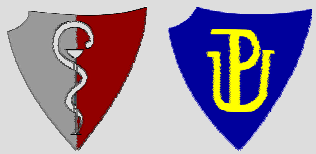
Opioids

Jan Strojil
Ústav farmakologie LF UP



May 4, 2006

Definitions

Pain - direct response to an untoward event associated with tissue damage such as injury, inflammation, cancer

nociceptive fibres - non-myelinated C fibres

nociception

hyperalgesia

allodynia

spontaneous pain

Definitions

Gate control theory

Substancia gelatinosa

Periaqueductal gray

Neuropathic pain

stroke, MS, injury, DM, shingles

Nociceptive and affective part of „pain“

Definitions

Chemical mediators of nociceptive pathways

(thermal and pressure stimuli can also cause pain, but only acute)

Vanilloid receptor (VR1) - capsaicin,

resiniferatoxin

Definitions

Kinins

Prostaglandins

5-HT

Histamine

lactic acid

…

Definitions

Transmitters

tachykinins

substance P

NKA

Opioid peptides (neuropeptides)

beta-endorphin

met-enkeohhalin

leu-enkephalin

dynorphin

Morphine-like drugs

Opiates vs. opioids

papaver somniferum

opium

mixture of alkaloids

papaverin

Opioid receptors

μ δ κ

G-protein coupled receptors

μ - analgesic, resp. depression, euphoria, sedation, dependence

δ - in the periphery

κ - analgesia on spinal level, sedation, dysphoria,

σ - psychomimetic effects, not purely opioid

Agonists, antagonists, dualists

pure agonists - high μ, less δ and. most typical drugs

morphinem nethadone, dextropropoxyphene, codeine, methadone, fentanyls

partial agonists - nalorphine

mixed agonists-antagonists - antagonists on μ and agonists on κ

antagonists - naloxone

Pharmacological action

CNS

analgesia - both nociceptive and affective component

euphoria - “abdominal orgasm”

respiratory depression - mediated by μ, coupled with analg.

cough suppresion - independent of respir. depression

nausea and vomiting - transient, 40 %, area postrema

pupillary constriction - important for diagnosis, μ and κ

Pharmacological action

GI tract

increases tonus and decreases motility

both central and peripheral

all receptors

note: increases pressure in biliary tract

Other

histamine release

Straub tail reaction

immunosuppressant

Tolerance and dependence

Tolerance

rapid, 12-24 hours

affects all but pupils and constipation

Physical dependence

abstinence syndrome - shakes, aggresion, irritability, influenze like symptoms, yaqning, dilated pupils, fever, sweating, piloerection, nausea, diarrhoea and insomnia

craving

Pharmacokinetics

variable absorption

half-life of most is 3-6 hours

hepatic metabolism

enterohepatic circulation

neonated can‘t conjugate as well

use „on demand“

Side effects

sedation,

respiratory depression,

constipation,

nausea and vomiting,

itching,

tolerance,

dependence,

euphoria/dysphoria

Other agonists

Heroin (diacetylmorphine, diamorphine)

like morphine

faster (better BBB crossing)

Codeine (methoxymorphine)

at most 20 % potency

not addictive, antitussic

some people can‘t demethylate

Other agonists

Pethidine = meperidine

like morphine, causes restlessness

better for neonates (no conjugation)

better for biliary pain

Fentanyl, sufentanil, remifentanil

more potent than morphine

short half-lives - 10-30 minutes

anaesthesia, PCA, TTS

Other agonists

etorphine

extremely potent, used for wild animals

methadone

T1/2 > 24 h

addiction treatment

tramadol

Antagonists

naloxone

all three receptors

no effect in healthy

hyperalgesia in inflammation…

T1/2 is only 2-4 hours!

naltrexone

similar, T1/2 is 10 hours

Thank you for your attention