdose patients. Acta Anaesthesiol Scand 2006;50:1266–1270. [PubMed: 17067327]
125. Boyd JJ, Kytta JV, Aittomaki JV, Rosenberg PH, Seppala TA, Randell TT. Cardiovascular changes after naloxone administration in propofol-sedated piglets during opioid overdose. Acta Anesthesiol Scand 2006;50:1271–1276.
126. Boyle EM, Freer Y, Wong CM, McIntosh N, Anand KJ. Assessment of persistent pain or distress and adequacy of analgesia in preterm ventilated infants. Pain 2006;124:87–91. [PubMed: 16725260]
127. Bradford CS, Walthers EA, Stanley DJ, Baugh MM, Moore FL. Delta and mu opioid receptors from the brain of a urodele amphibian, the rough-skinned newt, Taricha granulaosa: cloning, heterologous expression and pharmacological characterization. Gen Comp Endocrinol 2006;146:275–290. [PubMed: 16375901]
128. Bradshaw M, Sen A. Use of a prophylactic antiemetic with morphine in acute pain: randomized controlled trial. Emerg Med J 2006;23:210–213. [PubMed: 16498159]
129. Brady KT, Waldrop AE, McRae AL, Back SE, Saladin ME, Upadhyaya HP, Anton RF, Randall PK. The impact of alcohol dependence and posttraumatic stress disorder on cold pressor task response. J Stud Alcohol 2006;67:700–706. [PubMed: 16847538]
130. Bredeloux P, Constentin J, Dubuc I. Interactions between NTS2 neurotensin and opioid receptors on two nociceptive responses assessed on the hot plate test in mice. Behav Brain Res 2006;175:399–407. [PubMed: 17074405]
131. Brainin-Mattos J, Smith ND, Malkmus S, Rew Y, Goodman M, Taulane J, Yaksh TL. Cancer-related bone pain is attenuated by a systemically available delta-opioid receptor agonist. Pain 2006;122:174–181. [PubMed: 16545911]
132. Breit A, Gagnidze K, Devi LA, Lagace M, Bouvier M. Simultaneous activation of delta opioid receptor (deltaOR)/sensory neuron-specific receptor-4 (SNSR-4) hetero-oligomer by the mixed bivalent agonist bovine adrenal medulla peptide 22 activates SNSR-4, but inhibits deltaOR signaling. Mol Pharmacol 2006;70:686–696. [PubMed: 16682504]
133. Breslin HJ, Cai C, Miskowski TA, Coutinho SV, Zhang SP, Hornby P, He W. Identification of potent phenyl imidazoles as opioid receptor agonists. Bioorg Med Chem Lett 2006;16:2505–2508. [PubMed: 16483774]
134. Brink TS, Hellman KM, Lambert AM, Mason P. Raphe magnus neurons help protect reactions to visceral pain nfrom interruption by cutaneous pain. J Neurophysiol 2006;96:3423–3432. [PubMed: 16928792]
135. Brixner DI, Oderda GM, Roland CL, Rublee DA. Opioid expenditures and utilization in the Medicaid system. J Pain Palliat Care Pharmacother 2006;20:5–13. [PubMed: 16687350]

136. Brown CH, Leng G, Ludwig M, Bourque CW. Endogenous activation of supraoptic nucleus kappa-opioid receptors terminates spontaneous phasic bursts in rat magnocellular neurosecretory cells. J Neurophsysiol 2006;95:3235–3244.

137. Brown ES, Beard L, Dobbs L, Rush AJ. Naltrexone in patients with bipolar disorder and alcohol dependence. Depress Anxiety 2006;23:492–495. [PubMed: 16841344]

138. Brown JM, Gouty S, Iyer V, Rosenberger J, Cox BM. Differential protection against MPTP or methamphetamine toxicity in dopamine neurons by deletion of ppN/OFQ expression. J Neurochem 2006;98:495–505. [PubMed: 16749908]

139. Browning KN, Zheng Z, Gettys TW, Travagli RA. Vagal afferent control of opioidergic effects in rat brainstem circuits. J Physiol 2006;575:761–776. [PubMed: 16825311]

140. Bruce E, Franck L, Howard RF. The efficacy of morphine and Entonox analgesia during chest drain removal in children. Paediatr Anaesth 2006;16:302–308. [PubMed: 16490095]

141. Bruchas MR, Macey TA, Lowe JD, Chavkin C. Kappa opioid receptor activation of p38 MAPK is GRK3- and arrestin-dependent in neurons and astrocytes. J Biol Chem 2006;281:18081–18089. [PubMed: 16648139]

142. Bruehl S, Chung OY. Parental history of chronic pain may be associated with impairments in endogenous opioid analgesic systems. Pain 2006;124:287–294. [PubMed: 16725261]

143. Bruehl S, Chung OY, Burns JW. Trait anger and blood pressure recovery following acute pain: evidence for opioid-mediated effects. Int J Behav Med 2006;13:138–146. [PubMed: 16712431]

144. Bruehl S, Chung OY, Donahue BS, Burns JW. Anger regulation style, postoperative pain, and relationship to the A118G mu opioid gene polymorphism: a preliminary study. J Behav Med 2006;29:161–169. [PubMed: 16400534]

145. Bruijnzeel AW, Lewis B, Bajpal LK, Morey TE, Dennis DM, Gold M. Severe deficit in brain reward function associated with fentanyl withdrawal in rats. Biol Psychiatry 2006;59:477–480. [PubMed: 16169528]

146. Brunton PJ, Sabatier N, Leng G, Russell JA. Suppressed oxytocin neuron responses to immune challenge in late pregnant rats: arole for endogenous opioids. Eur J Neurosci 2006;23:1241–1247. [PubMed: 16553786]

147. Bryant CD, Eitan S, Sinchak K, Fanselow MS, Evans CJ. NMDA receptor antagonism disrupts the development of morphine analgesic tolerance in male, but not female C57BL/6J mice. Am J Physiol 2006;291:R315–R326.

148. Bryant CD, Roberts KW, Byun JS, Fanselow MS, Evans CJ. Morphine analgesic tolerance in 129P3/J and 129S6/SvEv mice. Pharmacol Biochem Behav 2006;85:769–779. [PubMed: 17196637]

149. Burattini C, Gill TM, Aicardi G, Janak PH. The ethanol self-administration context as a reinstatement cue: acute effects of naltrexone. Neurosci 2006;139:877–887.

150. Burford JH, Corley KT. Morphine-associated pruritus after single extradural administration in a horse. Vet Anaesth Analg 2006;33:193–198. [PubMed: 16634946]

151. Burghardt PR, Wilson MA. Microinjection of naltrexone into the central, but not the basolateral, amygdala blocks the anxiolytic effects of diazepam in the plus maze. Neuropsychopaharmacol 2006;31:1227–1240.

152. Burke MC, Letts PA, Krajewski SJ, Rance NE. Coexpression of dynorphin and neurokinin B immunoreactivity in the rat hypothalamus: morphologic evidence of interrelated function within the arcuate nucleus. J Comp Neurol 2006;498:712–726. [PubMed: 16917850]

153. Bush JA, Mastro AM, Kraemer WJ. Proenkephalin peptide F immunoreactivity in different circulatory biocompartments after exercise. Peptides 2006;27:1498–1506. [PubMed: 16406203]

154. Cabioglu MT, Ergene N. Changes in serum leptin and beta-endorphin levels with weight loss by electroacupuncture and diet restriction in obesity treatment. Am J Chin Med 2006;34:1–11. [PubMed: 16437734]

155. Caeiro X, Hansen C, Garcia N, Vivas L. Beta-endorphin involvement in the regulatory response to body sodium overload. Neurosci 2006;142:557–565.

156. Cagniard B, Balsam PD, Brunner D, Zhuang X. Mice with chronically elevated dopamine exhibit enhanced motivation, but not learning, for a food reward. Neuropsychopharmacol 2006;31:1362–1370.

157. Caille S, Parsons LH. Cannabinoid modulation of opiate reinforcement through the ventral striatopallidal pathway. Neuropsychopharmacol 2006;31:804–813.

158. Caldiero RM, Parran TV Jr, Adelman CL, Piche B. Inpatient initiation of buprenorphine maintenance vs. detoxification: can retention of opioid-dependent patients in outpatient counseling be improved? Am J Addict 2006;15:1–7. [PubMed: 16449087]

159. Calle M, Kozicz T, van der Linden E, Desfeux A, Veening JG, Barendregt HP, Roubos EW. Effect of starvation on Fos and neuropeptide immunoreactivities in the brain and pituitary gland of Xenopus laevis. Gen Comp Endocrinol 2006;147:237–246. [PubMed: 16483575]

160. Calsyn DA, Malcy JA, Saxon AJ. Slow tapering from methadone maintenance in a program encouraging indefinite maintenance. J Subst Abuse Treat 2006;30:159–163. [PubMed: 16490679]

161. Calvo F, Coimbra NC. Interactions between opioid peptides-containing pathways and GABA(A)-receptors-mediated systems modulate panic-like-induced behaviors elicited by electric and chemical stimulation of the inferior colliculus. Brain Res 2006;1104:92–102. [PubMed: 16797498]

162. Campbell VC, Taylor RE, Tizabi Y. Antinociceptive effects of alcohol and nicotine: involvement of the opioid system. Brain Res 2006;1097:71–77. [PubMed: 16730342]

163. Campos AR, Santos FA, Rao VS. Ketamine-induced potentiation of morphine analgesia in rat tail-flick test: role of opioid-, alpha2-adrenoceptors and ATP-sensitive potassium channels. Biol Pharm Bull 2006;29:86–89. [PubMed: 16394516]

164. Canciani L, Giaroni C, Zanetti E, Giuliani D, Pisani R, Moro E, Trinchera M, Crema F, Lecchini S, Frigo G. Functional interaction between alpha2-adrenoceptors, mu- and kappa-opioid receptors in the guinea pig myenteric plexus: effects of chronic desipramine treatment. Eur J Pharmacol 2006;553:269–279. [PubMed: 17055479]

165. Cao JL, Liu HL, Wang JK, Zeng YM. Cross-talk between nitric oxide and ERK1/2 signaling pathway in the spinal cord mediates naloxone-precipitated withdrawal in morphine-dependent rats. Neuropharmacol 2006;51:315–326.

166. Capasso A, Piacente S, DeTommasi N, Rastrelli L, Pizza C. The effect of isoquinoline alkaloids on opiate withdrawal. Curr Med Chem 2006;13:807–812. [PubMed: 16611069]

167. Capasso R, Borrelli F, Capasso F, Siebert DJ, Stewart DJ, Zjawiony JK, Izzo AA. The hallucinogenic herb Salvia divinorum and its active ingredient Salvinorin A inhibit enteric cholinergic transmission in the guinea-pig ileum. Neurogastroeneterol Motil 2006;18:69–75.

168. Carai MA, Colombo G, Gessa YL, Yalamanchili R, Basavarajappa BS, Hungund BL. Investigation on the relationship between cannabinoid CB1 and opioid receptors in gastrointestinal motility in mice. Br J Pharmacol 2006;148:1043–1050. [PubMed: 16847440]

169. Carlezon WA Jr, Beguin C, DiNieri JA, Baumann MH, Richards MR, Todtenkopf MS, Rothman RB, Ma Z, Lee DY, Cohen BM. Depressive-like effects of the kappa-opioid receptor agonist salvinorin A on behavior and neurochemistry in rats. J Pharmacol Exp Ther 2006;316:440–447. [PubMed: 16223871]

170. Carroll CP, Walsh SL, Bigelow GE, Strain EC, Preston KL. Assessment of agonist and antagonist effects of tramadol in opioid-dependent humans. Exp Clin Psychopharmacol 2006;14(8bii):109–120. [PubMed: 16756415]

171. Carroll FI, Melvin MS, Nuckols MC, Mascarella SW, Navarro HA, Thomas JB. N-substituted 4beta-methyl-5-(3-hydroxyphenyl)-7alpha-amidomorphans are potent, selective kappa opioid receptor antagonists. J Med Chem 2006;49:1781–1791. [PubMed: 16509593]

172. Carvalho B, Angst MS, Fuller AJ, Lin E, Mathusamy AD, Riley ET. Experimental heat pain for detecting pregnancy-induced analgesia in humans. Anesth Analg 2006;103:1283–1287. [PubMed: 17056970]

173. Casares FM, Mantione KJ, Oh K, Lee R, Stefano GB. Nitric oxide's pulsatile release in lobster heart and its regulation by opiate signaling: pesticide interference. Med Sci Monit 2006;12:BR373–BR378. [PubMed: 17136001]

174. Castro RR, Cunha FQ, Silva FS Jr, Rocha FA. A quantitative approach to measure joint pain in experimental ostoarthritis: evidence of a role for nitric oxide. Osteoarthritis Cartilege 2006;14:769–776.

175. Catheline G, Touquet B, Besson JM, Lombard MC. Parturition in the rat: a physiological pain model. Anesthesiol 2006;57:1265.

176. Ceccarelli I, De Padova AM, Fiorenzani P, Massafra C, Aloisi AM. Single opioid administration modifies gonadal steroids in both the CNS and plasma of male rats. Neurosci 2006;140:929–937.

177. Ceccarelli SM, Pinard E, Stalder H, Alberati D. Discovery of N-(2-hydroxy-2-aryl-cyclohexyl) substituted spiropiperidines as GlyT1 antagonists with improved pharmacological profile. Bioorg Med Chem Lett 2006;16:354–357. [PubMed: 16246561]

178. Cengiz S, Ulukan O, Ates I, Tugcu H. Determination of morphine in postmortem rabbit bone marrow and comparison with blood morphine concentrations. Forensic Sci Int 2006;156:91–94. [PubMed: 16410157]

179. Chan GM, Stajic M, Marker EK, Hoffman RS, Nelson LS. Testing positive for methadone and either a tricyclic antidepressant or a benzodiazepine is associated with an accidental overdose death: analysis of medical examiner data. Acad Emerg Med 2006;13:543–547. [PubMed: 16641481]

180. Chang AK, Bijur PE, Meyer RH, Kenny MK, Solorzano C, Gallagher EJ. Safety and efficacy of hydromorphone as an analgesia alternative to morphine in acute pain: a randomized clinical trial. Ann Emerg Med 2006;48:164–172. [PubMed: 16857467]

181. Chang L, Luo L, Palmer JA, Sutton S, Wilson SJ, Barbier AJ, Breitenbucher JG, Chaplan SR, Webb M. Inhibition of fatty acid amide hydrolase produces analgesia by multiple mechanisms. Br J Pharmacol 2006;148:102–113. [PubMed: 16501580]

182. Charleston C, Puana R, McAllister RK, Hunter FA, Childs EW. Morphine attenuates hemorrhagic shock-induced hyperpermeability. Anesth Analg 2006;103:156–161. [PubMed: 16790645]

183. Chartoff EH, Mague SD, Barhight MF, Smith AM, Carlezon WA Jr. Behavioral and molecular effects of dopamine D1 receptor stimulation during naloxone-precipitated morphine withdrawal. J Neurosci 2006;26(5biv):6450–6457. [PubMed: 16775132]

184. Chawarski MC, Mazlan M, Schottenfeld RS. Heroin dependence and HIV infection in Malaysia. Drug Alcohol Depend 2006;82(1):S39–S42. [PubMed: 16769444]

185. Chefer VI, Shippenberg TS. Paradoxical effects of prodynorphin gene deletion on basal and cocaine-evoked dopaminergic neurotransmission in the nucleus accumbens. Eur J Neurosci 2006;23:229–238. [PubMed: 16420432]

186. Chefer VI, Zapata A, Shippenberg TS, Bungay PM. Quantitative no-net-flux microdialysis permits detection of increases and decreases in dopamine uptake in mouse nucleus accumbens. J Neurosci Methods 2006;155:187–193. [PubMed: 16466808]

187. Chen C, Farooqui M, Gupta K. Morphine stimulates vascular endothelial growth factor-like signaling in mouse retinal endothelial cells. Curr Neurovasc Res 2006;3:171–180. [PubMed: 16918381]

188. Chen C, Li JG, Chen Y, Huang P, Wang Y, Liu-Chen LY. GEC1 interacts with the kappa opioid receptor and enhances its expression. J Biol Chem 2006;281:7983–7993. [PubMed: 16431922]

189. Chen CP, Boyadjieva NI, Advis JP, Sarkar DK. Ethanol suppression of the hypothalamic proopiomelanocortin level and the splenic NK cell cytolytic activity is associated with a reduction in the expression of proinflammatory cytokines, but not anti-inflammatory cytokines in neuroendocrine and immune cells. Alcohol Clin Exp Res 2006;30:1925–1932. [PubMed: 17067358]

190. Chen CP, Kuhn P, Advis JP, Sarkar DK. Prenatal ethanol exposure alters the expression of period genes governing the circadian function of BEND neurons in the hypothalamus. J Neurochem 2006;97:1026–1033. [PubMed: 16686691]

191. Chen CP, Kuhn P, Chaturvedi K, Boyadjieva N, Sarkar DK. Ethanol induces apoptotic death of developing beta-endorphin neurons via suppression of cyclic adenosine monophosphate production and activation of transforming growth factor-beta 1-linked apoptotic signaling. Mol Pharmacol 2006;69:706–717. [PubMed: 16326933]

192. Chen L, Thakker MM, Winston S, Bolortuya Y, Basheer R, McCarley RW. REM sleep changes in rats induced by siRNA-mediated orexin knockdown. Eur J Neurosci 2006;24:2039–2048. [PubMed: 17067300]

193. Chen MH, Liu TW, Xie L, Liu TW, Song FQ, He T. Does naloxone alone increase resuscitation rate during cardiopulmonary resuscitation in a rat asphyxia model? Am J Emerg Med 24:567–572. [PubMed: 16938595]

194. Chen MH, Xie L, Liu TW, Song FQ, He T. Naloxone and epinephrine are equally effective for cardiopulmonary resuscitation in a rat asphyxia model. Acta Anaesthesiol Scand 2006;50:1125–1130. [PubMed: 16987343]

195. Chen RZ, Frassetto A, Fong TM. Effects of the CB1 cannabinoid receptor inverse agonist AM251 on food intake and body weight in mice lacking mu-opioid receptors. Brain Res 2006;1108:176–178. [PubMed: 16828068]

196. Chen SA, O'Dell LE, Hoefer ME, Greenwell TN, Zorrilla EP, Koob GF. Unlimited access to heroin self-administration: independent motivational markers of opiate dependence. Neuropsychopharmacol 2006;31:2692–2707.

197. Chen SR, Pan HL. Loss of TRPV1-expressing sensory neurons reduces spinal mu opioid receptors but paradoxically potentiates opioid analgesia. J Neurophysiol 2006;95:3086–3096. [PubMed: 16467418]

198. Chen SR, Pan HL. Blocking mu opioid receptors in the spinal cord prevents the analgesic action by subsequent systemic opioids. Brain Res 2006;1081:119–125. [PubMed: 16499888]

199. Chen T, Cai Q, Hong Y. Intrathecal sensory neuron-specific receptor agonists bovine adrenal medulla 8–22 and (Tyr6)-gamma2-MSH-6–12 inhibit formalin-induced nociception and neuronal Fos-like immunoreactivity in the spinal cord of the rat. Neurosci 2006;141:965–975.

200. Chen Y, Chen C, Wang Y, Liu-Chen LY. Ligands regulate cell surface level of the human kappa opioid receptor activation-induced down-regulation and pharmacological chaperone-mediated enhancement: differential effects of nonpeptide and peptide agonists. J Pharmacol Exp Ther 2006;319:765–775. [PubMed: 16882876]

201. Chen Y, Samal B, Hamelink CR, Xiang CC, Chen Y, Chen M, Vaudry D, Brownstein MJ, Hallenbeck JM, Eiden LE. Neuroprotection by endogenous and exogenous PACAP following stroke. Regul Pept 2006;137:4–19. [PubMed: 17027094]

202. Chen Y, Sommer C. Nociceptin and its receptor in rat dorsal root ganglion neurons in neuropathic and inflammatory pain models: implications on pain processing. J Peripher Nerv Syst 2006;11:232–240. [PubMed: 16930285]

203. Chen ZX, Zhang HL, Gu ZL, Chen BW, Han R, Reid PF, Raymond LN, Qin ZH. A long-form alpha-neurotoxin from cobra venom produces potent opioid-independent analgesia. Acta Pharmacol Sin 2006;27:402–408. [PubMed: 16539838]

204. Chena LX, Qia YM, Wangb R, Duan X, Gao YF, Yang DJ. Roles of nitric oxide synthase inhibitor on antinociceptive effects of mu-opioid agonist in mice. Protein Pept Lett 2006;13:993–997. [PubMed: 17168821]

205. Cheng JT, Huang CC, Liu IM, Tzeng TF, Chang CJ. Novel mechanism for plasma glucose-lowering action of metformin in streptozotocin-induced diabetic rats. Diabetes 2006;55:819–825. [PubMed: 16505249]

206. Cheng WF, Chen LK, Chen CA, Chang MC, Hsiao PN, Su YN, Lee CN, Jeng HJ, Hsieh CY, Sun WZ. Chimeric DNA vaccine reverses morphine-induced immunosuppression and tumorigenesis. Mol Ther 2006;13:203–210. [PubMed: 16140583]

207. Chesterfield M, Janik J, Murphree E, Lynn C, Schmidt E, Callahan P. Orphanin FQ/nociceptin is a physiological regulator of prolactin sectrtion in female rats. Endocrinology 2006;147:5087–5093. [PubMed: 16887913]

208. Chieng BC, Christie MJ, Osborne PB. Characterization of neurons in the rat central nucleus of the amygdala: cellular physiology, morphology and opioid sensitivity. J Comp Neurol 2006;497:910–927. [PubMed: 16802333]

209. Chin TY, Chueh SH, Tao PL. S-nitroglutathione and glutathione act as NMDA receptor agonists in cultured hippocampal neurons. Acta Pharmacol Sin 2006;27:853–860. [PubMed: 16787569]

210. Chiu CT, Ma T, Ho IK. Methamphetamine-induced behavioral sensitization in mice: alterations in mu-opioid receptor. J Biomed Sci 2006;13:797–811. [PubMed: 16847721]

211. Chong RY, Oswald L, Yang X, Uhart M, Lin PI, Wand GS. The micro-opioid receptor polymorphism A118G predicts cortisol responses to naloxone and stress. Neuropsychopharmacol 2006;31:204–211.

212. Choi HS, Kim CS, Hwang CK, Song KY, Wang W, Qiu Y, Law PY, Wei LN, Loh HH. The opioid ligand binding of human mu-opioid receptor is modulated by novel splice variants of the receptor. Biochem Biophys Res Commun 2006;343:1132–1140. [PubMed: 16580639]

213. Chou WY, Wang CH, Liu PH, Liu CC, Tseng CC, Jawan B. Human opioid receptor A118G polymorphism affects intravenous patient-controlled analgesia morphine consumption after total abdominal hysterectomy. Anesthesiol 2006;105:334–337.

214. Chou WY, Yang LC, Lu HF, Ko JY, Wang CH, Lin SH, Lee TH, Concejero A, Hsu CJ. Association of mu-opioid receptor gene polymorphism (A118G) with variations in morphine consumption for analgesia after total knee arthroplasty. Acta Anesthesiol Scand 2006;50:787–792.

215. Christie MJ. Opioid and cannabinoid receptors: friends with benefits or just close friends? Br J Pharmacol 2006;148:385–386. [PubMed: 16682965]

216. Chritin M, Savasta M, Besson G. Benefit of tianeptine and morphine in a transgenic model of familial amyotrophic lateral sclerosis. Amyotroph Lateral Scler 2006;7:32–37. [PubMed: 16546757]

217. Chu LF, Clark DJ, Angst MS. Opioid tolerance and hyperalgesia in chronic pain patients after one motn of oral morphine therapy: a preliminary prospective study. J Pain 2006;7:43–48. [PubMed: 16414554]

218. Chu YC, Lin SM, Hsieh YC, Chan KH, Tsou MY. Intraoperative administration of tramadol for postoperative nurse-controlled analgesia resulted in earlier awkening and less sedation than morphine in children after cardiac surgery. Anesth Analg 2006;102:1668–1673. [PubMed: 16717306]

219. Chung E, Burke B, Bieber AJ, Doss JC, Ohgami Y, Quock RM. Dynorphin-mediated antinocicetive effects of L-arginine and SIN-1 (an NO donor) in mice. Brain Res Bull 2006;70:245–250. [PubMed: 16861110]

220. Chung S, Pohl S, Zeng J, Civelli O, Reinscheid RK. Endogenous orphanin FQ/nociceptin is involved in the development of morphine tolerance. J Pharmacol Exp Ther 2006;318:262–267. [PubMed: 16595734]

221. Church CA, Stewart C 4th, O-Lee TJ, Wallace D. Rofecoxib versus hydrocodone/acetaminophen for postoperative analgesia in functional endoscopic sinus surgery. Laryngoscope 2006;116:602–606. [PubMed: 16585866]

222. Churruca I, Portillo MP, Zumalabe JM, Macarulla MT, Del Burgo LS, Zarate J, Echevarria E. Fluoxetine alters mu opioid receptor expression in obese Zucker rat extrahypothalamic regions. Int J Neurosci 2006;116:289–298. [PubMed: 16484055]

223. Ciccocioppo R, Economidou D, Rimondini R, Sommer W, Massi M, Heilig M. Buprenorphine reduces alcohol drinking through activation of the nociceptin/orphanin FQ-NOP receptor system. Biol Psychiat 2006;61:4–12. [PubMed: 16533497]

224. Cifani C, Guerrini R, Massi M, Polidori C. Chronic intracerebroventricular infusion of nociceptin/orphanin FQ increases food and ethanol intake in alcohol-preferring rats. Peptides 2006;27:2803–2810. [PubMed: 16730389]

225. Ciofi P, Leroy D, Tramu G. Sexual dimorphism in the organization of the rat hypothalamic infindibular area. Neurosci 2006;141:1731–1745.

226. Ciraulo DA, Hitzemann RJ, Somoza E, Knapp CM, Rotrosen J, Sarid-Segal O, Ciraulo AM, Greenblatt DJ, Chiang CN. Pharmacokinetics and pharmacodynamics of multiple sublingual buprenorphine tablets in dose-escalation trials. J Clin Pharmacol 2006;46:179–192. [PubMed: 16432270]

227. Claiborne J, Nag S, Mokha SS. Activation of opioid receptor like-1 receptor in the spinal cord produces sex-specific antinociception in the rat: estrogen attenuates antinociception in the female, whereas testosterone is required for the expression of antinociception in the male. J Neurosci 2006;26:13048–13053. [PubMed: 17167094]

228. Clark MJ, Furman CA, Gilson TD, Traynor JR. Comparison of the relative efficacy and potency of mu-opioid agonists to activate Galpha(i/o) proteins containing a pertussis toxin-insensitive mutation. J Pharmacol Exp Ther 2006;317:858–864. [PubMed: 16436499]

229. Codd EE, Carson JR, Colburn RW, Dax SL, Desai-Krieger D, Martinez RP, McKown LA, Neilson LA, Pitis PM, Stahle PL, Stone DJ, Streeter AJ, Wu WN, Zhang SP. The novel, orally active, delta

opioid RWJ-394674 is biotransformed to the potent mu opioid RWJ-413216. J Pharmacol Exp Ther 2006;318:1273–1279. [PubMed: 16766719]

230. Colpaert FC, Deseure K, Stinus L, Adriansen H. High-efficacy 5-hydroxytryptamine 1A receptor activation counteracts opioid hyperallodynia and affective conditioning. J Pharmacol Exp Ther 2006;316:892–899. [PubMed: 16254131]
231. Comer SD, Sullivan MA, Yu E, Rothenberg JL, Kleber HD, Kampman K, Dackis C, O'Brien CP. Injectable, sustained-release naltrexone for the treatment of opioid dependence: a randomized, placebo-controlled trial. Arch Gen Psychiat 2006;63:210–218. [PubMed: 16461865]
232. Compton P, Ling W, Moody D, Chiang N. Pharmacokinetics, bioavailability and opioid effects of liquid versus tablet buprenorphine. Drug Alcohol Depen 2006;82:25–31.
233. Concas A, Sogliano C, Porcu P, Marra C, Brundu A, Biggio G. Neurosteroids in nicotine and morphine dependence. Psychopharmacol 2006;186:281–292.
234. Cone EJ, Heit HA, Caplan YH, Gourlay D. Evidence of morphine metabolism to hydromorphone in pain patients chronically treated with morphine. J Anal Toxicol 2006;30:1–5. [PubMed: 16620524]
235. Connor M, Kitchen I. Has the sun set on kappa3-opioid receptors? Br J Pharmacol 2006;147:349–350. [PubMed: 16402044]
236. Contet C, Gaveriaux-Ruff C, Matifas A, Caradec C, Champy MF, Kieffer BL. Dissociation of analgesic and hormonal responses to forced swim stress using opioid receptor knockout mice. Neuropsychopharmacol 2006;31:1733–1744.
237. Contreras MT, Hernandez AF, Gonzalez M, Gonzalez S, Ventura R, Pla A, Valverde JL, Segura J, de la Torre R. Application of pericardial fluid to the analysis of morphine (heroin) and cocaine in forensic toxicology. Forensic Sci Int 2006;164:168–171. [PubMed: 16442766]
238. Correia CJ, Walsh SL, Bigelow GE, Strain EC. Effects associated with double-blind omission of buprenorphine/naloxone over a 98-h period. Psychopharmacol 2006;189:297–306.
239. Cosola C, Albrizio M, Guaricci AC, DeSalvia MA, Zarrilli A, Sciorsci RL, Minoia R. Opioid agonist/antagonist of naloxone in modulating rabbit jejunum contractility in vitro. J Physiol Pharmacol 2006;57:439–449. [PubMed: 17033096]
240. Coulbault L, Beaussier M, Verstuyft C, Weickmans H, Dubert L, Tregouet D, Descot C, Parc Y, Lienhart A, Jaillon P, Becquemont L. Environmental and genetic factors associated with morphine response in the postoperative period. Clin Pharmacol Ther 2006;79:316–324. [PubMed: 16580900]
241. Coy RT, Kanarek RB. Chronic sucrose intake reduces the antagonist effect of beta-funaltrexamine on morphine-induced antincocieption in female, but not in male rats. Nutr Neurosci 2006;9:131–139. [PubMed: 17176635]
242. Craft RM, Clark JL, Hart SP, Pinckney MK. Sex differences in locomotor effects of morphine in the rat. Pharmacol Biochem Behav 2006;85:850–858. [PubMed: 17217999]
243. Craft RM, Leitl MD. Potentiation of morphine antinociception by pentobarbiatal in female vs. male rats Pain 2006;121:115–125.
244. Crandall CS, Kerrigan S, Blau RL, Lavalley J, Zumwalt R, McKinney PE. The influence of site of collection on postmortem morphine concentration in heroin overdose victims. J Forensic Sci 2006;51:413–420. [PubMed: 16566783]
245. Crawford HW, Hickey C, Zaarour C, Howard A, Naser B. Development of acute opioid tolerance during infusion of remifentanil for pediatric scoliosis surgery. Anesth Analg 2006;102:1662–1667. [PubMed: 16717305]
246. Crawford MW, Galton S, Naser B. Postoperative morphine consumption in children with sickle-cell disease. Pediatr Anaesth 2006;16:152–157.
247. Croissandeau G, Wahnon F, Yashpal K, Seidah NG, Coderre TJ, Chretien M, Mbikay M. Increased ostress-induced analgesia in mice lacking the proneuropeptide convertase PC2. Neurosci Lett 2006;406:71–75. [PubMed: 16905251]
248. Crooks PA, Kottayil SG, Al-Ghananeem AM, Byrn SR, Allan Butterfield D. Opiate receptor binding properties of morphine-, dihydromorphine- and codeine 6-O-sulfate ester congners. Bioorg Med Chem Lett 2006;16:4291–4295. [PubMed: 16777416]

249. Crosby SJ, Knapp CM, Kornetsky C. Nociceptive threshold and analgesic response to morphine in aged and young adult rats as determined by thermal radiation and intracerebral electrical stimulation. Pharmacol Biochem Behav 2006;84:148–157. [PubMed: 16759686]

250. Csaba G, Kovacs P, Pallinger E. Changes in the endorphin and serotonin content of rat immune cells during adulthood following maternal exposure to ethanol during pregnancy and lactation. Alcohol 2006;38:111–116. [PubMed: 16839857]

251. Csaba G, Kovacs P, Pallinger E. Influence of in vitro and in vivo insulin treatment on the hormone Histamine, serotonin, endorphin and triiodothyronine) content of thymus and spleen cells. Life Sci 2006;78:1034–1047. [PubMed: 16423370]

252. Csaba G, Kovacs P, Pallinger E. Hormones in the nucleus. Immunologically demonstrable biogenic amines (serotonin, histamine) in the nucleus of rat peritoneal mast cells. Life Sci 2006;78:1871–1877. [PubMed: 16332378]

253. Csaba G, Kovacs P, Pallinger E. Influence of paraformaldehyde and EDAC fixation on the demonstrability of hormones (histamine, endorphin, triiodothyrodine) in rat immune cells: an immunocytochemical comparative analysis. Cell Biol Int 2006;30:412–415. [PubMed: 16546412]

254. Cui Y, Chen Y, Zhi JL, Guo RX, Feng JQ, Chen PX. Activation of p38 mitogen-activated protein kinase in spinal microglia mediates morphine antinociceptive tolerance. Brain Res 2006;1069:235–243. [PubMed: 16403466]

255. Dahan A. Opioid-induced respiratory effects: new data on buprenorphine. Palliat Med 2006;20 (16a):S3–S8. [PubMed: 16764215]

256. Dai F, Yang JY, Gu PF, Hou Y, Wu CF. Effect of drug-induced ascorbic acid release in the striatum and the nucleus accumbens in hippocampus-lesioned rsts. Brain Res 2006;1125:163–170. [PubMed: 17112479]

257. Dai Z, Kang L, Wang L, Ma L. Different roles of dopamine receptor subtypes in footshock stress-induced enhancement of morphine conditioned place preference. Neurosci Lett 2006;409:52–56. [PubMed: 17000048]

258. Dallimore JE, Mickiewicz AL, Napier TC. Intra-ventral pallidal glutamate antagonists block expression of morphine-induced place preference. Behav Neurosci 2006;120:1103–1114. [PubMed: 17014261]

259. Damaj MI, Zheng J, Martin BR, Kuhar MJ. Intrathecal CART (55–102) attenuates hyperalgesia and allodynia in a mouse model of neuropathic, but not inflammatory pain. Peptides 2006;27:2019–2023. [PubMed: 16814901]

260. Danielsson I, Gasior M, Stevenson GW, Folk JE, Rice KC, Negus SS. Electroencephalographic and convulsant of the delta opioid agonist SNC80 in rhesus monkeys. Pharmacol Biochem Behav 2006;85:428–434. [PubMed: 17112570]

261. Dardonville C, Fernandez-Fernandez C, Gibbons SL, Ryan GJ, Jagerovic N, Gabilondo AM, Meana JJ, Callado LF. Synthesis and pharmacological studies of new hybrid derivatives of fentanyl active at the mu-opioid receptor and I2-imidazoline binding sites. Bioorg Med Chem 2006;14:6570–6580. [PubMed: 16797997]

262. da Silva VA Jr, Vieira A, Pinto CF, de Paula TA, Palma MB, Lins Amorim MJ, Amorim AA Jr, Manhaes-de-Castro R. Neonatal treatment with naloxone increases the population of Sertoli cells and sperm production in adult rats. Reprod Nutr Dev 2006;46:157–166. [PubMed: 16597421]

263. D'Astous M, Mickley KR, Dluzen DE, Di Paolo T. Differential protective properties of estradiol and tamoxifen against methamphetamine-induced nigrostriatal dopaminergic toxicity in mice. Neuroendocrinology 2006;82:111–120.

264. Davis KM, Esposito MA, Meyer BA. Oral analgesia compared with intravenous patient-controlled analgesia for pain after cesarean delivery: a randomized controlled trial. Am J Obstet Gynecol 2006;194:967–971. [PubMed: 16580284]

265. Davis S, Deo SH, Barlow M, Yoshishige D, Farias M, Caffrey JL. The monosialosyl ganglioside GM-1 reduces the vagolytic efficacy of delta2-opioid receptor stimulation. Am J Physiol Heart Circ Physiol 2006;291:H2318–H2326. [PubMed: 16815987]

266. Davison JW, Sweeney ML, Bush KR, davis Correale TM, Calsyn DA, Reoux JP, Sloan KL, Kiviahan DR. Outpatient treatment engagement and abstinence rates following inpatient opioid detoxification. J Addict Dis 2006;25:27–35. [PubMed: 17088223]

267. Dean AJ, Saunders JB, Jones RT, Young RM, Connor JP, Lawford BR. Does naltrexone treatment lead to depression? Findings from a randomized controlled trial in subjects with opioid dependence. J Psychiat Neurosci 2006;31:38–45.

268. Decaillot FM, Che FY, Fricker LD, Devi LA. Peptidomics of Cpefat/fat mouse hypothalamus and striatum: effect of chronic morphine administration. J Mol Neurosci 2006;28:277–284. [PubMed: 16691015]

269. De Castro E, Silva E, Luz PA, Magrani J, Andrade L, Miranda N, Pereira V, Fregoneze JB. Role of the central opioid system in the inhibition of water and salt intake induced by central administration of IL-1beta in rats. Pharmacol Biochem Behav 2006;83:285–295. [PubMed: 16554088]

270. Deciga-Campos M, Guerrero-Anaico JA, Quijano L, Mata R. Antinociceptive activity of 3-O-beta-d-glucopyranosyl-23,24-dihydrocucurbitacin F from Hintonia standleyana (Rubiaceae). Pharmacol Biochem Behav 2006;83:342–348. [PubMed: 16569425]

271. Del Gaudio A, Ciritella P, Perrotta F, Puopolo M, Lauta E, Mastronardi P, De Vivo P. Remifentanil vs fentanyl with a target controlled propofol infusion in patients undergoing craniotomy for supratentorial lesions. Minerva Anestesiol 2006;72:309–319. [PubMed: 16675939]

272. De Luca-Vinhas MC, Macedo CE, Brandao ML. Pharmacological assessment of the freezing, antinociception and exploratory behavior organized in the ventrolateral periaqueductal gray. Pain 2006;121:94–104. [PubMed: 16472918]

273. DeNoble VJ, Mele PC. Intravenous nicotine self-administration in rats: effects of mecamylamine, hexamethonium and naloxone. Psychopharmacol 2006;184:266–272.

274. Densmore VS, Morton NM, Mullins JJ, Secki JR. 11 beta-hydroxysteroid dehydrogenase type 1 induction in the arcuate nucleus by high-fat feeding: a novel constraint to hyperphagia? Endocrinol 2006;147:4486–4495.

275. Deo SH, Johnson-Davis S, Barlow MA, Yoshishige D, Caffrey JL. Repeated delta-1 opioid receptor stimulation reduces delta2-opioid receptor responses in the sinoarterial node. Am J Physiol Heart Circ Physiol 2006;291:H2246–H2254. [PubMed: 16782849]

276. De Pietri L, Siniscalchi A, Reggiani A, Masetti M, Begliomini B, Gazzi M, Gerunda GE, Pasetto A. The use of intrathecal morphine for postoperative pain relief after liver resection: a comparison with epidural analgesia. Anesth Analg 2006;102:1157–1163. [PubMed: 16551916]

277. Der-Avakian A, Bland ST, Scmid MJ, Watkins LR, Spencer RL, Maier SF. The role of glucocorticoids in the uncontrollable stress-induced potentiation of nucleus accumbens shell dopamine and conditioned place preference responses to morphine. Psychoneuroendocrinol 2006;31:653–663.

278. Dernedde M, Stadler M, Bardiau F, Seidel L, Boogaerts JG. Low vs. high concentration of levobupivacaine for post-operative epidural analgesia: influence of mode of delivery. Acta Anaesthesiol Scand 2006;50:613–621. [PubMed: 16643233]

279. D'Este L, Casini A, Pontieri FE, Renda TG. Changes in neuropeptide FF and NPY immunohistochemical patterns in rat brain under heroin treatment. Brain Res 2006;1083:151–158. [PubMed: 16529722]

280. Diana M, Spiga S, Acquas E. Persistent and reversible morphine withdrawal-induced morphological changes in the nucleus accumbens. Ann NY Acad Sci 2006;1074:446–457. [PubMed: 17105943]

281. Diaz SL, Barros VG, Antonelli MC, Rubio MC, Balerio GN. Morphine withdrawal syndrome and its prevention with baclofen: autoradiographic study of mu-opioid receptors in prepubertal male and female mice. Synapse 2006;60:132–140. [PubMed: 16715492]

282. Di Benedetto M, D'addario C, Candeletti S, Romualdi P. Chronic and acute effects of 3,4-methylenedioxy-N-methylamphetamine ('Ecstasy') administration on the dynorphinergic system in the rat brain. Neurosci 2006;137:187–196.

283. Dickson EW, Ludwig PS, Ackermann LW, Buresh CT, Denning GM. Met5-enkephalin-Arg6-Phe7 (MEAP): a cardioprotective hormonal opioid. Acad Emerg Med 2006;13:813–819. [PubMed: 16766738]

284. Dietze P, Jolley D, Fry CL, Bammer G, Moore D. When is a little knowledge dangerous? Circumstances of recent heroin overdose and links to knowledge of overdose risk factors. Drug Alchol Depend 2006;84:223–230.

285. Dijan MC, Blanchet B, Pesce F, Sermet A, Disdet M, Vazquez V, Gury C, Roux FX, Raggueneau JL, Coste J, Joly LM. Comparison of the time to extubation after use of remifentanil or sufentanil in combination with propofol as anesthesia in adults undergoing nonemergency intracranial surgery: a prospective, randomized, double-blind trial. Clin Ther 2006;28:560–568. [PubMed: 16750467]

286. Dimitriou H, Bakogeorgou E, Kampa M, Notas G, Stiakaki E, Kouroumalis E, Kalmanti M, Castanas E. Kappa-opioids induce a reversible inhibition of CFU-GM from CD133(+) cord blood cells. Cytotherapy 2006;8(17):367–374. [PubMed: 16923612]

287. Dobi A, Szemes M, Lee C, Palkovits M, Lim F, Gyorgy A, Mahan MA, Agoston DV. AUF-1 is expressed in the developing brain, binds to AT-rich double-stranded DNA, and regulates Enk gene expression. J Biol Chem 2006;281:28889–28900. [PubMed: 16769718]

288. Do Carmo GP, Mello NK, Rice KC, Folk JE, Negus SS. Effects of the selective delta opioid agonist SNC80 on cocaine- and food-maintained responding in rhesus monkeys. Eur J Pharmacol 2006;547:92–100. [PubMed: 16934797]

289. Doggrell SA. Which treatment for alcohol dependence: naltrexone, acamprosate and/or behavioural intervention? Expert Opin Pharmacother 2006;7:2169–2173. [PubMed: 17020440]

290. Dogrul A, Seyrek M. Systemic morphine produces antinociception mediated by spinal 5-HT7, but not 5-HT1A and 5-HT2 receptors in the spinal cord. Br J Pharmacol 2006;149:498–505. [PubMed: 16921395]

291. Doherty MM, Poon K, Tsang C, Pang KS. Transport is not rate-limiting in morphine glucuronidation in the single-pass perfused liver preparation. J Pharmacol Exp Ther 2006;317:890–900. [PubMed: 16464965]

292. Domingues A, Cunha Oliveira T, Laco ML, Macedo TR, Oliveira CR, Rego AC. Expression of NR1/NR2B N-methyl-D-aspartate receptors enhances heroin toxicity in HEK293 cells. Ann NY Acad Sci 2006;1074:458–465. [PubMed: 17105944]

293. Dominguez-Ramirez AM, Cortes-Arroyo AR, Pena MH, Aoki-Maki K, Lopez JR, Rios-Castaneda C, Lopez-Munoz FJ. High-performance liquid chromatography assay for morphine in small plasma samples: application to pharmacokinetic studies in rats. J Pharm Biomed Anal 2006;40:1172–1178. [PubMed: 16242894]

294. Dong Z, Mao R, Han H, Cao J, Xu L. Morphine withdrawal modified antinociceptive effects of acute morphine in rats. Biochem Biophys Res Commun 2006;346:578–582. [PubMed: 16762316]

295. Doron R, Fridman L, Yadid G. Dopamine-2 receptors in the arcuate nucleus modulate cocaine-seeking behavior. Neuroreport 2006;17:1633–1636. [PubMed: 17001283]

296. Dortch-Carnes J, Russell KR. Morphine-induced reduction of intraocular pressure and pupil diameter: role of nitric oxide. Pharmacol 2006;77:17–24.

297. Doyle GA, Sheng XR, Schwebel CL, Ferraro TN, Berrettini WH, Buono RJ. Identification and functional significance of polymorphisms in the mu-opioid receptor gene (Oprm) promoter of C57BL/6 and DBA/2 mice. Neurosci Res 2006;55:244–254. [PubMed: 16644048]

298. Doyon WM, Howard EC, Shippenberg TS, Gonzales RA. Kappa-opioid receptor modulation of accumbal dopamine concentration during operant ethanol self-administration. Neuropharm 2006;51:487–496.

299. Drake CT, Milner TA. Mu opioid receptors are extensively co-localized with parvalbumin, but not somatostatin, in the dentate gyrus. Neurosci Lett 2006;403:176–180. [PubMed: 16716508]

300. Drakenberg K, Nikoshkov A, Horvath MC, Fagergren P, Gharibyan A, Saarelainen K, Rahman S, Nylander I, Bakalkin G, Rajs J, Keller E, Hurd YL. Mu opioid receptor A118G polymorphism in association with striatal opioid neuropeptide gene expression in heroin abusers. Proc Natl Acad Sci (USA) 2006;103:7883–7888. [PubMed: 16682632]

301. Du G, Gao Y, Nie S, Pan W. The permeation of nalmefene hydrochloride across different regions of ovine nasal mucosa. Chem Pharm Bull (Tokyo) 2006;54:1722–1724. [PubMed: 17139110]

302. Dunbar JL, Turncliff RZ, Dong Q, Silverman BL, Ehrich EW, Lasseter KC. Single- and multiple-dose pharmacokinetics of long-acting injectable naltrexone. Alcohol Clin Exp Res 2006;30:480–490. [PubMed: 16499489]

303. Dunbar SA, Karamian I, Yeatman A, Zhang J. Effects of recurrent withdrawal on spinal GABA release during chronic morphine infusion in the rat. Eur J Pharmacol 2006;535:152–156. [PubMed: 16540107]

304. Du Pen S, Du Pen A, Hillyer J. Intrathecal hydromorphone for intractable nonmalignant pain: a retrospective study. Pain Med 2006;7:101–15. [PubMed: 16634721]

305. Ebrahimi F, Tavakoli S, Hajrasouliha AR, Sadgeghipour H, Dehghani M, Ahmadi SH, Dehpour AR. Involvement of endogenous opioid peptides and nitric oxide in the blunted chronotopic and inotropic responses to beta-adrenergic stimulation in cirrhotic rats. Fundam Clin Pharmacol 2006;20:461–471. [PubMed: 16968416]

306. Ebrahimkhani MR, Kiani S, Oakley F, Kendall T, Shariftabrizi A, Tavangar SM, Moezi L, Payabvash S, Karoon A, Hosieninik H, Mann DA, Moore KP, Mani AR, Dehpour AR. Naltrexone, an opioid receptor antagonist, attenuates liver fibrosis in bile duct ligated rats. Gut 2006;55:1606–1616. [PubMed: 16543289]

307. Economidou D, Fedeli A, Fardon RM, Weiss F, Massi M, Ciccocioppo R. Effect of novel nociceptin/orphanin FQ receptor ligands on ethanol drinking in alcohol-preferring rats. Peptides 2006;27:3299–3306. [PubMed: 17097763]

308. Economidou D, Policani F, Angellotti T, Massi M, Terada T, Ciccocioppo R. Effect of novel NOP receptor ligands on food intake in rats. Peptides 2006;27:775–783. [PubMed: 16483692]

309. Egashira N, Li JC, Mizuki A, Yamauchi K, Matsuda T, Osajima M, Matsushita M, Mishima K, Iwasaki K, Hara S, Ono N, Nishimura R, Nohara T, Fujiwara M. Antagonistic effects of methanolic extract of Polygala telephiodes on morphine responses in mice. J Ethnopharmacol 2006;104:193–198. [PubMed: 16202547]

310. Elhabazi K, Aboufatima R, Benharref A, Zyad A, Chait A, Dalal A. Study on the antinociceptive effects of Thymus broussonetli Boiss extracts in mice and rats. J Ethnopharmacol 2006;107:406–411. [PubMed: 16713159]

311. El-Hage N, Wu G, Ambati J, Bruce-Keller AJ, Knapp PE, Hauser KF. CCR2 mediates the increases in glial activation by exposure to HIV-1 Tat and opiates. J Neuroimmunol 2006;178:9–16. [PubMed: 16831471]

312. El-Hage N, Wu G, Wang J, Ambati J, Knapp PE, Reed JL, Bruce-Keller AJ, Hauser KF. HIV-1 Tat and opiate-induced changes in astrocytes promote chemotaxis of microglia through the expression of MCP-1 and alternative chemokines. Glia 2006;53:132–146. [PubMed: 16206161]

313. El-Haggar S, El-Ashmawy S, Attia A, Mostafa T, Roaiah MM, Fayez A, Ghazi S, Zohdy W, Roshdy N. Beta-endorphin in serum and seminal plasma in infertile men. Asian J Androl 2006;8:709–712. [PubMed: 16751995]

314. Elliott JC, Picker MJ, Sparrow AJ, Lysle DT. Dissociation between sex differences in the immunological, behavioral and physiological effects of kappa- and delta-opioids in Fischer rats. Psychopharmacol 2006;185:66–75.

315. Elliott JC, Wagner AF, Lysle DT. Neurokinin-1 receptor signaling mediates sex differences in mu and kappa opioid-induced enhancement of contact hypersensitivity. J Neuroimmunol 2006;181:100–105. [PubMed: 17023055]

316. El-Tahtawy A, Kokki H, Reidenberg BE. Population pharmacokinetics of oxycodone in children 6 months to 7 years old. J Clin Pharmacol 2006;46:433–442. [PubMed: 16554451]

317. Emeterio EP, Tramullas M, Hurle MA. Modulation of apoptosis in the mouse brain after morphine treatments and morphine withdrawal. J Neurosci Res 2006;83:1352–1361. [PubMed: 16496378]

318. Endepols H, Muhlenbrock-Lenter S, Roth G, Walkowiak W. The septal complex of the fire-bellied toad Bombina orientalis: chemoarchitecture. J Chem Neuroanat 2006;31:59–76. [PubMed: 16229986]

319. Endoh T. Pharmacological characterization of inhibitory effects of postsynaptic opioid and cannabinoid receptors on calcium currents in neonatal rat nucleus tractus solitarius. Br J Pharmacol 2006;147:391–401. [PubMed: 16402042]

320. Englberger W, Kogel B, Friderichs E, Strassburder W, Germann T. Reversibility of opioid receptor occupancy of buprenorphine in vivo. Eur J Pharmacol 2006;534:95–102. [PubMed: 16490191]

321. Engstrom L, Mackerlova L, Blomqvist A. Lipopolysaccharide induces preproenkephalin transcription in hypophysiotropic neurons of the rat paraventricualr hypothalamic nucleus suggesting a neuroendocrine role for enkephalins during immune stress. Neurosci 2006;142:781–788.

322. Erkent U, Iskit AB, Onur R, Ilhan M. The effect of nitric oxide on fentanyl and haloperidol-induced catalepsy in mice. Eur J Anesthesiol 2006;23:580–585.

323. Ernst A, Kohrie J, Bergmann A. Proenkephalin A 119–159, a stable Proenkephalin A precursor fragment identified in human circulation. Peptides 2006;27:1835–1840. [PubMed: 16621157]

324. Escher T, Mittleman G. Schedule-induced alcohol drinking: non-selective effects of acamprosate and naltrexone. Addict Biol 2006;11:55–63. [PubMed: 16759337]

325. Estebe JP, Legay F, Gentili M, Wodey E, Leduc C, Ecoffey C, Moulineaux JP. An evaluation of a polyamine-deficient diet for the treatment of inflammatory pain. Anesth Analg 2006;102:1781–1788. [PubMed: 16717326]

326. Estelles J, Rodriguez-Arias M, Maldanado C, Manzanedo C, Aguilar MA, Minarro J. Prenatal cocaine alters later responses to morphine in adult male mice. Prog Neuropsychopharmacol Biol Psychiatry 2006;30:1073–1082. [PubMed: 16737762]

327. Etgen AM, Gonzalez-Flores O, Todd BJ. The role of insulin-like growth factor and growth factor-associated signal transduction pathways in estradiol and progesterone facilitation of female reproductive behaviors. Front Neuroendocrinol 2006;27:363–375. [PubMed: 16904171]

328. Eun JS, Bae K, Yun YP, Hong JT, Kwon HN, Oh KW. Inhibitory effect of paeonol on morphine-induced locomotor sensitization and conditioned place preference in mice. Arch Pharm Res 2006;29:904–910. [PubMed: 17121187]

329. Fachin-Scheit DJ, Frozino Ribeiro A, Pigatto G, Oliveira Goeldner F, Boerngen de Lacerda R. Development of a mouse model of ethanol addiction: naltrexone efficacy in reducing consumption but not craving. J Neural Transm 2006;113:1305–1321. [PubMed: 16465467]

330. Falk T, Zhang S, Erbe EL, Sherman SJ. Neurochemical and electrophysiological characteristics of rat striatal neurons in primary culture. J Comp Neurol 2006;494:275–289. [PubMed: 16320238]

331. Fang Q, Guo J, He F, Pneg YL, Chang M, Wang R. In vivo inhibition of neuropeptide FF agonism by BIBP3226, an NPY Yi receptor antagonist. Peptides 2006;27:2207–2213. [PubMed: 16762456]

332. Fang X, Tang W, Sun S, Huang L, Huang Z, Weil MH. Mechanism by which activation of delta-opioid receptor reduces the severity of postresuscitation myocardial dysfunction. Crit Care Med 2006;34:2607–2612. [PubMed: 16775573]

333. Fanjun M, Junfa L, Bingxi Z, Fang J. nPKCepsilon and NMDA receptors participate in neuroprotection induced by morphine pretreatment. J Neurosurg Anesthesiol 2006;18:119–124. [PubMed: 16628065]

334. Farooqui M, Geng ZH, Stephenson EJ, Zaveri N, Yee D, Gupta K. Naloxone acts as an antagonist of estrogen receptor activity in MCF-7 cells. Mol Cancer Ther 2006;5:611–620. [PubMed: 16546975]

335. Fassoulaki A, Stamatakis E, Petropoulos G, Siafaka I, Hassiakos D, Sarantopoulos C. Gabapentin attenuates late, but not acute pain after abdominal hysterectomy. Eur J Anaesthesiol 2006;23:136–141. [PubMed: 16426468]

336. Favrat B, Zimmermann G, Zullino D, Krenz S, Dorogy F, Muller J, Zwahlen A, Broers B, Besson J. Opioid antagonist detoxification under anaesthesia versus traditional clonidine detoxification combined with an additional week of psychosocial support: a randomized clinical trial. Drug Alcohol Depend 2006;81:109–116. [PubMed: 16024184]

337. Fecho K, Manning EL, Maixner W, Schmitt CP. Effects of carrageenan and morphine on acute inflammation and pain in Lewis and Fischer rats. Brain Behav Immun 2006;21:68–78. [PubMed: 16603335]

338. Fedeli A, Policani F, Ubaldi M, Cippitelli A, Massi M, Ciccocioppo R. Activation of the nociceptin/orphanin FQ system is unable to reverse CRF2 receptor mediated anorexia in the rat. Peptides 2006;27:3284–3291. [PubMed: 17050037]

339. Feeney GF, Comnnor JP, Young RM, Tucker J, McPherson A. Combined acamprosate and naltrexone, with cognitive behavioural therapy is superior to either medication alone for alcohol abstinence: a singler centre's experience with pharmacotherapy. Alcohol Alcohol 2006;41:321–327. [PubMed: 16467406]

340. Feld JM, Hoffman WE, Stechert MM, Hoffman IW, Ananda RC. Fentanyl or dexmetdedetomidine combined with desflurane for bariatric surgery. J Clin Anesth 2006;18:24–28. [PubMed: 16517328]

341. Feng P, Rahim RT, Cowen A, Liu-Chen LY, Peng X, Gaughan J, Meissner JJ Jr, Adler MW, Eisenstein TK. Effects of mu, kappa or delta opioids administered by pellet or pump on oral Salmonella infection and gastrointestinal transit. Eur J Pharmacol 2006;534:250–257. [PubMed: 16513108]

342. Fenu S, Spina L, Rivas A, Longoni R, DiChiara G. Morphine-conditioned single-trial place preference: role of nucleus accumbens shell dopamine receptors in acquisition, but not expression. Psychopharmacol 2006;187:143–153.

343. Fichna J, do Rego JC, Kosson P, Schiller PW, Costenin J, Janecka A. [(35)S]GTPgammaS binding is stimulated by endomorphin-2 and morphiceptin analogs. Biochem Biophys Res Commun 2006;345:162–168. [PubMed: 16677613]

344. Fichna J, Gach K, Piestrzeniewicz M, Burgeon E, Poels J, Vanden Broeck J, Janecka A. Functional characterization of opioid receptor ligands by aequorin luminescence-based calcium assay. J Pharmacol Exp Ther 2006;317:1150–1154. [PubMed: 16497786]

345. Fichna J, Janecka A, Bailly L, Marsais F, Constentin J, do Rego JC. In vitro characterization of novel peptide inhibitors of endomorphin-degrading enzymes in the rat brain. Chem Biol Drug Des 2006;68:173–175. [PubMed: 17062015]

346. Fichna J, Piestrzeniewicz M, Gach K, Poels J, Burgeon E, Vanden Broeck J, Jancka A. [D-1-Nal4] enndomorphin-2 is a potent mu-opioid receptor antagonist in the aequorin luminescence-based calcium assay. Life Sci 2006;79:1094–1099. [PubMed: 16624333]

347. Fiellin DA, Pantalon MV, Chawarski MC, Moore BA, Sullivan LE, O'Connor PG, Schottenfeld RS. Counseling plus buprenorphine-naloxone maintenance therapy for opioid dependence. N Engl J Med 2006;355:365–374. [PubMed: 16870915]

348. Finn A, Fabre SF, Hellstrom PM, Brene S. Methodological aspects of rat beta-endorphin analysis – influence of diurnal variation. J Immunol Meth 2006;312:118–125.

349. Fischer BD, Dykstra LA. Interactions between an N-methyl-D-aspartate antagonist and low-efficacy opioid receptor agonists in assays of schedule-controlled responding and thermal nociception. J Pharmacol Exp Ther 2006;318:1300–1306. [PubMed: 16772537]

350. Flaten MA, Aslaksen PM, Finset A, Simonsen T, Johansen O. Cognitive and emotional factors in placebo analgesia. J Psychosom Res 2006;61:81–89. [PubMed: 16813849]

351. Flores JA, Galan-Rodriguez B, Ramiro-Fuentes S, Fernandez-Espejo E. Role of dopamine neurons in the rostral linear nucleus and periaqueductal gray in the rewarding and sensitizing properties of heroin. Neuropsychopharmacol 2006;31:1475–1488.

352. Foradori CD, Amstalden M, Goodman RL, Lehman MN. Colocalisation of dynorphin and neurokinin B immunoreactivity in the arcuate nucleus and median eminence of the sheep. J Neuroendocrinol 2006;18:534–541. [PubMed: 16774502]

353. Ford CP, Mark GP, Williams JT. Properties and opioid inhibition of mesolimbic dopamine neurons vary according to target location. J Neurosci 2006;26:2788–2797. [PubMed: 16525058]

354. Forster JG, Rosenberg PH, Niemi TT. Continuous spinal micocatheter (28 gauge) technique for arterial bypass surgery of the lower extremities and comparison of ropivacaine with or without morphine for postoperative analgesia. Br J Anaesth 2006;97:393–400. [PubMed: 16798772]

355. Fox MA, Stevenson GW, Rice KC, Riley AL. Naloxone, not proglumide or MK-801, alters effects of morphine preexposure on morphine-induced taste aversions. Pharmacol Biochem Behav 2006;84:169–177. [PubMed: 16777201]

356. Fox SH, Lang AE, Brotchie JM. Translation of nondopaminergic treatments for levodopa-induced dyskinesia from MPTP-lesioned nonhuman primates to phase Iia clinical studies: keys to success and roads to failure. Mov Disord 2006;21:1578–1594. [PubMed: 16874752]

357. Franca DS, Ferreira-Alves DL, Duarte ID, Ribeiro MC, Rezende RM, Bakhle YS, Francischi JN. Endogenous opioids mediate the hypoalgesia induced by selective inhibitors of cyclo-oxygenase 2 in rat paws treated with carrageenan. Neuropharmacol 2006;51:37–43.

358. Franklin SO, Jiminez R. Increases in preproeEnkephalin mRNA levels in the Syrian hamster: the influence of glucorticoids is dependent on age and tissue. Brain Res 2006;1086:65–75. [PubMed: 16597437]

359. Fredheim OM, Kassa S, Dale O, Klepstad P, Lando NI, Borchgrevink PC. Opioid switching from oral slow release morphine to oral methadone may improve pain control in chronic non-malignant pain: a nine-month follow-up study. Palliat Med 2006;20:35–41. [PubMed: 16482756]

360. Freitas RM, Vasconcelos SM, Sousa FC, Viana GS, Fonteles MM. Pharmacological studies of the opioids, mood stabilizer and dopaminergic drugs on pilocarpine-induced seizures and status epilepticus. Neurosci Lett 2006;408:84–88. [PubMed: 17011127]

361. Frenklakh L, Bhat RS, Bhaskaran M, Sharma S, Sharma M, Dinda A, Singhal PC. Morphine-induced degradation of the host defense barrier role of intestinal mucosal injury. Dig Dis Sci 2006;51:318–325. [PubMed: 16534675]

362. Freye E, Latasch L, Levy JV. S(+)-ketamine attenuates increase in electroencephalograph activity and amplitude height of sensory-evoked potentials during rapid opioid detoxification. Anesth Analg 2006;102:1439–1444. [PubMed: 16632823]

363. Frithiof R, Rundgren M. Activation of central opioid receptors determines the timing of hypotension during acute hemorrhage-induced hypovolemia in conscious sheep. Am J Physiol 2006;291:R987–R996.

364. Fu CY, Yang Q, Wang KR, Kong ZQ, Chen Q, Wang R. Rat/mouse hemokinin-1, a mammalian tachykinin peptide, markedly potentiates the antinociceptive effects of morphine administered at the peripheral and supraspinal level. Behav Brain Res 2006;170:293–301. [PubMed: 16621052]

365. Fu X, Wang YQ, Wu GC. Involvement of nociceptin/orphanin FQ and its receptor in electroacupuncture-produced anti-hyperalgesia in rats with peripheral inflammation. Brain Res 2006;1078:212–218. [PubMed: 16563360]

366. Fuchigami T, Kakinohana M, Nakamura S, Murata K, Sugahara K. Intrathecal nicorandil and small-dose morphine can induce spastic paraparesis after a noninjurious interval of spinal cord ischemia in the rat. Anesth Analg 2006;102:1217–1222. [PubMed: 16551926]

367. Fuentealba JA, Gysling K, Magendzo K, Andres ME. Repeated administration of the selective kappa-opioid receptor agonist U-69593 increases stimulated dopamine extracellular levels in the rat nucleus accumbens. J Neurosci Res 2006;84:450–459. [PubMed: 16676328]

368. Fujii H, Nagase H. Rational drug design of selective epsilon opioid receptor agonist TAN-821 and antagonist TAN-1014. Curr Med Chem 2006;13:1109–1118. [PubMed: 16719773]

369. Fujii M, Nabe T, Tomozawa J, Kohno S. Involvement of skin barrier dysfunction in itch-related scratching in special diet-fed hairless mice. Eur J Pharmacol 2006;530:152–156. [PubMed: 16359656]

370. Fujita T, Kumamoto E. Inhibition by endomorphin-1 and endomorphin-2 of excitatory transmission in adult rat substantia gelatinosa neurons. Neurosci 2006;139(12a):1095–1105.

371. Fukada H, Suenaga K, Tsuchida D, Mantyh CR, Pappas TN, Hicks GA, Dehaven-Hudkins DL, Takahashi T. The selective mu opioid receptor antagonist, alvimopan, improves delayed GI transit of postoperative ileus in rats. Brain Res 2006;1102:63–70. [PubMed: 16797494]

372. Fukuda T, Hisano S, Toyooka H. Moderate hypercapnia-induced anesthetic effects and endogenous opioids. Neurosci Lett 2006;403:20–23. [PubMed: 16701947]

373. Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. CMAJ 2006;174:1589–1594. [PubMed: 16717269]

374. Furudono Y, Ando C, Yamamoto C, Kobashi M, Yamamoto T. Involvement of specific orexigenic neuropeptides in sweetener-induced overconsumption in rats. Behav Brain Res 2006;175:241–248. [PubMed: 17010451]

375. Gale SD, Perkel DJ. Physiological properties of zebra finch ventral tegmental area and substantia nigra pars compacta neurons. J Neurophysiol 2006;96:2295–2306. [PubMed: 16870835]

376. Galea S, Worthington N, Piper TM, Nandi VV, Curtis M, Rosenthal DM. Provision of naloxone to injection drug users as an overdose prevention strategy: early evidence from a pilot study in New York City. Addict Behav 2006;31:907–912. [PubMed: 16139434]

377. Galeote L, Kieffer BL, Maldanado R, Berrendero F. Mu-opioid receptors are involved in the tolerance to nicotine antinociception. J Neurochem 2006;97:416–423. [PubMed: 16539669]

378. Galeotti N, Stefano GB, Guarna N, Bianchi E, Ghelardini C. Signaling pathway of morphine induced acute thermal hyperalgesia in mice. Pain 2006;123:294–305. [PubMed: 16650582]

379. Galietta G, Loizzo A, Loizzo S, Trombetta G, Spampinato S, Campana G, Capasso A, Palermo M, Guarino I, Franconi F. Administration of antisense oligodeoxynucleotide against proopiomelanocortin prevents enduring hormonal alterations induced by neonatal handling in male mice. Eur J Pharmacol 2006;550:180–185. [PubMed: 17045988]

380. Galizio M, Miller L, Ferguson A, McKinney P, Pitts RC. Olfactory repeated discrimination reversal in rats: effects of chlordiazepoxide, dizocilpine and morphine. Behav Neurosci 2006;120:1175–1179. [PubMed: 17014269]

381. Gallagher EJ, Esses D, Lee C, Lahn M, Bijur PE. Randomized clinical trial of morphine in acute abdominal pain. Ann Emerg Med 2006;48:150–160. [PubMed: 16953529]

382. Gameiro GH, Gameiro PH, Andrade Ada S, Pereira LF, Arthuri MT, Marcondes FK, Veiga MC. Nociception- and anxiety-like behavior in rats submitted to different periods of restraint stress. Physiol Behav 2006;87:643–649. [PubMed: 16488452]

383. Gao F, Hu X, Chen D. Naloxone or vagotomy does not influence centrally octreotide-induced inhibition of gastric acid secretion in rats. J Huazhong Univ Sci Technolog Med Sci 2006;26:432–435. [PubMed: 17120741]

384. Gao Y, Liu X, Liu W, Qi Y, Liu X, Zhou Y, Wang R. Opioid receptor binding and antinociceptive activity of the analogues of endomorphin-2 and morphiceptin with phenylalanine mimics in position 3 or 4. Bioorg Med Chem Lett 2006;16:3688–3692. [PubMed: 16682191]

385. Garcia-Martinez D, Portilla-de Buen E, Leal C, Santillan P, Muniz J. The immediate response to severe shock in a canine model with a combination of hypertonic-hyperoncotic solution with naloxone. Shock 2006;26:379–385. [PubMed: 16980885]

386. Gardell LR, King T, Ossipov MH, Rice KC, Lai J, Vanderah TW, Porreca F. Opioid receptor-mediated hyperalgesia and antinociceptive tolerance induced by sustained opiate delivery. Neurosci Lett 2006;396:44–49. [PubMed: 16343768]

387. Garland M, Abildskov KM, Taylor S, Benzeroual K, Caspersen CS, Arroyo SE, Kiu TW, Reznik B, Weldy P, Daniel SS, Stark RI. Fetal morphine metabolism and clearance are constant during late gestation. Drug Metab Dispos 2006;34:636–646. [PubMed: 16443669]

388. Gavioli EC, Calo' G. Antidepressant-and anxiolytic-like effects of nociceptin/orphanin FQ receptor ligands. Naunyn Schmied Arch Pharmacol 2006;372:319–330.

389. Gear RW, Lee JS, Miaskowski C, Gordon NC, Paul SM, Levine JD. Neuroleptics antagonize nalbuphine antianalgesia. J Pain 2006;7:187–191. [PubMed: 16516824]

390. Gehlert DR, Gackenheimer SL, Shaw JL. Distribution of nociceptin and Ro64–6198 activated [35S]-GTPgammaS binding in the rat brain. Neuropeptides 2006;40:95–105. [PubMed: 16403422]

391. Geib AJ, Babu K, Ewald MB, Boyer EW. Adverse effects in children after unintentional buprenorphine exposure. Pediatrics 2006;118:1746–1751. [PubMed: 17015570]

392. Genazzani AR, Bernardi F, Pluchino N, Giretti MS, Begliuomini S, Casarosa E, Luisi M, Kloosterboer HJ. Effect of tibolone administration on central and peripheral levels of allopregnanolone and beta-endorphin in female rats. Menopause 2006;13:57–64. [PubMed: 16607099]

393. Gendron L, Lucido AL, Mennicken F, O'Donnell D, Vincent JP, Stroh T, Beaudet A. Morphine and pain-related stimuli enhance cell surface availability of somatic delta-opioid receptors in rat dorsal root ganglia. J Neurosci 2006;26:953–962. [PubMed: 16421315]

394. Gentili F, Cardinaletti C, Carrieri A, Ghelfi F, Mattioli L, Perfumi M, Vesprini C, Pigini M. Involvement of I2-imidazoline binding sites in positive and negative morphine analgesia modulatory effects. Eur J Pharmacol 2006;553:73–81. [PubMed: 17081513]

395. Georges F, LeMoine C, Aston-Jones G. No effect of morphine on ventral tegmental dopmine neurons during withdrawal. J Neurosci 2006;26:5720–5726. [PubMed: 16723528]

396. Gerald TM, Ward GR, Howlett AC, Franklin SO. CB1 knockout mice display significant changes in striatal opioid peptide and D4 dopamine receptor gene expression. Brain Res 2006;1093:20–24. [PubMed: 16684513]

397. Gerra G, Fantoma A, Zaimovic A. Naltrexone and buprenorphine combination in the treatment of opiate dependence. J Psychopharmacol 2006;20:806–814. [PubMed: 16401652]

398. Ghahremani MH, Eghtesad E, Tahsili-Fahadan P, Sharifzadeh M, Amini M, Tootian Z. Inhibition of the cyclooxygenase pathway attenuates morphine-induced conditioned place preference in mice. Pharmacol Biochem Behav 2006;85:356–361. [PubMed: 17049975]

399. Gharagozlou P, Hashemi E, DeLorey TM, Clark JD, Lameh J. Pharmacological profiles of opioid ligands at kappa opioid receptors. BMC Pharmacol 2006;6:3. [PubMed: 16433932]

400. Giacomuzzi S, Kemmler G, Ertl M, Riemer Y. Opioid addicts at admission vs. slow-release oral morphine, methadone and sublingual buprenorphine maintenance treatment participants. Subst Use Misuse 2006;41:223–244. [PubMed: 16393744]

401. Gibson PR, Johnston S, Lagopoulos J, Cummine JL. Transient loss of motor-evoked responses associated with caudal injection of morphine in a patient with spondylolisthesis undergoing spinal fusion. Pediatr Anaesth 2006;16:568–572.

402. Gintzler AR, Chakrabarti S. Post-opioid receptor adaptations to chronic morphine; altered functionality and associations of signaling molecules. Life Sci 2006;79:717–722. [PubMed: 16581089]

403. Glick SD, Ramirez RL, Livi JM, Maisonneuve IM. 18-methoxycoronaridine acts in the medial habenula and/or interpedunuclar nucleus to decrease morphine self-administration in rats. Eur J Pharmacol 2006;537:94–98. [PubMed: 16626688]

404. Goktalay G, Cavun S, Levendusky MC, Hamilton JR, Millington WR. Glycyl-glutamine inhibits nicotine conditioned place preference and withdrawal. Eur J Pharmacol 2006;530:95–102. [PubMed: 16364288]

405. Goktalay G, Cavun S, Levendusky MC, Resch GE, Veno PA, Millington WR. Hemorrhage activates proopiomelanococrtin neurons in rat hypothalamus. Brain Res 2006;1070:45–55. [PubMed: 16403465]

406. Gold MS, Melker RJ, Dennis DM, Morey TE, Bajpai LK, Pomm R, Frost-Pineda K. Fentanyl abuse and dependence: further evidence for second hand exposure hypotheis. J Addict Dis 2006;25:15–21. [PubMed: 16597569]

407. Goldfarb Y, Reinscheid RK, Kusnecov AW. Orphanin FQ/nociceptin interactions with the immune system in vivo: gene expression changes in lymphoid organs and regulation of the cytokine response to staphylococcal enterotoxin A. J Neuroimmunol 2006;176:76–85. [PubMed: 16762423]

408. Gonzalez D, Riba J, Bouso JC, Gomez-Jarabo D, Barbanoj MJ. Pattern of use and subjective effects of Salvia divinorum among recreational users. Drug Alcohol Depend 2006;85:157–162. [PubMed: 16720081]

409. Gonzalez-Nunez V, Barrallo A, Traynor JR, Rodriguez RE. Characterization of opioid-binding sites in the zebrafish brain. J Pharamcol Exp Ther 2006;316:900–904.

410. Goto Y, Arai-Otsuki S, Tachibana Y, Ichikawa D, Ozaki S, Takahashi H, Iwasawa Y, Okamoto O, Okuda S, Ohta H, Sagara T. Identification of a novel spiropiperidine opioid receptor-like 1 antagonist class by a focused library approach featuring 3D-pharmacophore similarity. J Med Chem 2006;49:847–849. [PubMed: 16451050]

411. Goumon Y, Muller A, Glattard E, Marban C, Gasnier C, Strub JM, Chasserot-Golaz S, Rohr O, Stefanho GB, Welters ID, Van Dorsselaer A, Schoentgen F, Aunis D, Metz-Boutigue MH. Identification of morphine-6-glucuronide in chromaffin cell secretory granules. J Biol Chem 2006;281:8082–8089. [PubMed: 16434406]

412. Grakalic I, Schindler CW, Baumann MH, Rice KC, Riley AL. Effects of stress modulation on morphine conditioned place preferences and plasma corticosterone levels in Fischer, Lewis and Sprague-Dawley rat strains. Psychopharm 2006;189:277–286.

413. Grant JE, Potenza MN, Hollander E, Cunningham-Williams R, Nurminen T, Smits G, Kallio A. Multicenter investigation of the opioid antagonist nalmefene in the treatment of pathological gambling. Am J Psychiat 2006;163:303–312. [PubMed: 16449486]

414. Granstrem O, Adriani W, Shumilina M, Izykenova G, Dambinova S, Laviola G. Specific changes in levels of autoantibodies to glutamate and opiate receptors induced by morphine administration in rats. Neurosci Lett 2006;403:1–5. [PubMed: 16687214]

415. Gray AC, Coupar IM, White PJ. Comparison of opioid receptor distributions in the rat central nervous system. Life Sci 2006;79:674–685. [PubMed: 16546223]

416. Grecksch G, Bartzsch K, Widera A, Becker A, Hollt V, Koch T. Development of tolerance and sensitization to different opioid agonists in rats. Psychopharmacol 2006;186:177–184.

417. Greenwald MK, Hursh SR. Behavioral economic analysis of opioid consumption in heroin-dependent individuals: effects of unit price and pre-session drug supply. Drug Alcohol Depend 2006;85:35–48. [PubMed: 16616994]

418. Gross ER, Hsu AK, Gross GJ. The JAK/STAT pathway is essential for opioid-induced cardioprotection: JAK2 as a mediator of STAT3, Akt and GSK-beta. Am J Physiol 2006;291:H827–H834.

419. Grosse Hartiage MA, Theisen MM, Monteiro de Oliveira NP, Van Aken H, Fobker M, Weber TP. Kappa-opioid receptor antagonism improves recovery from myocardial stunning in chronically instrumented dogs. Anesth Analg 2006;103:822–832. [PubMed: 17000788]

420. Grusser SM, Thalemann CN, Platz W, Golz J, Partecke G. A new approach to preventing relapse in opiate addicts: a psychometric evaluation. Biol Psychiat 2006;71:231–235.

421. Gu PF, Wu CF, Yang JY, Shang Y, Hou Y, Bi XL, Dai F. Differential effects of drug-induced ascorbic acid release in the striatum and nucleus accumbens of freely moving rats. Neurosci Lett 2006;399:79–84. [PubMed: 16480820]

422. Guan Y, Borzan J, Meyer RA, Raja SN. Windup in dorsal horn neurons is modulated by endogenous spinal mu-opioid mechanisms. J Neurosci 2006;26:4298–4307. [PubMed: 16624950]

423. Guedes AG, Rude EP, Rider MA. Evaluation of histamine release during constant rate infusion of morphine in dogs. Vet Anaesthes Analg 2006;33:28–35.

424. Guieu R, Fenouillet E, Devaux C, Fajloun Z, Carrega L, Sabatier JM, Sauze N, Marguet D. CD26 modulates nociception in mice via its didpeptidyl-peptidase IV activity. Behav Brain Res 2006;166:230–235. [PubMed: 16154213]

425. Guitart-Masip M, Giminez-Llort L, Fernandez-Tereul A, Canete T, Tobena A, Ogren SO, Terenius L, Johansson B, et al. Reduced ethanol response in the alcohol-preferring RHA rats and neuropeptide mRNAs in relevant structures. Eur J Neurosci 2006;23:531–540. [PubMed: 16420460]

426. Gultekin H, Ahmedov V. Role of the opioidergic system and nitric oxide in the analgesic effect of venlafaxine. Yakugaku Zasshi 2006;126:117–121. [PubMed: 16462101]

427. Gunduz O, Rizzi A, Baldisserotto A, Guerrini R, Spagnolo B, Gavioli EC, Kocsis L, Magyar A, Benyhe S, Borsodi A, Calo G. In vitro and in vivo pharmacological characterization of the nociceptin/orphanin FQ receptor ligand Ac-RYYRIK-ol. Eur J Pharmacol 2006;539:39–48. [PubMed: 16682024]

428. Gunduz O, Sipos F, Spagnolo B, Kocsis L, Magyar A, Orosz G, Borsodi A, Calo G, Benyhe S. In vitro binding and functional studies of Ac-RYYRIK-ol and its derivatives, novel partial agonists of the nociceptin/orphanin F/Q receptor. Neurosignals 2006;15:91–101. [PubMed: 16874009]

429. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces postoperative analgesic requirements. Can J Anaesth 2006;53:646–652. [PubMed: 16803911]

430. Guerrero AT, Verri WA Jr, Cunha TM, Silva TA, Rocha FA, Ferreira SH, Cunha FQ, Parada CA. Hypernociception elicited by tibio-tarsal joint flexion in mice: a novel experimental arthritis model for pharmacological screening. Pharmacol Biochem Behav 2006;84:244–251. [PubMed: 16797062]

431. Gursoy S, Bagcivan I, Yildirim MK, Berkan O, Kaya T. Vasorelaxant effect of opioid analgesics on the isolated human radial artery. Eur J Anesthesiol 2006;23:496–500.

432. Guzman DC, Vazquez IE, Brizuela NO, Alvarez RJ, Mejia GB, Garcia EH, Santamaria D, de Apreza MR, Olguin HJ. Assessment of oxidative damage induced by acute doses of morphine sulfate in postnatal and adult rat brain. Neurochem Res 2006;31:549–554. [PubMed: 16758364]

433. Hacker J, Pederson NP, Chieng BC, Keay KA, Christie MJ. Enhanced Fos expression in glutamic acid decarboxylase immunoreactive neurons of the mouse periaqueductal gray during opioid withdrawal. Neurosci 2006;137:1389–1396.

434. Hadziomerovic D, Rabenbauer B, Wildt L. Normalization of hyperinsulinemia by chronic opioid receptor blockade in hyperandrogenemic women. Fertil Steril 2006;86:651–657. [PubMed: 16901484]

435. Haeseler G, Foadi N, Ahrens J, Dengler R, Hecker H, Leuwer M. Tramadol, fentanyl and sufentanil but not morphine block voltage-operated sodium channels. Pain 2006;126:234–244. [PubMed: 16949748]

436. Haller CA, Stone J, Burke V, Branch J, Chen K, Gross S. Comparison of an automated and point-of-care immunoassay for GC-MCS for urine oxycodone in the clinical laboratory. J Anal Toxicol 2006;30:106–111. [PubMed: 16620541]

437. Haller VL, Cichewicz DL, Welch SP. Non-cannabinoid CB1, non-cannabinoid CB2 antinociceptive effects of several novel compounds in the PPQ stretch test in mice. Eur J Pharmacol 2006;546:60–68. [PubMed: 16919265]

438. Hama A, Basler A, Sagen J. Enhancement of morphine antinociception with the peptide N-methyl-D-aspartate receptor antagonist [Ser1]-histogranin in the formalin test. Brain Res 2006;1095:59–64. [PubMed: 16712813]

439. Hamabe W, Maeda T, Fukazawa Y, Kumamoto K, Shang LQ, Yamamoto A, Yamamoto C, Tokuyama S, Kishioka S. P-glycoprotein ATPase activating effect of opioid analgesics and their P-glycoprotein-dependent antinociception in mice. Pharmacol Biochem Behav 2006;85:629–636. [PubMed: 17134744]

440. Hamad MO, Kiptoo PK, Stinchcomb AL, Crooks PA. Synthesis and hydrolytic behavior of two novel tripartite codrugs of naltrexone and 6beta-naltrexol with hydroxybupropion as potential alcolhol abuse and smoking cessation agents. Bioorg Med Chem 2006;14:7051–7061. [PubMed: 16798000]

441. Hamidi GA, Manaheji H, Janahmadi M, Noorbakhsh SM, Salami M. Co-administration of MK-801 and morphine attenuates neuropathic pain in rat. Physiol Behav 2006;88:628–635. [PubMed: 16815501]

442. Han MH, Bolanos CA, Green TA, Olson VG, Neve RL, Liu RJ, Aghajanian GK, Nestler EJ. Role of cAMP response element –binding protein in the rat locus coeruleus: regulation of neuronal activity and opiate withdrawal behaviors. J Neurosci 2006;26:4624–4629. [PubMed: 16641242]

445. Han W, Hata M, Imbe H, Liu QR, Takamatsu Y, Koizumi M, Murphy NP, Senba E, Uhl GR, Sora I, Ikeda K. Increased body weight in mice lacking mu-opioid receptors. Neuroreport 2006;17:941–944. [PubMed: 16738492]

446. Han W, Kasai S, Hata H, Takahashi T, Takamatsu Y, Yamamoto H, Uhl GR, Sora I, Ikeda K. Intracisternal A-particle element in the 3′ noncoding region of the mu-opioid receptor gene in CXBK mice: a new genetic mechanism underlying differences in opioid sensitivity. Pharmacogenet Genomics 2006;16:451–460. [PubMed: 16708053]

447. Hanif K, Gupta K, Gupta S, Gupta YK, Maiti S, Pasha S. Chimeric peptide of met-enkephalin and FMRFa: effect of chlorination on confirmation and analgesia. Neurosci Lett 2006;403:131–135. [PubMed: 16764989]

448. Hanson JE, Emond MR, Madison DV. Blocking polysysnaptic inhibition via opioid receptor activation isolates excitatory synaptic currents without triggering epileptiform activity in organoatypic hippocampal slices. J Neurosci Meth 2006;150:8–15.

449. Hara Y, Yakoleva T, Bakalkin G, Pickel VM. Dopamine D1 receptors have subcellular distributions conducive to interactions with prodynorphin in the nucleus accumbens shell. Synapse 2006;60:1–19. [PubMed: 16575853]

450. Harris AC, Atkinson DM, Aase DM, Gewirtz JC. Double dissociation in the neural substrates of acute opiate dependence as measured by withdrawal-potentiated startle. Neurosci 2006;139:1201–1210.

451. Harris CL, Hamid B, Rosenquist RW, Schultz-Stubner SH. Ganglionic local opioid application (GLOA) for treatment of chronic headache and facial pain. Reg Anesth Pain Med 2006;31:460–462. [PubMed: 16952820]

452. Hartrick CT, Martin G, Kantor G, Koncelik J, Manvelian G. Evaluation of a single-dose extended-release epidural morphine formulation for pain after knee arthroplasty. J Bone Joint Surg Am 2006;88:273–281. [PubMed: 16452737]

453. Hasegawa M, Ohno H, Tanaka H, Hatakeyama M, Kawaguchi H, Takahashi T, Handa H. Affinity identification of delta-opioid receptors using latex nanoparticles. Bioorg Med Chem Lett 2006;16:158–161. [PubMed: 16216499]

454. Hashimoto T, Saito Y, Yamada K, Hara N, Kirihara Y, Tsuchiya M. Enhancement of morphine analgesic effect with induction of mu-opioid receptor endocytosis in rats. Anesthesiol 2006;105:574–580.

455. Hatami H, Oryan S, Semnanian S, Kazemi B, Ahmadiani A. Additive effect of dextromethorphan on the inhibitory effect of anti-NT4 on morphine tolerance. Pharmacol 2006;78:105–112.

456. Hatsukari I, Hitosugi N, Dinda A, Singhal PC. Morphine modulates the monocyte-macrophage conversion phase. Cell Immunol 2006;239:41–48. [PubMed: 16698002]

457. Hawes JJ, Narasimhaiah R, Picciotto MR. Galanin attenuates cyclic AMP regulatory element-binding protein (CREB) phosphorylation induced by chronic morphine and naloxone challenge in Cath. a cells and primary striatal cultures. J Neurochem 2006;96:1160–1168. [PubMed: 16417577]

458. Haywood MD, Schaich-Borg A, Pintar JE, Low MJ. Differential involvement of endogenous opioids in sucrose consumption and food reinforcement. Pharmacol Biochem Behav 2006;85:601–611. [PubMed: 17166571]

459. He S, Grasing K. L-methamphetamine and selective MAO inhibitors decrease morphine-reinforced and non-reinforced behavior in rats; insights towards selegiline's mechanism of action. Pharmacol Biochem Behav 2006;85:675–688. [PubMed: 17157368]

460. Heidari MR, Azad EM, Mehrabani M. Evaluation of the analgesic effect of Echium amonenum Fisch & C.A. Mey. Extract in mice: possible mechanism involved. J Ethnopharmacol 2006;103:345–349. [PubMed: 16185831]

461. Heidari P, Sahebgharani M, Riazi G, Zarrindast MR. Influence of morphine and dopamine receptor sensitization on locomotor activity in mice. Pharmacol 2006;78:185–192.

462. Heinz AJ, Epstein DH, Schroeder JR, Singleton EG, Heishman SJ, Preston KL. Heroin and cocaine craving and use during treatment: measurement validation and potential relationships. J Subst Abuse Treat 2006;31:355–364. [PubMed: 17084789]

463. Hellemans KG, Everitt BJ, Lee JL. Disrupting reconsolidation of conditioned withdrawal memories in the basolateral amygdala reduces suppression of heroin seeking in rats. J Neurosci 2006;26:12694–12699. [PubMed: 17151272]

464. Hellemans KG, Dickinson A, Everitt BJ. Motivational control of heroin seeking by conditioned stimuli associated with withdrawal and heroin taking by rats. Behav Neurosci 2006;120:103–114. [PubMed: 16492121]

465. Helwig M, Khorooshi RM, Tups A, Barrett P, Archer ZA, Exner C, Rozman N, Braulke LJ, Mercer JG, Klingenspor M. PC1/3 and PC/2 gene expression and post-translational endoproteolytic pro-opiomelanocortin processing is regulated by photoperiod in the seasonal Siberian hamster (Phodopus sungorus). J Neuroendocrinol 2006;18:413–425. [PubMed: 16684131]

466. Hernandez-Avila CA, Song C, Kuo L, Tennen H, Armeli S, Kranzler HR. Targeted versus daily naltrexone: secondary analysis of effects on average daily drinking. Alcohol Clin Exp Res 2006;30:860–865. [PubMed: 16634855]

467. Hernandez-Delgadillo GP, Cruz SL. Endogenous opioids are involved in the morphine and dipyrone analgesic potentiation in the tail-flick test in rats. Eur J Pharmacol 2006;546:54–59. [PubMed: 16914138]

468. Hess PE, Snowman CE, Hahn CJ, Kunze LJ, Ingold VJ, Pratt SD. Chloroprocaine may not affect epidural morphine for postcesarean deleivery analgesia. J Clin Anesth 2006;18:29–33. [PubMed: 16517329]

469. Hesselgard K, Stromblad LG, Romner B, Reinstrup P. Postoperative continuous intrathecal pain treatment in children after selective dorsal rhizotomy with bupivacaine and two different morphine doses. Pediatr Anaeth 2006;16:436–443.

470. Hill-Pryor C, Dunbar JC. The effect of high fat-induced obesity on cardiovascular and physical activity and opioid responsiveness in conscious rats. Clin Exp Hypertens 2006;28:133–145. [PubMed: 16546839]

471. Hiller A, Meretoja DA, Korpela R, Pliparinen S, Taivainen T. The analgesic efficacy of acetaminophen, ketoprofen or their combination for pediatric surgical patients having soft tissue or orthopedic procedures. Anesth Analg 2006;102:1365–1371. [PubMed: 16632811]

472. Himukashi S, Takeshima H, Koyanagi S, Shichino T, Fukuda K. The involvement of the nociceptin receptor in the antinociceptive action of nitrous oxide. Anesth Analg 2006;103:738–741. [PubMed: 16931689]

473. Hiramatsu M, Mizuno N, Kanematsu K. Pharmacological characterization of the ameliorating effect on learning and memory impairment and antinociceptive effect of KT-95 in mice. Behav Brain Res 2006;167:219–225. [PubMed: 16223533]

474. Hiramatsu M, Watanabe E. Dynorphin A(2–13) improves mecamylamine-induced learning impairment accompanied by reversal of reductions in acetylcholine release in rats. Neuropep 2006;40:47–56.

475. Hogen Esch AJ, van der Heide S, van den Brink W, van Ree JM, Bruynzeel DP, Coenraads PJ. Contact allergy and respiratory and mucosal complaints from heroin (diacetylmorphine). Contact Dermatitis 2006;54:42–49. [PubMed: 16426293]

476. Holstein SE, Phillips TJ. GABAB receptor stimulation attenuates the locomotor effects of morphine in mice bred for extreme sensitivity to the stimulant effects of ethanol. Pharmacol Biochem Behav 2006;85:697–704. [PubMed: 17161860]

477. Holtman JR Jr, Wala EP. Characterization of the antinociceptive effect of oxycodone in male and female rats. Pharmacol Biochem Behav 2006;83:100–108. [PubMed: 16434089]

478. Hope BT, Simmons DE, Mitchell TB, Kreuter JD, Mattson BJ. Cocaine-induced locomotor activity and Fos expression in nucleus accumbens are sensitized for 6 months after repeated cocaine administration outside the home cage. Eur J Neurosci 2006;24:867–875. [PubMed: 16930414]

479. Horner KA, Keefe KA. Regulation of psychostimulant-induced preprodynorphin, c-fos and zif/268 messenger RNA expression in the rat dorsal striatum by mu opioid receptor blockade. Eur J Pharmacol 2006;532:61–73. [PubMed: 16443216]

480. Horta ML, Morejon LC, da Cruz AW, Dos Santos GR, Welling LC, Terhorst L, Costa RC, Alam RU. Study of the prophylactic effect of droperidol, allzapride, propofol and promethazine on spinal morphine-induced pruritus. Br J Anaesth 2006;96:796–800. [PubMed: 16597655]

481. Horvat S, Mlinaric-Majerski K, Glavas-Obrovac L, Jakas A, Veljkovic J, Marczi S, Kragol G, Roscic M, Matkovic M, Milostic-Srb A. Tumor-cell-targeted methionine-enkephalin analogues containing unnatural amino acids: design, synthesis and in vitro antitumor activity. J Med Chem 2006;49:3136–3142. [PubMed: 16722632]

482. Horvath MC, Hurd YL, Rajs J, Keller E. Variations in respiratory distress characterize the acute agonal period during heroin overdose death: relevance to postmortem mRNA studies. Brain Res Bull 2006;70:251–259. [PubMed: 16861111]

483. Hou Y, Belcheva MM, Clark AL, Zahm DS, Coscia CJ. Increased opioid receptor binding and G protein coupling in the accumbens and ventral tegmental area of postnatal day 2 rats. Neurosci Lett 2006;395:244–248. [PubMed: 16300888]

484. Hough LB, de Esch IJ, Janssen E, Phillips J, Svokos K, Kern B, Trachler J, Abood ME, Leurs R, Nalwalk JW. Antinociceptive activity of chemical congeners of improgan: optimization of side chain length leads to the discovery of a new, potent, non-opioid analgesic. Neuropharm 2006;51:447–456.

485. Hua S, Hermanussen S, Tang L, Monteith GR, Cabot PJ. The neural cell adhesion molecule asntibody blocks cold-water swim stress-induced analgesia and cell adhesion between lymphocytes and cultured dorsal root ganglion neurons. Anesth Analg 2006;103:1558–1564. [PubMed: 17122239]

486. Huang J, Mahavadi S, Sirwai W, Hu W, Murthy KS. Gi-coupled receptors mediate phosphorylation of CPI-17 and MLC20 via preferential activation of the PI3K/ILK pathway. Biochem J 2006;396:193–200. [PubMed: 16472257]

487. Huang MK, Dai YS, Lee CH, Liu C, Tsay WI, Li JH. Performance characteristics of DRI, CEDIA, and REMEDi systems for preliminary tests of opiates in human urine. J Anal Toxicol 2006;30:61–64. [PubMed: 16620534]

488. Huang W, Moody DE, McCance-Katz EF. The in vivo glucuronidation of buprenorphine and norbuprenorphine determined by liquid chromatography-electrospray ionization-tandem mass spectrometry. Ther Drug Monit 2006;28:245–251. [PubMed: 16628138]

489. Hubert GW, Kuhar MJ. Colocalization of CART with prodynorphin and dopamine D1 receptors in the rat nucleus accumbens. Neuropeptides 2006;40:409–415. [PubMed: 17064765]

490. Hugonin L, Vukojevic V, Bakalkin G, Graslund A. Membrane leakage induced by dynorphins. FEBS Lett 2006;580:3201–3205. [PubMed: 16697372]

491. Hui CK, Huang CH, Lin CJ, Lau HP, Chan WH, Yeh HM. A randomized double-blind controlled study evaluating the hypothermic effect of 150 microg morphine during spinal anaesthsia for Caesarean section. Anaesthesia 2006;61:29–31. [PubMed: 16409339]

492. Hui R, Chen T, Li YQ. The reciprocal connections of endomorphin 1- and endomorphin 2-containing neurons between the hypothalamus and nucleus tractus solitarii in the rat. Neurosci 2006;138(2bi): 171–181.

493. Huleihel R, Yanai J. Disruption of the development of cholinergic-induced translocation and activation of PKC isoforms after prenatal heroin exposure. Brain Res Bull 2006;69:174–181. [PubMed: 16533667]

494. Hullett BJ, Chambers NA, Pascoe EM, Johnson C. Tramadol vs morphine during adenotonsillectomy for obstructive sleep apnea in children. Paediatr Anaesth 2006;16:648–653. [PubMed: 16719881]

495. Hummel M, Schroeder J, Liu-Chen LY, Cowan A, Unterwald EM. An antisense oligodeoxynucleotide to the mu opioid receptor attenuates cocaine-induced behavioral sensitization and reward. Neurosci 2006;142:481–491.

496. Hung HF, Kao PF, lin YS, Chen FC, Chen FC, Tsai JC, Chan P. Changes of serum beta-endorphin by programmed exercise training are correlated with improvement of clinical symptoms and quality of life in female mitral valve prolapse patients. Cardiol 2006;108:252–257.

497. Ibrahim MM, Rude ML, Stagg NJ, Mata HP, Lai J, Vanderah TW, Porreca F, Buckley NE, Makriyannis A, Malan TP Jr. CB2 cannabinoid receptor modulation of antinociception. Pain 2006;122:36–42. [PubMed: 16563625]

498. Ide S, Kobayashi H, Ujike H, Ozaki N, Sekine Y, Inada T, Harano M, Komiyama T, Yamada M, Iyo M, Iwata N, Tanaka K, Shen H, Iwahashi K, Itokawa M, Minami M, Satoh M, Ikeda K, Sora I. Linkage disequilibrium and association with methamphetamine dependence/psychosis of mu-opioid receptor gene polymorphisms. Pharmacogenetics J 2006;6:179–188.

499. Ide S, Minami M, Ishihara K, Uhl GR, Sora I, Ikeda K. Mu opioid receptor-dependent and independent components in effects of tramadol. Neuropharm 2006;51:651–658.

500. Ikeda Y, Miura T, Sakamoto J, Miki T, Tanno M, Kobayashi H, Ohori K, Takahashi A, Shimamoto K. Activation of ERK and suppression of calcineurin are interacting mechanisms in cardioprotection afforded by delta-opioid receptor activation. Basic Res Cardiol 2006;101:418–426. [PubMed: 16619106]

501. Imai S, Narita M, Hashimoto S, Nakamura A, Miyoshi K, Nozaki H, Hareyama N, Takagi T, Suzuki M, Narita M, Suzuki T. Differences in tolerance to anti-hyperalgesic effects between chronic treatment with morphine and fentanyl under a state of pain. Nihon Shinkei Seishin Yakurigaku Zasshi 2006;26:183–192. [PubMed: 17240843]

502. Inan S, Cowan A. Nalfurafine, a kappa opioid receptor agonist, inhibits scratching behavior secondary to cholestasis induced by chronic ethynylestradiol injections in rats. Pharmacol Biochem Behav 2006;85:39–43. [PubMed: 16919318]

503. Inyushkin AN. The effects of leucine-enkephalin on the membrane potential and activity of rat respiratory center neurons in vitro. Neurosci Behav Physiol 2006;36(16a):573–579. [PubMed: 16783508]

504. Iordanova MD, McNally GP, Westbrook RF. Opioid receptors in the nucleus accumbens regulate attentional learning in the blocking paradigm. J Neurosci 2006;26:4036–4045. [PubMed: 16611820]

505. Ishikawa K, Nitta A, Mizoguchi H, Mohri A, Murai R, Miyamoto Y, Noda Y, Kitaichi K, Yamada K, Nabeshima T. Effects of single and repeated administration of methamphetamine or morphine on neuroglycan C gene expression in the rat brain. Int J Neuropsychopharmacol 2006;9:407–415. [PubMed: 16146580]

506. Ito S, Mori T, Sawaguchi T. Differental effects of mu,-opioid, delta-opioid and kappa-opioid receptor agonists on dopamine receptor agonist-induced climbing behavior in mice. Behav Pharmacol 2006;17(13):691–701. [PubMed: 17110795]

507. Izawa R, Jaber M, Deroche-Gamonet V, Sillaber I, Kellendonk C, Le Moal M, Tronche F, Piazza PV. Gene expression regulation following behavioral sensitization to cocaine in transgenic mice lacking the glucocorticoid receptor in the brain. Neurosci 2006;137:915–924.

508. Jacobsen KX, Hoistad M, Staines WA, Fuxe K. The distribution of dopamine D1 receptor and mu-opioid receptor 1 immunoreactivities in the amygdala and interstitial nucleus of the posterior limb of the anterior commissure: relationships to tyrosine hydroxylase and opioid peptide terminal systems. Neurosci 2006;141:2007–2018.

509. Jacobson DA, Cho J, Landa LR Jr, Tamarina NA, Roe MW, Buxbaum JD, Philipson LH. Downstream regulatory element antagonistic modulator regulates islet prodynorphin expression. Am J Physiol 2006;291:E587–E595.

510. Jafari MR, Zarrindast MR, Djahanguiri B. Influence of cholinergic system modulators on morphine state-dependent memory of passive avoidance in mice. Physiol Behav 2006;88:146–151. [PubMed: 16678225]

511. Janczewski WA, Feldman JL. Distinct rhythm generators for inspiration and expiration in the juvenile rat. J Physiol 2006;570:407–420. [PubMed: 16293645]

512. Janecka A, Kruszynski R, Fichna J, Sosson P, Janecki T. Enzymatic degradation studies of endomorphin-2 and its analogues containing N-methylated amino acids. Peptides 2006;27:131–135. [PubMed: 16087275]

513. Jang S, Kim H, Kim D, Jeong MW, Ma T, Kim S, Ho IK, Oh S. Attenuation of morphine tolerance and withdrawal syndrome by coadministration of nalbuphine. Arch Pharm Res 2006;29:677–684. [PubMed: 16964763]

514. Janicki PK, Schuler G, Francis D, Bohr A, Gordin V, Jarzembowski T, Ruiz-Velasco V, Mets B. A genetic association study of the functional A118G polymorphism of the human mu-opioid receptor gene in patients with acute and chronic pain. Anesth Analg 2006;103:1011–1017. [PubMed: 17000822]

515. Jardinaud F, Roques BP, Noble F. Tolerance to the reinforcing effects of morphine in delta9-tetrahydrocannibinol-treated mice. Behav Brain Res 2006;173:255–261. [PubMed: 16884789]

516. Jarosz PA, Sekhon P, Coscina DV. Effect of opioid antagonism on conditioned place preferences to snack foods. Pharmacol Biochem Behav 2006;83:257–264. [PubMed: 16540156]

517. Jasmin L, Narasaiah M, Tien D. Noradrenaline is necessary for the hedonic properties of addictive drugs. Vascul Pharmacol 2006;45:243–250. [PubMed: 16899413]

518. Javan M, Kazemi B, Ahmadiani A, Motamedi F. Dexamethasone mimics the inhibitory effect of chronic pain on the development of tolerance to morphine analgesia and compensates for morphine induced changes in G protein gene expression. Brain Res 2006;1104:73–79. [PubMed: 16828064]

519. Jhamandas K, Milne B, Sutak M, Gouarderes C, Zajac JM, Yang HY. Facilitation of spinal morphine analgesia in normal and morphine tolerant animals by neuropeptide SF and related peptides. Peptides 2006;27:953–963. [PubMed: 16515821]

520. Jhaveri MD, Richardson D, Kendall DA, Barrett DA, Chapman V. Analgesic effects of fatty acid amide hydrolase inhibition in a rat model of neuropathic pain. J Neurosci 2006;26:13318–13327. [PubMed: 17182782]

521. Ji GC, Zhou ST, Shapiro G, Reubi JC, Jurczyk S, Carlton SM. Analgesic activity of a non-peptide imidazolidinedione somatostatin agonist: in vitro and in vivo studies in rat. Pain 2006;124:34–49. [PubMed: 16650579]

522. Ji Y, Murphy AZ, Traub RJ. Sex differences in morphine analgesia of visceral pain are supraspinally and peripherally mediated. Amer J Physiol Regul Integr Comp Physiol 2006;291:R307–R314. [PubMed: 16556902]

522. Jiang B, Shi Y, Li H, Kang L, Ma L. Decreased morphine analgesia in rat overexpressing beta-arrestin 2 at periaqueductal gray. Neurosci Lett 2006;400:150–153. [PubMed: 16563622]

523. Jiang J, Huang J, Hong Y. Bovine adrenal medulla 22 reverses antinociceptive morphine tolerance in the rat. Behav Brain Res 2006;168:167–171. [PubMed: 16337015]

524. Jimenez N, Puig MM, Pol O. Antiexudative effects of opioids and expression of kappa and delta receptors during intestinal inflammation in mice: involvement of nitric oxide. J Pharmacol Exp Ther 2006;316:261–270. [PubMed: 16183704]

525. Jin C, Araki H, Kawasaki Y, Nagata M, Suemaru K, Shibata K, Hamamura T, Kawasaki H, Gomita Y. The glutamate release inhibitor riluzole attenuates the formation of conditioned place aversion induced by naloxone in rats undergoing a single morphine exposure. Brain Res 2006;1069:120–126. [PubMed: 16360647]

526. Jin YH, Nishioka H, Wakabayashi K, Fujita T, Yonehara N. Effect of morphine on the release of excitatory amino acids in the rat hind instep: pain is modulated by the interaction between the peripheral opioid and glutamate systems. Neurosci 2006;138:1329–1339.

527. Jinsmaa Y, Marczak E, Fujita Y, Shiotani K, Miyazaki A, Li T, Tsuda Y, Ambo A, Sasaki Y, Bryant SD, Okada Y, Lzarus LH. Potent in vivo antinociception and opioid receptor preference of the novel analogue [Dmt1]endomorphin-1. Pharmacol Biochem Behav 2006;84:252–258. [PubMed: 16782179]

528. John TF, French LG, Erlichman JS. The antinociceptive effects of salvinorin A in mice. Eur J Pharmacol 2006;545:129–133. [PubMed: 16905132]

529. Johnson EA, Oldfield S, Braksator E, Gonzalez-Cuello A, Couch D, Hall KJ, Mundell SJ, Bailey CP, Kelly E, Henderson G. Agonist-selective mechanisms of mu-opioid receptor desensitization in human embryonic kidney 293 cells. Mol Pharmacol 2006;70:676–685. [PubMed: 16682505]

530. Johnson EE, Chieng B, Napier I, Connor M. Decreased mu-opioid receptor signalling and a reduction in calcium current density in sensory neurons from chronically morphine-treated mice. Br J Pharmacol 2006;148:947–955. [PubMed: 16783402]

531. Jolivalt CG, Jiang Y, Freshwater JD, Bartoszyk GD, Calcutt NA. Dynorphin A, kappa opioid receptors and the antinociceptive efficacy of asimadoline in streptozotocin-induced diabetic rats. Diabetologia 2006;49:2775–2785. [PubMed: 16924480]

532. Jones HE, Suess P, Jasinski DR, Johnson RE. Transferring methadone-stabilized pregnant patients buprenorphine using an immediate release morphine transition: an open-label exploratory study. Am J Addict 2006;15:61–70. [PubMed: 16449094]

533. Jongkamonwiwat N, Phansuwan-Pujito P, Casalotti SO, Forge A, Dodson H, Govitapong P. The existence of opioid receptors in the cochlea of guinea pigs. Eur J Neurosci 2006;23:2701–2711. [PubMed: 16817873]

534. Joseph T, Lee TL, Ning C, Nishiuchi Y, Kimura T, Jikuya H, Ou K, Chin YC, Tachibana S. Identification of mature nocistatin and nociceptin in human brain and cerebrospinal fluid by mass spectrometry combined with affinity chromatography and HPLC. Peptides 2006;27:122–130. [PubMed: 16043263]

535. Joshi SK, Hernandez G, Mikusa JP, Zhu CZ, Zhong C, Salyers A, Wismer CT, Chandran P, Decker MW, Honore P. Comparison of antinociceptive actions of standard analgesics in attenuating capsaicin and nerve-injury-induced mechanical hypersensitivity. Neurosci 2006;143:587–596.

536. Joyce AR, Easterling K, Holtzman SG, Kuhar MJ. Modeling the onset of drug dependence: a consideration of the requirement for protein synthesis. J Theor Biol 2006;240:531–537. [PubMed: 16352315]

537. Juarez J, Camargo G, Gomez-Pinedo U. Effects of estradiol valerate on voluntary alcohol consumption, beta-endorphin content and neuronal population in hypothalamic arcuate nucleus. Pharmacol Biochem Behav 2006;85:132–139. [PubMed: 16970984]

538. Julien N, Marchand S. Endogenous pain-inhibitory systems activated by spatial summation are opioid-mediated. Neurosci Lett 2006;401:256–260. [PubMed: 16600506]

539. Jung JY, Yang HR, Jeong YJ, Vang MS, Park SW, Oh WM, Kim SH, Youn DH, Na CS, Kim WJ. Effects of acupuncture on c-Fos expression in brain after noxious tooth stimulation of the rat. Am J Chin Med 2006;34:989–1003. [PubMed: 17163588]

540. Jungbauer C, Lindig TM, Schrodl F, Neuhuber W, Brehmer A. Chemical coding of myenteric neurons with different axonal projection patterns in the porcine ileum. J Anat 2006;209:733–743. [PubMed: 17118061]

541. Juni A, Klein G, Kest B. Morphine hyperalgesia in mice is unrelated to opioid activity, analgesia or tolerance: evidence for multiple diverse hyperalgesic systems. Brain Res 2006;1070:35–44. [PubMed: 16409995]

542. Jutkiewicz EM, Baladi MG, Folk JE, Rice KC, Woods JH. The convulsive and electroencephalographic changes produced by nonpeptide delta-opioid agonists in rats: comparison with pentylenetetrazol. J Pharmacol Exp Ther 2006;317:1337–1348. [PubMed: 16537798]

543. Jutkiewicz EM, Torregrossa MM, Sobczyk-Kojiro K, Mosberg HI, Folk JE, Rice KC, Watson SJ, Woods JH. Behavioral and neurobiological effects of the enkephalinase inhibitor RB101 relative to its antidepressant effects. Eur J Pharmacol 2006;531:151–159. [PubMed: 16442521]

544. Kahveci N, Gulec G, Ozluk K. Effects of intracerebroventricularly-injected morphine on anxiety, memory retrieval and locomotor activity in rats: involvement of vasopressinergic system and nitric oxide pathway. Pharmacol Biochem Behav 2006;85:859–867. [PubMed: 17223187]

545. Kakinohana M, Nakamura S, Fduchigami T, Davison KJ, Marsala M, Sugahara K. Mu and delta, but not kappa, opioid agonists induce spastic paraparesis after a short period of spinal cord ischaemia in rats. Br J Anaesth 2006;96:88–94. [PubMed: 16317029]

546. Kaminski T. The involvement of protein kinases in signaling of opioid agonist FK33–824 in porcine granulaosa cells. Anim Reprod Sci 2006;91:107–122. [PubMed: 16310101]

547. Kanamori C, Kanamori T, Hayashi M, Yorioka H, Kanzaki H. Three-cycle fentanyl patch system significantly improves pain control in gynecologic cancer. J Obstet Gynaecol Res 2006;32:605–609. [PubMed: 17100824]

548. Kane BE, Nieto MJ, McCurdy CR, Ferguson DM. A unique binding epitope for salvinorin A, a non-nitrogenous kappa opioid receptor agonist. FEBS J 2006;273:1966–1974. [PubMed: 16640560]

549. Karakucuk EH, Yamanoglu T, Demirel O, Bora N, Zengil H. Temporal variation in drug interaction between lithium and morphine-induced analgesia. Chronobiol Int 2006;23:675–682. [PubMed: 16753949]

550. Karaman S, Gunusen I, Uyar M, Firat V. The effect of pre-operative lornoxicam and ketoprofen application on the morphine consumption of post-operative patient-controlled analgesia. J Int Med Res 2006;34:168–175. [PubMed: 16749412]

551. Karaman S, Kocabas S, Uyar M, Hayzaran S, Firat V. The effects of sufantenil or morphine added to hyperbaric bupivacaine in supraspinal anaesthesia for caesarean section. Eur J Anaesthesiol 2006;23:285–291. [PubMed: 16438758]

552. Karaman S, Kocababs S, Uyar M, Zincircioglu C, Firat V. Intrathecal morphine: effects on perioperative hemodynamics, postoperative analgesia and stress response for total abdominal hysterectomy. Adv Ther 2006;23:295–306. [PubMed: 16751162]

553. Karcz-Kubicha M, Ferre S, Diaz-Ruiz O, Quiroz-Molina C, Goldberg SR, Hope BT, Morales M. Stimulation of adenosine receptors selectively activates gene expression in striatal enkephalinergic neurons. Neuropsychopharmacol 2006;31:2173–2179.

554. Kariv R, Tiomny E, Grenshpon R, Dekel R, Waisman G, Ringel Y, Halpern Z. Low-dose naltrexone for the treatment of irritable bowel syndrome: a pilot study. Dig Dis Sci 2006;51:2128–2133. [PubMed: 17080248]

555. Kasai S, Han W, Ide S, Hata H, Takamatsu Y, Yamamoto H, Uhl GR, Sora I, Ikeda K. Involvement of the 3′ non-coding region of the mu-opioid receptor gene is important is morphine-induced analgesia. Psychiatry Clin Neurosci 2006;60:S11–S17.

556. Kathmann M, Flau K, Redmer A, Trankle C, Schlicker E. Cannabidiol is an allosteric modulator at mu- and delta-opioid receptors. Naunyn Schmidebergs Arch Pharmacol 2006;372:354–361.

557. Katsuki R, Fujita T, Koga A, Liu T, Nakatsuka T, Nakashima M, Kumamoto E. Tramadol, but not its major metabolite (mono-O-demethyl tramadol) depresses compound action potentials in frog sciatic nerves. Br J Pharmacol 2006;149:319–327. [PubMed: 16921387]

558. Kaur M, Liguori A, Lang W, Rapp SR, Fleischer AB, Feldman SR. Induction of withdrawal-like symptoms in a small randomized, controlled trial of opioid blockade in frequent tanners. J Am Acad Dermatol 2006;54:709–711. [PubMed: 16546596]

559. Kawano H, Masuko S. Peptidergic and catecholaminergic synaptic contacts onto nucleus preopticus medianus neurons projecting to the subfornical organ of the rat. Neurosci Res 2006;55:211–217. [PubMed: 16443298]

560. Kawano S, Ambo A, Sasaki Y. Synthesis and receptor binding properties of chimeric peptides contiaining a mu opioid receptor ligand and nociceptin/orphanin FQ receptor ligand Ac-RYYRIK-amide. Bioorg Med Chem Lett 2006;16:4839–4841. [PubMed: 16814543]

561. Kawasaki Y, Kohno T, Ji RR. Different effects of opioid and cannabinoid receptor agonists on C-fiber-induced extracellular signal-related kinase activation in dorsal horn neurons in nomal and spinal-ligated rats. J Pharmacol Exp Ther 2006;316:601–607. [PubMed: 16221738]

562. Kaye AD, Baluch A, Phelps J, Baber SR, Ibrahim IN, Hoover JM, Zhang C, Fields A. An analysis of remifentanil in the pulmonary vascular bed of the cat. Anesth Analg 2006;102:118–123. [PubMed: 16368815]

563. Kaye AD, Hoover JM, Baber SR, Ibrahim IN, Phelps J, Fields A, Baluch A, Huffman S. The effects of meperidine in the pulmonary vascular bed of the cat. J Cardiothorac Vasc Anesth 2006;20:691–695. [PubMed: 17023290]

564. Kaye AD, Hoover JM, Ibrahim IN, Phelps J, Balcuh A, Fields A, Huffman S. Analysis of the effects of fentanyl in the feline pulmonary vascular bed. Am J Ther 2006;13:478–484. [PubMed: 17122527]

565. Kaye AD, Phelps J, Baluch A, Ibrahim IN, Hoover JM, Baber SR, Zhang C, Armstrong C, Huffman S, Fields A. The effects of sufentanil in the feline pulmonary vascular bed. Eur J Pharmacol 2006;534:159–164. [PubMed: 16507307]

566. Kee WD, Khaw KS, Ma KC, Wong AS, Lee BB, Ng FF. Maternal and neonatal effects of remifentanil at induction of general anesthesia for cesarean delivery: a randomized, double-blind, controlled trial. Anesthesiol 2006;104:14–20.

567. Kennedy SE, Koeppe RA, Young EA, Zubieta JK. Dysregulation of endogenous opioid emotion regulation circuitry in major depression in women. Arch Gen Psychiat 2006;63:1199–1208. [PubMed: 17088500]

568. Kenny PJ, Chen SA, Kitamura O, Markou A, Koob GF. Conditioned withdrawal drives heroin consumption and decreases reward sensitivity. J Neurosci 2006;26:5894–5900. [PubMed: 16738231]

569. Keresztes A, Toth G, Fulop F, Szucs M. Synthesis, radiolabeling and receptor binding of [3H][(1S, 2R)ACPC2]endomorphin-2. Peptides 2006;27:3315–3321. [PubMed: 17084945]

570. Kersante F, Mollereau C, Zajac JM, Roumy M. Anti-opioid activities of NPFF1 receptors in a SH-SY5Y model. Peptides 2006;27:980–989. [PubMed: 16488058]

571. Kho ST, Lopez IA, Evans C, Ishiyama A, Ishiyama G. Immunolocalization of orphanin FQ in rat cochlea. Brain Res 2006;1113:146–152. [PubMed: 16935273]

572. Khorasni MZ, Hajizadeh S, Fathollahi Y, Semnanian S. Interaction of adenosine and naloxone on regional cerebral blood flow in morphine-dependent rats. Brain Res 2006;1084:61–66. [PubMed: 16626652]

573. Khorram-Manesh A, Ardakani JV, Behjatyi HR, Nylund G, Delbro D. The effects of opioids on the development of postoperative intra-abdominal adhesions. Dig Dis Sci 2006;51:560–565. [PubMed: 16614967]

574. Khoshnoodi MA, Motiei-Langroudi R, Tahsisli-Fahadan P, Yahyavi-Firouz-Abadi N, Ghahremani MH, Dehpour AR. Involvement of nitric oxide system in enhancement of morphine-induced conditioned place preference by agmatine. Neurosci Lett 2006;399:234–239. [PubMed: 16490306]

575. Kiefer F, Jahn H, Otte C, Naber D, Wiedemann K. Hypothalamic-pituitary-adrenocortical axis activity: a target of pharmacological anticraving treatment. Biol Psychiat 2006;60:74–76. [PubMed: 16483549]

576. Kiefer F, Jahn H, Otte C, Nakovics H, Wiedemann K. Effects of treatment with acamprosate on beta-endorphin plasma concentration in humans with high alcohol preference. Neurosci Lett 2006;404:103–106. [PubMed: 16782270]

577. Kim CS, Choi HS, Hwang CK, Song KY, Lee BK, Law PY, Wei LN, Loh HH. Evidence of the neuron-restrictive silencer factor (NRSF) interaction with Sp3 and its synergic repression to the mu opioid receptor (MOR) gene. Nucleic Acids Res 2006;34:6392–6403. [PubMed: 17130167]

578. Kim E, Clark AL, Kiss A, Hahn JW, Wesselschmidt R, Coscia CJ, Belcheva MM. Mu and kappa opioids induce the differentiation of embryonic stem cells to neural progenitors. J Biol Chem 2006;281:33749–33760. [PubMed: 16954126]

579. Kim H, Mittal DP, Iadarolas MJ, Dionne RA. Genetic predictors for acute experimental cold and heat pain sensitivity in humans. J Med Genet 2006;43:e40. [PubMed: 16882734]

580. Kim HW, Roh DH, Yoon SY, Kang SY, Kwon YB, Han HJ, Lee HJ, Choi SM, Ryu YH, Beitz AJ, Lee JH. The anti-inflammatory effects of low- and high-frequency electroacupuncture are mediated

by peripheral opioids in a mouse air pouch inflammation model. J Altern Complement Med 2006;12:39–44. [PubMed: 16494567]

581. Kim JS, Lemasters JJ. Opioid receptor-independent protection of ischemic rat hepatocytes by morphine. Biochem Biophys Res Commun 2006;351:958–964. [PubMed: 17097606]
582. Kim KS, Lee KW, Lee KW, Im JY, Yoo JY, Kim SW, Lee JK, Nestler EJ, Han PL. Adenylyl cyclase type 5 (AC5) is an essential mediator of morphine action. Proc Natl Acad Sci (USA) 2006;103:3908–3913. [PubMed: 16537460]
583. Kim SK, Moon HJ, Na HS, Kim KJ, Kim JH, Park JH, Lee SH, Rhim SS, Lee SG, Min BI. The analgesic effects of automatically controlled rotating acupuncture in rats: mediation by endogenous opioid system. J Physiol Sci 2006;56:259–262. [PubMed: 16839460]
584. Kim SW, Grant JE, Yoon G, Williams KA, Remmel RP. Safety of high-dose naltrexone treatment: hepatic transaminase profiles among outpatients. Clin Neuropharmacol 2006;29:77–79. [PubMed: 16614539]
585. Kimura M, Tokumura M, Itoh T, Inoue O, Abe K. Lack of cyclic AMP-specific phosphodiesterase 4 activation during naloxone-precipitated morphine withdrawal in rats. Neurosci Lett 2006;404:107–111. [PubMed: 16753260]
586. Kimura T. Human opioid peptide met-enkephalin binds to anionic phosphatidylserine in high preference to zwitterionic phosphatidylchlorine: natural abundance (13)c NMR study on the binding state in large unilamellar vesicles. Biochem 2006;45:15601–15609. [PubMed: 17176081]
587. King A, de Wit H, Riley RC, Cao D, Niaura R, Hatsukami D. Efficacy of naltrexone in smoking cessation: a preliminary study and an examination of sex differences. Nicotine Tob Res 2006;8:671–682. [PubMed: 17008194]
588. Kiptoo PK, Hamad MO, Crooks PA, Stinchcomb AL. Enhancement of transdermal delivery of 6-beta-naltrexol via a codrug linked to hydroxybupropion. J Control Release 2006;113:137–145. [PubMed: 16750868]
589. Kiraly KP, Riba P, D'Addario C, Di Benedetto M, Landuzzi D, Candeletti S, Romualdi P, Furst S. Alterations in prodynorphin gene expression and dynorphin levels in different brain regions after chronic administration of 14-methoxymetopon and oxycodone-6-oxime. Brain Res Bull 2006;70:233–239. [PubMed: 16861108]
590. Kitahara T, Kaneko T, Horii A, Fukushima M, Kizawa-Okumura K, Takeda N, Kubo T. Fos-enkephalin signaling in the rat medial vestibular nucleus facilitates vestibular compensation. J Neurosci Res 2006;83:1573–1583. [PubMed: 16547969]
591. Kitanaka N, Kitanaka J, Takemura M. Modification of morphine-induced hyperlocomotion and antinociception in mice by clorgyline, a monoamine oxidase-A inhibitor. Neurochem Res 2006;31:829–837. [PubMed: 16794857]
592. Kitto KF, Fairbanks CA. Supraspinally administered agmatine prevents the development of supraspinal morphine analgesic tolerance. Eur J Pharmacol 2006;536:133–137. [PubMed: 16546161]
593. Kivitz A, Ma C, Aedieh H, Galer BS. A 2-week, multicenter, randomized, double-blind, placebo-controlled, dose-ranging, phase III trial comparing the efficacy of oxymorphone extended release and placebo in adults with pain associated with osteoarthritis of the hip or knee. Clin Ther 2006;28:352–364. [PubMed: 16750450]
594. Kleppner SR, Patel R, McDonough J, Constantini LC. In-vitro and in-vivo characterization of a buprenorphine delivery system. J Pharm Pharmacol 2006;58:295–302. [PubMed: 16536895]
595. Klous MG, Lee W, Hillebrand MJ, van den Brink W, van Ree JM, Beijnen JH. Analysis of diacetylmorphine, caffeine and degradation products after votilization of pharmaceutical heroin for inhalation. J Anal Toxicol 2006;30:6–13. [PubMed: 16620525]
596. Klous MG, Lee WC, van den Brink W, van Ree JM, Beijnen JH. Votilization of diacetylmorphine: in vitro simulation of 'chasing the dragon'. Pharmazie 2006;61:438–445. [PubMed: 16724542]
597. Knudsen HK, Ducharne LJ, Roman PM. Early adoption of buprenorphine in substance abuse treatment centers: data from the private and public sectors. J Subst Abuse Treat 2006;30:363–373. [PubMed: 16716852]
598. Ko MC, Divin MF, Lee H, Woods JH, Traynor JR. Differential in vivo potencies of naltrexone and 6beta-naltrexol. J Pharmacol Exp Ther 2006;316:772–779. [PubMed: 16258020]

599. Ko MC, Wei H, Woods JH, Kennedy RT. Effects of intrathecally administered nociceptin/orphanin FQ in monkeys: behavioral and mass spectrometric studies. J Pharmacol Exp Ther 2006;318:1257–1264. [PubMed: 16766718]

600. Ko SW, Jia Y, Xu H, Yim SJ, Jang DH, Lee YS, Zhao MG, Toyoda H, Wu LJ, Chatila T, Keang BK, Zhuo M. Evidence for a role of CaMKIV in the development of opioid analgesic tolerance. Eur J Neurosci 2006;23:2158–2168. [PubMed: 16630062]

601. Ko WC, Liu TP, Cheng JT, Tzeng TF, Liu IM. Effect of opioid mu-receptors activation on insulin signals damaged by tumor necrosis factor alpha in myoblast C2C12 cells. Neurosci Lett 2006;397:274–278. [PubMed: 16406665]

602. Kobayashi H, Hata H, Ujike H, Harano M, Inada T, Komiyama T, Yamada M, Sekine Y, Iwata N, Iyo M, Ozaki N, Itokawa M, Naka M, Ide S, Ikeda K, Numachi Y, Sora I. Association analysis of delta-opioid receptor gene polymorphisms in methamphetamine dependence/psychosis. Am J Med Genet B Neuropsychiatr Genet 2006;141:482–486. [PubMed: 16741914]

603. Koch AL, Arfken CL, Schuster CR. Characteristics of U.S. substance abuse treatment facilities adopting buprenorphine in its initial stage of availability Drug. Alcohol Depend 2006;83:274–278.

604. Koch T, Wu DF, Yang LQ, Brandenberg LO, Hollt V. Role of phospholipase D2 in the agonist-induced and constitutive endocytosis of G-protein coupled receptors. J Neurochem 2006;97:365–372. [PubMed: 16539674]

605. Kokki H, Rasanen I, Lasalmi M, Lehtola S, Ranta VP, Vanamo K, Ojanpera I. Comparison of oxycodone pharmacokinetics after buccal and sublingual administration in children. Clin Pharmacokinet 2006;45:745–754. [PubMed: 16802855]

606. Kong LL, Yu LC. Involvement of mu- and delta-opioid receptors in the antinociceptive effects induced by AMPA receptor antagonist in the spinal cord of rats. Neurosci Lett 2006;402:180–183. [PubMed: 16644121]

607. Kostopanagiotou G, Pandazi A, Matiatou S, Kontogiannopoulou S, Matsota P, Niokou D, Kitsou M, Crepi E, Christdoulaki K, Grigoropoulou I. The impact of intraoperative propofol in the prevention of postoperative pruritus induced by epidural morphine. Eur J Anaesthesiol 2006;23:418–421. [PubMed: 16469206]

608. Kotwica G, Staszkiewicz J, Skowronski MT, Siawrys G, Bogacka I, Franczak A, Kurowicka B, Krazinski B, Okrasa S. Effects of oxytocin alone and incombination with selected hypothalamic hormones on ACTH, beta-endorphin, LH and PRL secretion by anterior pituitary cells of cyclic pigs. Reprod Biol 2006;6:115–131. [PubMed: 17173093]

609. Koya E, Spijker S, Voorn P, Binnekada R, Schmidt ED, Schoffelmeer AN, De Vries TJ, Smit AB. Enhanced cortical and accumbal molecular reactivity associated with conditioned heroin, but not sucrose-seeking behaviour. J Neurochem 2006;98:905–915. [PubMed: 16787418]

610. Kozak AT, Spates CR, McChargue DE, Bailey KC, Schneider KL, Liepman MR. Naltrexone renders one-session exposure less effective: a controlled pilot study. J Anxiety Disord 2006;21:142–152. [PubMed: 16647240]

611. Kraemer WJ, Sim SK, Bush JA, Nindl BC, Volek JS, Spiering BA, Hatfield DL, Fragala MS, Putukian M, Sebastianelli WJ. Influence of the menstrual cycle of proenkephalin peptide F responses to maximal cycle exercise. Eur J Appl Physiol 2006;96:581–586. [PubMed: 16408233]

612. Kraus J, Borner C, Lendeckel U, Hollt V. Interferon-gamma down-regulates transcription of the mu-opioid receptor gene in neuronal and immune cells. J Neuroimmunol 2006;181:13–18. [PubMed: 16914208]

613. Krivski JA, Soffel EC, Sumner JE, Inman BC, Craft RM. Role of ventral tegmental area, periaqueductal gray and parabrachial nucleus in the discriminative stimulus effects of morphine in the rat. Behav Pharmacol 2006;17:259–270. [PubMed: 16572004]

614. Krowicki ZK, Kapusta DR. Tonic nociceptinergic inputs to neurons in the hypothalamic paraventricular nucleus contribute to sympathetic vasomotor tone and water and electrolyte homeostasis in conscious rats. J Pharmacol Exp Ther 2006;317:446–453. [PubMed: 16407463]

615. Krupitsky EM, Zvartau EE, Masalov DV, Tsoy MV, Burakov AM, Egorova VY, Didenko TY, Romanova TN, Ivanova EB, Bespalov AY, Verbitskaya EV, Neznanov NG, Grinenko AY, O'Brien CP, Woody GE. Naltrexone with or without fluoxetine for preventing relapse to heroin addiction in St. Petersburg, Russia J Subst Abuse Treat 2006;31:319–328.

616. Krystal JH, Madonick S, Perry E, Gueorguieva R, Brush L, Wray Y, Belger A, D'Souza DC. Potentiation of low dose ketamine effects by naltrexone: potential implications for the pharmacotherapy of alcoholism. Neuropsychopharmacol 2006;31:1793–1800.

617. Ku YH. Role of limbic peptidergic circuits in regulation of arterial pressure, relevant to development of essential hypertension. Neuropep 2006;40:299–308.

618. Ku YH, Wang M, Li YH, Sun ZJ, Guo T, Wu JS. Repetition rates of specific interval patterns in single spike train reflect excitation of specific receptor types, shown by high-speed favored pattern detection method. Brain Res 2006;1113:110–128. [PubMed: 16934232]

619. Kudryavtseva N, Gerrits MA, Avgustinovich DF, Tenditnik MV, Van Ree JM. Anxiety and ethanol consumption in victorious and defeated mice: effect of kappa-opioid receptor activation. Eur Neuropsychopharmacol 2006;16:504–511. [PubMed: 16524701]

620. Kumar R, Orsoni S, Norman L, Verma AS, Tirado G, Giavedoni LD, Staprans S, Miller GM, Buch SJ, Kumar A. Chronic morphine exposure causes pronounced virus replication in cerebral compartment and accelerated onset of AIDS in SIV/SHIV-infected Indian rhesus macaques. Virology 2006;354:192–206. [PubMed: 16876224]

621. Kuzmin A, Madjid N, Terenius L, Ogren SO, Bakalkin G. Bif dynorphin, a prodynorphin-derived peptide produces NMDA receptor-mediated effects on memory, anxiolytic-like and locomotor behavior in mice. Neuropsychopharmacol 2006;31:1928–1937.

622. Labuz D, Berger S, Mousa SA, Zollner C, Rittner HL, Shaqura MA, Segovia-Silvestre T, Przewlocka B, Stein C, Machelska H. Peripheral antinociceptive effects of exogenous and immune cell-derived endomorphins in prolonged inflammatory pain. J Neurosci 2006;26:4350–4358. [PubMed: 16624955]

623. LaGraize SC, Borzan J, Peng YB, Fuchs PN. Selective regulation of pain affect following activation of the opioid anterior cingulated cortex system. Exp Neurol 2006;197:22–30. [PubMed: 15996657]

624. Lagu T, Anderson BJ, Stein M. Overdoses among friends: drug users are willing to administer naloxone to others. J Subst Abuse Treat 2006;30:129–133. [PubMed: 16490676]

625. Lai DM, Tu YK, Liu IM, Chen PF, Cheng JT. Mediation of beta-endorphin by ginsenoside Rh2 to lower plasma glucose in streptozotocin-induced diabetic rats. Planta Med 2006;72:9–13. [PubMed: 16450289]

626. Lai J, Luo MC, Chen Q, Ma S, Gardell LR, Ossipov MH, Porreca F. Dynorphin A activates bradykinin receptors to maintain neuropathic pain. Nat Neurosci 2006;9:1534–1540. [PubMed: 17115041]

627. Lalovic B, Kharasch E, Hoffer C, Risler L, Liu-Chen LY, Shen DD. Pharmacokinetics and pharmacodynamics of oral oxycodone in healthy human subjects: role of circulating active metabolites. Clin Pharmacol Ther 2006;79:461–479. [PubMed: 16678548]

628. Lam HC, Kuo SM, Chuang MJ, Keng HM, Lin PR, Liu GS, Hsu CM, Howng SL, Tai MH. Blockade of endothelin-1 release contributes to the anti-angiogenic effect of pro-opiomelanocortin overexpression in endothelial cells. Exp Biol Maywood 2006;231:782–788.

629. Lansac G, Dong W, Dubois CM, Benlarbi N, Afonso C, Fourneir I, Salzet M, Day R. Lipopolysaccharide mediated regulation of neuroendocrine associated proprotein convertases and neuropeptide precursor processing in the rat spleen. J Neuroimmunol 2006;171:57–71. [PubMed: 16337011]

630. Lau B, Bretaud S, Huang Y, Lin E, Guo S. Dissociation of food and opiate preference by a genetic mutation in zebrafish. Genes Brain Behav 2006;5:497–505. [PubMed: 17010096]

631. Lazzeri M, Calo G, Spinelli M, Malaguti S, Guerrini R, Salvadori S, Beneforti P, Regoli D, Turini D. Daily intravesical instillation of 1 mg nociceptin/orphanin FQ for the control of neurogenic detrusor overactivity: a multicenter, placebo controlled, randomized exploratory study. J Urol 2006;176:2098–2102. [PubMed: 17070267]

632. Leal T, Lebacq J, Vanbinst R, Lederman CH, De Kock M, Wallemacq P. Successful protocol of anaestehesia for measuring trnasepithelial nasal potential difference in spontaneously breathing mice. Lab Anim 2006;40:43–52. [PubMed: 16460587]

633. Le Bourdonnec B, Goodman AJ, Graczyk TM, Belanger S, Seida PR, DeHaven RN, Dolle RE. Synthesis and pharmacological evaluation of novel octahydro-1H-pyrido[1,2-a]pyrazine as mu-opioid receptor antagonists. J Med Chem 2006;49:7290–7306. [PubMed: 17149859]

634. Le Bourdonnec B, Goodman AJ, Michaut M, Ye HF, Graczyk TM, Belanger S, Herbertz T, Yap GP, DeHaven RN, Dolle RE. Elucidation of the bioactive confirmation of the N-substituted trans-3,4-dimethyl-4-(3-hydroxyphenyl) piperadine class of mu-opioid receptor antagonists. J Med Chem 2006;49:7278–7289. [PubMed: 17149858]

635. Lee CH, Chuang HY, Shih CC, Jong SB, Chang CH, Yu HS. Transepidermal water loss, serum IgE and beta-endorphin as important and independent biological markers for development of itch intensity in atopic dermatitis. Br J Dermatol 2006;154:1100–1107. [PubMed: 16704640]

636. Lee DY, He M, Liu-Chen LY, Wang Y, Li JG, Xu W, Ma Z, Carlezon WA Jr, Cohen B. Synthesis and in vitro pharmacological studies of new C(4)-modified salvinorin A analogues. Bioorg Med Chem Lett 2006;16:5498–5502. [PubMed: 16945525]

637. Lee HK, Lewis LD, Tsongalis GJ, McMullin M, Schur BC, Wong SH, Yeo KT. Negative urine opioid screening caused by rifampin-mediated induction of oxycodone hepatic metabolism. Clin Chim Acta 2006;367:196–200. [PubMed: 16414038]

638. Lee J, Alrubaian J, Dores RM. Are lungfish living fossils? Observations on the evolution of the opioid/orphanin gene family. Gen Comp Endocrinol 2006;148:306–314. [PubMed: 16930601]

639. Lee JH, Shin EJ, Jeong SM, Kim JH, Lee BH, Yoon IS, Lee JH, Choi SH, Lee SM, Lee PH, Kim HC, Nah SY. Effects of dextrorotatory morphinans on alpha3beta4 nicotinic acetylcholine receptors expressed in Xenopus oocytes. Eur J Pharmacol 2006;536:85–92. [PubMed: 16563374]

640. Lee MG, Undem BJ, Brown C, Carr MJ. Effect of nociceptin in acid-evoked cough and airway sensory nerve activation in guinea pigs. Am J Respir Crit Care Med 2006;173:271–275. [PubMed: 16239621]

641. Lee YS, Agnes RS, Badghisi H, Davis P, Ma SW, Lai J, Porreca F, Hruby VJ. Design and synthesis of novel hydrazide-linked bifunctional peptides as delta/mu opioid receptor agonists and CCK1/CCK2 receptor antagonists. J Med Chem 2006;49:1773–1780. [PubMed: 16509592]

642. Leggett JD, Harbuz MS, Jessop DS, Fulford AJ. The nociceptin receptor antagonist [Nphe1, Arg14, Lys15] nociceptin/orphanin FQ-NH2 blocks the stimulatory effects of nociceptin/orphanin FQ on the HPA axis in rats. Neurosci 2006;141:2051–2057.

643. Lelong-Boulouard V, Quentin T, Moreaux F, Debruyne D, Boulouard M, Coquerel A. Interactions of buprenorphine and dipotassium clorazepate on anxiety and memory functions in the mouse. Drug Alchol Depend 2006;85:103–113.

644. Le Maitre E, Daubeuf F, Duterte-Boucher D, Constentin J, Leroux-Nicollet I. Coupling of ORL1 (NOP) receptors to G proteins was decreased in the nucleus accumbens of anxious relative to non-anxious mice. Brain Res 2006;1110:144–149. [PubMed: 16860781]

645. Lemberg K, Kontinen VK, Siiskonen AO, Viljakka KM, Yli-Kauhaluoma JT, Korpi ER, Kalso EA. Antinociception by spinal and systemic oxycodone: why does the route make a difference? In vitro and in vivo studies in rats. Anesthesiol 2006;105:801–812.

646. Lemberg K, Kontinen VK, Viljakka K, Kylanlahti I, Yli-Kauhaluoma J, Kalso E. Morphine, oxycodone, methadone and its enantiomers in different models of nociception in the rat. Anesth Analg 2006;102:1768–1774. [PubMed: 16717324]

647. Le Merrer J, Cagniard B, Cazala P. Modulation of anxiety by mu-opioid receptors of the lateral septal region in mice. Pharmacol Biochem Behav 2006;83:465–479. [PubMed: 16626794]

648. LeMerrer J, Stephens DN. Food-induced behavioral sensitization, its cross-sensitization to cocaine and morphine, pharmacological blockade, and effect on food intake. J Neurosci 2006;26:7163–7171. [PubMed: 16822973]

649. Lessa MA, Tibirica E. Pharmacologic evidence for the involvement of central and peripheral opioid receptors in the cardioprotective effects of fentanyl. Anesth Analg 2006;103:815–821. [PubMed: 17000787]

650. Lester PA, Traynor JR. Comparison of the in vitro efficacy of mu, delta, kappa and ORL1 receptor agonists and non-selective opioid agonists in dog brain membranes. Brain Res 2006;1073–1074:290–296.

651. Lewanowitsch T, Miller JH, Irvine RJ. Reversal of morphine, methadone and heroin induced effects in mice by naloxone methiodide. Life Sci 2006;78:682–688. [PubMed: 16102783]

652. Li D, Olszewski PK, Shi Q, Grace MK, Billington CJ, Kotz CM, Levine AS. Effect of opioid receptor ligands injected into the rostral lateral hypothalamus on c-fos and feeding behavior. Brain Res 2006;1096:120–124. [PubMed: 16716266]

653. Li J, Zeng SJ, Zhang XW, Zuo MX. The distribution of substance P and met-enkephalin in vocal control nuclei among oscine species and its relation to song complexity. Behav Brain Res 2006;172:202–211. [PubMed: 16806516]

654. Li KW, Jimenez CR, van der Schors RC, Hornshaw MP, Schoffelmeer AN, Smit AB. Intermittent administration of morphine alters protein expression in the rat nucleus accumbens. Proteomics 2006;6:2003–2008. [PubMed: 16447156]

655. Li S, Lee ML, Bruchas MR, Chan GC, Storm DR, Chavkin C. Calmodulin-stimulated adenylyl cyclase gene deletion affects morphine responses. Mol Pharmacol 2006;70:1742–1749. [PubMed: 16914643]

656. Li W, Tang Y, Xie Q, Sheng W, Qiu ZB. 3D-QSAR studies of orvinol analogs as kappa-opioid agonists. J Mol Model 2006;12:877–884. [PubMed: 16552460]

657. Li Y, Saito Y, Suzuki M, Ueda H, Endo M, Maruyama K. Kytorphin has a novel action on rat cardiac muscle. Biochem Biophys Res Commun 2006;339:805–809. [PubMed: 16325776]

658. Li Y, van den Pol AN. Differential target-dependent actions of coexpressed inhibitory dynorphin and excitatory hypocretin/orexin neuropeptides. J Neurosci 2006;26:13037–13047. [PubMed: 17167093]

659. Li Z, Guo L, Ye C, Zhang D. U50488H inhibits outwardly rectifying potassium channel in PC12 cells via pertussis toxin-sensitive G-protein. Biochem Biophys Res Commun 2006;340:1184–1191. [PubMed: 16405915]

660. Liang DY, Guo T, Liao G, Kingery WS, Peltz G, Clark JD. Chronic pain and genetic background interact and influence opioid analgesia, tolerance and physical dependence. Pain 2006;121:232–240. [PubMed: 16516386]

661. Liang DY, Liao G, Lighthall GK, Peltz G, Clark JD. Genetic variants of the P-glycoprotein gene Abcb1b modulate opioid-induced hyperalgesia, tolerance and dependence. Pharmacogenet Genomics 2006;16:825–835. [PubMed: 17047491]

662. Liang DY, Liao G, Wang J, Usaka J, Guo Y, Peltz G, Clark JD. A genetic analysis of opioid-induced hyperalgesia in mice. Anesthesiology 2006;104:1054–1062. [PubMed: 16645459]

663. Liang J, Li Y, Ping X, Yu P, Zuo Y, Wu L, Han JS, Cui C. The possible involvement of endogenous ligands for mu-, delta- and kappa-opioid receptors in modulating morphine-induced CPP expression in rats. Peptides 2006;27:3307–3314. [PubMed: 17097192]

664. Liao M, Lester MJ, Eger EI, Tang M, Sonner JM. Naloxone does not increase the minimum alveolar anesthetic concentration of sevoflurane in mice. Anesth Analg 2006;102:1452–1455. [PubMed: 16632825]

665. Ligeti M, Bosze S, Csampai A, Gunduz O, Al-Khrasani M, Ronai AZ, Medzihradszky-Schweiger H, Benyhe S, Borsin A, Hudecz F, Magyar A. Synthesis of enzymatically-resistant nociceptin-related peptide containing a carbamic acid residue. J Pept Sci 2006;12:481–490. [PubMed: 16550501]

666. Lilja J, Endo T, Hofstetter C, Westman E, Young J, Olson L, Spenger C. Blood oxygenation level-dependent visualization of synaptic relay stations of sensory pathways along the axis in response to graded sensory stimulation of a limb. J Neurosci 2006;26:6330–6336. [PubMed: 16763041]

667. Lim PC, McIntyre PE. An audit of intrathecal morphine analgesia for non-obstetric postsurgical patients at an adult tertiary hospital. Anaesth Intensive Care 2006;34:776–781. [PubMed: 17183897]

668. Lima-Junior RC, Oliveira FA, Gurgel LA, Cavalcante IJ, Santos KA, Campos DA, Vale CA, Silva RM, Chaves MH, Rao VS, Santos FA. Attenuation of visceral nociception by alpha- and beta-amyrin, a triterpenoid mixture isolated from the resin of Protium heptaphyllum, in mice. Planta Med 2006;72:34–39. [PubMed: 16450293]

669. Lin S, Boey D, Lee N, Schwarzer C, Sainsbury A, Herzog H. Distribution of prodynorphin mRNA and its interaction with the NPY system in the mouse brain. Neuropep 2006;40:115–123.

670. Lin X, Xue LY, Wang R, Zhao QY, Chen Q. Protective effects of endomorphins, endogenous opioid peptides in the brain, on human low density lipoprotein oxidation. FEBS J 2006;273:1275–1284. [PubMed: 16519691]

671. Lin YH, Li JH, Ko WK, Wu SM. Direct and sensitive analysis of methamphetamine, ketamine, morphine and codeine in human urine by cation-selective exhaustive injection and sweeping micellar electrokinetic chromatography. J Chromatr A 2006;1130:281–286.

672. Linari G, Agostini S, Broccardo M, Petrella C, Improta G. Regulation of pancreatic secretion in vitro by nociceptin/orphanin FQ and opioid receptors: a comparative study. Pharmacol Res 2006;54:356–360. [PubMed: 16979347]

673. Lind J, Graslund A, Maier L. Membrane interactions of dynorphins. Biochem 2006;45:15931–15940. [PubMed: 17176116]

674. Lindemeyer K, Leemhuis J, Loffler S, Grass N, Norenberg W, Meyer DK. Metabotropic glutamate receptors modulate the NMDA- and AMPA-induced gene expression in neocortical interneurons. Cereb Cortex 2006;16:1662–1677. [PubMed: 16407481]

675. Liou SS, Liu IM, Lai MC. The plasma glucose lowering action of Hei-Shug-Pian, the fire-processed product of the root of Aconitum (Aconitum carmichaeli), in streptozotocin-induced diabetic rats. J Ethnopharmacol 2006;106:256–262. [PubMed: 16443340]

676. Lisboa AC, Mello IC, Nunes RS, Dos Santos MA, Antoniolli AR, Marcal RM, Cavalcanti SC. Antinociceptive effect of Hyptis pectinata leaveves extract. Fitoterapia 2006;77:439–443. [PubMed: 16908108]

677. Lisi TL, Sluka KA. A new electrochemical HPLC method for analysis of enkephalins and endomorphins. J Neurosci Meth 2006;150:74–79.

678. Liu GS, Liu LF, Lin CJ, Tseng JC, Chuang MJ, Lam HC, Lee JK, Yang LC, Chan JH, Howng SL, Tai MH. Gene transfer of pro-opiomelanocortin prohormone suppressed the growth and metastasis of melanoma: involvement of alpha-melanocyte-stimulating hormone-mediated inhibition of the nuclear factor kappaB/cyclooxygenase-2 pathway. Mol Pharmacol 2006;69:440–451. [PubMed: 16269535]

679. Liu H, Ni J, Wang J. In vitro release performance and analgesic activity of endomorphin-1 loaded nanoparticles. Pharmazie 2006;61:450–452. [PubMed: 16724544]

680. Liu HC, Ho HO, Liu RH, Yeh GC, Lin DL. Urinary excretion of morphine and codeine following the administration of single and multiple doses of opium preparations prescribed in Taiwan as “brown mixture”. J Anal Toxiol 2006;30:225–231.

681. Liu HM, Liu XF, Yao JL, Wng CL, Yu Y, Wang R. Utilization of combined chemical modifications to enhance the blood-brain barrier permeability and pharmacological activity of endomorphin-1. J Pharmacol Exp Ther 2006;319:308–316. [PubMed: 16803861]

682. Liu IM, Liou SS, Cheng JT. Mediation of beta-endorphin by myricetin to lower plasma glucose in streptozotocin-induced diabetic rats. J Ethnopharmacol 2006;104:199–206. [PubMed: 16203117]

683. Liu J, Wu WM, Che JJ, Zhang J, Wang R. Endomorphins restored the endothelium-dependent relaxation of the rabbit aorta rings exposed to high D-glucose condition via NO-c-GMP pathway. Protein Pet Lett 2006;13:1037–1044.

684. Liu KS, Kao CH, Liu SY, Sung KC, Kuei CH, Wang JJ. Novel depots of buprenorphine have a long-acting effect for the management of physical dependence to morphine. J Pharm Pharmacol 2006;58:337–344. [PubMed: 16536900]

685. Liu NJ, vonGizycki H, Gintzler AR. Phospholipase Cbeta1 modulates pain sensitivity, opioid antinociception and opioid tolerance formation. Brain Res 2006;1069:47–53. [PubMed: 16405873]

686. Liu S, Liu J, Chen JD. Neural mechanisms involved in the inhibition of intestinal motility induced by intestinal electrical stimulation in conscious dogs. Neurogastroenterol Motil 2006;18:62–68. [PubMed: 16371084]

687. Liu S, Shibata A, Ueno S, Xu F, Baba Y, Jiang D, Li Y. Investigation of interaction of Leu-enkephalin with lipid membranes. Colloids Surf B Biointerfaces 2006;48:148–158. [PubMed: 16542826]

688. Liu SL, Li YH, Shi GY, Chen YH, Huang CW, Hosng JS, Wu HL. A novel inhibitory effect of naloxone on macrophage activation and atherosclerosis formation in mice. J Am Coll Cardiol 2006;48:1871–1879. [PubMed: 17084265]

689. Liu W, Wang CH, Cui Y, Mo LQ, Zhi JL, Sun SN, Wang YL, Yu HM, Zhao CM, Feng JQ, Chen PX. Inhibition of neuronal nitric oxide synthase antagonizes morphine antinociceptive tolerance by decreasing the activation of p38 MAPK in the spinal microglia. Neurosci Lett 2006;410:174–177. [PubMed: 17101217]

690. Liu X, Sullivan KA, Madi JE, Legare M, Tjalkens RB. Manganese-induced neurotoxicity: the role of astroglial-derived nitric oxide in striatal interneuron degeneration. Toxicol Sci 2006;91:521–531. [PubMed: 16551646]

691. Liu Y, Sunderland VB, O'Neill AG. In vitro and in vivo release of naltrexone from biodegradable dept systems. Drug Devel Ind Pharm 2006;32:85–94. [PubMed: 16455607]

692. Lizarraga I, Chambers JP. Involvement of opioidergic and alpha2-adrenergic mechanisms in the central analgesic effects of non-steroidal anti-inflammatory drugs in sheep. Res Vet Sci 2006;80:194–200. [PubMed: 16085153]

693. Loitman JE. Enhanced analgesia with opioid antagonist administration. J Palliat Med 2006;9:1250–1253. [PubMed: 17187530]

694. Lomanowska AM, Rana SA, McCutcheon D, Parler LA, Wainwright PE. Artificial rearing alters the response of rats to natural and drug-mediated rewards. Dev Psychobiol 2006;48:301–314. [PubMed: 16617460]

695. Lotsch J, Geisslinger G. Relevance of frequent mu-opioid receptor polymorphisms for opioid activity in healthy volunteers. Pharmacogenetics J 2006;6:200–210.

696. Lotsch J, Skarke C, Schmidt H, Rohrbacher M, Hofmann U, Scwab M, Geisslinger G. Evidence for morphine-independent centrl nervous opioid effects after administration of codeine: contribution of other codeine metabolites. Clin Pharmacol Ther 2006;79:35–48. [PubMed: 16413240]

697. Lotsch J, Skarke C, Wieting J, Oertel BG, Schmidt H, Brockmoller J, Geisslinger G. Modulation of the central nervous effects of levomethadone by genetic polymorphisms potentially affecting its metabolism, distribution and drug action. Clin Pharmacol Ther 2006;79:72–89. [PubMed: 16413243]

698. Loughlin SE, Islas MI, Cheng MY, Lee AG, Villegier AS, Leslie FM. Nicotine modulation of stress-related peptide neurons. J Comp Neurol 2006;497:575–588. [PubMed: 16739166]

699. Love EJ, Lane JG, Murison PJ. Morphine administration in horses anaesthetized for upper respiratory tract surgery. Vet Anaesth Analg 2006;33:179–188. [PubMed: 16634944]

700. Loyd DR, Murphy AZ. Sex differences in the anatomical and functional organization of the periaqueductal gray-rostral ventromedial medullary pathway in the rat: a potential circuit mediating the sexually dimorphic actions of morphine. J Comp Neurol 2006;496:723–738. [PubMed: 16615128]

701. Lu Y, Lum TK, Leow Augustine YW, Weltrowska G, Nguyen TM, Lemieux C, Chung NN, Schiller PW. Replacement of the N-terminal tyrosine residue in opioid peptides with 3-(2,6-dimethyl-4-carbamoylphenyl)propanoic acid (Dcp) results in a novel mu opioid antagonist. J Med Chem 2006;49:5382–5385. [PubMed: 16913729]

702. Luccarini P, Childeric A, Gaydier AM, Voisin D, Dallel R. The orofacial formalin test in the mouse: a behavioral model for studying physiology and modulation of trigeminal nociception. J Pain 2006;7:908–914. [PubMed: 17157777]

703. Lufty K, Brown MC, Nerio N, Aimiuwu O, Tran B, Anghel A, Friedman TC. Repeated stress alters the ability of nicotine to activate the hypothalamic-pituitary-adrenal axis. J Neurochem 2006;99:1321–1327. [PubMed: 17064351]

704. Lugo JN Jr, Wilson MA, Kelly SJ. Perinatal ethanol exposure alters met-enkephalin levels of male and female rats. Neurotoxicol Teratol 2006;28:238–244. [PubMed: 16457985]

705. Lugo-Chinchilla AM, Baez D, Velez M, Ildefonso C, Renaud FL. Altered subcellular signaling in murine peritoneal macrophages upon chronic morphine exposure. J Neuroimmunol 2006;176:86–94. [PubMed: 16750574]

706. Luis-Delgado OE, Barrot M, Rodeau JL, Schott G, Benbouzid M, Poisbeau P, Freund-Mercier MJ, Lasbennes F. Calibrated forceps: a sensitive and reliable tool for pain and analgesia studies. J Pain 2006;7:32–39. [PubMed: 16414552]

707. Lundeberg S, Hatava P, Lagerkranser M, Olsson GL. Perception of pain following rectal administration of morphine in children: a comparison of a gel and a solution. Paediatr Anaesth 2006;16:164–169. [PubMed: 16430413]

708. Luz PA, Andrade L, Miranda N, Pereira V, Fregoneze J, De Castro e Silva E. Inhibition of water intake by the central administration of IL-1beta in rats: role of the central opioid system. Neuropep 2006;40:85–94.

709. Ma J, Pan ZZ. Contribution of brainstem GABA(A) synaptic transmission to morphine analgesic tolerance. Pain 2006;122:163–173. [PubMed: 16527406]

710. Ma J, Zhang Y, Kalyizhny AE, Pan ZZ. Emergence of functional delta-opioid receptors induced by long-term treatment with morphine. Mol Pharmacol 2006;69:1137–1145. [PubMed: 16399848]

711. Ma YY, Guo CY, Yu P, Lee DY, Han JS, Cui CL. The role of NR2B containing NMDA receptor in place preference conditioned with morphine and natural reinforcers in rats. Exp Neurol 2006;200:343–355. [PubMed: 16631172]

712. Macey TA, Lowe JD, Chavkin C. Mu opioid receptor activation of ERK 1/2 is GRK3 and arresin dependent in striatal neurons. J Biol Chem 2006;281:34515–34524. [PubMed: 16982618]

713. Mahurter L, Garceau C, Marino J, Scmidhammer H, Toth G, Pasternak GW. Separation of binding affinity and intrinsic activity of the potent mu-opioid 14-methoxymetopon. J Pharmacol Exp Ther 2006;319:247–253. [PubMed: 16801454]

714. Maia JL, Lima-Junior RC, David JP, David JM, Santos FA, Rao VS. Oleanolic acid, a pentacyclic triterpene attenuates the mustard oil-induced colonic nociception in mice. Biol Pharm Bull 2006;29:82–85. [PubMed: 16394515]

715. Malavasi LM, Nyman G, Augustsson H, Jacobson M, Jensen-Waern M. Effects of epidural morphine and transdermal fentanyl on physiology and behaviour after abdominal surgery in pigs. Lab Anim 2006;40:16–27. [PubMed: 16460586]

716. Malik AK, Flock KE, Godavarthi CL, Loh HH, Ko JL. Molecular basis underlying the poly C binding protein 1 as a regulator of the proximal promoter of the mouse mu-opioid receptor gene. Brain Res 2006;1112:33–45. [PubMed: 16904079]

717. Malinowski K, Shock EJ, Rochelle P, Kearns CF, Guirnalda PD, McKeever KH. Plasma beta-endorphin, cortisol and immune responses to acute exercise are altered by age and exercise training in horses. Equine Vet J Suppl 2006;36:267–273. [PubMed: 17402430]

718. Mangold DL, Wand GS. Cortisol and adrenocroticotrophic hormone responses to naloxone in subjects with high and low neuroticism. Biol Psychiatry 2006;60:850–855. [PubMed: 16950229]

719. Mannelli P, Gottheil E, Van Bockstaele EJ. Antagonist treatment of opioid withdrawal translational low dose approach. J Addict Dis 2006;25:1–8. [PubMed: 16785213]

720. Manoir BD, Bourget P, Langlois M, Szekely B, Fischler M, Chauvin M, Paci A, Fletcher D. Evaluation of the pharmacokinetic profile and analgesic efficacy of oral morphine after total hip arthroplasty. Eur J Anaesthesiol 2006;23:748–754. [PubMed: 16723055]

721. Mansour-Ghanaei F, Taheri A, Froutan H, Ghofrani H, Nasiri-Toosi M, Bagerzadeh AH, Farahvash MJ, Mirmomen S, Ebrahimi-Dariani N, Farhangi E, Pourrasouli Z. Effect of oral naltrexone on pruitus in cholestatic patients. World J Gastroenterol 2006;12:1125–1128. [PubMed: 16534857]

722. Mantione KJ, Kim C, Stefano GB. Morphine regulates gill ciliary activity via coupling to nitric oxide release in a bivalve mollusk: opiate receptor expression in gill tissues. Med Sci Mont 2006;12:BR195–BR200.

723. Mantovani M, Kaster MP, Pertile R, Calixto JB, Rodrigues AL, Santos AR. Mechanisms involved in the antinociception caused by melatonin in mice. J Pineal Res 2006;41:382–389. [PubMed: 17014696]

724. Marchand S, Betourne A, Marty V, Daumas S, Halley H, Lassalle JM, Zajac JM, Frances B. A neuropetide FF agonist blocks the acquisition of conditioned place preference to morphine in C57Bl/6J mice. Peptides 2006;27:964–972. [PubMed: 16494968]

725. Maresh CM, Sokmen B, Kraemer WJ, Hoffman JR, Watson G, Judalson DA, Gabaree-Boulant CL, Deschenes MR, Vanheest JL, Armstrong LE. Pituitary-adrenal responses to arm versus leg exercise in untrained man. Eur J Appl Physiol 2006;97:471–477. [PubMed: 16685546]

726. Margolis EB, Lock H, Chefer VI, Shippenberg TS, Hjelmstad GO, Fields HL. Kappa opioids selectively control dopaminergic neurons projecting to the prefrontal cortex. Proc Natl Acad Sci (USA) 2006;103:2938–2942. [PubMed: 16477003]

727. Marinelli PW, Lam M, Bai L, Quirion R, Gianoulakis C. A microdialysis profile of dynorphin A(1–8) release in the rat nucleus accumbens following alcohol administration. Alcohol Clin Exp Res 2006;30:982–990. [PubMed: 16737456]

728. Marinho BG, Miranda LS, Gomes NM, Matheus ME, Leitao SG, Vasconcellos ML, Fernandes PD. Antinociceptive action of (+/−)-cis-(6-ethyl-tetrahydropyran-2-yl)-formic acid in mice. Eur J Pharmacol 2006;550:47–53. [PubMed: 17030031]

729. Marker CL, Lujan R, Colon J, Wickman K. Distinct populations of spinal cord lamina II interneurons expressing G-protein-gated potassium channels. J Neurosci 2006;26:12251–12259. [PubMed: 17122050]

730. Marlowe DB. Depot naltrexone in lieu of incarceration: a behavioral analysis of coerced treatment for addicted offenders. J Subst Abuse Treat 2006;31:131–139. [PubMed: 16919739]

731. Marquez P, Baliram R, Gajawada N, Friedman TC, Lufty K. Differential involvement of enkephalins in analgesic tolerance, locomotor sensitization, and conditioned place preference induced by morphine. Behav Neurosci 2006;120:10–15. [PubMed: 16492112]

732. Marshall DA, Strauss ME, Pericak D, Buitendyk M, Codding C, Torrance GW. Economic evaluation of controlled-release oxycodone verus oxycodone-acetaminophen for osteoarthritis pain of the hip or knee. Am J Manage Care 2006;12:205–214.

733. Martin TJ, Kahn W, Cannon DG, Smith JE. Self-administration of heroin, cocaine and their combination under a discrete trial schedule of reinforcement in rats. Drug Alcohol Depend 2006;82:282–286. [PubMed: 16413144]

734. Martin TJ, McIntosh S, Smith JE. Alkylation of opioid receptors occurred following 5′-naltrindole-isothiocyanate injected into the nucleus accumbens of rats: receptor selectivity and anatomical diffusion. Synapse 2006;60:384–391. [PubMed: 16847946]

735. Martins MA, de Castro Bastos L, Tonussi CR. Formalin injection into knee joints of rats: pharmacologic characterization of a deep somatic nociceptive model. J Pain 2006;7:100–107. [PubMed: 16459275]

736. Marzioni M, Alpini G, Saccomanno S, de Minicis S, Glaser S, Francis H, Trozzi L, Venter J, Orlando F, Fava G, Candelaresi C, Macarri G, Benedetti A. Endogenous opioids modulate the growth of the biliary tree in the development of cholestasis. Gastroenterology 2006;130:1831–1847. [PubMed: 16697745]

737. Masand G, Hanif K, Sen S, Ahsan A, Maiti S, Pasha S. Synthesis, conformational and pharmacologic studies of glycosylated chimeric peptides of Met-enkephalin and FMRFa. Brain Res Bull 2006;68:329–334. [PubMed: 16377439]

738. Maslov LN, Barzakh EI, Platonov AA, Minin SM, Ovchinnikov MV. Chronotropic effect of D-Ala2, Leu5, Arg6-enkephalin (dalargin) is associated with activation of peripheral kappa-opioid receptors. Bull Exp Biol Med 2006;140:682–686. [PubMed: 16848223]

739. Maslov LN, Lishmanov YB, Barzakh EI, Lasukova TV, Rice KK, Oeltgen PR. Negative inotropic and chronotropic effects of delta-opioid receptor antagonists are mediated via non-opioid receptors. Bull Exp Biol Med 2006;141:420–423. [PubMed: 17152360]

740. Maswood N, Cosmi S, Alfinito PD, Leventhal L, Deecher DC. The role of the selective serotonin reuptake inhibitor fluoxetine in temperature regulation in ovariectomized rat models. Neuroend 2006;84:330–338.

741. Matejec R, Harbach HW, Bodeker RH, Hempelmann G, Teschmacher H. Plasma levels of corticotroph-type pro-opiomelanocortin derivatives such as beta-lipotropin, beta-endorphin(1–31), or adrenocorticotropic hormone are correlated with severity of postoperative pain. Clin J Pain 2006;22:113–121. [PubMed: 16428944]

742. Matejec R, Schulz A, Muhling J, Uhlich H, Bodeker RH, Hempellmann G, Teschmacher H. Preoperative concentration of beta-lipotropin immunoreactive material in cerebrospinal fluid: a predictor of postoperative pain? Neuropeptides 2006;40:11–21. [PubMed: 16289330]

743. Matejec R, Uhlich H, Hotz C, Muhling J, Harnbach HW, Bodeker RH, Hempelmann G, Teschmacher H. Corticotropin-releasing hormone reduces pressure pain sensitivity in humans without

involvement of beta-endorphin(1–31), but does not reduce heat pain sensitivity. Neuroendocrinol 2006;82:185–197.

744. Mathes WF, Kanarek RB. Chronic wheel running activity attenuates the antinociceptive actions of morphine and morphine-6-glucuronide administration into the periaqueductal gray of rats. Pharmacol Biochem Behav 2006;83:578–584. [PubMed: 16712909]
745. Mathon DS, Vanderschuren LJ, Ramakers GM. Reduced psychostimulant effects on dopamine dynamics in the nucleus accumbens of mu-opioid receptor knockout mice. Neurosci 2006;141:1679–1684.
746. Matsumoto K, Hatori Y, Murayama T, Tashima K, Wongseripipatana S, Misawa K, Kitajima M, Takayama H, Horie S. Involvement of mu-opioid receptors in anitnociception and inhibition of gastrointestinal transit induced by 7-hydroxymitragynine, isolated from Thai herbal medicine Mitragyna speciosa. Eur J Pharmacol 2006;549:63–70. [PubMed: 16978601]
747. Matsumoto K, Takayama H, Ishikawa H, Aimi N, Ponglux D, Watanabe K, Horie S. A partial agonistic effect of 9-hydroxycorynatheidine on mu-opioid receptor in the guinea pig ileum. Life Sci 2006;78:2265–2271. [PubMed: 16266723]
748. Matwyshyn GA, Bhalla S, Gulati A. Endothelin ETA receptor blockade potentiates morphine analgesia but does not affect gastrointestinal transit in mice. Eur J Pharmacol 2006;543:48–53. [PubMed: 16814278]
749. Maxwell S, Bigg D, Stanczykiewicz K, Carlberg-Racich S. Prescribing naloxone to actively injecting heroin users: a program to reduce heroin overdose deaths. J Addict Dis 2006;25:89–96. [PubMed: 16956873]
750. Mazieres L, Jiang CH, Lindstrom S. Recurrent inhibition of the bladder C fibre reflex in the cat and its response to naloxone. J Physiol 2006;575:603–615. [PubMed: 16809367]
751. Mazlan M, Schottenfeld RS, Chawarski MC. New challenges and opportunities in managing substance abuse in Malaysia. Drug Alcohol Rev 2006;25:473–478. [PubMed: 16939945]
752. McCance-Katz EF, Moody DE, Morse GD, Friedland G, Pade P, Baker J, Alvanzo A, Smith P, Ogundele A, Jatlow P, Rainey PM. Interactions between buprenorphine and antiretrovirals. I. The nonnucleoside reverse-transcriptase inhibitors efavierenz and delavirdine. Clin Infect Dis 2006;43 (4):S224–S234. [PubMed: 17109309]
753. McCance-Katz EF, Moody DE, Smith PF, Morse GD, Friedland G, Pade P, Baker J, Alvanzo A, Jatlow P, Rainey PM. Interactions between buprenorphine and antiretrovirals. II. The protease inhibitors nelfinavir, lopinavir/ritonavir, and ritonavir. Clin Infect Dis 2006;43(4):S235–S246. [PubMed: 17109310]
754. McCubbin JA, Helfer SG, Switzer FS III, Galloway C, Griffith WV. Opioid analgesia in persons at risk for hypertension. Psychosom Med 2006;68:116–120. [PubMed: 16449421]
755. McCurdy CR, Sukfa KJ, Smith GH, Warnick JE, Nieto MJ. Antinociceptive profile of salvinorin A, a structurally unique kappa opioid receptor agonist. Pharmacol Biochem Behav 2006;83:109–113. [PubMed: 16434091]
756. McDougall JJ, Larson SE. Nociceptin/orphanin FQ evokes knee joint pain in rats via a mast cell independent mechanism. Neurosci Lett 2006;398:135–138. [PubMed: 16423460]
757. McGeary JE, Monti PM, Rohsenow DJ, Tidey J, Swift R, Miranda R Jr. Genetic moderators of naltrexone's effects on alcohol cue reactivity. Alcohol Clin Exp Res 2006;30:1288–1296. [PubMed: 16899031]
758. McLaughlin JP, Land BB, Li S, Pintar JE, Chavkin C. Prior activation of kappa opioid receptors with U50488H mimics repeated forced swim stress to potentiate cocaine place preference conditioning. Neuropsychopharmacol 2006;31:787–794.
759. McLaughlin JP, Li S, Valdez J, Chavkin TA, Chavkin C. Social defeat stress-induced behavioral responses are mediated by the endogenous kappa opioid system. Neuropsychopharmacol 2006;31:1241–1248.
760. McLaughlin PJ, Zagon IS. Progression of squamous cell carcinoma of the head and neck is associated with down-regulation of the opioid growth factor receptor. Int J Oncol 2006;28:1577–1583. [PubMed: 16685459]

761. McNally GP, Carrive P. A telemetric examination of cardiovascular function during the development of, and recovery from, opiate dependence in rats. Physiol Behav 2006;88:55–60. [PubMed: 16624345]

762. McNally GP, Cole S. Opioid receptors in the midbrain periaqueductal gray regulate prediction errors during Pavlovian fear conditioning. Behav Neurosci 2006;120:313–323. [PubMed: 16719696]

763. Megarbane B, Hreiche R, Pirnay S, Marie N, Baud FJ. Does high-dose buprenorphine cause respiratory depression? Possible mechanisms and therapeutic consequences. Toxicol Rev 2006;25:79–85. [PubMed: 16958555]

764. Melo CM, Maia JL, Cavaicante IJ, Lima MA, Vieira GA, Silveira ER, Rao VS, Santos PA. 12-acetyoxyhawtriwaic acid lactone, a diterpene from Egletes viscose, attenuates capsaicin-induced ear edema and hindpaw nociception in mice: possible mechanisms. Planta Med 2006;72:584–589. [PubMed: 16636964]

765. Mendez M, Morales-Mulia M. Ethanol exposure differentially alters pro-enkephalin mRNA expression in regions of the mesocorticolimbic system. Psychopharmacol 2006;189:117–124.

766. Mendizabel V, Zimmer A, Maldanado R. Involvement of kappa/dynorphin system in WIN 55, 212–2 self-administration in mice. Neuropsychopharamcol 2006;31:1957–1966.

767. Mensah-Brown EP, Garey LJ. The superior colliculus of the camel: a neuronal-specific nuclear protein (NeuN) and neuropeptide study. J Anat 2006;208:239–250. [PubMed: 16441568]

768. Meotti FC, Luiz AP, Pizzolatti MG, Kassuya CA, Calixto JB, Santos AR. Analysis of the antinociceptive effects of the flavenoid myricitrin: evidence for a role of the L-arginine-nitric oxide and protein kinase C pathways. J Pharmacol Exp Ther 2006;316:789–796. [PubMed: 16260583]

769. Mercadante S, Porzio G, Ferrera P, Fulfaro F, Aielli F, Ficorella C, Verna L, Tirelli W, Villari P, Arcuri E. Low morphine doses in opioid-naïve cancer patients with pain. J Pain Symptom Manage 2006;31:242–247. [PubMed: 16563318]

770. Merchant RC, Schwartzapfel BL, Wolf FA, Li W, Carlson L, Rich JD. Demographic, geographic and temporal patterns of ambulance runs for suspected opiate overdose in Rhode Island, 1997–2002. Subst Use Misuse 2006;41:1209–1226. [PubMed: 16861173]

771. Merg F, Filliol D, Usynin I, Bazov I, Bark N, Hurd YL, Yakoleva T, Kieffer BL, Bakalkin G. Big dynorphin as a putative endogenous ligand for the kappa-opioid receptor. J Neurochem 2006;97:292–301. [PubMed: 16515546]

772. Messmer D, Hatsukari I, Hitosugi N, Schmidt-Wolf IG, Singhal PC. Morphine reciprocally regulates IL-10 and IL-12 production by monocyte-derived human dendritic cells and enhances T cell activation. Mol Med 2006;12:284–290. [PubMed: 17380193]

773. Metrebian N, Carnwath Z, Mott J, Carnwath T, Stimson GL, Sell L. Patients receiving a prescription for diamorphine (heroin) in the United Kingdom. Drug Alcohol Rev 2006;25:115–121. [PubMed: 16627300]

774. Metz JR, Huising MO, Leon K, Verburg-van Kemenade BM, Flik G. Central and peripheral interleukin-1beta and interleukin-1 receptor I expression and their role in the acute stress response of common carp, Cyprinus carpio L. J Endocrinol 2006;191:25–35. [PubMed: 17065386]

775. Meymandi MS, Sepehri G, Mobasher M. Gabapentin enhances the analgesic response to morphine in acute model of pain in male rats. Pharmacol Biochem Behav 2006;85:185–189. [PubMed: 16979227]

776. Meyza KZ, Sotowska-Brochocka J. Photoperiod affects distribution of dynorphin A in the brain of Siberian hamster. Acta Neurobiol Exp (Wars) 2006;66:207–213. [PubMed: 17133952]

777. Milekic MH, Brown SD, Castellini C, Alberini CM. Persistent disruption of an established morphine conditioned place preference. J Neurosci 2006;26:3010–3020. [PubMed: 16540579]

778. Miller EI, Torrance HJ, Oliver JS. Validation of the immunalysis microplate ELISA for the detection of buprenorphine and its metabolite norbuprenorphine in urine. J Anal Toxicol 2006;30:115–119. [PubMed: 16620543]

779. Milman A, Weizman R, Rigai T, Rice KC, Pick CG. Behavioral effects of opiate subtypes compared with benzodiazepines in the staircase paradigm. Behav Brain Res 2006;170:141–147. [PubMed: 16574254]

780. Milo S, Ansonoff M, King M, Rossi GC, Zuckerman A, Pintar J, Pasternak GW. Codeine and 6-acetylcodeine analgesia in mice. Cell Mol Neurobiol 2006;26:1011–1019. [PubMed: 16868817]

781. Miranda A, De La Cruz F, Zamudio SR. Immobility response elicited by clamping the neck induces antinociception in a “tonic pain” test in mice. Life Sci 2006;79:1108–1113. [PubMed: 16624327]

782. Miranda-Cardenas Y, Rojas-Piloni G, Martinez-Lorenzana G, Rodriguez-Jimenez J, Lopez-Hidalgo M, Freund-Mercier MJ, Condes-Lara M. Oxytocin and electrical stimulation of the paraventricular hypothalamic nucleus produce antinociceptive effects that are reversed by an oxytocin antagonist. Pain 2006;122:182–189. [PubMed: 16527400]

783. Mitchell JM, Bergren LJ, Chen KS, Fields HL. Cholecystokinin is necessary for the expression of morphine conditioned place preference. Pharmacol Biochem Behav 2006;85:787–795. [PubMed: 17196636]

784. Mitchell TB, Lintzeris N, Bond A, Strang J. Feasibility and acceptability of an intranasal diamorphine spray as an alternative to injectable diamorphine for maintenance treatment. Eur Addict Res 2006;12:91–95. [PubMed: 16543744]

785. Miyatake M, Miyagawa K, Mizuo K, Narita M, Suzuki T. Dynamic changes in dopaminergic neurotransmission induced by a low concentration of bisphenol-A in neurons and astrocytes. J Neuroendocrinol 2006;8:434–444. [PubMed: 16684133]

786. Mizoguchi H, Ito K, Watannabe H, Watanabe C, Katsuyama S, Fujimora T, Sakurada T, Sakurada S. Contribution of spinal mu(1)-opioid receptors and dynorphin B to the antinociception induced by Tyr-d-Arg-Phe-Sar. Peptides 2006;27:2786–2793. [PubMed: 16919848]

787. Mizoguchi H, Nakayama D, Watanabe H, Ito K, Sakurada W, Sawai T, Fujimura T, Sato T, Sakurada T, Sakurada S. Involvement of spinal mu(1)-opioid receptors on the Tyr-d-Arg-Phe-sarcosine-induced antinocieption. Eur J Pharmacol 2006;540:67–72. [PubMed: 16730704]

788. Mizoguchi H, Watananbe H, Hayashi T, Sakurada W, Sawai T, Fujimura T, Sakurada T, Sakurada S. Possible involvement of dynorphin A(1–7) release via mu1-opioid receptors in spinal antinociception by endomorphin-2. J Pharmacol Exp Ther 2006;317:362–368. [PubMed: 16394196]

789. Mizushige T, Kawai T, Matsumura S, Yoneda T, Kawada T, Tsuzuki S, Inoue K, Fushiki T. POMC and orexin mRNA expressions induced by anticipation of a corn-oil emulsion feeding are maintained at the high levels until oil ingestion. Biomed Res 2006;27:227–232. [PubMed: 17099287]

790. Mobarekah JI, Takahashi K, Sakurada S, Kuramasu A, Yanei K. Enhanced antinociceptive effects of morphine in histamine H2 receptor gene knockout mice. Neuropharmacol 2006;51:612–622.

791. Moezi L, Shafaroodi H, Sarkar S, Emami-Razavi SH, Sanatkar M, Mirzi N, Dehpour AR. Involvement of nitergic and opioidergic systems in the hypothermia induced by cholestasis in rats. Pathophysiol 2006;13:227–232.

792. Mohan S, Stevens CW. Systemic and spinal administration of the mu opioid, remifentanil produces antinociception in amphibians. Eur J Pharmacol 2006;534:89–94. [PubMed: 16487509]

793. Mombeini T, Roushanzamir F, Jorjani M, Pourpak Z, Gaskari SA, Mehr SE, Dehpour AR. Alteration in specific opioid-receptor labeling on peripheral blood leukocytes of bile duct-ligated rats. Pathophysiol 2006;13:111–117.

794. Monstein HJ, Grahn N, Ohlsson B. Proenkephalin-A mRNA is widely expressed in tissues of the human gastrointestinal tract. Eur Surg Res 2006;38:464–468. [PubMed: 16940731]

795. Morgan MM, Fossum EN, Levine CS, Ingram SL. Antinociceptive tolerance revealed by cumulative intracranial microinjections of morphine into the periaqueductal gray in the rat. Pharmacol Biochem Behav 2006;85:214–219. [PubMed: 16979226]

796. Morgan MM, Fossum EN, Stalding BM, King MM. Morphine antinocieptive potency on chemical, mechanical and thermal nociceptive tests in the rat. J Pain 2006;7:358–366. [PubMed: 16632325]

797. Morgan O, Griffiths C, Hickman M. Association between availability of heroin and methadone and fatal poisoning in England and Wales 1993–2004. Int J Epidemiol 2006;35:1579–1585. [PubMed: 17077102]

798. Morgan OW, Johnson H, Rooney C, Seagroatt V, Griffiths C. Changes in the pattern of methadone-related deaths in England and Wales 1993–2003. J Public Health (Oxf) 2006;28:318–323. [PubMed: 17060353]

799. Mori T, Ito S, Kita T, Narita M, Suzuki T, Sawaguchi T. Effects of mu-, delta- and kappa-opioid receptor agonists on methamphetamine-induced self-injurious behavior in mice. Eur J Pharmacol 2006;532:81–87. [PubMed: 16464448]

800. Mori T, Nomura M, Yoshizawa X, Nagase H, Sawaguchi T, Narita M, Suzuki T. Generalization of NMDA-receptor antagonists to the discriminative stimulus effects of kappa-opioid receptor agonists U50488H, but not TRK-820 in rats. J Pharmacol Sci 2006;100:157–161. [PubMed: 16474203]

801. Morin LP, Shivers KY, Blanchard JH, Muscat L. Complex organization of mouse and rat suprachiasmatic nucleus. Neurosci 2006;137:1285–1297.

802. Morissette M, Dridl M, Calon F, Tahar AH, Meltzer LT, Bedard PJ, Di Paolo T. Prevention of levodopa-induced dyskinesias by a selective NR1A/2B N-methyl-D-aspartate receptor antagonist in parkinsonian monkeys: implication of proenkephalin. Mov Disord 2006;21:9–17. [PubMed: 16127720]

803. Morley KC, Teesson M, Reid SC, Sannibale C, Thomson C, Phung N, Weltman M, Bell JR, Richardson K, Haber PS. Naltrexone versus acamprosate in the treatment of alcohol dependence: a multi-centre, randomized, double-blind, placebo-controlled trial. Addiction 2006;101:1451–1462. [PubMed: 16968347]

804. Morrish GA, Foster DJ, Somogyi AA. Differential in vitro inhibition of M3G and M6G formation from morphine by (R)- and (S)-methadone and structurally related opioids. Br J Clin Pharmacol 2006;61:326–335. [PubMed: 16487227]

805. Moss IR, Brown KA, Laferriere A. Recurrent hypoxia in rats during development increases subsequent respiratory sensitivity to fentanyl. Anesthesiol 2006;105:715–718.

806. Mudie AS, Holland GR. Local opioids in the inflamed dental pulp. J Endod 2006;32:319–323. [PubMed: 16554202]

807. Muhlfeld C, Urru M, Rumelin R, Mirzaie M, Schondube F, Richter J, Dorge H. Myocardial ischemic tolerance in the newborn rat involving opioid receptors and mitochondrial K+ channels. Anat Rec A Discov Mol Cell Evol Biol 2006;288:297–303. [PubMed: 16456873]

808. Murphy GS, Szokol JW, Marymont JH, Avram MJ, Vender JS. Opioids and cardioprotection: the impact of morphine and fentanyl on recovery of ventricular function after cardiopulmonary bypass. J Cardiothorac Vasc Anesth 2006;20:493–502. [PubMed: 16884978]

809. Mustazza C, Borioni A, Sestili I, Sbraccia M, Rodomonte A, Ferretti R, Del Giudice MR. Synthesis and evaluation as NOP ligands of some spiro-[piperidine-4,2′ (1′H)-quinazolin]-4′ (3′H)-ones and spiro-[piperidine-4,5′ (6′H)-[1,2,4]triazolo[1,5-c]quinazolines]. Chem Pharm Bull (Tokyo) 2006;54:611–622. [PubMed: 16651754]

810. Nadal X, Banos JE, Kieffer BL, Maldonado R. Neuropathic pain is enhanced in delta-opioid receptor knockout mice. Eur J Neurosci 2006;23:830–834. [PubMed: 16487163]

811. Nadjar A, Brotchie JM, Guigoni C, Li Q, Zhou SB, Wang GJ, Ravenscroft P, Georges F, Crossman AR, Bezard E. Phenotype of striatofugal medium spiny neurons in parkinsonian and dyskinetic nonhuman primates: a call for reappraisal of the functional organization of the basal ganglia. J Neurosci 2006;26:8653–8661. [PubMed: 16928853]

812. Narita M, Kaneko C, Miyoshi K, Nagumo Y, Kuzumaki N, Nakajima M, Nanjo K, Matsuzawa K, Yamazaki M, Suzuki T. Chronic pain induces anxiety with concomitant changes in opioidergic function in the amygdala. Neuropsychopharmacol 2006;31:739–750.

813. Narita M, Kato H, Kasukawa A, Narita M, Suzuki M, Takeuchi T, Suzuki T. Role of Src family kinase in the rewarding effect and hyperlocomotion induced by morphine. Neuroreport 2006;17:115–119. [PubMed: 16407755]

814. Narita M, Kuzumaki N, Miyatake M, Sato F, Wachi H, Seyama Y, Suzuki T. Role of delta-opioid receptor function in neurogenesis and neuroprotection. J Neurochem 2006;97:1494–1505. [PubMed: 16696856]

815. Narita M, Kuzumaki N, Narita M, Kaneko C, Hareyama N, Miyatake M, Shindo K, Miyoshi K, Nakajima M, Nagumo Y, Sato F, Wachi H, Seyama Y, Suzuki T. Chronic pain-induced emotional dysfunction is associated with astrogliosis due to cortical delta-opioid receptor dysfunction. J Neurochem 2006;97:1369–1378. [PubMed: 16696849]

816. Narita M, Kuzumaki N, Narita M, Kaneko C, Tamai E, Khotib J, Miyatake M, Shindo K, Nagumo Y, Tanaka S, Suzuki T. Age-related emotionality is associated with cortical delta-opioid receptor dysfunction-dependent astrogliosis. Neurosci 2006;137:1359–1367.

817. Narita M, Miyagawa K, Mizuo K, Yoshida T, Suzuki T. Prenatal and neonatal exposure to low-dose of bisphenol-A enhance the morphine-induced hyperlocomotion and rewarding effect. Neurosci Lett 2006;402:249–252. [PubMed: 16678967]

818. Narita M, Miyatake M, Narita M, Shibasaki M, Shindo K, Nakamura A, Kuzumaki N, Nagumo Y, Suzuki T. Direct evidence of astrocytic modulation in the development of rewarding effects induced by drugs of abuse. Neuropsychopharmacol 2006;31:2476–2488.

819. Narita M, Nagumo Y, Hashimoto S, Narita M, Khotib J, Miyatake M, Sakurai T, Yanagisawa M, Nakamachi T, Shioda S, Suzuki T. Direct involvement of orexigenic systems in the activation of the mesolimbic dopamine pathway and related behaviors induced by morphine. J Neurosci 2006;26:398–405. [PubMed: 16407535]

820. Narita M, Suzuki M, Narita M, Niikura K, Nakamura A, Miyatake M, Yajima Y, Suzuki T. mu-Opioid receptor internalization-development and-independent mechanisms of the development of tolerance to mu-opioid receptor agonists: Comparison between etorphine and morphine. Neurosci 2006;138:609–619.

821. Nason MW Jr, Mason P. Medullary raphe neurons facilitate brown adipose tissue activation. J Neurosci 2006;26:1190–1198. [PubMed: 16436606]

822. Natalini CC, Linardi RL. Analgesic effects of epidural administration of hydromorphone in horses. Am J Vet Res 2006;67:11–15. [PubMed: 16426205]

823. Natalini CC, Polydoro Ada D, Linardi RL. Analgesic effects of subarachnoidally administered hyperbaric opioids in horses. Am J Vet Res 2006;67:941–946. [PubMed: 16740084]

824. Naude R, Oelofsen W, Takahashi A, Amano M, Kawauchi H. Molecular cloning and characterization of preproopiomelanocortin (PrePOMC) cDNA from the ostrich (Struthio camelus). Gen Comp Endocrinol 2006;146:310–317. [PubMed: 16457826]

825. Nava F, Caldiroli E, Premi S, Lucchini A. Relationship between plasma cortisol levels, withdrawal symptoms and craving in abstinet and treated heroin addicts. J Addict Dis 2006;25:9–16. [PubMed: 16785214]

826. Nava F, Premi S, Manzato E, Lucchini A. Comparing treatments of alcoholism on craving and biochemical measures of alcohol consumptionst. J Psychoactive Drugs 2006;38:211–217. [PubMed: 17165363]

827. Navigante AH, Cerchietti LC, Castro MA, Lutteral MA, Cabalar ME. Midazolam as adjunct therapy to morphine in the alleviation of severe dyspnea perception in patients with advanced cancer. J Pain Symptom Manage 2006;31:38–47. [PubMed: 16442481]

828. Naydenova ED, Zhivkova VI, Zamfirova RN, Vezenkov LT, Dobrinova YG, Mateeva PI. Synthesis and biological activity of nociceptin/orphanin FQ (1–13)NH2 analogues modified in the 9 and/or 13 positions. Bioorg Med Chem Lett 2006;16:4701–4704.

829. Nayebi AR, Charkhpour M. Role of 5-HT(1A) and 5-HT(2) receptors of dorsal and median raphe nucleus in tolerance to morphine analgesia in rats. Pharmacol Biochem Behav 2006;83:203–207. [PubMed: 16516955]

830. Neasta J, Uttenweiler-Joseph S, Chaoui K, Monsarrat B, Meunier JC, Mouledous L. Effect of long-term exposure of SH-SY5Y cells to morphine: a whole cell proteomic analysis. Proteome Sci 2006;4:23. [PubMed: 17184524]

831. Nefzi A, Ostresh JM, Appel JR, Bidlack J, Dooley CT, Houghten RA. Identification of potent and highly selective chiral tri-amine and tetra-amine mu opioid receptors ligands: an example of lead optimaztion using mixture-based libraries. Bioorg Med Chem Lett 2006;16:4331–4338. [PubMed: 16750366]

832. Negus SS. Choice between heroin and food in nondependent and heroin-dependent rhesus monkeys: effects of naloxone, buprenorphine, and methadone. J Pharmacol Exp Ther 2006;317:711–723. [PubMed: 16456085]

833. Nelson L, Vergnolle N, D'Mello C, Chapman K, Le T, Swain MG. Endogenous opioid-mediated antinociception in cholestatic mice is peripherally, not centrally, mediated. J Hepatol 2006;44:1141–1149. [PubMed: 16466825]

834. Nestler EJ, Carlezon WA Jr. The mesolimbic dopamine reward circuit in depression. Biol Psychiat 2006;59:1151–1159. [PubMed: 16566899]

835. Neubert JK, Rossi HL, Malphurs W, Vierck CJ Jr, Caudle RM. Differentiation between capsaicin-induced allodynia and hyperalgesia using a thermal operant assay. Behav Brain Res 2006;170:308–315. [PubMed: 16675039]

836. Neumeyer JL, Peng X, Knapp BI, Bidlack JM, Lazarus LH, Salvadori S, Trapella C, Balboni G. New opioid designed multiple ligands from Dmt-Tic and morphinan pharmacophores. J Med Chem 2006;49:5640–5643. [PubMed: 16942040]

837. Newby NC, Mendonca PC, Gamperi K, Stevens ED. Pharmacokinetics of morphine in fish: winter flounder (Pseudopleuronectes americnaus) and seawater-acclimated rainbow trout (Oncorhynchus mykiss). Comp Biochem Physiol C Toxicol Pharmacol 2006;143:275–283. [PubMed: 16631414]

838. Ng HP, Nordstrom U, Axelsson K, Pernoiola AD, Gustav E, Ryttberg L, Gupta A. Efficacy of intra-articular ropivacaine, or a combination of ropivacaine, morphine and ketorolac on postoperative pain relief after ambulatory arthroscopic knee surgery: a randomized double-blind study. Reg Anesth Pain Med 2006;31:26–33. [PubMed: 16418021]

839. Ng KF, Yuen TS, Ng VM. A comparison of postoperative cognitive function and pain relief with fentanyl or tramadol patient-controlled analgesia. J Clin Anesth 2006;18:205–210. [PubMed: 16731323]

840. Nicholson B, Ross E, Weil A, Sasaki J, Sacks G. Treatment of chronic moderate-to-severe non-malignant pain with polymer-coated extended-release morphine sulfate capsules. Curr Med Res Opin 2006;22:539–550. [PubMed: 16574037]

841. Nicolas LB, Kolb Y, Prinssen EP. A combined marble burying-locomotor activity test in mice: a practical screening test with sensitivity to difference classes of anxiolytics and antidepressants. Eur J Pharmacol 2006;547:106–115. [PubMed: 16934246]

842. Nie H, Wang H, Zhang RX, Gao WC, Qiao JT, Dafny N. Is protein kinase C (PKC) involved in nociception? Int J Neurosci 2006;116:1115–1124. [PubMed: 16861172]

843. Niedfeldt RL, Robertson SA. Postanesthetic hyperthermia in cats: a retrospective comparison between hydromorphone and buprenorphine. Vet Anaesth Analg 2006;33:381–389. [PubMed: 17083610]

844. Nieland NP, Moynihan HA, Carrington S, Broadbear J, Woods JH, Traynor JR, Husbands SM, Lewis JW. Structural determinants of opioid activity in derivatives of 14-aminomorphinones: effect of substitution in the aromatic ring of cinnamoylaminomorphinones and codeinones. J Med Chem 2006;49:5333–5338. [PubMed: 16913723]

845. Nishizawa D, Han W, Hasegawa J, Ishida T, Numata Y, Sato T, Kawai A, Ikeda K. Association of mu-opioid receptor gene polymorphism A118G with alcohol dependence in a Japanese population. Neuropsychobiol 2006;53:137–141.

846. Nizhnikov ME, Varlinskaya EI, Petrov ES, Spear NE. Reinforcing properties of ethanol in neonatal rats: involvement of the opioid system. Behav Neurosci 2006;120:267–280. [PubMed: 16719691]

847. Noel RJ Jr, Marrero-Otero Z, Kumar R, Chompre-Gonzalez GS, Verma AS, Kumar A. Correlation between SIV Tat evolution and AIDS progression in cerebrospinal fluid of morphine-dependent and control macaques infected with SIV and SHIV. Virology 2006;349:440–452. [PubMed: 16643974]

848. Noh HS, Kim DW, Kang SS, Kim YH, Cho GJ, Choi WS. Ketogenic diet decreases the level of proenkephalin mRNA induced by kainic acid in the mouse hippocampus. Neurosci Lett 2006;395:87–92. [PubMed: 16300887]

849. Nomura A, Ujike H, Tanaka Y, Otani K, Morita Y, Kishimoto M, Morio A, Harano M, Inada T, Yamada M, Komiyama T, Sekine Y, Iwata N, Sora I, Iyo M, Ozaki N, Kuroda S. Genetic variant of prodynorphin gene is risk factor for methamphetamine dependence. Neurosci Lett 2006;400:158–162. [PubMed: 16529859]

850. Nordt C, Stohler R. Incidence of heroin use in Zurich, Switzerland: a treatment case register analysis. Lancet 2006;367:1830–1834. [PubMed: 16753485]

851. Nozaki C, Kamei J. Possible involvement of opioidergic systems in the antinociceptive effect of the selective serotonin reuptake inhibitors in sciatic nerve-injured mice. Eur J Pharmacol 2006;552:99–104. [PubMed: 17056034]

852. Nozaki C, Saitoh A, Kamei J. Characterization of the antinociceptive effects of oxycodone in diabetic mice. Eur J Pharmacol 2006;535:145–151. [PubMed: 16533506]

853. Nunes EV, Rothenberg JL, Sullivan MA, Carpenter KM, Kleber HD. Behavioral therapy to augment oral naltrexone for opioid dependence: a ceiling on effectiveness. Am J Drug Alcohol Abuse 2006;32:503–517. [PubMed: 17127538]

854. O'Brien B, Cody C. Analgesia and sedation in the presence of a naltrexone implant: a novel pharmacological challenge. Eur J Emerg Med 2006;13:315–316. [PubMed: 16969243]

855. O'Brien C, Cornish JW. Naltrexone for probationers and parolees. J Subst Abuse Treat 2006;31:107–111. [PubMed: 16919734]

856. Oertel BG, Schmidt R, Schneider A, Geisslinger G, Lotsch J. The mu-opioid receptor gene polymorphism 118>G depletes alfentanil-induced analgesia and protects against respiratory depression in homozygous carriers. Pharmacogent Genomics 2006;16:625–636.

857. Oh DY, Jung KH, Yang BH, Lee JS, Choi IG, Chai YG. Naltrexone influences protein kainaseCe and integrin alpha7 activity in SH-SY5Y neuroblastoma cells. Exp Mol Med 2006;38:100–106. [PubMed: 16520558]

858. Ohtsubo K, Watanabe H, Yao F, Okada G, Mouri H, Yamaguchi Y, Sawabu N. Preproenkephalin hypermethylation in the pure pancreatic juice compared with p53 mutation in the diagnosis of pancreatic carcinoma. J Gastroenterol 2006;41:791–797. [PubMed: 16988769]

859. Ojanen SP, Hyytia P, Klianmaa K. Enhanced morphine-induced ethanol drinking in alcohol-preferring alko rats sentitized to morphine. Alcohol Clin Exp Res 2006;30:621–629. [PubMed: 16573579]

860. Okuda-Ashitaka E, Minami T, Matsumura S, Takeshima H, Reinscheid RK, Civelli O, Ito S. The opioid peptide nociceptin/orphanin FQ mediates prostaglandin E2-induced allodynia, tactile pain associated with nerve injury. Eur J Neurosci 2006;23:995–1004. [PubMed: 16519664]

861. Okutsu H, Watananbe S, Takahashi I, Aono Y, Saigusa T, Koshikawa N, Cools AR. Endomorphin-2 and endomorphin-1 promote the extracellular amount of accumbal dopamine via nonopioid and mu-opioid receptors, respectively. Neuropsychopharmacol 2006;31:375–383.

862. Olianas MC, Concas D, Onali P. Agonist activity of naloxone benzoylhydrazone at recombinant and native opioid receptors. Br J Pharmacol 2006;147:360–370. [PubMed: 16402046]

863. Oliveira AR, Barros HM. Ultrasonic vocalizations during the formalin test: a measure of the affective dimension of pain? Anesth Analg 2006;102:832–839. [PubMed: 16492837]

864. Olson VG, Griner NB, Heusner CL, Palmiter RD. Lack of neuropeptide Y attenuates the somatic signs of opiate withdrawal. Synapse 2006;60:553–556. [PubMed: 16952158]

865. Olson VG, Heusner CL, Bland RJ, During MJ, Weinshenker D, Palmiter RD. Role of noradrenergic signaling by the nucleus tractus solitarius in mediating opiate reward. Science 2006;311:1017–1020. [PubMed: 16484499]

866. O'Malley SS, Cooney JL, Jrishnan-Sarin S, Dubin JA, McKee SA, Cooney NL, Blakeslee A, Meandzija B, Romano-Dahlgard D, Wu R, Makuch R, Jatlow P. A controlled trial of naltrexone augmentation of nicotine replacement therapy for smoking cessation. Arch Intern Med 2006;166:667–674. [PubMed: 16567607]

867. Onimaru H, Kumagawa Y, Homma I. Respiration-related rhythmic activity in the rostral medulla of newborn rats. J Neurophysiol 2006;96:55–61. [PubMed: 16495360]

868. Ordaz-Sanchez I, Weber RJ, Rice KC, Zhang X, Rodriguez-Padilla C, Tamex-Guerra R, Mendez-Vazquez JL, Gomez-Flores R. Chemotaxis of human and rat leukocytes by the delta-selective non-peptidic opioid SNC 80. Rev Latinoam Microbiol 2006;45:16–23. [PubMed: 17061517]

869. Ortiz MI, Medina-Tato DA, Sarmiento-Heredia D, Palma-Martinez J, Granados-Soto V. Possible activation of NO-cyclic GMP-K+ channels pathway by gabapentin on the formalin test. Pharmacol Biochem Behav 2006;83:420–427. [PubMed: 16630650]

870. Ott J. Obviation of opioid withdrawal syndrome by concomitant administration of naltrexone in microgram doses: two psychonautic bioassays. J Psychoactive Drugs 2006;38:101–105. [PubMed: 16681181]

871. Ottinger MA, Corbitt C, Hoffman R, Thompson N, Russek-Cohen E, Deviche P. Reproductive aging in Japanese quail, Cortunix japonica is associated with changes in central opioid receptors. Brain Res 2006;1126:167–175. [PubMed: 17045975]

872. Otto B, Riepl RL, Otto C, Klose J, Enck P, Klosterhalfen S. mu-opiate receptor agonists – a new pharmacological approach to prevent motion sickness? Br J Clin Pharmacol 2006;61:27–30. [PubMed: 16390348]

873. Ou HY, Cheng JT, Yu EH, Wu TJ. Metaformin increases insulin sensitivity and plasma beta-endorphin in human subjects. Horm Metab Res 2006;38:106–111. [PubMed: 16523411]

874. Ozdogan UK, Lahdesmaki J, Scheinin M. The analgesic efficacy of partial opioid agonists is increased in mice with targeted inactivation of the alpha2A-adrenoceptor gene. Eur J Pharmacol 2006;529:105–113. [PubMed: 16325800]

875. Ozturk Y, Aydin S, Beis R, Herekman-Demir T. The involvement of endogenous opioid mechanisms in the antinociceptive effects induced by antidepressant drugs, desipramine and trimipramine. Pharmacol Biochem Behav 2006;83:592–597. [PubMed: 16712910]

876. Papaleo F, Contarino A. Gender- and morphine dose-liked expression of spontaneous somatic opiate withdrawal in mice. Behav Brain Res 2006;170:110–118. [PubMed: 16580078]

877. Park HS, Lee HY, Kim YH, Park JK, Zvartau EE, Lee H. A highly selective kappa-opioid receptor agonist with low addictive potential and dependence liability. Bioorg Med Chem Lett 2006;16:3609–3613. [PubMed: 16650985]

878. Parker LA, Limebeer CL, Slomke J. Renewal effect: context-dependent extinction of a cocaine- and a morphine-induced floor preference. Psychopharmacol 2006;187:133–137.

879. Parkhill AL, Bidlack JM. Reduction of lipopolysaccharide-induced interleukin-6 production by the kappa opioid U50488H in a mouse monocyte-like cell line. Int Immunopharmacol 2006;6:1013–1019. [PubMed: 16644488]

880. Parkitna JR, Obara I, Wawrzczak-Bargiela A, Makuch W, Przewlocka B, Przewlocki R. Effects of glycogen synthase kinase 3beta and cyclin-dependent kinase 5 inhibitors on morphine-induced analgesia and tolerance in rats. J Pharmacol Exp Ther 2006;319:832–839. [PubMed: 16902054]

881. Pastor R, Aragon CM. The role of opioid receptor subtypes in the development of behavioral sensitization to ethanol. Neuropsychopharmacol 2006;31:1489–1499.

882. Patel HH, Head BP, Peterson HN, Niesman IR, Huang D, Gross GJ, Insel PA, Roth DM. Protection of adult rat cardiac myocytes from ischemic cell death: role of caveolar microdomains and delta-opioid receptors. Am J Physiol Heart Circ Physiol 291:H344–H350. [PubMed: 16501018]

883. Patel JP, Sengupta R, Bardi G, Khan MZ, Mullen-Przeworski A, Meucci O. Modulation of neuronal CXCR4 by the mu-opioid agonist DAMGO. J Neurovirol 2006;12:492–500. [PubMed: 17162664]

884. Paterson S, Cordero R. Comparison of the various opiate alkaloid contaminants and their metabolites found in illicit heroin with 6-monoacetylmorphine as indicators of heroin ingestion. J Anal Toxicol 2006;30:267–273. [PubMed: 16803666]

885. Patwardhan AM, Diogenes A, Berg KA, Fehrenbacher JC, Clarke WP, Akopian AN, Hargreaves KM. PAR-2 agonists activate trigeminal nociceptors and induce functional competence in the delta opioid receptor. Pain 2006;125:114–124. [PubMed: 16781076]

886. Pawlyk AC, Cosmi S, Alfinito PD, Maswood N, Deecher DC. Effects of the 5HT2A antagonist mirtazapine in rat models of thermoregulation. Brain Res 2006;1123:135–144. [PubMed: 17067560]

887. Payabvash S, Beheshtian A, Salmasi AH, Kiumehr S, Ghahremani MH, Tavangar SM, Sabzevari O, Dehpour AR. Chronic morphine treatment induces oxidant and apoptotic damage in the mice liver. Life Sci 2006;79:972–980. [PubMed: 16750225]

888. Peart JN, Gross GJ. Cardioprotective effects of acute and chronic opioid treatment are mediated via different signaling pathways. Am J Physiol 2006;291:H1746–H1753.

889. Peddyreddy MK, Dkhar SA, Ramaswamy S, Naveen AT, Shewade DG. An inherent acceleratory effect of insulin on small intestinal transit and its pharmacological characterization in normal mice. World J Gastroenterol 2006;12:2592–2600.

890. Pederson LH, Blackburn-Munro G. Pharmacological characterization of place escape/avoidance behaviour in the rat chronic constriction injury model of neuropathic pain. Psychopharmaocl 2006;185:208–217.

891. Peixoto AJ, Celich MF, Zardo L, Peixoto Filho AJ. Ondansteron, or droperidol for prophylaxis of nausea and vomiting after intrathecal morphine. Eur J Anaesthesiol 2006;23:670–675. [PubMed: 16805932]

892. Pellicano MP, Sadile AG. Differential alcohol drinking behaviour and dependence in the Naples low- and high-excitability rat lines. Behav Brain Res 2006;171:199–206. [PubMed: 16712974]

893. Pello OM, Duthey B, Garcia-Bernal D, Rodriguez-Frade JM, Stein JV, Teixido J, Martinez C, Mellado M. Opioids trigger alpha5 beta 1 integrin-mediated monocyte adhesion. J Immunol 2006;176:1675–1685. [PubMed: 16424197]

894. Pelloux Y, Constentin J, Duterte-Boucher D. Novelty preference predicts place preference conditioning to morphine and its oral consumption in rats. Pharmacol Biochem Behav 2006;84:43–50. [PubMed: 16733065]

895. Peng X, Knapp BI, Bidlack JM, Neumeyer JL. Synthesis and preliminary in vitro investigation of bivalent ligands containing homo- and heterodimeric pharmacophores at mu, delta and kappa opioid receptors. J Med Chem 2006;49:256–262. [PubMed: 16392810]

896. Peng YL, Chang M, Dong SL, Li W, Han RW, Fu GX, Chen Q, Wang R. Novel potent agonist [(pF) Phe4, Aib7, Aib11, Arg14, Lys15]N/OFQ-NH2 and antagonist [Nphe1,(pF)Phe4, Aib7, Aib11, Arg14, Lys15]N/OFQ-NH2 of nociceptin/orphanin FQ receptor. Regul Pept 2006;134:75–81. [PubMed: 16516988]

897. Pereira FC, Lourenco E, Milhazes N, Morgadinho T, Ribeiro CF, Ali SF, Macedo TR. Methamphetamine, morphine and their combination: acute changes in striatal dopamine transmission evaluated by microdialysis in awake rats. Ann NY Acad Sci 2006;1074:160–173. [PubMed: 17105914]

898. Perrine SA, Hoshaw BA, Unterwald EM. Delta opioid receptor ligands modulate anxiety-like behaviors in the rat. Br J Pharmacol 2006;147:864–872. [PubMed: 16491101]

899. Persson AI, Bull C, Eriksson PS. Requirement for Id1 in opioid-induced oligodendrogenesis in cultured adult rat hippocampal progenitors. Eur J Neurosci 2006;23:2277–2288. [PubMed: 16706836]

900. Petaja-Repo UE, Hogue M, Leskela TT, Markkanen PM, Tuusa JT, Bouvier M. Distinct subcellular localization for constitutive and agonist-modulated palmitoylation of the human delta opioid receptor. J Biol Chem 2006;281:15780–15789. [PubMed: 16595649]

901. Peters JW, Anderson BJ, Simons SH, Uges DR, Tibboel D. Morphine metabolite pharmacokinetics during vasoarterial extra corporeal membrane oxygenation in neonates. Clin Pharmacokinet 2006;45:705–714. [PubMed: 16802851]

902. Peterson JB, Conrod P, Vassileva J, Gianoulakis C, Pihl RO. Differential effects of naltrexone on cardiac, subjective and behavioural reactions to acute ethanol intoxication. J Psychiatry Neurosci 2006;31:386–393. [PubMed: 17136216]

903. Petrakis IL, Nich C, Ralevski E. Psychotic spectrum disorders and alcohol abuse: a review of pharmacotherapeutic strategies and a report on the effectiveness of naltrexone and disulfiram. Schizophr Bull 2006;32:644–654. [PubMed: 16887890]

904. Petrakis IL, Poling J, Levinson C, Nich C, Carroll K, Ralevski E, Rounsaville B. Naltrexone and disulfiram in patients with alcohol dependence and comorbid post-traumaticstress disorder. Biol Psychiatry 2006;60:777–783. [PubMed: 17008146]

905. Petrov ES, Nizhnikov ME, Varlinskaya EI, Spear NE. Dynorphin A(1–13) and responsiveness of the newborn rat to a surrogate nipple: immediate behavioral consequences and reinforcement effects in conditioning. Behav Brain Res 2006;170:1–14. [PubMed: 16621051]

906. Petrov RR, Vardanyan RS, Lee YS, Ma SW, Davis P, Begay LJ, Lai JY, Porreca F, Hruby VJ. Synthesis and evaluation of 3-aminopropionyl substituted fentanyl analogs for opioid activity. Bioorg Med Chem Lett 2006;16:4946–4950. [PubMed: 16828552]

907. Pettinati HM, O'Brien CP, Rabinowitz AR, Wortman SP, Oslin DW, Kampman KM, Dackis CA. The status of naltrexone in the treatment of alcohol dependence: specific effects on heavy drinking. J Clin Psychopharmacol 2006;26:610–625. [PubMed: 17110818]

908. Phansuwan-Pujito P, Ebadi M, Govitrapong P. Immunocytochemical characterization of delta-opioid and mu-opioid receptor protein in the bovine pineal gland. Cells Tissues Organs 2006;182:48–56. [PubMed: 16651829]

909. Pietrovski EF, Rosa KA, Facundo VA, Rios K, Marques MC, Santos AR. Anticociceptive properties of the ethanolic extract and of the triterpene 3beta,6beta,16beta-trihidroxilup-20(29)-ene obtained

from the flowers of Combretum leprosum in mice. Pharmacol Biochem Behav 2006;83:90–99. [PubMed: 16458954]

910. Pimpinelli F, Parenti M, Guzzi F, Piva F, Hokfelt T, Maggi R. Presence of delta opioid receptors on a subset of hypothalamic gonadotropin releasing hormone (GnRH) neurons. Brain Res 2006;1070:15–23. [PubMed: 16405927]
911. Pinal-Seoane N, Martin IR, Gonzalez-Nunez V, de Velasco EM, Alvarez FA, Sarmiento RG, Rodriguez RE. Characterization of a new duplicate delta-opioid receptor from zebrafish. J Mol Endocrinol 2006;37:391–403. [PubMed: 17170080]
912. Pisanu A, Acquas E, Fenu S, Di Chiara G. Modulation of Delta(9)-THC-induced increase of cortical and hippocampal acetylcholine release by mu opioid and D(1) dopamine receptors. Neuropharmacol 2006;50:661–670.
913. Pitts RC, Buda DR, Keith JR, Cerutti DT, Galizio M. Chlordiazepoxide and dizocilpine, but not morphine, selectively impair acquisition under a novel repeated-acquisition and performance task in rats. Psychopharmacol 2006;189:135–143.
914. Placenza FM, Fletcher PJ, Vaccarino FJ, Erb S. Effects of central neurokinin-1 receptor antagonism on cocaine- and opiate-induced locomotor activity and self-administration behaviour in rats. Pharmacol Biochem Behav 2006;84:94–101. [PubMed: 16757018]
915. Pluchino N, Luisi M, Lenzi L, Centofanti M, Begliuomini S, Freschi L, Ninni F, Genazzani AR. Progesterone and progestins: effects on brain, allopregnanolone and beta-endorphin. J Steroid Biochem Mol Biol 2006;102:205–213. [PubMed: 17052903]
916. Poisnel G, Quentin T, Barre L, Coqueral A, Debruyne D. Competitive displacement binding assay on rat brain sections and using a beta-imager: application to mu-opioid ligands. J Neurosci Meth 2006;154:60–67.
917. Polgar E, Furuta T, Kaneko T, Todd A. Characterization of neurons that express preprotachykinin B in the dorsal horn of the spinal cord. Neurosci 2006;139:687–697.
918. Porcu P, Grant KA, Green HL, Rogers LS, Morrow AL. Hypothalamic-pituitary-adrenal axis and ethanol modulation of deoxycorticosterone levels in cynomolgus monkeys. Psychopharmacol 2006;186:293–301.
919. Portnoy RK, Sibirceva U, Smout R, Horn S, Connor S, Blum RH, Spence C, Fine PG. Opioid use and survival at the end of life: a survey of a hospice population. J Pain Symptom Manage 2006;32:532–540. [PubMed: 17157755]
920. Poulin JF, Chevalier B, Laforest S, Drolet G. Enkephalinergic afferents of the corticomedial amygdala in the rat. J Comp Neurol 2006;496:859–876. [PubMed: 16628615]
921. Pozos-Guillen AJ, Aguirre-Banuelos P, Arellano-Guerrero A, Castanneda-Hernandez G, Hoyo-Vadillo C, Perez-Urizar J. Isobolographic analysis of the dual-site synergism in the antinociceptive response of tramadol in the formalin test in rats. Life Sci 2006;79:2275–2282. [PubMed: 16934842]
922. Pradhan AA, Siau C, Constantin A, Clarke PB. Chronic morphine administration results in tolerance to delta opioid receptor-mediated antinociception. Neurosci 2006;141:947–954.
923. Primeaux SD, Wilson SP, McDonald AJ, Mascagni F, Wilson MA. The role of delta opioid receptors in the anxiolytic actions of benzodiazepines. Pharmacol Biochem Behav 2006;85:545–554. [PubMed: 17109943]
924. Prokopp CR, Rubin MA, Sauzem PD, de Souza AH, Berlese DB, Lourega RV, Muniz MN, Bonacorso HG, Zanatta N, Martins MA, Mello CF. A pyrazolyl-thiazole derivative causes antinociception in mice. Braz J Med Biol Res 2006;39:795–799. [PubMed: 16751986]
925. Proudfoot CJ, Garry EM, Cottrell DF, Rosie R, Anderson H, Robertson DC, Fleetwood-Walker SM, Mitchell R. Analgesia mediated by the TRPM8 cold receptor in chronic neuropathic pain. Curr Biol 2006;16:1591–1605. [PubMed: 16920620]
926. Puehler W, Rittner HL, Mousa SA, Brack A, Krause H, Stein C, Schafer M. Interleukin-1 beta contributes to the upregulation of kappa opioid receptor mRNA in dorsal root ganglion in response to peripheral inflammation. Neurosci 2006;141:989–998.
927. Puppala BL, Bhalla S, Matwyshyn G, Gulati A. Involvement of central endothelin receptors in neonatal morphine withdrawal. Exp Biol Med 2006;231:1157–1160.

928. Qi CT, Zou H, Zhang CH, Xie QL, Jin ML, Yu L. Effect of GNTI, a kappa opioid receptor antagonist, on MK-801-induced hyperlocomotion and stereotypy in mice. Acta Pharmacol Sin 2006;27:1401–1408. [PubMed: 17049114]

929. Qi W, Smith FG. Modulation of systemic and renal haemodynamics by kappa-opioids in conscious lambs. Exp Physiol 2006;91:877–885. [PubMed: 16728455]

930. Qu CL, Tang JS, Jia H. Involvement of GABAergic modulation of antinociception induced by morphine microinjected into the ventrolateral orbital cortex. Brain Res 2006;1073–1074:281–289.

931. Quesada A, Micevych P. Estrogen and CCK1 receptor modification of mu-opioid receptor binding in the cortex of female rats. Brain Res 2006;1073–1074:316–320.

932. Quezada M, Henriquez S, Vargas M, Cardenas H, Tapia A, Rios M, Salvatierra AM, Orihuela PA, Croxatto HB, Velasquez L. Fertil Steril 2006;86:1750–1757. [PubMed: 17074347]

933. Rabbani M, Sadeghi HM, Gudarzi S. Protective effects of calcium-magnesium soft gels in morphine tolerant and dependent mice. Magnes Res 2006;19:28–34. [PubMed: 16846098]

934. Raffa RB, Baron DA, Tallarida RJ. Schild (apparent pA2) analysis of a kappa-opioid antagonist in Planaria. Eur J Pharmacol 2006;540:200–201. [PubMed: 16737694]

935. Raffa RB, Stagliano GW, Tallarida RJ. Subadditive withdrawal from cocaine/kappa-opioid agonist combinations in Planaria. Brain Res 2006;1114:31–35. [PubMed: 16914122]

936. Raffa RB, Tallarida RJ. Modified 'Joyce model' of opioid dependence/withdrawal. Eur J Pharmacol 2006;551:54–57. [PubMed: 17045985]

937. Raffaeli W, Marconi G, Fanelli G, Taddei S, Borghi GB, Casati A. Opioid-related side-effects after intrathecal morphine: a prospective, randomized, double-blind dose-response study. Eur J Anaesthesiol 2006;23:605–610. [PubMed: 16507190]

938. Raffaeli W, Samolsky Dekel BG, Landuzzi D, Caminiti A, Righetti D, Balestri M, Montanari F, Romualdi P, Candeletti S. Nociceptin levels in the cerebrospinal fluid of chronic pain patients with or without intrathecal administration of morphine. J Pain Symptom Manage 2006;32:372–377. [PubMed: 17000354]

939. Raimundo JM, Sudo RT, Pontes LB, Antunes F, Trachez MM, Zapata-Sudo G. In vitro and in vivo vasodilator activity of racemic tramadol and its enantiomers in Wistar rats. Eur J Pharmacol 2006;530:117–123. [PubMed: 16371227]

940. Rasheed A, Haq MA, Ghori MU. Effect of opioid antagonists in stress-induced analgesia in uromastix hardwickii and gallus domesticus. Pediatr Blood Cancer 2006;46:15–24.

941. Raut A, Iglewski M, Ratka A. Differential effects of impaired mitochondrial energy production on the function of mu and delta opioid receptors in neuronal SK-N-SH cells. Neurosci Lett 2006;404:242–246. [PubMed: 16808998]

942. Rawls SM, Allebach C, Cowan A. Nitric oxide synathase mediates delta opioid receptor-induced hypothermia in rats. Eur J Pharmacol 2006;536:109–112. [PubMed: 16566919]

943. Rawls SM, Cowan A. Modulation of delta opioid-evoked hypothermia in rats by WAY100635 and fluoxetine. Neurosci Lett 2006;398:319–324. [PubMed: 16483716]

944. Ray R, Jepson C, Patterson F, Strasser A, Rukstalis M, Perkins K, Lynch KG, O'Malley S, Berrettini WH, Lerman C. Association of the OPRM1 A118G variant with the relative reinforcing value of nicotine. Psychopharm 2006;188:355–363.

945. Reeta, Kh; Mediratta, PK.; Rathi, N.; Jain, H.; Chugh, C.; Sharma, KK. Role of kappa- and delta-opioid receptors in the antinociceptive effect of oxytocin in formalin-induced pain responses in mice. Regul Pept 2006;135:85–90. [PubMed: 16712978]

946. Reid CM, Martin RM, Sterne JA, Davies AN, Hanks GW. Oxycodone for cancer-related pain: meta-analysis of randomized controlled trials. Arch Intern Med 2006;166:837–843. [PubMed: 16636208]

947. Renzelli CM, Capretto NA. Less pain, more gain: buprenorphine-nalaoxone and patient retention in treatment. J Addict Dis 2006;25:97–104. [PubMed: 16956874]

948. Reyes BA, Glaser JD, Magtoto R, Van Bockstaele EJ. Pro-opiomelanocortin co-localizes with corticotrophin-releasing factor in axon terminals of the noradrenergic nucleus locus coeruleus. Eur J Neurosci 2006;23:2067–2077. [PubMed: 16630054]

949. Rezayof A, Amini R, Rassouli Y, Zarrindast MR. Influence of nitric oxide on morphine-induced amnesia and interactions with dopaminergic receptor agents. Physiol Behav 2006;88:124–131. [PubMed: 16631214]

950. Ribeiro Do Couto B, Aguilar MA, Manzanedo C, Rodriguez-Arias M, Armario A, Minarro J. Social stress is as effective as physical stress in reinstating morphine-induced place preference in mice. Psychopharmacol 2006;185:459–470.

951. Riest G, Peters J, Weiss M, Pospiech J, Hoffmann O, Neuhauser M, Beiderlinden M, Eikermann M. Does perioperative administration of rofecoxib improve analgesia after spine, breast and orthopaedic surgery? Eur J Anaesthesiol 2006;23:219–226. [PubMed: 16430794]

952. Riley MA, Vathy I. Mid- to late gestational morphine exposure does not alter the rewarding properties of morphine in adult male rats. Neuropharmacol 2006;51:295–304.

953. Rimanoczy A, Slamberova R, Bar N, Vathy I. Morphine exposure prevents up-regulation of MR and GR binding sites in the brain of adult male and female rats due to prenatal stress. Int J Dev Neurosci 2006;24:241–248. [PubMed: 16698219]

954. Ring RH, Alder J, Fennell M, Kouranova E, Black IB, Thakker-Varia S. Transcriptional profiling of brain-derived-neurotrophic factor-induced neuronal plasticity: a novel role for nociceptin in hippocampal neurite outgrowth. J Neurobiol 2006;66:361–377. [PubMed: 16408296]

955. Rios C, Gomes I, Devi LA. Mu opioid and CB1 cannabinoid receptor interactions: reciprocal inhibition of receptor signaling and neuritogenesis. Br J Pharmacol 2006;148:387–395. [PubMed: 16682964]

956. Ripamonti C, Fagnoli E, Campa T, Brunelli C, De Conno F. Is the use of transdermal fentanyl inappropriate according to the WHO guidelines and the EPAC recommendations? A study of cancer patients in Italy Support Care. Cancer 2006;14:400–407.

957. Ripoli H, Hascoet M, Bourin M. The four-plates test: anxiolytic or analgesic paradigm? Prog Neuropsychopharmacol Biol Psychiatry 2006;30:873–880. [PubMed: 16644084]

958. Rittner HL, Labuz D, Schaefer M, Mousa SA, Schulz S, Scafer M, Stein C, Brack A. Pain control by CXCR2 ligands through Ca2+-regulated release of opioid peptides from polymorphonuclear cells. FASEB J 2006;20:2627–2629. [PubMed: 17060402]

959. Rivera JM, Locketz AJ, Fritz KD, Horlocker TT, Lewallen DG, Prasad A, Bresnahan JF, Kinney MO. “Broken heart syndrome” after separation (from OxyContin). Mayo Clin Proc 2006;81:825–828. [PubMed: 16770984]

960. Rivera-Gines A, Cook RJ, Loh HH, Ko JL. Interplay of Sps and poly C binding protein 1 on the mu-opioid receptor gene expression. Biochem Biophys Res Commun 2006;345:530–537. [PubMed: 16682008]

961. Rizzi A, Nazzaro C, Marzola GG, Zucchini S, Trapella C, Guerrini R, Zeilhofer HU, Regoli D, Calo’ G. Endogenous nociceptin/orphanin FQ signaling produces opposite spinal antinociception and supraspinal pronociceptive effects in the mouse formalin test: pharmacological and genetic evidences. Pain 2006;124:100–108. [PubMed: 16697109]

962. Roberto M, Siggins GR. Nociceptin/orphanin FQ presynaptically decreases GABA transmission and blocks the ethanol-induced increase of GABA release in the central amygdala. Proc Natl Acad Sci (USA) 2006;103:9715–9720. [PubMed: 16788074]

963. Rocha L, Arida RM, Carvalho Rde A, Scorza FA, Neri-Bazan L, Cavalheiro EA. GABA and opioid binding distribution in the brain of the seizure-resistenat Proechimys guyannensis: an autoradiography study. Synapse 2006;60:392–398. [PubMed: 16847947]

964. Rock RB, Hu S, Sheng WS, Peterson PK. Morphine stimulates CCL2 production by human neurons. Neuroinflammation 2006;3:32.

965. Rodgers RJ, Augar R, Berryman N, Hansom CJ, O’Mahony ML, Palmer RM, Stevens A, Tallett AJ. Atypical anxiolytic-like response to naloxone in benzodiazepine-resistant 129S2/SvHsd mice: role of opioid receptor subtypes. Psychopaharm 2006;187:345–355.

966. Roman E, Ploj K, Gustafsson L, Meyerson BJ, Nylander I. Variations in opioid peptide levels during the estrous cycle in Sprague-Dawley rats. Neuropeptides 2006;40:195–206. [PubMed: 16540166]

967. Ronai AZ, Al-Khrasani M, Betnyhe S, Lengyei I, Kocsis L, Orosz G, Toth G, Kato E, Tothfalusi L. Partial and full agonism in endomorphin derivatives: comparison by null and operational model. Peptides 2006;27:1507–1513. [PubMed: 16413634]

968. Ronai AZ, Szemenyei E, Kato E, Kocsis L, Orosz G, Al-Khransi M, Toth G. Endomorphin synthesis in rat brain from intracerebroventricularly injected [3H]-Tyr-Pro: a possible biosynthetic route for endomorphins. Regul Pept 2006;134:54–60. [PubMed: 16464510]

969. Rook EJ, Huitema AD, van den Brink W, van Ree JM, Beijnen JH. Population pharmacokinetics of heroin and its major metabolites. Clin Pharmacokinet 2006;45:401–417. [PubMed: 16584286]

970. Rook EJ, van Ree JM, van den Brink W, Hillebrand MJ, Huitema AD, Hendriks VM, Beijnen JH. Pharmacokinetics and pharmacodynamics of high doses of pharmaceutically prepared heroin, by intravenous or inhalation route in opioid-dependent patients. Basic Clin Pharmacol Toxicol 2006;98:86–96. [PubMed: 16433897]

971. Rook EJ, van Zanten AP, van den Brink W, van Ree JM, Beijnen JH. Mast cell tyrptase levels after inhalation or intravenous administration of high doses pharmaceutically prepared heroin. Drug Alcohol Depend 2006;85:185–190. [PubMed: 16765536]

972. Roozen HG, VanBeers SE, Weevers HJ, Breteler MH, Willemsen MC, Postmus PE, Kerkhof AJ. Effects of smoking cessation: naltrexone combined with a cognitive behavioral treatment based on the community reinforcement approach. Subst Use Misuse 2006;41:45–60. [PubMed: 16393735]

973. Roth TL, Moriceau S, Sullivan RM. Opioid modulation of Fos protein expression and olfactory circuitry plays a pivotal role in what neonates remember. Learn Mem 2006;13:590–598. [PubMed: 17015856]

974. Roth TL, Sullivan RM. Examining the role of endogenous opioids in learned odor-stroke associations in infant rats. Dev Psychobiol 2006;48(6d):71–78. [PubMed: 16381030]

975. Roth-Deri I, Mayan R, Yadid G. A hypothalamic endorphinergic lesion attenuates acquisition of cocaine self-administration in the rat. Eur Neuropsychopharmacol 2006;16:25–32. [PubMed: 16043329]

976. Ruangkittisakul A, Ballanyi K. Reversal by phosphodiesterase-4 blockers of in vitro apnea in the isolated brainstem-spinal cord preparation from newborn rats. Neurosci Lett 2006;401:194–198. [PubMed: 16581183]

977. Ruangkittisakul A, Schwarzacher SW, Secchia L, Poon BY, Ma Y, Funk GD, Ballanyi K. High sensitivity to neuromodulator-activated signaling pathways at physiological [K+] of confocally imaged respiratory center neurons in on-line-calibrated newborn rat brainstem slices. J Neurosci 2006;26:11870–11880. [PubMed: 17108160]

978. Sabino V, Cottone P, Koob GF, Steardo L, Lee MJ, Rice KC, Zorrilla EP. Dissociation between opioid and CRF1 antagonist sensitive drinking in Sardinian alcohol-preferring rats. Psychopharm 2006;189:175–186.

979. Sable HJ, Bell RL, Rodd ZA, McBride WJ. Effects of naltrexone on the acquisition of alcohol intake in male and female periadolescent and adult alcohol-preferring rats. Int J Adolesc Med Health 2006;18:139–149. [PubMed: 16639868]

980. Sadri-Vakili G, Menon AS, Farrell LA, Keller-McGandy CE, Cantuti-Castelvetri I, Standaert DG, Augood SJ, Yohrling GJ, Cha JH. Huntingtin inclusions do not down-regulate specific genes in the R6/2 Huntington's disease mouse. Eur J Neurosci 2006;23:3171–3175. [PubMed: 16820007]

981. Sahraei H, Barzegari AA, Shams J, Zarrindast MR, Haeri-Rohani A, Ghoshooni H, Sepehri H, Salimi SH. Theophylline inhibits tolerance and sensitization induced by morphine: a conditioned place preference paradigm study in female mice. Behav Pharmacol 2006;17:621–628. [PubMed: 17021395]

982. Sahraei H, Faghih-Monzavi Z, Fatemi SM, Pashaei-Rad S, Salimi SH, Kamalinejad M. Effects of Papaver rhoeas on the acquisition and expression of morphine-induced behavioral sensitization in mice. Phytother Res 2006;20:737–741. [PubMed: 16807881]

983. Saidek Z, Blake-Palmer K, Hay DL, Northup JK, Glass M. Differential activation of G-proteins by mu-opioid receptor agonists. Br J Pharmacol 2006;147:671–680. [PubMed: 16415903]

984. Sakaguchi M, Koseki M, Wakamatsu M, Matsumura E. Effects of systemic administration of beta-casomorphin-5 on learning and memory in mice. Eur J Pharmacol 2006;530:81–87. [PubMed: 16360145]

985. Sakharkar AJ, Singru PS, Mazumdar M, Subhedar N. Reproduction phase-related expression of beta-endorphin-like immunoreactivity in the nucleus lateralis tuberis of the female Indian major carp cCirrhinus mrigala: correlation with the leutinising hormone cells-ovary axis. J Neuroendocrinol 2006;18:319–329. [PubMed: 16629830]

986. Sanabria ER, D'Andrea Vieira I, da Silveira Pereira MF, Faria LC, da Silva AC, Cavalheiro EA, da Silva Fernandes MJ. Pro-epileptic effect of alfentanil in rats subjected to pilocarpine-induced chronic epilepsy. Brain Res Bull 2006;69:535–545. [PubMed: 16647582]

987. San-Emeterio EP, Hurle MA. Modulation of brain apoptosis-related proteins by the opioid antagonist naltrexone in mice. Neurosci Lett 2006;403:276–279. [PubMed: 16716514]

988. Sarvela PJ, Halonen PM, Soikkeli AI, Kainu JP, Korttila KT. Ondansetron and tropisetron do not prevent intraspinal morphine- and fentanyl-induced pruritus in elective cesarean delivery. Acta Anaesthesiol Scand 2006;50:239–244. [PubMed: 16430549]

989. Sasaki Y, Kawano S, Kohara H, Watanabe H, Ambo A. ORL-1 and opioid receptor preferences of nociceptin and dynorphin A analogues with Dmp substituted for N-terminal aromatic residues. Bioorg Med Chem 2006;14:2433–2437. [PubMed: 16321540]

990. Sauliere A, Gaibelet G, Millot C, Mazeres S, Lopez A, Salome L. Diffusion of the mu opioid receptor at the surface of human neuroblastoma SH-SY5Y cells is restricted to permeable domains. FEBS Lett 2006;580:5227–5231. [PubMed: 16963028]

991. Saunier-Rebori BT, Pazo JH. Inhibition of the jaw opening reflex and single neurons in the trigeminal subnucleus caudalis by activation of striatal D2 dopamine receptors. Neuropharm 2006;51:263–271.

992. Saurer TB, Ijames SG, Lysle DT. Neuropeptide Y Y1 receptors mediate morphine-induced reductions of natural killer cell activity. J Neuroimmunol 2006;177:18–26. [PubMed: 16766046]

993. Savegnano L, Jesse CR, Moro AV, Borges VC, Santos FW, Rocha JB, Nogueira CW. Bis selenide derivatives: a class of potential antioxidant and antinociceptive agents. Pharmacol Biochem Behav 2006;83:221–229. [PubMed: 16545442]

994. Schallmach E, Steiner D, Vogel Z. Adenylyl cyclase type II activity is regulated by two different mechanisms: implications for acute and chronic opioid exposure. Neuropharm 2006;50:998–1005.

995. Schallmach E, Steiner D, Vogel Z. Inhibition of AC-II activity following chronic agonist exposure is modulated by phosphorylation. J Mol Neurosci 2006;29:115–122. [PubMed: 16954601]

996. Scherrer G, Tryoen-Toth P, Filliol D, Matifas A, Laustriat D, Cao YQ, Basbaum AI, Dierich A, Vonesh JL, Gaveriaux-Ruff C, Kieffer BL. Knockin mice expressing fluorescent delta opioid receptors uncover G protein-coupled receptor dynamics in vivo. Proc Natl Acad Sci (USA) 2006;103:9691–9696. [PubMed: 16766653]

997. Schmid-Grendelmeier P, Pokorny R, Gasser UE, Richarz U. A comparison of the skin irritation potential of transdermal fentanyl versus transdermal buprenorphine in middle-aged to elderly healthy volunteers. Curr Med Res Opin 2006;22:501–509. 998. [PubMed: 16574034]

998. Schmitt PM, Gohil K, Kaufman MP. Spinal estrogen attenuates the exercise pressor reflex but has little effect on the expression of genes regulating neurotransmitters in the dorsal root ganglia. J Appl Physiol 2006;100:958–964. [PubMed: 16306253]

999. Schoffelmeer AN, Hogenboom F, Wardeh G, De Vries TJ. Interactions between CB1 cannabinoid and mu opioid receptors mediating inhibition of neurotransmitter release in rat nucleus accumbens core. Neuropharm 2006;51:773–781.

1000. Schreiber S, Pick CG. From selective to highly selective SSRIs: a comparison of the antinociceptive properties of fluoxetine, fluvoxamine, citalopram and escitalopram. Eur Neuropsychopharmacol 2006;16:464–468. [PubMed: 16413173]

1001. Schroeder MB, Riters LV. Pharmacological manipulations of dopamine and opioids have differential effects on sexually motivated song in male European starlings. Physiol Behav 2006;88:575–584. [PubMed: 16784760]

1002. Schulte H, Segerdahl M, Graven-Nielsen T, Grass S. Reduction in human experimental muscle pain by alfentanil and morphine. Eur J Pain 2006;10:733–741. [PubMed: 16414295]

1003. Schwilke EW, Barnes AJ, Kacinko SL, Cone EJ, Moolchan ET, Huestis MA. Opioid disposition in human sweat after controlled oral codeine administration. Clin Chem 2006;52:1539–1545. [PubMed: 16740647]

1004. Seet E, Leong WL, Yeo AS, Fook-Chang S. Effectiveness of 3-in-1 continuous femoral block of differing concentrations compared to patient controlled intravenous morphine for post total knee arthroplasty analgesia and knee rehabilitation. Anaesth Intensive Care 2006;34:25–30. [PubMed: 16494145]

1005. Seib RK, Paul JE. Posoperative gabapentin for postoperative analgesia: a meta-analysis. Can J Anaesth 2006;53:461–469. [PubMed: 16636030]

1006. Seidel M, Billert H, Kurpisz M. Regulation of eNOS expression in HCAEC cell line treated with opioids and proinflammatory cytokines. Kardiol Pol 2006;64:153–158. [PubMed: 16502366]

1007. Sen S, Aydin ON, Aydin K. Beneficial effect of low-dose ketamine addition to epidural administration of morphine-bupivacaine mixture for cancer pain in two cases. Pain Med 2006;7:166–169. [PubMed: 16634730]

1008. Sevcik MA, Jonas BM, Lindsay TH, Halvorson KG, Ghilardi JR, Kuskowski MA, Mukherjee P, Maggio JE, Mantyh PW. Endogenous opioids inhibit early-stage pancreatic pain in a mouse model of pancreatic cancer. Gastroenterology 2006;131:900–910. [PubMed: 16952558]

1009. Sevostianova N, Danysz W. Analgesic effects of mGlu1 and mGlu5 receptor antagonists in the rat formalin test. Neuropharm 2006;51:623–630.

1010. Shahabi NA, McAllen K, Sharp BK. Delta opioid receptors stimulate Akt-dependent phosphorylation of c-jun in T cells. J Pharmacol Exp Ther 2006;316:933–939. [PubMed: 16249373]

1011. Shahabi S, Hashemi M, Hassan ZM, Javan M, Bathaie SZ, Toraihi T, Zakeri Z, Ilkhanizadeh B, Jazani NH. The effect of post-burn local hyperthermia on the reducing burn injury: the possible role of opioids. Int J Hyperthermia 2006;22:421–431. [PubMed: 16891244]

1012. Shalev U, Finnie PS, Quinn T, Tobin S, Wahi P. A role for corticotrophin-releasing factor, but not corticosterone, in acute food-deprivation-induced reinstatement of heroin seeking in rats. Psychopharmacol 2006;187:376–384.

1013. Shams J, Sahraei H, Gholami A, Haeri-Rohani A, Alaf-Javadi M, Sepehri H, Salimi SH, Ghoshooni H. Effects of ultra-low doses of nicotine on the expression of morphine-induced conditioned place preference in mice. Behav Pharmacol 2006;17:629–635. [PubMed: 17021396]

1014. Shanahan MD, Doran CM, Digiusto E, Bell J, Lintzeris N, White J, Ali R, Saunders JB, Mattick RP, Gilmour S. A cost-effectiveness analysis of heroin detoxification methods in the Australian National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD). Addict Behav 2006;31:371–387. [PubMed: 15972245]

1015. Shang GW, Liu DN, Yan LH, Cui XY, Zhang KP, Qi C, Chen J. Nociceptive stimulus modality-related differences in pharmacokinetic-pharmacodynamic modeling of morphine in the rat. Pharmacol Biochem Behav 2006;85:464–473. [PubMed: 17126387]

1016. Shariftabrizi A, Nifli AP, Ansari M, Saadat F, Ebrahimkhani MR, Alizadeh N, Nasseh A, Alexaki VI, Dehpour AR, Castanas E, Khorramizadeh MR. Matrix metalloproteinase 2 secretion in WEHI 164 fibrosarcoma cells is nitric oxide-related and modified by morphine. Eur J Pharmacol 2006;530:33–39. [PubMed: 16386243]

1017. Sharifzadeh M, Hadjiakhoondi A, Khanavi M, Susanabadi M. Effects of aqueous, methanolic and chloroform extracts of rhizome and aerial parts of Valeriana officinalis L on naloxone-induced jumping in morphine-dependent mice. Addict Biol 2006;11:145–151. [PubMed: 16800827]

1018. Sharifzadeh M, Haghighat A, Tahsili, Fahadan P, Khalaj S, Zarrindast MR, Zamanian AR. Intrahippocampal inhibition of protein kinase A attenuates morphine-induced conditioned place preference. Pharmacol Biochem Behav 2006;85:705–712. [PubMed: 17174386]

1019. Sharma HS. Hyperthermia influences excitatory and inhibitory amino acid neurotransmitters in the central nervous system. An experimental study in the rat using behavioral, biochemical, pharmacological and morphological approaches. J Neural Transm 2006;113:497–519. [PubMed: 16550328]

1020. Sharma HS, Ali SF. Alterations in blood-brain barrier function by morphine and methamphetamine. Ann NY Acad Sci 2006;1074:198–224. [PubMed: 17105918]

1021. Sharma HS, Lundstedt T, Boman A, Lek P, Seifert E, Wiklund L, Ali SF. A potent serotonin-modulating compound AP-267 attenuates morphine withdrawal-induced blood-brain barrier dysfunction in rats. Ann NY Acad Sci 2006;1074:482–496. [PubMed: 17105947]

1022. Sharma HS, Nyberg F, Gordh T, Alm P. Topical application of dynorphin A(1–17) antibodies attenuates neuronal nitric oxide synthase up-regulation, edema formation and cell injury following focal trauma to the rat spinal cord. Acta Neurochir Suppl 2006;96:309–315. [PubMed: 16671477]

1023. Sharma M, Mohta M, Chawla R. Efficacy of intrathecal adenosine for postoperative pain relief. Eur J Anaesthesiol 2006;23:449–453. [PubMed: 16507193]

1024. Shekunova EV, Bespalov AY. Effects of memantine on estrogen-dependent acute tolerance to the morphine analgesia in female rats. Eur J Pharmacol 2006;535:78–85. [PubMed: 16546163]

1025. Shen H, Sprott H, Aeschlimann A, Gay RE, Michel BA, Gay S, Sprott H. Analgesic action of acetaminophen in symptomatic osteoarthritis of the knee. Rheumatol (Oxford) 2006;45:765–770.

1026. Sher L, Cooper TB, Mann JJ, Oquendo MA. Modified dexamethasone suppression-corticotropin-releasing hormone stimulation test: a pilot study of young healthy volunteers and implications for alcoholism research in adolescents and young adults. Int J Adolesc Med Health 2006;18:133–137. [PubMed: 16639867]

1027. Shi X, McGinty JF. Extrcellular signal-related mitogen-activated protein kinase inhibitors decrease amphetamine-induced behavior and neuropeptide gene expression in the striatum. Neurosci 2006;138:1289–1298.

1028. Shibasaki M, Katsura M, Tsujimura A, Ohkuma S. Up-regulated L-type high voltage-gated calcium channels cause increase in diazepam binding inhibitor induced by sustained morphine exposure in mouse cerebrocortical neurons. Life Sci 2006;80:166–172. [PubMed: 17023003]

1029. Shimura T, Imaoka H, Yamamoto T. Neurochemical modulation of ingestive behavior in the ventral pallidum. Eur J Neurosci 2006;23:1596–1604. [PubMed: 16553623]

1030. Shin IW, Sohn JT, Park KE, Chang KC, Choi JY, Lee HK, Chung YK. A supraclinical dose of tramadol stereoselectively attenuates endothelium-dependent relaxation in isolated rat aorta. Anesth Analg 2006;103:366–371. [PubMed: 16861418]

1031. Shiotani K, Li T, Miyazaki A, Tsuda Y, Bryant SD, Ambo A, Sasaki Y, Lazarus LH, Okada Y. Synthesis of 3,6-bis{H-Tyr/H-Dmt-NH(CH2)m, n]-2(1H)pyrazinone derivatives: function of alkyl chain length on opioid activity. Bioorg Med Chem Lett 2006;16:5793–5796. [PubMed: 16949282]

1032. Shoblock JR, Maidment NT. Constitutively active mu opioid receptors mediate the enhanced conditioned aversive effect of naloxone in morphine-dependent mice. Neuropsychopharmacol 2006;31:171–177.

1033. Short JL, Drago J, Lawrence AJ. Comparison of ethanol preference and neurochemical measures of mesolimbic dopamine and adenosine systems across different strains of mice. Alcohol Clin Exp Res 2006;30:606–620. [PubMed: 16573578]

1034. Shu H, Arita H, Hayashida M, Chiba S, Sekiyama H, Hanaoka K. Inhibition of morphine tolerance by processed Aconiti tuber is mediated by kappa-opioid receptors. J Ethnopharmacol 2006;106:263–271. [PubMed: 16446067]

1035. Shukla PK, Tang L, Wang ZJ. Phosphorylation of neurogranin, protein kinase C and Ca2+/calmodulin dependent protein kinase II in opioid tolerance and dependence. Neurosci Lett 2006;404:266–269. [PubMed: 16824682]

1036. Sibanda S, Hughes JM, Pawson PE, Kelly G, Bellenger CR. The effects of preoperative extradural bupivacaine and morphine on the stress response in dogs undergoing femoral-tibial joint surgery. Vet Anaesth Analg 2006;33:246–257. [PubMed: 16764590]

1037. Sibilia V, Lattuada N, Rapetti D, Pagani F, Vincenza D, Bulgarelli I, Locatelli V, Guidobono F, Netti C. Ghrelin inhibits inflammatory pain in rats: involvement of the opioid system. Neuropharm 2006;51:497–505.

1038. Simmen U, Kelber O, Okpanyi SN, Jaeggi R, Bueter B, Weiser D. Binding of STW 5 (Iberoglast) and its components to intestinal 5-HT, muscarinic M3 and opioid receptors. Phytomedicine 2006;13:51–55. [PubMed: 16973340]

1039. Simonin F, Schmitt M, Laulin JP, Laboureyras E, Jhamandas JH, MacTavish D, Matifas A, Mollereau C, Laurent P, Parmentier M, Kieffer BL, Bourguignon JJ, Simonnet G. RF9, a potent and selective neuropeptide FF receptor antagonist, prevents opioid-induced tolerance associated with hyperalgesia. Proc Natl Acad Sci 2006;103:466–471. [PubMed: 16407169]

1040. Sinchak K, Romeo HE, Micevych PE. Site-specific estrogen and progestin regulation of orphanin FQ/nociceptin and nociceptin opioid receptor mRNA expression in the female rat limbic hypothalamic system. J Comp Neurol 2006;496:252–268. [PubMed: 16538678]

1041. Singh N, Cheve G, Ferguson DM, McCurdy CR. A combined ligand-based and target-based drug design approach for G-protein coupled receptors: application to salvinorin A, a selective kappa opioid receptor agonist. J Computer Aided Mol Des 2006;20:471–493.

1042. Singhal AK, Mishra S, Bhatnagar S, Singh R. Epidural morphine analgesia compared with intravenous morphine for oral cancer surgery with pectoralis major myocutaneous flap reconstruction. Acta Anaesthesiol Scand 2006;50:234–238. [PubMed: 16430548]

1043. Singleton PA, Lingen MW, Fekete MJ, Garcia JG, Moss J. Methylnaltrexone inhibits opiate and VEGF-induced angiogenesis: role of receptor transactivation. Microvasc Res 2006;72:3–11. [PubMed: 16820176]

1044. Sivam SP, Cox J. Postnatal administration of D1 dopamine agonist reverses neonatal dopaminergic lesion-induced changes in striatal enkephalin and substance P systems. Brain Res 2006;1073–1074:159–163.

1045. Smith FL, Javed RR, Smith PA, Dewey WL, Gabra BH. PKC and PKA inhibitors reinstate morphine-induced behaviors in morphine tolerant mice. Pharmacol Res 2006;54:474–480. [PubMed: 17056270]

1046. Smith J, Owen E, Earis J, Woodcock A. Effect of codeine on objective measurement of cough in chronic obstructive pulmonary disease. J Allergy Clin Immunol 2006;117:831–835. [PubMed: 16630941]

1047. Smith LJ, Valenzuela JR, Krugner-Higby LA, Brown C, Heath TD. A single dose of liposome-encapsulated hydromorphone provides extended analgesia in a rat model of neuropathic pain. Comp Med 2006;56:487–492. [PubMed: 17219779]

1048. Smith MA, Lyle MA. Chronic exercise decreases sensitivity to mu opioids in female rats: correlation with exercise output. Pharmacol Biochem Behav 2006;85:12–22. [PubMed: 16904173]

1049. Smith VA, Beyer CE, Brandt MR. Neurochemical changes in the RVM associated with peripheral inflammatory pain stimuli. Brain Res 2006;1095:65–72. [PubMed: 16730668]

1050. Smith YR, Stohler CS, Nichols TE, Bueller JA, Koeppe RA, Zubieta JK. Pronociceptive and antinociceptive effects of estradiol through endogenous opioid neurotransmission in women. J Neurosci 2006;26:5777–5785. [PubMed: 16723535]

1051. Snook LA, Milligan G, Kieffer BL, Massotte D. Mu-delta opioid receptor functional interaction: insight using receptor-G protein fusions. J Pharmacol Exp Ther 2006;318:683–690. [PubMed: 16690720]

1052. Soaje M, Valdez S, Bregonzio C, Penissi A, Deis RP. Dopaminergic mechanisms involved in prolactin release after mifepristone and naloxone treatment during late pregnancy in the rat. Neuroendocrinol 2006;84:58–67.

1053. Sobocanec S, Kusic B, Sverko V, Balog T, Marotti T. Methionine-enkephalin modulated regulation of oxidant/antioxidant status in liver of CBA mice. Biogerontol 2006;7:53–62.

1054. Solbrig MV, Adrian R, Baratta J, Lauterborn JC, Koob GF. Kappa opioid control of seizures produced by a virus in an animal model. Brain 2006;129:642–654. [PubMed: 16399805]

1055. Solbrig MV, Adrian R, Chang DY, Perng GC. Viral risk factor for seizures: pathobiology of dynorphin in herpes simplex viral (HSV-1) seizures in an animal model. Neurobiol Dis 2006;23:612–620. [PubMed: 16843674]

1056. Sorge RE, Stewart J. The effects of long-term chronic buprenorphine treatment on the locomotor and nucleus accumbens dopamine response to acute heroin and cocaine in rats. Pharmacol Biochem Behav 2006;84:300–305. [PubMed: 16806444]

1057. Soverchia L, Mosconi G, Ruggeri B, Ballarini P, Catone G, Degl'Innocenti S, Nabissi M, Polzonetti-Magni AM. Proopiomelanocortin gene expression and beta-endorphin in the pituitary, testis and epididymis of stallion. Mol Reprod Dev 2006;73:1–8. [PubMed: 16177984]

1058. Spadaro A, Ajello A, Luigiano C, Morace C, Resta ML, Berlinghieri G, Campo S, Scisca C, Alibrandi A, D'Arrigo G, Alessi N, Ferrau O, Freni MA. Low utility of plasma nociceptin/orphanin in the diagnosis of hepatocellular carcinoma. World J Gastroenterol 2006;12:4716–4720. [PubMed: 16937445]

1059. Spampinato S, Baiula M. Agonist-induced endocytosis and desensitization of the human nociceptin receptor. Neuroreport 2006;17:173–177. [PubMed: 16407766]

1060. Spies C, Eggers V, Szabo G, Lau A, von Dossow V, Schoenfeld H, Althoff H, Hegenscheid K, Bohm B, Schroeder T, Pfeiffer S, Ziemer S, Paschen C, Klein M, Marks C, Miller P, Sander M, Wernecke KD, Achterberg E, Kaisers U, Volk HD. Intervention at the level of the neuroendocrine-

immune axis and post-operative pneumonia rate in long-term alcoholics. Am J Respir Crit Care Med 2006;174:408–414. [PubMed: 16728716]

1061. Spivak CE, Oz M, Beglan CJ, Shrager RI. Diffusion delays and unstirred layer effects at monolayer cultures of Chinese hamster ovary cells: radioligand binding, confocal microscopy and mathematical simulations. Cell Biochem Biophys 2006;45:43–58. [PubMed: 16679563]

1062. Sprenger T, Valet M, Boecker H, Henriksen G, Spilker ME, Willoch F, Wagner KJ, Wester HJ, Tolle TR. Opioidergic activation in the medial pain system after heat pain. Pain 2006;122:63–67. [PubMed: 16527398]

1063. Sprung J, Sanders MS, Warner ME, Gebhart JB, Stanhope CR, Jankowski CJ, Liedl L, Schroeder DR, Brown DR, Warner DO. Pain relief and functional status after vaginal hysterectomy: intrathecal versus general anesthesia. Can J Anaesth 2006;53:690–700. [PubMed: 16803917]

1064. Staahl C, Christrup LL, Anderson SD, Arendt-Nielsen L, Drewes AM. A comparative study of oxycodone and morphine in a multi-modal, tissue-differentiated experimental pain model. Pain 2006;123:28–36. [PubMed: 16600508]

1065. Stanojevic S, Mitic K, Vujic V, Kovacevic-Jovanovic V, Dimitrijevic M. Beta-endorphin differentially affects inflammation in two inbred rats strains. Eur J Pharmacol 2006;549:157–165. [PubMed: 16978600]

1066. Statler KD, Alexander H, Vagni V, Dixon CE, Clark RS, Jenkins L, Kochanek PM. Comparison of seven anesthetic agents on outcome after experimental traumatic brain injury in adult, male rats. J Neurotrauma 2006;23:97–108. [PubMed: 16430376]

1067. Steagall PV, Carnicelli P, Taylor PM, Luna SP, Dixon M, Ferreira TH. Effects of subcutaneous methadone, morphine, buprenorphine or saline on thermal and pressure thresholds in cats. J Vet Pharmacol Ther 2006;29:531–537. [PubMed: 17083457]

1068. Steffensen SC, Stobbs SH, Colago EE, Lee RS, Koob GF, Gallegos RA, Henriksen SJ. Contingent and non-contingent effects of heroin on mu-opioid receptor-contining ventral tegmental area GABA neurons. Exp Neurol 2006;202:139–151. [PubMed: 16814775]

1069. Stevenson GW, Bilsky EJ, Negus SS. Targeting pain-suppressed behaviors in preclinical assays of pain and analgesia: effects of morphine on acetic acid-suppressed feeding in C57BL/6J mice. J Pain 2006;7:408–416. [PubMed: 16750797]

1070. Stewart DJ, Fahmy H, Roth BL, Yan F, Zjawiony JK. Bioisosteric modification of salvinorin A, a potent and selective kapp-opioid receptor agonist. Arzneimittelforschung 2006;56:269–275. [PubMed: 16724512]

1071. St-Hilaire M, Bourhis E, Levesque D, Rouillard C. Impaired behavioural and molecular adaptations to deopamine denervation and repeated L-DOPA treatment in Nur77-knockout mice. Eur J Neurosci 2006;24:795–805. [PubMed: 16930409]

1072. Strandberg JJ, Kugelberg FC, Alkass K, Gustavsson A, Zahlsen K, Spigset O, Druid H. Toxicological analysis in rats subjected to heroin and morphine overdose. Toxicol Lett 2006;166:11–18. [PubMed: 16793228]

1073. Streel E, Dan B, Campanella S, Meyvaert A, Hanak C, Pelc I, Verbanck P. A pharmacological modulation of opiate withdrawal using an up-/down-regulation of the noradrenergic system in opiate-dependent rats. Int J Neuropsychopharmacol 2006;9:621–626. [PubMed: 16146582]

1074. Strong JA, Dalvi A, Revilla A, Sahay A, Samaha FJ, Welge JA, Gong J, Gartner M, Yue X, Yu L. Genotype and smoking history affect risk of levodopa-induced dyskinesias in Parkinson's disease. Mov Disord 2006;21:654–659. [PubMed: 16435402]

1075. Suarez-Roca H, Silva JA, Arcaya JL, Quintero L, Maixner W, Pinerua-Shuhaibar L. Role of mu-opioid and NMDA receptors in the development and maintenance of repeated swim stress-induced thermal hyperalgesia. Behav Brain Res 2006;167:205–211. [PubMed: 16214233]

1076. Succu S, Mascia MS, Melis T, Sanna F, Boi A, Melis MR, Argiolas A. Morphine reduces penile erections induced by the cannabinoid receptor antagonist SR 141716A in male rats: role of paraventricular glutamic acid and nitric oxide. Neurosci Lett 2006;404:1–5. [PubMed: 16725257]

1077. Suder P, Bierczynska-Krzysik A, Kraj A, Borstedt P, Mak P, Stawikowski M, Rolka K, Nyberg F, Fries E, Silberring J. Identification of bikunin as an endogenous inhibitor of dynorphin convertase in human cerebrospinal fluid. FEBS J 2006;273:5113–5120. [PubMed: 17087727]

1078. Sugaya I, Qu T, Sugaya K, Pappas GD. Genetically-engineered human mesenchymal stem cells produce met-enkephalin at augmented higher levels in vitro. Cell Transplant 2006;15:225–230. [PubMed: 16719057]

1079. Sugimoto Y, Shimizu A, Kato T, Satoh A, Ozaki S, Ohta H, Okamoto O. Design, synthesis and biological evaluation of indole derivatives as novel nociceptin/orphanin FQ (N/OFQ) receptor antagonists. Bioorg Med Chem Lett 2006;16:3569–3573. [PubMed: 16621546]

1080. Sugino T, Shimazoe T, Ikeda M, Watananbe S. Role of nociceptin and opioid receptor like 1 on entrainment function in the rat suprachiasmatic nucleus. Neurosci 2006;137:537–544.

1081. Sukikara MH, Mota-Ortiz SR, Baldo MV, Felicio LF, Canteras NS. A role for the periaqueductal gray in switching adaptive behavioral responses. J Neurosci 2006;26:2583–2589. [PubMed: 16510737]

1082. Sullivan LE, Barry D, Moore BA, Chawarski MC, Tetrault JM, Pantalon MV, O'Connor PG, Schottenfeld RS, Fiellin DA. A trial of integrated buprenorphine/naloxone and HIV clinical care. Clin Infect Dis 2006;43(4):S184–S190. [PubMed: 17109305]

1083. Sullivan MA, Rothernberg JL, Vosburg SK, Church SH, Feldman SJ, Epstein EM, Kleber HD, Nunes EV. Predictors of retention in naltrexone maintenance for opioid dependence: analysis of a stage I trial. Am J Addict 2006;15:150–159. [PubMed: 16595353]

1084. Sullivan MA, Vosburg SK, Comer SD. Depot naltrexone: antagonism of the reinforcing, subjective and physiological effects of heroin. Psychopharm 2006;189:37–46.

1085. Sumner JE, Ulibarri C, Craft RM. Testosterone modulation of reproductive indices vs. morphine antinociception in male rats. Life Sci 2006;79:2119–2127. [PubMed: 16914166]

1086. Sun B, Tipton CM, Bidlack JM. The expression of pro-dynorphin gene is down-regulated by activation with lipopolysaccharide in U-937 macrophage cells. J Neuroimmunol 2006;174:52–62. [PubMed: 16483672]

1087. Sun JJ, Chuang Kung J, Wang CC, Chen SL, Shyu BC. Short-term facilitation in the anterior cingulate gyrus following stimulation of the medial thalamus in the rat. Brain Res 2006;1097:101–115. [PubMed: 16725116]

1088. Sun X, Ma S, Zang YM, Lu SY, Guo HT, Bi H, Wang YM, Ma H, Ma XL, Pei JM. Vasorelaxing effect of U50488H in pulmonary artery and underlying mechanism in rats. Life Sci 2006;78:2516–2522. [PubMed: 16336977]

1089. Susce MT, Murray-Carmichael E, de Leon J. Response to hydrocodone, codeine and oxycodone in a CYP2D6 poor metabolizer. Prog Neuropsychopharmacol Biol Psychiatry 2006;30:1356–1358. [PubMed: 16631290]

1090. Suzuki M, Narita M, Nakamura A, Suzuki T. Role of gap junction in the expression of morphine-induced antinociception. Eur J Pharmacol 2006;535:169–171. [PubMed: 16522320]

1091. Suzuki M, Narita M, Narita M, Niikura K, Suzuki T. Chronic morphine treatment increases the expression of the neural cell adhesion molecule in the dorsal horn of the mouse spinal cord. Neurosci Lett 2006;399:202–205. [PubMed: 16510246]

1092. Suzuki M, Narita M, Narita M, Suzuki T. Chronic morphine treatment increases the expression of vesicular glutamate transporter 1 in the mouse spinal cord. Eur J Pharmacol 2006;535:166–168. [PubMed: 16522322]

1093. Suzuki R, Porreca F, Dickenson AH. Evidence for spinal dorsal horn hyperexcitability following sustained morphine exposure. Neurosci Lett 2006;407:156–161. [PubMed: 16959420]

1094. Svensson J, Diez M, Engel J, Wass C, Tivesten A, Jannson JO, Isaksson O, Archer T, Hokfelt T, Ohlsson C. Endocrine, liver-derived IGF-I is of importance for spatial learning and memory in old mice. J Endocrinol 2006;189:617–627. [PubMed: 16731792]

1095. Szegedi V, Juhasz G, Rozsa E, Juhasz-Vedres G, Datki Z, Fulop L, Bozso Z, Lakatos A, Laczko I, Farkas T, Kis Z, Toth G, Soos K, Zarandi M, Budai D, Toldi J, Penke B. Endomorphin-2, an endogenous tetrapeptide, protects against Abeta1–42 in vitro and in vivo. FASEB J 2006;20:1191–1193. [PubMed: 16636106]

1096. Taddio A, Lee C, Yip A, Parvez B, McNamara PJ, Shah V. Intravenous morphine and topical tetracaine for treatment of pain in neonates undergoing central line placement. JAMA 2006;295:793–800. [PubMed: 16478902]

1097. Taha SA, Norsted E, Lee LS, Lang PD, Lee BS, Woolley JD, Fields HL. Endogenous opioids encode relative taste preference. Eur J Neurosci 2006;24:1220–1226. [PubMed: 16925586]

1098. Tahsali-Fahadan P, Yahyavi-Firouz-Abadi N, Khoshnoodi MA, Motiei-Langroudi R, Tahaei SA, Ghahremani MH, Dehpour AR. Agmatine potentiates morphine-induced conditioned place preference in mice: modulation by alpha2-adrenoceptors. Neuropsychopharamcol 2006;31:1722–1732.

1099. Tai YH, Wang YH, Wang JJ, Tao PL, Tung CS, Wong CS. Amitriptyline suppresses neuroinflammation and up-regulates glutamate transporters in morphine-tolerant rats. Pain 2006;124:77–86. [PubMed: 16697108]

1100. Tajalli S, Jonaidi H, Abbasnejad M, Denbow DM. Interaction between nociceptin/orphanin FQ (N/OFQ) and GABA in response to feeding. Physiol Behav 2006;89:410–413. [PubMed: 16904711]

1101. Takahashi A, Amano M, Amiya N, Yamanome T, Yamamori K, Kawauchi H. Expression of three proopiomelanocortin subtype genes and mass spectrometric identification of POMC-derived peptides in pars distalis and pars intermedia of barfin flounder pituitary. Gen Comp Endocrinol 2006;145:280–286. [PubMed: 16242690]

1102. Takasaki I, Nojima H, Shiraki K, Kuraishi Y. Specific down-regulation of spinal mu-opioid receptor and reduced analgesic effects of morphine in mice with postherpetic pain. Eur J Pharmacol 2006;550:62–67. [PubMed: 17026987]

1103. Takasu K, Honda M, Ono H, Tanabe M. Spinal alpha-2 adrenergic and muscarinic receptors and the NO release cascade mediate supraspinally-produced effectiveness of gabapentin at decreasing mechanical hypersensitivity in mice after partial nerve injury. Br J Pharmacol 2006;148:233–244. [PubMed: 16582934]

1104. Takeuchi R, Hoshijima N, Nagasaka H, Chowdhury SA, Kikuchi H, Kanda Y, Kunii S, Kawase M, Sakagami H. Induction of non-apoptotic cell death by morphinone in human promyelocytic leukemia HL-60 cells. Anticancer Res 2006;26:3343–3348. [PubMed: 17094451]

1105. Talley P, Heitkemper M, Chicz-Demet A, Sandman CA. Male violence, stress, and neuroendocrine parameters in pregnancy: a pilot study. Biol Res Nurs 2006;7:222–233. [PubMed: 16552950]

1106. Tamura Y, Monden M, Shintani M, Kawai A, Shiomi H. Neuroprotective effects of hibernation-regulating substances against low-temperature-induced cell death in cultured hamster hippocampal neurons. Brain Res 2006;1108:107–116. [PubMed: 16854391]

1107. Tanabe M, Murakami H, Honda M, Ono H. Gabapentin depresses C-fiber-evoked field potentials in rat spinal dorsal horn only after induction of long-term potentiaion. Exp Neurol 2006;202:280–286. [PubMed: 16857192]

1108. Tang L, Shukla PK, Wang ZJ. Attenuation of opioid tolerance by antisense oligodeoxynucleotides targeting neurogranin. Eur J Pharmacol 2006;542:106–107. [PubMed: 16797003]

1109. Tang L, Shukla PK, Wang LX, Wang ZJ. Reversal of morphine antinociceptive tolerance and dependence by the acute supraspinal inhibition of Ca(2+)/calmodulin-depdnent protein kinase II. J Pharmacol Exp Ther 2006;317:901–909. [PubMed: 16505162]

1110. Tao PL, Liang KW, Sung WY, Wu YT, Huang EY. Nalbuphine is effective in decreasing the rewarding effect induced by morphine in rats. Drug Alcohol Depend 2006;84:175–181. [PubMed: 16517095]

1111. Taracha E, Lehner M, Wislowska-Stanek A, Zienowicz M, Maciejak P, Bidzinski A, Skorzewska A, Turzynska D, Plaznik A. Effects of methadone and morphine on c-Fos expression in the rat brain: similarities and differences. Pharmacol Rep 2006;58:120–124. [PubMed: 16531639]

1112. Tavakoli S, Hajrasouliha AR, Jabehdar-Maralani P, Ebrahimi F, Sadeeghipor H, Dehghani M, Shafaroodi H, Dehpour AR. Modulated hemodynamic response to clonidine in bile duct-ligated rats: the role of nitric oxide. Eur J Pharmacol 2006;542:148–153. [PubMed: 16824510]

1113. Teodorov E, Modena CC, Sukikara MH, Felicio LF. Preliminary study of the effects of morphine treatment in opioid receptor gene expression in brain structures of the female rat. Neurosci 2006;141:1225–1231.

1114. Teoh WH, Thomas E, Tan HM. Ultra-low dose combined spinal-epidural anesthesia with intrathecal bupivacaine 3.75 mg for cesarean delivery: a randomized controlled trial. Int J Obstet Anesth 2006;15:273–278. [PubMed: 16774830]

1115. Terner JM, Barrett AC, Lomas LM, Negus SS, Picker MJ. Influence of low doses of naltrexone on morphine antinociception and morphine tolerance in male and female rats of four strains. Pain 2006;122:90–101. [PubMed: 16527399]

1116. Teyin E, Derbent A, Balcioglu T, Cokmez B. The efficacy of caudal morphine or bupivacaine combined with general anesthesia on postoperative pain and neuroendocrine stress response in children. Paediatr Anaesth 2006;16:290–296. [PubMed: 16490093]

1117. Thomas JB, Zhang L, Navarro HA, Carroll FI. Highly potent and selective phenylmorphan-based inverse agonists of the opioid delta receptor. J Med Chem 2006;49:5597–5609. [PubMed: 16942033]

1118. Thomson LM, Zeng E, Terman GW. An N-methyl-D-aspartate receptor mediated large, low frequency, spontaneous excitatory postsynaptic current in neonatal rat spinal dorsal horn neurons. Neurosci 2006;141:1489–1501.

1119. Thomson LM, Zeng E, Terman GW. Differential effect of glutamate transporter inhibition on EPSCs in the morphine naïve and morphine tolerant neonatal spinal cord slice. Neurosci Lett 2006;407:64–69. [PubMed: 16949209]

1120. Tidgewell K, Harding WW, Lozama A, Cobb H, Shah K, Kannan P, Dersch CM, Parrish D, Deschamps JR, Rothman RB, Prisinzano TE. Synthesis of salvinorin A analogues as opioid receptor probes. J Nat Prod 2006;69:914–918. [PubMed: 16792410]

1121. Tirado G, Kumar A. Evolution of SIV envelope in morphine-dependent rhesus macaques with rapid disease progression. AIDS Res Hum Retroviruses 2006;22:114–119. [PubMed: 16438654]

1122. Tiras S, Haas V, Chevret L, Decobert M, Buisine A, Devictor D, Durnad P, Tissieres P. Nonketotic hyperglycemia coma in toddlers after unintentional methadone ingestion. Ann Emerg Med 2006;48:448–451. [PubMed: 16997682]

1123. Tofil NM, Benner KW, Faro SJ, Winkler MK. The use of enteral naloxone to treat opioid-induced constipation in a pediatric intensive care unit. Pediatr Crit Care Med 2006;7:252–254. [PubMed: 16575353]

1124. Toit LD, Bennett NC, Gutjahr GH, Coen CW. Reproductive suppression in subordinate female highveld mole-rats (Cryptomys hottentotus pretoriae): no role for endogenous opioid peptides. Physiol Behav 2006;87:897–902. [PubMed: 16574170]

1125. Tong C, Conklin D, Eisenach JC. A pain model after gynecologic surgery: the effect of systemic and intrathecal morphine. Anesth Analg 2006;103:1288–1293. [PubMed: 17056971]

1126. Tongjaroenbuangam W, Jongkamonwiwat N, Phansuwan-Pujito P, Casalotti SO, Forge A, Dodson H, Govitrapong P. Relationship of opioid receptors with GABAergic neurons in the rat inferior colliculus. Eur J Neurosci 2006;24:1987–1994. [PubMed: 17040471]

1127. Torregrossa MM, Jutkiewicz EM, Mosberg HI, Balboni G, Watson SJ, Woods JH. Peptidic delta opioid receptor agonists produce antidepressant-like effects in the forced swim test and regulate BDNF mRNA expression in rats. Brain Res 2006;1069:172–181. [PubMed: 16364263]

1128. Toske SG, Cooper SD, Morello DR, Hays PA, Casale JF, Casale E. Natural heroin impurities from tetrahydrobenzylisoquinoline alkaloids. J Forensic Sci 2006;51:308–320. [PubMed: 16566764]

1129. Towett PK, Kanui TI, Juma FD. Stimulation of mu and delta opioid receptors induces hyperalgesia while stimulation of kappa receptors induces antinociception in the hot-plate test in the naked mole-rat (Heterocephalus glaber). Brain Res Bull 2006;71:60–68. [PubMed: 17113929]

1130. Trafton JA, Minkel J, Humphreys K. Determing effective methadone doses for individual opioid-dependent patients. PloS Med 2006;3:e80. [PubMed: 16448216]

1131. Trang T, Ma W, Chabot JG, Quirion R, Jhamandas K. Spinal modulation of calcitonin gene-related peptide by endocannabinoids in the development of opioid physical dependence. Pain 2006;126:256–271. [PubMed: 16935424]

1132. Trapella C, Guerrini R, Piccagli L, Calo' G, Carra' G, Spagnolo B, Rubini S, Fanton G, Hebbes C, McDonald J, Lambert DG, Regoli D, Salvadori S. Identification of an achiral analogue of J-113397 as potent nociceptin/orphanin FQ receptor antagonist. Bioorg Med Chem 2006;14:692–704. [PubMed: 16202610]

1133. Tsai NP, Bi J, Loh HH, Wei LN. Netrin-1 signaling regulates de novo protein synthesis of kappa opioid receptor by facilitating polysomal partition of its mRNA. J Neurosci 2006;26:9743–9749. [PubMed: 16988045]

1134. Tsai YF, Doufas AG, Huang CS, Liou FC, Lin CM. Postoperative coma in a patient with complete basilar syndrome after anterior cervical disectomy. Can J Anaesth 2006;53:202–207. [PubMed: 16434763]

1135. Tsikauri N, Gurtskaia G, Tsagareli M. Is endogenous opioid system involved in non-opioid analgesics tolerance? Georgian Med News 2006;137:121–125. [PubMed: 16980767]

1136. Tso PH, Wong YH. Opioid receptor-like (ORL1) receptor utilizes both G(oA) and G(oB) for signal transduction. Protein Pept Lett 2006;13:437–441. [PubMed: 16800795]

1137. Turchan-Cholewo J, Liu Y, Gartner S, Reid R, Jie C, Peng X, Chen KC, Chauhan A, Haughey N, Cutler R, Mattson MP, Pardo C, Conant K, Sacktor N, McArthur JC, Hauser KF, Gairola C, Nath A. Increased vulnerability of ApoE4 neurons to HIV proteins and opiates: protection by diosgenin and L-deprenyl. Neurobiol Dis 2006;23:109–119. [PubMed: 16697650]

1138. Ueda Y, Inoue T, Rahman MA, Yatsuzuka R, Jiang S, Kamei C. A new chronic itch model accompanied by skin lesions in hairless mice. Int Immunopharmacol 2006;6:1609–1615. [PubMed: 16919833]

1139. Uhart M, Chong RY, Oswald L, Lin PI, Wand GS. Gender differences in hypothalamic-pituitary-adrenal (HPA) axis reactivity. Psychoneuroendocrinol 2006;31:642–652.

1140. Ulugol A, Dokmeci D, Guray G, Sapolyo N, Ozyigit F, Tamer M. Antihyperalgesic, but not antiallodynic, effect of melatonin in nerve-injured neuropathic mice: Possible involvements of the L-arginine-NO pathway and opioid systems. Life Sci 2006;78:1592–1597. [PubMed: 16107259]

1141. Urayama A, King K, Gaskin FS, Farr A, Banks WA. Effects of chronic ethanol administration on brain interstitial levels of Methionine-enkephalin as measured by microdialysis in vivo. Peptides 2006;27:2201–2206. [PubMed: 16672169]

1142. Vale ML, Cunha FQ, Brito GA, Benevides VM, Ferreira SH, Poole S, Ribeiro RA. Anti-nociceptive effect of thalidomide on zymosan-induced experimental articular incapacitation. Eur J Pharmacol 2006;536:309–317. [PubMed: 16597438]

1143. Valjent E, Corbille AG, Bertran-Gonzalez J, Herve D, Girault JA. Inhibition of ERK pathway or protein synthesis during re-exposure to drugs of abuse erases previously learned place preference. Proc Natl Acad Sci (USA) 2006;103:2932–2937. [PubMed: 16473939]

1144. van Alfen-van der Velden AA, Hopman JC, Klaessens JH, Feuth T, Sengers RC, Liem KD. Effects of midazolam and morphine on cerebral oxygenation and hemodynamics in ventilated premature infants. Biol Neonate 2006;90:197–202. [PubMed: 16717443]

1145. Van Bockstaele EJ, Rudoy C, Mannelli P, Oropeza V, Qian Y. Elevated mu-opioid receptor expression in the nucleus of the solitary tract accompanies attenuated withdrawal signs after chronic low dose naltrexone in opiate-dependent rats. J Neurosci Res 2006;83:508–514. [PubMed: 16385558]

1146. van den Munckhof P, Gilbert F, Chamberland M, Levesque D, Drouin J. Striatal neuroadaptation and rescue of locomotor deficit by L-dopa in aphakia mice, a model of Parkinson's disease. J Neurochem 2006;96:160–170. [PubMed: 16269007]

1147. van Dorp E, Yassen A, Sarton E, Romberg R, Olofsen E, Teppema L, Danhof M, Dahan A. Naloxone reversal of buprenorphine-induced respiratory depression. Anesthesiol 2006;105:51–57.

1148. Vasilev GN, Alexieva DZ, Pavlova RZ. Safety and efficacy of oral slow release morphine for maintenance treatment in heroin addicts: a 6-month open noncomparative study. Eur Addict Res 2006;12:53–60. [PubMed: 16543739]

1149. Vazquez ME, Blanco JB, Salvadori S, Trapella C, Argazzi R, Bryant SD, Jinsmaa Y, Lazarus LH, Negri L, Giannini E, Lattanzi R, Colucci M, Balboni G. 6-N, N-dimethylamino-2,3-napthalimide: a new environment-sensitive probe in delta- and mu-selective opioid peptides. J Med Chem 2006;49:3653–3658. [PubMed: 16759107]

1150. Vazquez V, Giros B, Dauge V. Maternal deprivation specifically enhances vulnerability to opiate dependence in rats. Behav Pharmacol 2006;17:715–724. [PubMed: 17110797]

1151. Vazquez V, Penit-Soria J, Durand C, Besson MJ, Giros B, Dauge V. Brief early handling increased morphine dependence in adult rats. Behav Brain Res 2006;170:211–218. [PubMed: 16567006]

1152. Vecchio L, Soldani C, Bottone MG, Malatesta M, Martin TE, Rothblum LI, Pellicciari C, Biggiogera M. DADLE induces a reversible hibernation-like state in HeLa cells. Histochem Cell Biol 2006;125:193–201. [PubMed: 16235044]

1153. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, Varin F. A multimodal analgesia protocol for total knee arthroplasty: a randomized controlled study. J Bone Joint Surg Am 2006;88:282–289. [PubMed: 16452738]

1154. Vera-Portocarrero LP, Xie JY, Kowal J, Ossipov MH, King T, Porreca F. Descending facilitation from the rostral ventromedial medulla maintains visceral pain in rats with experimental pancreatitis. Gastroenterology 2006;130:2155–2164. [PubMed: 16762636]

1155. Vergura R, Valenti E, Hebbes CP, Gavioli EC, Spagnolo B, McDonald J, Lambert DG, Balboni G, Salvadori S, Regoli D, Calo' G. Dmt-Tic-CH2-Bid (UFP-502), a potent DOP receptor agonist: in vitro and in vivo studies. Peptides 2006;27:3322–3330. [PubMed: 16963157]

1156. Verma-Gandhu M, Bercik P, Motomura Y, Verdu EF, Khan WI, Blennerhassett PA, Wang L, El-Sharkawy RT, Collins SM. CD4+ T-cell modulation of visceral nociception in mice. Gastroenterology 2006;130:1721–1728. [PubMed: 16697736]

1157. Verster JC, Veldhuijzen DS, Volkerts ER. Effects of an opioid (oxycodone/paracetamol) and an NSAID (bromfenac) on driving, ability, memory functioning, psychomotor performance, pupil size and mood. Clin J Pain 2006;22:499–504. [PubMed: 16772806]

1158. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with the use of morphine and opiates. J Intern Med 2006;260:76–87. [PubMed: 16789982]

1159. Vetter I, Kapitzke D, Hermanussen S, Monteith GR, Cabot PJ. The effects of pH on beta-endorphin and morphine inhibition of calcium transients in dorsal root ganglion neurons. J Pain 2006;7:488–499. [PubMed: 16814688]

1160. Vetter I, Wyse BD, Monteith GR, Roberts-Thompson SJ, Cabot PJ. The mu opioid agonist morphine modulates potentiation of capsaicin-evoked TRPV1 responses through a cyclic AMP-dependent protein kinase A pathway. Mol Pain 2006;2:22. [PubMed: 16842630]

1161. Viard E, Sapru HN. Endomorphin-2 in the medial NTS attenuates the responses to baroreflex activation. Brain Res 2006;1073–1074:365–373.

1162. Vihavainen T, Mijatovic J, Piepponen TP, Tuominen RK, Ahtee L. Effect of morphine on locomotor activity and striatal metabolism in nicotine-withdrawn mice. Behav Brain Res 2006;173:85–93. [PubMed: 16846651]

1163. Villeda SA, Akopians AL, Bbayan AH, Basbaum AI, Phelps PE. Absence of Reelin results in altered nociception and aberrant neuronal positioning in the dorsal spinal cord. Neurosci 2006;139:1385–1396.

1164. Villesen HH, Foster DJ, Upton RN, Somogyi AA, Martinez A, Grant C. Cerebral kinetics of oxycodone in conscious sheep. J Pharm Sci 2006;95:1666–1676. [PubMed: 16729270]

1165. Vindenes V, Handal M, Ripel A, Boix F, Morland J. Conditioned place preference induced by morphine and morphine-6-glucuronide in mice. Pharmacol Biochem Behav 2006;85:292–297. [PubMed: 17011617]

1166. Vissers KC, Geenen F, Biermans R, Meert TF. Pharmacological correlation between the formalin test and the neuropathic pain behavior in different species with chronic constriction injury. Pharmacol Biochem Behav 2006;84:479–486. [PubMed: 16860855]

1167. Vit Clauw DJ, Moallem T, Boudah A, Ohara PT, Jasmin L. Analgesia and hyperalgesia from CRF receptor modulation in the central nervous system of Fischer and Lewis rats. Pain 2006;121:241–260. [PubMed: 16495007]

1168. Vit JP, Ohara PT, Tien DA, Fike JR, Eikmeier L, Beitz A, Wilcox GL, Jasmin L. The analgesic effect of low dose focal irradiation in a mouse model of bone cancer is associated with spinal changes in neuro-mediators of nociception. Pain 2006;120:188–201. [PubMed: 16360279]

1169. Vitale G, Arletti R, Ruggieri V, Cifani C, Massi M. Anxiolytic-like effects of nociceptin/orphanin FQ in the elvated plus maze and in the conditioned defensive burying test in rats. Peptides 2006;27:2193–2200. [PubMed: 16730097]

1170. Vogiatzidis K, Hatzoglou C, Zarogiannis S, Matafia G, Gourgoulianis K, Molyvdas PA. Mu-Opioid influence on transmesothelial resistance of isolated sheep pleura and parietal pericardium. Eur J Pharmacol 2006;530:276–280. [PubMed: 16405886]

1171. Vogl SE, Worda C, Egarter C, Bieglmayer C, Szekeres T, Huber J, Husslein P. Mode of delivery is associated with maternal and fetal endocrine stress response. BJOG 2006;113:441–445. [PubMed: 16489937]

1172. Waal H, Frogopsahl G, Olsen L, Christophersen AS, Morland J. Naltrexone implants – duration, tolerability and clinical usefulness: a pilot study. Eur Addict Res 2006;12:138–144. [PubMed: 16778434]

1173. Waara-Wolleat KL, Hildebrand KR, Stewart GR. A review of intrathecal fentanyl and sufentanil for the treatment of chroic pain. Pain Med 2006;7:251–259. [PubMed: 16712626]

1174. Walczak JS, Pichette V, Leblond F, Desbiens K, Beaulieu P. Characterization of chronic constriction of the saphenous nerve, a model of neuropathic pain in mice showing rapid molecular and electrophysiological changes. J Neurosci Res 2006;83:1310–1322. [PubMed: 16511871]

1175. Walker EA. In vivo pharmacological resultant analysis reveals noncompetitive interactions between opioid antagonists in the rat tail-withdrawal assay. Br J Pharmacol 2006;149:1071–1082. [PubMed: 17075571]

1176. Wallace DR, Dodson SL, Nath A, Booze RM. Delta opioid agonists attenuate TAT(1-72)-induced oxidative stress in SK-N-SH cells. Neurotoxicol 2006;27:101–107.

1177. Wallace MS, Moulin D, Clark AJ, Wasserman R, Neale A, Morley-Forster P, Castaigne JP, Teichman S. A Phase II, multicenter, randomized, bouble-blind, placebo-controlled crossover study of CJC-1008-- a long-acting parenteral opioid analgesic -- in the treatment of postherpetic neuralgia. J Opioid Manag 2006;2:167–173. [PubMed: 17319450]

1178. Wallace OB, Lauwers KS, Dodge JA, May SA, Calvin JR, Hinklin R, Bryant HU, Shetler PK, Adrian MD, Geiser AG, Sato M, Burris TP. A selective estrogen receptor modulator for the treatment of hot flushes. J Med Chem 2006;49:843–846. [PubMed: 16451049]

1179. Wallage HR, Palmentier JP. Hydrocodone-related fatalities in Ontario. J Anal Toxicol 2006;30:202–209. [PubMed: 16803655]

1180. Walwyn WM, Wei W, Xie CW, Chiu K, Kieffer BL, Evans CJ, Maidment NT. Mu opioid receptor-effector coupling and trafficking in dorsal root ganglion neurons. Neurosci 2006;142:493–503.

1181. Wan Q, Douglas SD, Wang X, Kolson DL, O'Donnell LA, Ho WZ. Morphine upregulates functional expression of neurokinin-1 receptor in neurons. J Neurosci Res 2006;84:1588–1596. [PubMed: 16983662]

1182. Wang H, Wei H, Chen B, Zhou Y. Chronic morphine exposure impairs short-term synaptic depression of geniculo-cortical visual pathway in vivo. Neurosci Lett 2006;410:228–233. [PubMed: 17052847]

1183. Wang HB, Laverghetta AV, Foehring R, Deng YP, Sun Z, Yamamoto K, Lei WL, Jiao Y, Reiner A. Single-cell RT-PCR, in situ hybridization histochemical and immunohistochemical studies of substance P and enkephalin co-occurrence in striatal projection neurons in rats. J Chem Neuroanat 2006;31:178–199. [PubMed: 16513318]

1184. Wang HY, Burns LH. Gbetagamma that interacts with adenylyl cyclase in opioid tolerance originates from a Gs protein. J Neurobiol 2006;66:1302–1310. [PubMed: 16967511]

1185. Wang J, Hogenkamp DJ, Tran M, Li WY, Yoshimura RF, Johnstone TB, Shen WC, Gee KW. Reversible lipidization for the oral delivery of leu-enkephalin. J Drug Target 2006;14:127–136. [PubMed: 16753826]

1186. Wang JY, Zeng XY, Fan GX, Yuan YK, Tang JS. Mu-, but not delta- and kappa-opioid receptor mediates the nucleus submedius interferon-alpha-evoked antinociception in the rat. Neurosci Lett 2006;397:254–258. [PubMed: 16406668]

1187. Wang JY, Zhao M, Yuan YK, Fan GX, Jia H, Tang JS. The roles of different subtypes of opioid receptors in mediating the nucleus submedius opioid-evoked antiallodynia in a neuropathic pain model of rats. Neurosci 2006;138:1319–1327.

1188. Wang T, Li SR, Dai X, Peng YL, Chen Q, Wang R. Effects of melatonin on orphanin FQ/nociceptin-induced hyperalgesia in mice. Brain Res 2006;1085:43–48. [PubMed: 16566906]

1189. Wang X, Douglas SD, Peng JS, Metzger DS, O'Brien CP, Zhang T, Ho WZ. Naltrexone inhibits alcohol-mediated enhancement of HIV infection of T lymphocytes. J Leukoc Biol 2006;79:1166–1172. [PubMed: 16574767]

1190. Wang X, Douglas SD, Peng JS, Zhou DJ, Wan Q, Ho WZ. An in vitro model of morphine withdrawal manifests the enhancing effect of human immunodeficiency virus infection of human T lymphocytes through the induction of substance P. Am J Pathol 2006;169:1663–1670. [PubMed: 17071590]

1191. Wang X, Dow-Edwards D, Anderson V, Minkoff H, Hurd YL. Discrete opioid gene expression impairment in the human fetal brain associated with maternal marijuana use. Pharmacogenomics 2006;6:255–264.

1192. Wang X, Traub RJ, Murphy AZ. Persistent pain model reveals sex difference in morphine potency. Am J Physiol Regul Integr Comp Physiol 2006;291:R300–R306. [PubMed: 16497818]

1193. Wang X, Wang Y, Xin H, Liu Y, Wang Y, Zheng H, Jiang Z, Wan C, Wnag Z, Ding JM. Altered expression of circadian clock gene, mPer1, in mouse brain and kidney under morphine dependence and withdrawal. J Circadian Rhythms 2006;4:9. [PubMed: 16925815]

1194. Wang XH, Tang Y, Xie Q, Qiu ZB. QSAR study of 4-phenylpiperidine derivatives as mu opioid agonists by neural network method. Eur J Med Chem 2006;41:226–232. [PubMed: 16403590]

1195. Wang Y, Xie WY, He Y, Wang M, Yang YR, Zhang Y, Yin DM, Jordan-Sciutto KL, Han JS, Wang Y. Role of CDK5 in neuroprotection from serum deprivation by mu-opioid receptor agonist. Exp Neurol 2006;202:313–323. [PubMed: 16879821]

1196. Wang ZY, Wang CQ, Yang JJ, Sun J, Huang YH, Tang QF, Qian YN. Which has the least immunity depression during postoperative analgesia – morphine, tramadol or tramadol with lornoxicam? Clin Chim Acta 2006;369:40–45. [PubMed: 16487501]

1197. Ward HG, Nicklous DM, Aloyo VJ, Simansky KJ. Mu-opioid receptor cellular function in the nucleus accumbens is essential for hedonically driven eating. Eur J Neurosci 2006;23:1605–1613. [PubMed: 16553624]

1198. Ward HG, Simansky KJ. Chronic prevention of mu-opioid receptor (MOR) G-protein coupling in the pontine parabrachial nucleus persistently decreases consumption of standard but not palatable food. Psychopharmacol 2006;187:435–446.

1199. Ward SJ, Lack C, Morgan D, Roberts DC. Discrete-trials heroin self-administration produces sensitization to the reinforcing effects of cocaine in rats. Psychopharm 2006;185:150–159.

1200. Waterman GD Jr, Leder MS, Cohen DM. Adverse events in pediatric ketamine sedations with or without morphine pretreatment. Pediatr Emerg Care 2006;22:408–411. [PubMed: 16801840]

1201. Watson MJ, Holt JD, O'Neill SJ, Wei K, Pendergast W, Gross GJ, Gengo PJ, Chang KJ. ARD-353 [4-((2R,5S)-4-R-(4-diethylcarbamoylphenl)(3-hydroxyphenyl)methyl)-2,5-dimethylpiperazin-1ylmethyl)benzoic acid], a novel nonpetide delta receptor agonist, reduces myocardial infarct size without central effects. J Pharmacol Exp Ther 2006;316:423–430. [PubMed: 16188952]

1202. Weber M, McNally GP, Richardson R. Opioid receptors regulate retrieval of infant fear memories: effect of naloxone on infantile amnesia. Behav Neurosci 2006;120:702–709. [PubMed: 16768621]

1203. Weber M, Modemann S, Schipper P, Trauer H, Franka H, Illes P, Geiger KD, Hengstier JG, Kleemann WJ. Increased polysialic neural cell adhesion molecule expression in the human hippocampus of heroin addicts. Neurosci 2006;138:1215–1223.

1204. Webster DE, Lu J, Chen SN, Farnsworth NR, Wang ZJ. Activation of the mu-opiate receptor by Vitex agnus-castus methanol extracts: implications for its use in PMS. J Ethnopharmacol 2006;106:216–221. [PubMed: 16439081]

1205. Webster LR, Butera PG, Moran LV, Wu N, Burns LH, Friedmann L. Oxytrex minimizes physical dependence while providing effective analgesia: a randomized controlled trial in low back pain. J Pain 2006;7:937–946. [PubMed: 17157780]

1206. Weed MR, Heinz RD. Effects of morphine on circadian rhythms of motor activity and body temperature in pig-tailed macaques. Pharmacol Biochem Behav 2006;84:487–496. [PubMed: 16860378]

1207. Wei F, Zhanf M, Feng YQ. Application of poly(methacrylic acid-ethylene gycol dimethacrylate) monolith microextraction coupled with capillary zone electrophoresis to the determination of opiates in human urine. Electrophoresis 2006;27:1939–1948. [PubMed: 16619301]

1208. Wei H, Pertovaara A. 5HT(1A) receptors in endogenous regulation of neuropathic hypersensitivity in the rat. Eur J Pharmacol 2006;535:157–165. [PubMed: 16545367]

1209. Wei J, Dong M, Xiao C, Jiang F, Castellino FJ, Prorok M, Dai Q. Conantokins and variants derived from cone snail venom inhibit naloxone-induced withdrawal jumping in morphine-dependent mice. Neurosci Lett 2006;405:137–141. [PubMed: 16859831]

1210. Weil J, Zolk O, Griepentrog J, Wenzel U, Zimmermann WH, Eschenhagen T. Alterations of the preproenkephalin system in cardiac hypertrophy and its role in atrioventricular conduction. Cardiovasc Res 2006;69:412–422. [PubMed: 16376326]

1211. Weinstein SM, Shi M, Buckley BJ, Kwarcinski MA. Multicenter, open-label, prospective evaluation of the conversion from previous opioid analgesics to extended-release hydromorphone hydrochloride administered every 24 hours to patients with persistent moderate to severe pain. Clin Ther 2006;28:86–98. [PubMed: 16490582]

1212. Weir C, McNeill A, Hook S, Harvie M, La Flamme AC, Le Gros G, Backstrom BT. Critical role of preproenkephalin in experimental autoimmune encephalomyelitis. J Neuroimmunol 2006;179:18–25. [PubMed: 16904193]

1213. Wenk HN, Brederson JD, Honda CN. Morphine directly inhibits nociceptors in inflamed skin. J Neurophysiol 2006;95:2083–2097. [PubMed: 16339007]

1214. Wentland MP, VanAlstine M, Kucejko R, Lou R, Cohen DJ, Parkhill AL, Bidlack JM. Redefining the structure-activity relationships of 2,6-methano-3-benzazocines. 4. Opioid receptor binding properties of 8-[N-(4′-phenyl)-phenethyl)carboxyamido] analogues of cyclazocine and ethylketocyclazocine. J Med Chem 2006;49:5635–5639. [PubMed: 16942039]

1215. Werkheiser JL, Rawls SM, Cowan A. Mu and kappa opioid receptor agonists antagonize icilin-induced wet-dog shaking in rats. Eur J Pharmacol 2006;547:101–105. [PubMed: 16945367]

1216. Westin UE, Bostrom E, Grasjo J, Hammarlund-Udenaes M, Bjork E. Direct nose-to-brain transfer of morphine after nasal administration to rats. Pharm Res 2006;23:565–572. [PubMed: 16489488]

1217. Wiktelius D, Khalil Z, Nyberg F. Modulation of peripheral inflammation by the substance P N-terminal metabolite substance P 1–7. Peptides 2006;27:1490–1497. [PubMed: 16414148]

1218. Will MJ, Pratt WE, kelley AE. Pharmacological characterization of high-fat feeding induced by opioid stimulation of the ventral striatum. Physiol Behav 2006;89:226–234. [PubMed: 16854442]

1219. Williams IJ, Edwards S, Rubo A, Haller VL, Stevens DL, Welch SP. Time course of the enhancement and restoration of the analgesic efficacy of codeine and morphine by delta9-tetrahydrocannabinol. Eur J Pharmacol 2006;539:57–63. [PubMed: 16687136]

1220. Willuhn I, Steiner H. Motor-skill learning-associated gene regulation in the striatum: effects of cocaine. Neuropsychopharm 2006;31:2669–2682.

1221. Wilson AW, Medhurst SJ, Dixon CI, Bontoft NC, Winyard LA, Brackenborough KT, De Alba J, Clarke CJ, Gunthorpe MJ, Hicks GA, Bountra C, McQueen DS, Chessell IP. An animal model of chronic inflammatory pain: pharmacological and temporal differentiation from acute models. Eur J Pain 2006;10:537–549. [PubMed: 16199187]

1222. Winkler CW, Hermes SM, Chavkin CI, Drake CT, Morrison SF, Aicher SA. Kappa opioid receptor (KOR) and GAD67 immunoreactivity are found in OFF and NEUTRAL cells in the rostral ventromedial medulla. J Neurophysiol 2006;96:3465–3473. [PubMed: 17005613]

1223. Wisner A, Dufour E, Messaoudi M, Nejdi A, Marcel A, Ungeheuer MN, Rougeot C. Human Opiorphin, a natural antinociceptive modulator of opioid-dependent pathways. Proc Natl Acad Sci (USA) 2006;103:17979–17984. [PubMed: 17101991]

1224. Witkowski G, Szulczyk P. Opioid mu receptor activation inhibits sodium currents in prefrontal cortical neurons via a protein kinase A- and C-dependent mechanism. Brain Res 2006;1094:92–106. [PubMed: 16733049]

1225. Wittmann M, Peters I, Schaaf T, Wartenberg HC, Wirz S, Nadstawek J, Urban BW, Barann M. The effects of morphine on human 5-HT3A receptors. Anesth Analg 2006;103:747–752. [PubMed: 16931691]

1226. Wong RH, Lee TW, Sihoe AD, Wan IY, Ng CS, Chan SK, Wong WW, Liang YM, Yim AP. Analgesic effect of electroacupuncture in postthoracotomy pain: a prospective randomized trial. Ann Thorc Surg 2006;81:2031–2036.

1227. Wood E, Stoltz JA, Li K, Montaner JS, Kerr T. Changes in Canadian heroin supply coinciding with the Austalian heroin shortage. Addiction 2006;101:689–695. [PubMed: 16669902]

1228. Woods AS, Kaminski R, Oz M, Wang Y, Hauser K, Goody R, Wang HY, Jackson SN, Zeitz P, Zolkowska D, Schepers R, Nold M, Danielson J, Graslund A, Vukojeviv V, Bakalkin G, Basbaum A, Shippenberg T. Decoy peptides that bind dynorphin noncovalently prevent NMDA receptor-mediated neurotoxicity. J Proteome Res 2006;5:1017–1023. [PubMed: 16602711]

1229. Woolcock K, Specht SC. Modulation of the Na, K-ATPase activity by prostaglandin E1 and [D-Ala2, N-Me-Phe4, Gly5-ol]-enekephalin. Life Sci 2006;78:1653–1661. [PubMed: 16460765]

1230. Wooley JD, Lee BS, Fields HL. Nucleus accumbens opioids regulate flavor-based preferences in food consumption. Neurosci 2006;143:309–317.

1231. Worthington N, Markham Piper T, Galea S, Rosenthal D. Opiate users' knowledge about overdose prevention and naloxone in New York City: a focus group study. Harm Reduct J 2006;3:19. [PubMed: 16822302]

1232. Wright N, Oldham N, Francis K, Jones L. Homeless drug users' awareness and risk perception of peer "Take Home Naltrexone" use – a qualitative study. Subst Abuse Treat Prev Policy 2006;1:28. [PubMed: 17014725]

1233. Wu HE, Sun HS, Cheng CW, Terashvili M, Tseng LF. Dextro- and levo-naloxone reverses the attenuation of morphine antinociception induced by lipopolysaccharides in the mouse spinal cord via a non-opioid mechanism. Eur J Neurosci 2006;24:2575–2580. [PubMed: 17100845]

1234. Wu HE, Sun HS, Cheng CW, Tseng LF. p38 mitogen-activated protein kinase inhibitor SB203580 reverses the antianalgesia induced by dextro-morphine or morphine in the mouse spinal cord. Eur J Pharmacol 2006;550:91–94. [PubMed: 17026985]

1235. Wu HE, Sun HS, Terashvili M, Scwashinger E, Sora I, Hall FS, Uhl GR, Tseng LF. Dextro- and levo-morphine attenuate opioid delta and kappa receptor agonist produced analgesia in mu-opioid receptor knockout mice. Eur J Pharmacol 2006;531:103–107. [PubMed: 16445907]

1236. Wu N, Su RB, Liu Y, Lu XQ, Zheng JQ, Cong B, Li J. Modulation of agmatine on calcium signal in morphine-dependent CHO cells by activation of IRAS, a candidate for imidazoline I1 receptor. Eur J Pharmacol 2006;548:21–28. [PubMed: 16962578]

1237. Wu S, Campbell C, Koda Y, Blanchfield JT, Toth I. Investigation of the route of absorption of lipid and sugar modieifed leu-enkephalin analogues and their enzymatic stability using the caco-2 monolayer system. Med Chem 2006;2:203–211. [PubMed: 16787368]

1238. Wu X, Yu LC. Alternation of galanin in nociceptive modulation in the central nervous system of rats during morphine tolerance: a behavioral and immunohistochemical study. Brain Res 2006;1086:85–91. [PubMed: 16626663]

1239. Wu ZQ, Li M, Chen J, Chi ZQ, Liu JG. Involvement of cAMP/cAMP-dependent protein kinase signalin pathway in regulation of Na+, K+-ATPase upon activation of opioid receptors by morphine. Mol Pharmacol 2006;69:866–876. [PubMed: 16317112]

1240. Xia P, Pei G, Schwarz W. Regulation of the glutamate transporter EAAC1 by expression and activation of delta-opioid receptor. Eur J Neurosci 2006;24:87–93. [PubMed: 16882010]

1241. Xiang XH, Wang HL, Wu WR, Guo Y, Cao DY, Wang HS, Zhao Y. Ethological analysis of scopolamine treatment or pretreatment in morphine dependent rats. Physiol Behav 2006;88:183–190. [PubMed: 16690091]

1242. Xiang Y, Gao H, Zhu H, Sun N, Ma Y, Lei H. Neurochemical changes in brain induced by chronic morphine treatment: NMR studies in thalamus and somatosensory cortex of rats. Neurochem Res 2006;31:1255–1261. [PubMed: 17004128]

1243. Xiao ZW, Cao CY, Wang ZX, Li JX, Liao HY, Zhang XX. Changes in dopamine transporter function in striatum during acute morphine addiction and its abstinence in rhesus monkey. Chin Med J 2006;119:1802–1807. [PubMed: 17097035]

1244. Xiong W, Yu LC. Involvements of mu- and kappa-opioid receptors in morphine-induced antinociception in the nucleus accumbens of rats. Neurosci Lett 2006;399:167–170. [PubMed: 16490317]

1245. Xiong W, Yu LC. Involvement of endogenous cholecystokinin in tolerance to morphine antinociception in the nucleus accumbens of rats. Behav Brain Res 2006;173:116–121. [PubMed: 16837074]

1246. Xu B, Wang Z, Li G, Li B, Lin H, Zheng R, Zheng Q. Heroin-administered mice involved in oxidative stress and exogenous antioxidant-alleviated withdrawal syndrome. Basic Clin Pharmacol Toxicol 2006;99:153–161. [PubMed: 16918717]

1247. Xu H, Arita H, Hayashida M, Zhang L, Sekiuyama H, Hanaoka K. Pain-relieving effects of processed Aconiti tuber in CCI-neuropathic rats. J Ethnopharmacol 2006;103:392–397. [PubMed: 16183224]

1248. Xu J, Xin S, Li H, Liu L, Xia W, Li P, Liu X, Li G. Involvement of caspase-3 pathway in antiapoptotic action of methionine-enkephalin on CEM x 174 cells in prolonged infection with simian immunodeficiency virus in vitro. Cell Biol Int 2006;30:114–121. [PubMed: 16458026]

1249. Xu J, Xu M, Pan YX. Chracterizing exons 11 and 1 promoters of the mu opioid receptor (Oprm) gene in transgenic mice. BMC Mol Biol 2006;7:41. [PubMed: 17101047]

1250. Xu W, Yoon SI, Huang P, Wang Y, Chen C, Chong PL, Liu-Chen LY. Localization of the kappa opioid receptor in lipid rafts. J Pharmacol Exp Ther 2006;317:1295–1306. [PubMed: 16505160]

1251. Xuei X, Dick D, Flury-Wetherill L, Tian HJ, Agrawal A, Bierut L, Goate A, Bucholz K, Schuckit M, Nurnberger J Jr, Tischfield J, Kuperman S, Porjesz B, Begleiter H, Foroud T, Edenberg HJ. Association of the kappa-opioid system with alcohol dependence. Mol Psychiatry 2006;11:1016–1024. [PubMed: 16924269]

1252. Yakimova KS. Effects of GABAB-agonist on rat hypothalamic neurons: functional antagonism with mu-receptor agonist. Neurosci Res 2006;54:281–287. [PubMed: 16427715]

1253. Yakovleva T, Bazov I, Cebers G, Marinova Z, Hara Y, Ahmed A, Vlaskovska M, Johansson B, Hochgeschwender U, Singh IN, Bruce-Keller AJ, Hurd YL, Kaneko T, Terenius L, Ekstrom TJ, Hauser KF, Pickel VM, Bakalkin G. Prodynorphin storage and processing in axon terminals and dendrites. FASEB J 2006;20:2124–2126. [PubMed: 16966485]

1254. Yamada H, Shimoyama N, Sora I, Uhl GR, Fukuda Y, Moriya H, Shimoyama M. Morphine can produce analgesia via spinal kappa opioid receptors in the absence of mu opioid receptors. Brain Res 2006;1083:61–69. [PubMed: 16530171]

1255. Yamamoto S, Honda M, Tanabe M, Ono H. Spinal ventral root after-discharges as a pain index: involvement of NK-1 and NMDA receptors. Brain Res 2006;1082:115–123. [PubMed: 16507302]

1256. Yamamoto T, Saito O, Shono K, Tanabe S. Effects of intrathecal and i.c.v. administration of neuropeptide W-23 and neuropeptide B on the mechanical allodynia induced by partial sciatic nerve ligation in rats. Neurosci 2006;137:265–273.

1257. Yamamoto T, Shono K, Tanabe S. Buprenorphine activates mu and opioid receptor like-1 receptors simultaneously, but the analgesic effect is mainly mediated by mu receptor activation in the rat formalin test. J Pharmacol Exp Ther 2006;318:206–213. [PubMed: 16565164]

1258. Yamashita K, Fukusaki M, Ando Y, Fujinaga A, Tanabe T, Terao Y, Sumikawa K. Preoperative administration of intravenous flurbiprofen axetil reduces postoperative pain for spinal fusion surgery. J Anesth 2006;20:92–95. [PubMed: 16633764]

1259. Yan Y, Nitta A, Mizuno T, Nakajima A, Yamada K, Nabeshima T. Discriminative-stimulus effects of methamphetamine and morphine are attenuated by cAMP-related compounds. Behav Brain Res 2006;173:39–46. [PubMed: 16857277]

1260. Yang J, Chen JM, Liu WY, Song CY, Lin BC. Through V2, not V1 receptor relating to endogenous opiate peptides, arginine vasopressin in periaqueductal gray regulates antinociception in the rat. Regul Pept 2006;137:156–1261. [PubMed: 17011056]

1261. Yang J, Li W, Liu X, Li Z, Li H, Yang G, Xu L, Li L. Enriched environment treatment counteracts enhanced addictive and depressive-like behavior induced by prenatal chronic stress. Brain Res 2006;1125:132–137. [PubMed: 17109826]

1262. Yang J, Liu WY, Song CY, Lin BC. Through central arginine vasopressin, not oxytocin and endogenous opiate peptides, glutamate sodium induces hypothalamic paraventricular nucleus enhancing acupuncture analgesia in the rat. Neurosci Res 2006;54:49–56. [PubMed: 16310878]

1263. Yang J, Yang Y, Xu HT, Chen JM, Liu WY, Lin BC. Arginine vasopressin enhances PAG synthesis and secretion of enkephalin and endorphin in the rat. Brain Res Bull 2006;71:193–199. [PubMed: 17113946]

1264. Yang JP, Yao M, Jiang XH, Wang LN. Establishment of model of visceral pain due to colorectal distension and its behavioral assessment in rats. World J Gastroenterol 2006;12:2781–2784. [PubMed: 16718770]

1265. Yang JW, Shih HC, Shyu BC. Intracortical circuits in rat anterior cingulate cortex are activated by nociceptive inputs mediated by medial thalamus. J Neurophysiol 2006;96:3409–3422. [PubMed: 16956990]

1266. Yang L, Zhu CJ, Cao JL, Zeng YM. Inhibition of the spinal phosphoinositide 3-kinase exacerbates morphine withdrawal responses. Neurosci Lett 2006;404:237–241. [PubMed: 16806705]

1267. Yang Q, Chen Y, Fu C, Chang M, Peng Y, Wang R. Effects of [Nphe1]nociceptin(1–13)NH2, [Phe1(CH2-NH)Gly2]nociceptin(1–13)NH2, and nocistatin on nociceptin inhibited constrictions of guinea pig isolated bronchus. Protein Pept Lett 13:185–188. [PubMed: 16472082]

1268. Yang SN, Liu CA, Chung MY, Huang HC, Yeh GC, Wong CS, Lin WW, Yang CH, Tao PL. Alterations of postsynaptic density proteins in the hippocampus of rat offspring from the morphine-addicted mother: beneficial effect of dextromethorphan. Hippocampus 2006;16:521–530. [PubMed: 16598705]

1269. Yao L, McFarland K, Fan P, Jiang Z, Ueda T, Diamond I. Adenosine A2a blockade prevents synergy between mu-opiate and cannabinoid CB1 receptors and eliminates heroin-seeking behavior in addicted rats. Proc Natl Acad Sci (USA) 2006;103:7877–7882. [PubMed: 16684876]

1270. Yen MH, Ko HC, Tang FI, Lu RB, Hong JS. Study of hepatotoxicity in the treatment of alcoholism. Alcohol 2006;38:117–120. [PubMed: 16839858]

1271. Yeomans DC, Lu Y, Laurito CE, Peters MC, Vota-Vellis G, Wilson SP, Pappas GD. Recombinant herpes vector-mediated nalgesia in a primate model of hyperalgesia. Mol Ther 2006;13:589–597. [PubMed: 16288901]

1272. Yim AJ, Moraes CR, Ferreira TL, Oliveira MG. Protein synthesis inhibition in the basolateral amygdala following retrieval does not impair expression of morphine-associated conditioned place preference. Behav Brain Res 2006;171:162–169. [PubMed: 16677727]

1273. Yin D, Woodruff M, Zhang Y, Whaley S, Miao J, Ferslew K, Zhao J, Stuart C. Morphine promotes Jurkat cell apoptosis through pro-apoptotic FADD/P53 and anti-apoptotic PI3K/Akt/NF-kappaB pathways. J Neuroimmunol 2006;174:101–107. [PubMed: 16529824]

1274. Yoo JH, Yang EM, Cho JH, Lee JH, Jeong SM, Nah SY, Kim HC, Kim HW, Kim SH, Lee SY, Jang CG. Inhibitory effects of berberine against morphine-induced locomotor sensitization and analgesic tolerance in mice. Neurosci 2006;142:953–961.

1275. Yoon MH, Bae HB, Choi JI, Kim SJ, Chung ST, Kim CM. Lack of reciprocity between opioid and 5HT3 receptors for antinociception in rat spinal cord. Pharmacol 2006;77:195–202.

1276. Yoon MH, Choi JI, Kim SJ, Kim CM, Bae HB, Chung ST. Synergistic antinociception between zaprinast and morphine in the spinal cord of rats on the formalin test. Eur J Anaesthesiol 2006;23:65–70. [PubMed: 16390569]

1277. Yoshida M, Kiyofuji H, Koyanagi S, Matsuo A, Fujioka T, To H, Higuchi S, Ohdo S. Glucocorticoid is involved in food-entrainable rhythm of mu-opioid receptor expression in mouse brainstem and analgesic effect of morphine. J Pharmacol Sci 2006;101:77–84. [PubMed: 16682786]

1278. Younger JW, Lawler-Row KA, Moe KA, Kratz AL, Keenum AJ. Effects of naltrexone on repressive coping and disclosure of emotional material: a test of the opioid-peptide hypothesis of repression and hypertension. Psychosom Med 2006;68:734–741. [PubMed: 17012527]

1279. Yu G, Yue YJ, Cui MX, Gong ZH. Thienorphine is a potent long-acting partial opioid agonist: a comparative study with buprenorphine. J Pharmacol Exp Ther 2006;318:282–287. [PubMed: 16569757]

1280. Yu Y, Cui Y, Wang X, Fan YZ, Liu J, Yan X, Wang R. Endomorphin1 and endomorphin2, endogenous potent inhibitors of electrical field stimulation (EFS)-induced cholinergic contractions of rat isolated bronchus. Peptides 2006;27:1846–1851. [PubMed: 16564113]

1281. Yu Y, Wang CL, Cui Y, Fan YZ, Liu J, Shao X, Liu HM, Wang R. C-terminal amide to alcohol conversion changes the cardiovascular effects of endomorphins in anesthetized rats. Peptides 2006;27:136–143. [PubMed: 16139930]

1282. Yu Y, Wang X, Cui Y, Fan YZ, Liu J, Wang R. Abnormal modulation of cholinergic neurotransmission by endomorphin 1 and endomorphin 2 in isolated bronchus of type 1 diabetic rats. Peptides 2006;27:2770–2777. [PubMed: 16901587]

1283. Yue X, Varga EV, Stropova D, Vanderah TW, Yamamura HI, Roeske WR. Chronic morphine-mediated adenylyl cyclase superactivation is attenuated by the Raf-1 inhibitor, GW5074. Eur J Pharmacol 2006;540:57–59. [PubMed: 16750187]

1284. Zachariou V, Bolanos CA, Selley DE, Theobald D, Cassidy MP, Kelz MB, Shaw-Lutchman T, Berton O, Sim-Selley LJ, Dileone RJ, Kumar A, Nestler EJ. An essential role of DeltaFosB in the nucleus accumbens in morphine action. Nat Neurosci 2006;9:205–211. [PubMed: 16415864]

1285. Zagon IS, Klocek MS, Sassani JW, Mauger DT, McLaughlin PJ. Corneal safety of topically applied naltrexone. J Ocul Pharmacol Ther 2006;22:37–387.

1286. Zagon IS, McLaughlin PJ. Opioid growth factor receptor is unaltered with the progression of human pancreatic and colon cancers. Int J Oncol 2006;29:489–494. [PubMed: 16820893]

1287. Zagon IS, Sassani JW, Malefyt KJ, McLaughlin PJ. Regulation of corneal repair by particle-mediated gene transfer of opioid growth factor receptor complementary DNA. Arch Opthamol 2006;124:1620–1624.

1288. Zagon IS, Sassani JW, McLaughlin PJ. Adaptation of the homeostatic ocular surface epithelium to chronic treatment with the opioid antagonist naltrexone. Cornea 2006;25:821–829. [PubMed: 17068460]

1289. Zalewska-Kaszubska J, Gorska D, Dyr W, Czarnecka E. Effect of acute administration of ethanol on beta-endorphin plasma level in ethanol preferring and non-preferring rats chronically treated with naltrexone. Pharmacol Biochem Behav 2006;85:155–159. [PubMed: 16934320]

1290. Zapata A, Shippenberg TS. Endogenous kappa opioid receptor systems modulate the responsiveness of mesoaccumbal Da neurons to ethanol. Alcohol Clin Exp Res 2006;30:592–597. [PubMed: 16573576]

1291. Zarnegar P, Persson AI, Ming Y, Terenius L. Opioid-induced regulation of gene expression in PC12 cells stably transfected with mu-opioid receptor. Neurosci Lett 2006;396:197–201. [PubMed: 16377088]

1292. Zarrindast MR, Askari E, Khalilzadeh A, Nouraei N. Morphine state-dependent learning and interaction with nitric oxide. Pharmacol 2006;78:66–71.

1293. Zarrindast MR, Azami BN, Rostami P, Rezayof A. Repeated administration of dopaminergic agents in the nucleus accumbens and morphine-induced place preference. Behav Brain Res 2006;169:248–255. [PubMed: 16472879]

1294. Zarrindast MR, Bananej M, Khalilzadeh A, Fazli-Tabaei S, Haeri-Rohani A, Rezayof A. Influence of intracerebroventricular administration of dopaminergic drugs on morphine state-dependent memory in the step-down passive avoidance task. Neurobiol Learn Mem 2006;86:286–292. [PubMed: 16723261]

1295. Zarrindast MR, Ghadimi M, Ramezani-Tehrani B, Sahebgharani M. Effect of GABA receptor agonists or antagonists on morphine-induced Straub tail in mice. Int J Neurosci 2006;116:963–973. [PubMed: 16861161]

1296. Zarrindast MR, Jafari-Sabet M, Rezayat M, Djahanguirl B, Rezayof A. Involvement of NMDA receptors in morphine state-dependent learning in mice. Int J Neurosci 2006;116:731–743. [PubMed: 16753898]

1297. Zarrindast MR, Kangarlu-Haghighi K, Khalilzadeh A, Fazli-Tabaei S. Influence of intracerebroventricular administration of cannabinergic drugs on morphine state-dependent memory in the step-down passive avoidance test. Behav Pharmacol 2006;17:231–237. [PubMed: 16572001]

1298. Zarrindast MR, Khalilzadeh A, Malekmohammadi N, Fazli-Tabaei S. Influence of morphine- or apomorphine-induced sensitization on histamine state-dependent learning in the step-down passive avoidance test. Behav Brain Res 2006;171:50–55. [PubMed: 16677725]

1299. Zarrindast MR, Mohajeri S. Influence of ATP-dependent K+ channels on nicotine-induced inhibition of withdrawal in morphine-dependent rats. Eur J Pharmacol 2006;552:90–98. [PubMed: 17049514]

1300. Zarrindast MR, Nouraei N, Khallilzadeh A, Askari E. Influence of acute and sub-chronic nicotine pretreatment on morphine state-dependent learning. Behav Brain Res 2006;173:268–273. [PubMed: 16893575]

1301. Zaveri NT, Waleh N, Toll L. Regulation of the prepronociceptin gene and its effect on neuronal differentiation. Gene 2006;384:27–36. [PubMed: 16935438]

1302. Zeng J, Thomson LM, Aicher SA, Terman GW. Primary afferent NMDA receptors increase dorsal horn excitation and mediate opiate tolerance in neonatal rats. J Neurosci 2006;26:12033–12042. [PubMed: 17108177]

1303. Zhang C, McDougall JJ. Stimulation of sensory neuropeptide release by nociceptin/orphanin FQ leads to hyperaemia in acutely inflamed rat knees. Br J Pharmacol 2006;148:938–946. [PubMed: 16783411]

1304. Zhang H, Torregrossa MM, Jutkiewicz EM, Shi YG, Rice KC, Woods JH, Watson SJ, Ko MC. Endogenous opioids upregulate brain-derived neurotrophic factor mRNA through delta- and mu-opioid receptors independent of antidepressant effects. Eur J Neurosci 2006;23:984–994. [PubMed: 16519663]

1305. Zhang HL, Han R, Chen ZX, Chen BW, Gu ZL, Reid PF, Raymond LN, Qin ZH. Opiate and acetylcholine-independent analgesic actions of crotoxin isolated from crotalus durissus terrificus venom. Toxicon 2006;48:175–182. [PubMed: 16857228]

1306. Zhang J, Frassetto A, Huang RR, Lao JZ, Pasternak A, Wang SP, Metzger JM, Strack AM, Fong TM, Chen RZ. The mu-opioid receptor subtype is required for the anorectic effect of an opioid receptor antagonist. Eur J Pharmacol 2006;545:147–152. [PubMed: 16876155]

1307. Zhang J, Qian H, Zhao P, Hong SS, Xia Y. Rapid hypoxia preconditioning protects cortical neurons from glutamate toxicity through delta-opioid receptor. Stroke 2006;37:1094–1099. [PubMed: 16514101]

1308. Zhang J, Xu M. Opposite regulation of cocaine-induced intracellular signaling and gene expression by dopamine D1 and D3 receptors. Ann NY Acad Sci 2006;1074:1–12. [PubMed: 17105899]

1309. Zhang L, Kendler KS, Chen X. The mu-opioid receptor gene and smoking initiation and nicotine dependence. Behav Brain Funct 2006;2:28. [PubMed: 16887046]

1310. Zhang L, Sykes KT, Buhler AV, Hammonds DL. Electrophysiological heterogeneity of spinally projecting serotonergic and nonserotonergic neurons in the rostral ventromedial medulla. J Neurophysiol 2006;95:1853–1863. [PubMed: 16338998]

1311. Zhang L, Tetrault J, Wang W, Loh HH, Law PY. Short- and long-term regulation of adenylyl cyclase activity by delta-opioid receptor are mediated by Galphai2 in neuroblastoma N2A cells. Mol Pharmacol 2006;69:1810–1819. [PubMed: 16525132]

1312. Zhang SZ, Wang NF, Xu J, Gao Q, Lin GH, Bruce IC, Xia Q. Kappa-opioid receptors mediate cardioprotection by remote preconditioning. Anesthesiol 2006;105:550–556.

1313. Zhang X, Bao L, Guan JS. Role of delivery and trafficking of delta-opioid peptide receptors in opioid analgesia and tolerance. Trends Pharmacol Sci 2006;27:324–329. [PubMed: 16678916]

1314. Zhang Y, Pan YX, Kolesnikov Y, Pasternak GW. Immunohistochemical labeling of the MOR carboxy terminal splice variant mMOR-1B4 in the mouse central nervous system. Brain Res 2006;1099:33–43. [PubMed: 16793025]

1315. Zhao H, Loh HH, Law PY. Adenylyl cyclase superactivation induced by long-term treatment with opioid agonist is dependent on receptor localized within lipid rafts and is independent of receptor internalization. Mol Pharmacol 2006;69:1421–1432. [PubMed: 16415176]

1316. Zhao M, Joo DT. Subpopulation of dorsal horn neurons displays enhanced N-methyl-D-aspartate receptor function after chronic morphine exposure. Anesthesiol 2006;104:815–825.

1317. Zhao M, Li Q, Tang JS. The effects of microinjection of morphine into thalamic nucleus submedius on formalin-evoked Nociceptive responses in the rat spinal dorsal horn. Neurosci Lett 2006;401:103–107. [PubMed: 16556485]

1318. Zhao M, Wang JY, Jia H, Tang JS. Mu- but not delta- and kappa-opioid receptors in the ventrolateral orbital cortex mediate opioid-induced antiallodynia in a rat neuropathic pain model. Brain Res 2006;1076:68–77. [PubMed: 16476416]

1319. Zhao P, Huang Y, Zuo Z. Opioid preconditioning induces opioid receptor-dependent neuroprotection against ischemia in rats. J Neuropathol Exp Neurol 2006;65:945–952. [PubMed: 17021399]

1320. Zhong W, Dong Z, Tian M, Cao J, Xu T, Xu L, Luo J. Opiate withdrawal induces dynamic expressions of AMPA receptors and its regulatory molecule CaMKIIalpha in hippocampal synapses. Life Sci 2006;79:861–869. [PubMed: 16616767]

1321. Zhou H, Aziza J, Sol JC, Courtade-Saidi M, Chatelin S, Evra C, Parant O, Lazorthes Y, Jozan S. Cell therapy of pain: characterization of human fetal chromaffin cells at early adrenal medulla development. Exp Neurol 2006;198:370–381. [PubMed: 16443224]

1322. Zhou LF, Zhu YP. Changes of CREB in rat hippocampus, prefrontal cortex and nucleus accumbens during three phases of morphine-induced conditioned place preference in rats. J Zhejiang Univ Sci B 2006;7:107–113. [PubMed: 16421965]

1323. Zhou Y, Bendor J, Hofmann L, Randesi M, Ho A, Kreek MJ. Mu opioid receptor and orexin/hypocretin mRNA levels in the lateral hypothalamus and striatum are enhanced by morphine withdrawal. J Endocrinol 2006;191:137–145. [PubMed: 17065397]

1324. Zhou Yi Syuu W, Hsiao I, Lin VW, Longhurst JC. Modulation of cardiovascular excitatory responses in rats by trnascutaneous magnetic stimulation: role of the spinal cord. J Appl Physiol 2006;100:926–932. [PubMed: 16269522]

1325. Zhu CZ, Nikkel AL, Martino B, Bitner RS, Decker MW, Honore P. Dissociation between post-surgical pain behaviors and spinal Fos-like immunoreactivity in the rat. Eur J Pharmacol 2006;531:108–117. [PubMed: 16438960]

1326. Zhu W, Mantione KJ, Casares FM, Cadet P, Kim JW, Bilfinger TV, Kream RM, Khalil S, Singh S, Stefano GB. Alcohol-, nicotine- and cocaine-evoked release of morphine from invertebrate ganglia: model system for screening drugs of abuse. Med Sci Monit 2006;12:BR155–BR161. [PubMed: 16641868]

1327. Zhu W, Mantione KJ, Casares FM, Sheehan MH, Kream RM, Stefano GB. Cholinergic regulation of endogenous morphine release from lobster nerve cord. Med Sci Monit 2006;12:BR295–BR301. [PubMed: 16940924]

1328. Zhu W, Mantione KJ, Shen L, Lee B, Stefano GB. Norlaudanosoline and nicotine increase endogenous ganglionic morphine levels: nicotine addiction. Cell Mol Neurobiol 2006;26:1037–1045. [PubMed: 16645895]

1329. Zhu X, Vincler MA, Parker R, Eisenach JC. Spinal cord dynorphin expression increases, but does not drive microglial prostaglandin production or mechanical hypersensitivity after incisional surgery in rats. Pain 2006;125:43–52. [PubMed: 16740361]

1330. Zhu YP, Long ZH, Zheng ML, Binsack R. Effect of glycine site/NMDA receptor antagonist MRZ2/576 on the conditioned place preference and locomotor activity induced by morphine in mice. J Zhejiang Univ Sci B 2006;7:998–1005. [PubMed: 17111470]

1331. Ziolkowska B, Stefanski R, Mierzejewski P, Zapart G, Kostowski W, Przewlocki R. Contingency does not contribute to the effects of cocaine self-administration on prodynorphin and proenkephalin gene expression in the rat forebrain. Brain Res 2006;1069:1–9. [PubMed: 16412997]

1332. Zissen MH, Zhang G, Kendig JJ, Sweitzer SM. Acute and chronic morphine alters formalin pain in neonatal rats. Neurosci Lett 2006;400:154–157. [PubMed: 16517072]