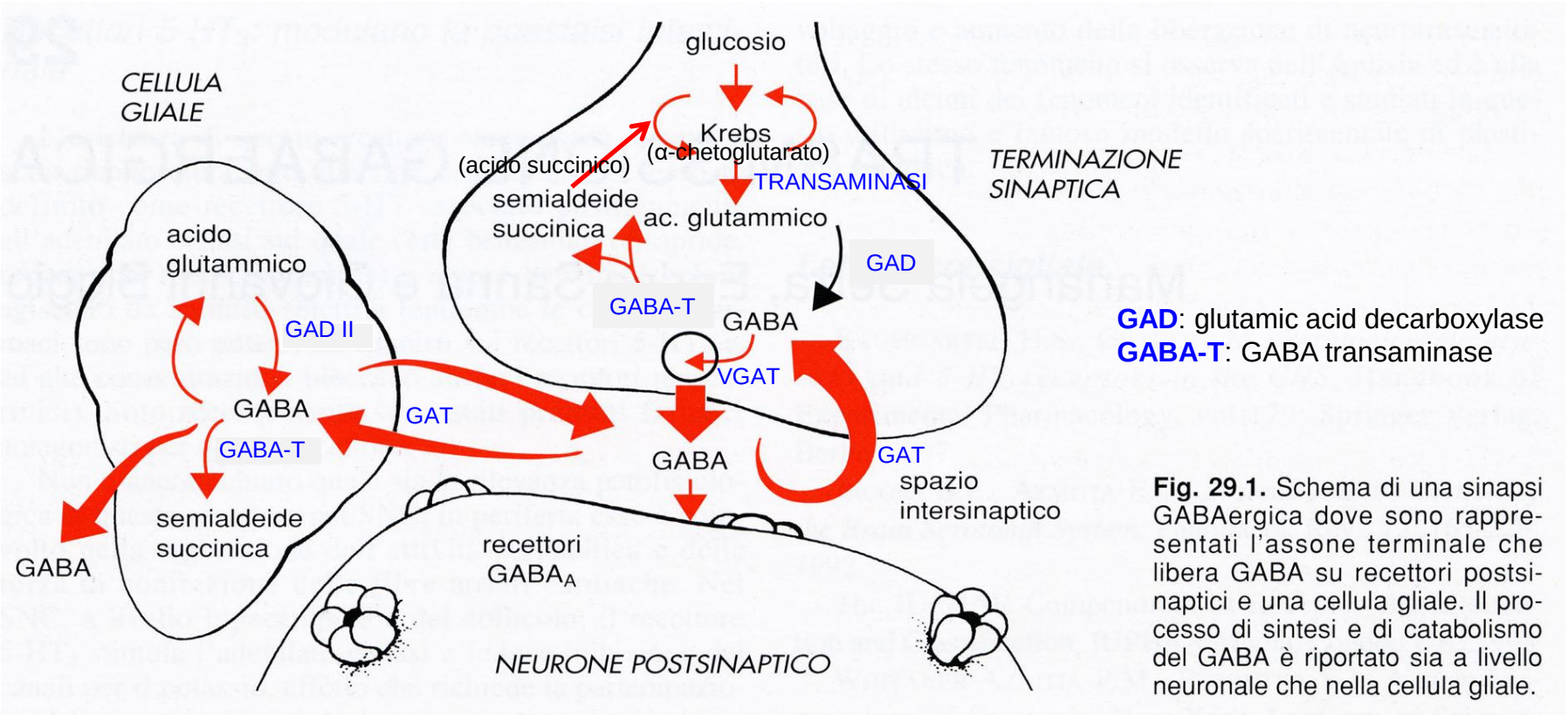
AMINO-ACIDI
GABA - Glutamato

GABA

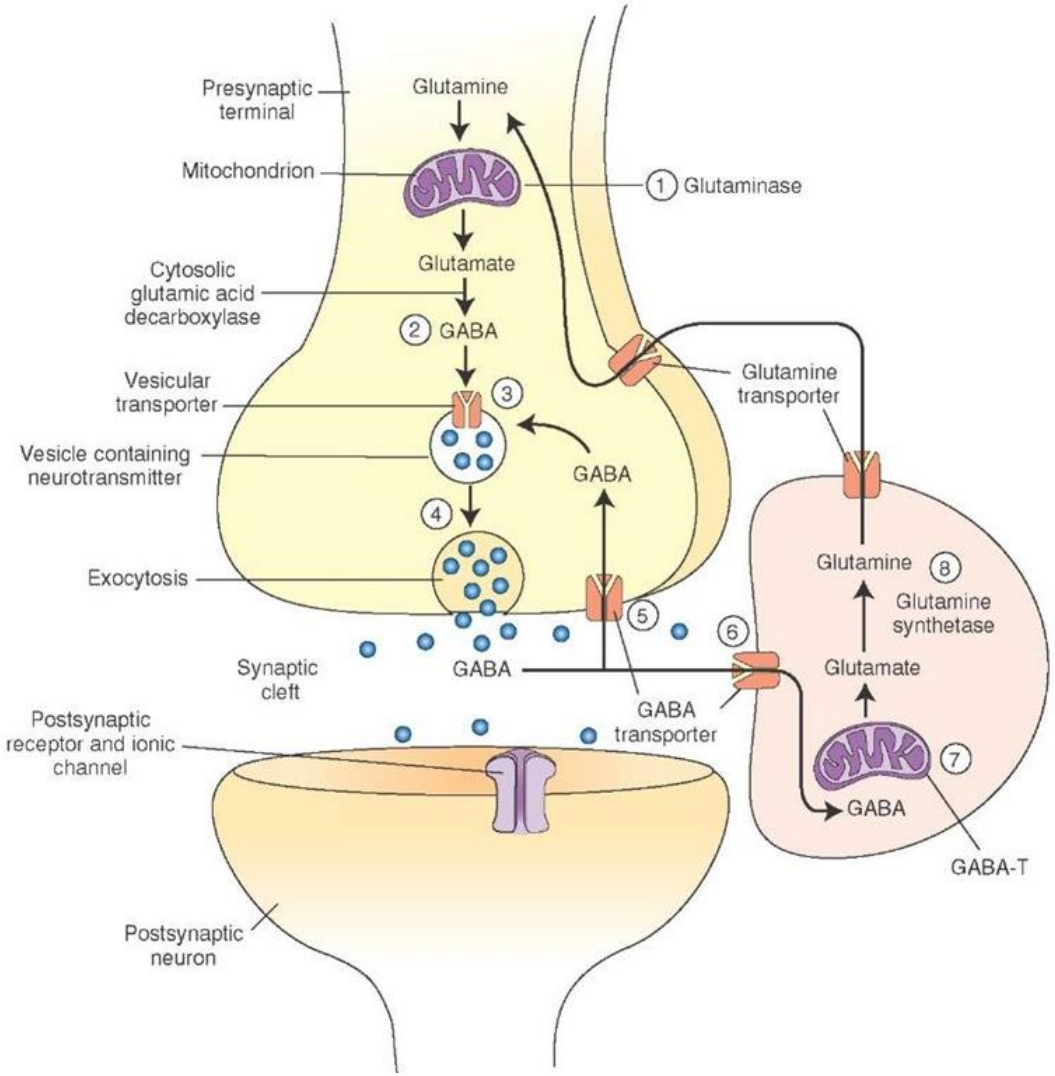
SINTESI E RILASCIO DEL GABA



GAD: glutamic acid decarboxylase
GABA-T: GABA transaminase

Fig. 29.1. Schema di una sinapsi GABAergica dove sono rappresentati l'assone terminale che libera GABA su recettori postsinaptici e una cellula gliale. Il processo di sintesi e di catabolismo del GABA è riportato sia a livello neuronale che nella cellula gliale.

SINTESI E RILASCIO DEL GABA



DISTRIBUZIONE DEL GABA

- Ampiamente distribuito in tutto il nevrasse.
- Prevalentemente interneuroni ad assone breve.
- Spesso co-rilasciato con altri trasmettitori.

RECETTORI GABA-A

$GABA_A$ Receptors

Currently Accepted Terminology	Transmitter Recognition Site	Allosteric Modulatory Sites
Agonists	Isoguvacine (G-002) Muscimol (G-019, M 1523) THIP (Gaboxadol) (T-101) Piperidine-4-sulphonic acid (P 9159)	—
Antagonists	Bicuculline (B 6889, B 9130) SR 95531 (Gabazine) (S-106)	Ro 15-1788 (Flumazenil) (F 6300) ZK 93426
Indirect Agonist	γ-Vinyl GABA (V 8261)	—
Positive Modulators	—	Allopregnanolone (P 0666) Barbiturates (Phenobarbital (P 5178), Pentobarbital (P 3761), Thiopental (T 1019)) Flunitrazepam (F 9261) Zolpidem (Z-103) Abecarnil
Negative Modulators	—	Pregnenolone sulfate (P 9129) DMCM (E-007) Ro 19-4603 Ro 05-3663 TBPS (B-104) Picrotoxin (P 1675)
Partial Modulators	—	Bretazenil Imidazenil
Signal Transduction Mechanisms	Cl^- influx	Cl^- influx, modulation GABA gating
Radioligands of Choice	[^{3}H]-Muscimol [^{3}H]-SR 95531	[^{3}H]-Flunitrazepam [^{3}H]-Zolpidem [^{3}H]-Ro 15-1788 [^{35}S]-TBPS [^{3}H]-Ro 15-4513

Sigma-RBI Product Numbers are shown in red; for detailed product information, visit the Sigma-RBI eHandbook at www.sigma-aldrich.com/sigma-rbiehandbook.

Abbreviations
DMCM: Methyl 6,7-dimethoxy-4-ethyl-β-carboline-3-carboxylate
Ro 05-3663: 5-Methyl-1,4-benzodiazepin-2(3H)-one
Ro 19-4603: Imidazo[1,5a]-1,4-thienodiazepinone
SR 95531: 2-(3-Carboxypropyl)-3-amino-6-(4-methoxyphenyl)-pyridazinium bromide
TBPS: t-Butylbicyclophosphorothionate
THIP: 4,5,6,7-Tetrahydroisoxazolo[5,4-c]pyridin-3-ol
ZK 93426: 5-Isopropyl-4-methyl-β-carboline-3-carboxylate ethyl ester

RECETTORI GABA-A

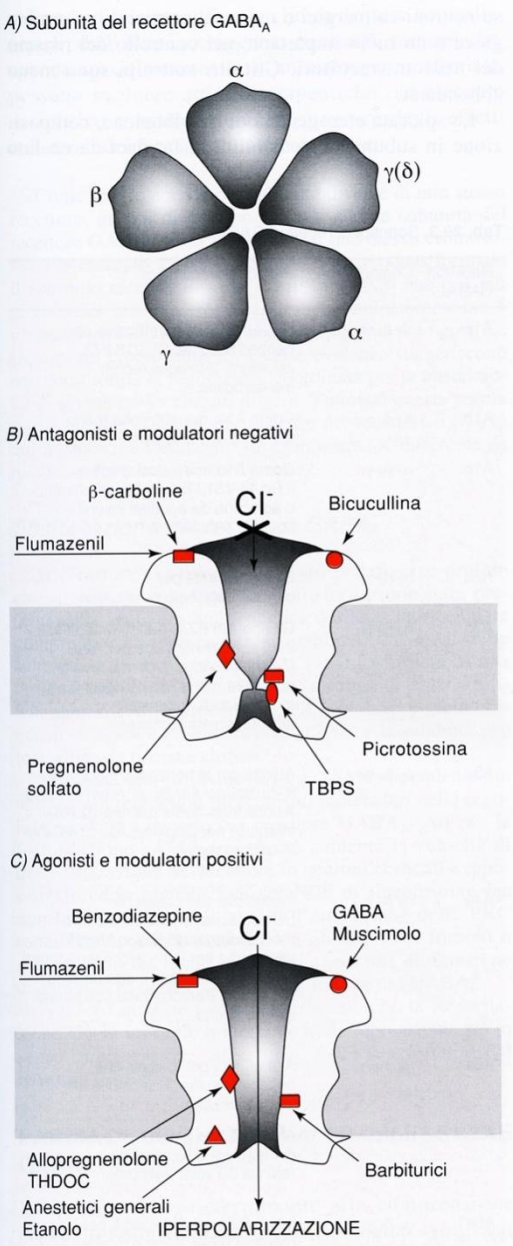


Fig. 29.2. Schema ipotetico della struttura molecolare del recettore GABA$_A$. In (*A*) sono indicate le tre differenti subunità α, β, γ (o δ in alternativa) necessarie per costituire un recettore funzionalmente sensibile sia all'azione dei barbiturici (α-β) che delle benzodiazepine (α, β, γ). Il rapporto tra subunità (nella figura 2α, 1β, 2γ) può variare nelle diverse aree del SNC. In (*B*) e (*C*) sono ipotizzati due differenti momenti funzionali del canale allo ione cloro: (*B*) inibito, (*C*) attivato. Sono riportati i siti di legame di differenti modulatori negativi (*B*) e positivi (*C*).

RECETTORI GABA-B

$GABA_B$ Receptor

Currently Accepted Name	$GABA_B$
Structural Information	$GABA_{B1a}$ 960 aa (rat) 961 aa (human) $GABA_{B2}$ 941 aa (rat) 941 aa (human)
Receptor Selective Agonists	(R)-Baclofen (G-013) 3-Aminopropylphosphonic acid (A 7162) 3-Aminopropylphosphinic acid 3-Aminopropylmethylphosphinic acid (A-196)
Receptor Selective Antagonists	Phaclofen (P-118) 2-Hydroxysaclofen (A 6566) CGP35348 (C 5851) CGP36742 CGP52432 CGP54626 CGP55845 CGP62349 SCH-50911
Signal Transduction Mechanisms	G_s (increase cAMP) G_i (cAMP modulation) ↑ K^+ (G) ↓ Ca^{2+} (G)
Radioligands of Choice	[^{3}H]-R-Baclofen [^{3}H]-3-Aminopropylphosphinic acid [^{3}H]-CGP54626 [^{125}I]-CGP64213 [^{3}H]-CGP62349 [^{125}I]-CGP71872

Sigma-RBI Product Numbers are shown in red; for detailed product information, visit the Sigma-RBI eHandbook at www.sigma-aldrich.com/sigma-rbiehandbook.

Abbreviations
CGP35348: 3-Aminopropyl-diethoxymethyl-phosphinic acid
CGP36742: 3-Aminopropyl-n-butyl-phosphinic acid
CGP52432: [3-[[(3,4-Dichlorophenyl)methyl]amino]propyl](diethoxy-methyl)phosphinic acid
CGP54626: (3-N[[1-(S)-(3,4-Dichlorophenyl)ethyl]amino-2-(S)-hydroxypropyl)-cyclohexylmethylphosphinic acid
CGP55845: (3-N[[1-(S)-(3,4-Dichlorophenyl)ethyl]amino-2-(S)-hydroxypropyl)-benzyl-phosphinic acid
CGP64213: 3-{1-(R)-[2-(S)-Hydroxy-3-[hydroxy-(5-[3-(4-hydroxy-3-iodo-phenyl)-propionylamino]-pentyl-phosphinoyl)-propylamino]-ethyl}-benzoic acid
CGP62349: 3-{1-(R)-[2-(S)-Hydroxy-3-[hydroxy-(4-methoxy-benzyl)-phosphinoyl]-propylamino]-ethyl}-benzoic acid
CGP71872: 3-{[1-(R)-(3-[[5-(4-Azido-2-hydroxy-5-iodo-benzoylamino)-pentyl]-hydroxy-phosphinoyl]-2-(S)-hydroxy-propylamino)-ethyl}-benzoic acid
SCH-50911: (+)-(S)-5,5-Dimethylmorpholinyl-2-acetic acid

Footnotes

EFFETTI

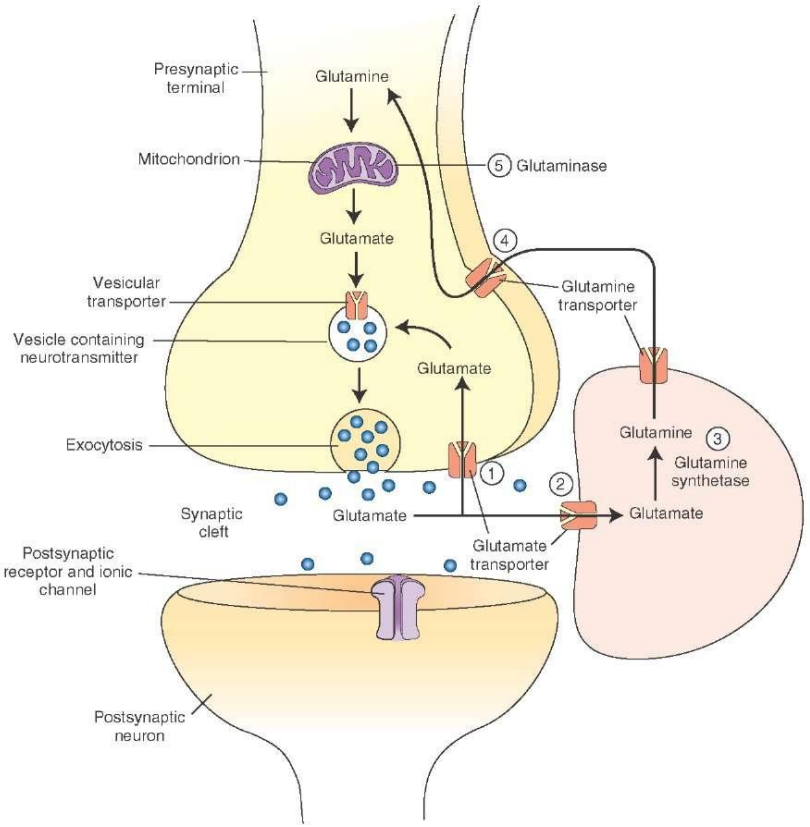
- Sedazione e riduzione dell’ansia.
- Induzione del sonno.
- Muscolo-rilassante.
- Anti-convulsivante.

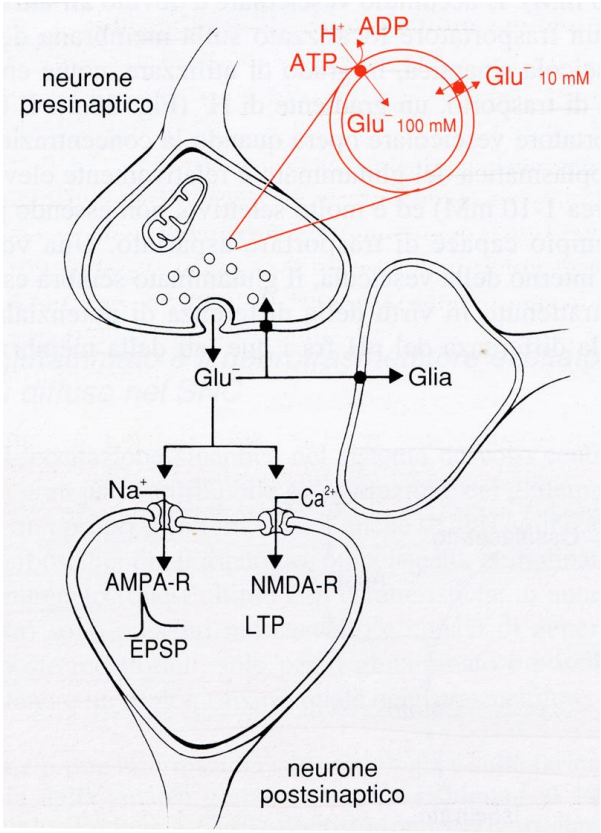
FARMACI

Ipnotici Sedativi
Ansiolitici
Muscolo-rilassanti
Anti-epilettici

Glutamato

BIOSINTESI E RILASCIO DEL GLUTAMATO





Glutamate is synthesized in the brain by two processes. **(A)** ***(-ketoglutarate*** (generated during the ***Krebs*** cycle) is transaminated to glutamate. **(B)** Nerve terminals and glial cells reuptake the glutamate released from the nerve terminals via specific transporters (Figure, 1 and 2). In the glia, glutamate is converted into ***glutamine*** by glutamine synthetase (3). Glutamine is transported out of the glia into the neuronal terminal via glutamine ***transporters*** (4). In the neuronal terminal, glutamine is converted into glutamate by glutaminase (5). Glutamate is taken up into the vesicles by active transport, stored, and subsequently released by exocytosis.

DISTRIBUZIONE DEL GLUTAMATO

- Ampiamente distribuito in tutto il nevrasse.
- Sia neuroni ad assone lungo che interneuroni ad assone breve.
- Spesso co-rilasciato con altri trasmettitori.

RECETTORI IONOTROPI GLUTAMATERGICI

Glutamate Receptors (Ion Channel Family) [a]

Currently Accepted Name	Glutamate site	NMDA Glycine site	Other	AMPA	Kainate
Alternate Name	—	—	—	Quisqualate	—
Structural Information	NR1 (920 aa human) NR2A (1464 aa human) NR2B (1484 aa human) NR2C (1233 aa human) NR2D (1329 aa rat) NR3A (1115 aa rat)	—	—	GluR1 (889 aa human) GluR2 (883 aa human) GluR3 (894 aa human) GluR4 (881 aa rat)	GluR5 (978 aa human) GluR6 (877 aa rat) GluR7 (919 aa human) KA1 (956 aa human) KA2 (962 aa human)
Subtype Selective Agonists	N-Methyl-D-aspartic acid (M 3262) Quinolinic acid (P 6,320-4)	Glycine (G 7126) D-Serine (S 4250) R(+)-HA-966 (partial) (H-130)	—	AMPA (A 0326) S(–)-5-Fluorowillardiine (F 2417) CX-614 [d] Cyclothiazide (C 9847) [d]	Kainic acid (K 0250) Domoic acid (D 6152) 4-Methylglutamate (G-137) ATPA (GluR5) (A-263)
Subtype Selective Antagonists	D(–)-AP-5 (A-169) D(–)-AP-7 (A-167) CGS19755 (C-105) CGP37849 CPP, (±)-, D- (C-104, C-189) D-CPPene EAA-090	7-Chlorokynurenic acid (C 0306) 5,7-Dichlorokynurenic acid (D-138) MNQX L-689,560 L-701,324 (L 0258) GV 150526	Ro 25-6981 (NR2B) (R 7150) Ro 8-4304 (NR2B) (R 8900) CP 101,606 (NR2B) Ifenprodil (NR2B) (I 2892)	NBQX (N-183) GYKI 52466 (G-119) [c] GYKI 53655 (G 3166) [c] CNQX (C-239) DNQX (D 0540) YM90K LY-294486 Ro 48-8587 SPD-502	CNQX (C-239) DNQX (D 0540) NS 102 (N-179) [b] LY-294486 (GluR5)
Channel Blockers	MK-801 (Dizocilpine) (M-107) Phencyclidine (PCP) (P 3029) CNS-1102 (Cerestat) Ketamine (K 2753)	—	—	Joro Spider Toxin (J-100)	—
Channel Permeability	Intrinsic ion channel ($Na^+/K^+/Ca^{2+}$)	—	—	Intrinsic ion channel ($Na^+/K^+/Ca^{2+}$)	Intrinsic ion channel ($Na^+/K^+/Ca^{2+}$)
Radioligands of Choice	[^{3}H]-CPP [^{3}H]-L-Glutamate	[^{3}H]-5,7-Dichlorokynurenate [^{3}H]-L-689,560	[^{3}H]-MK-801 (channel) [^{3}H]-Ro 25-6981 (NR2B)	[^{3}H]-AMPA [^{3}H]-Ro 48-8587	[^{3}H]-Kainic acid [^{3}H]-NBQX

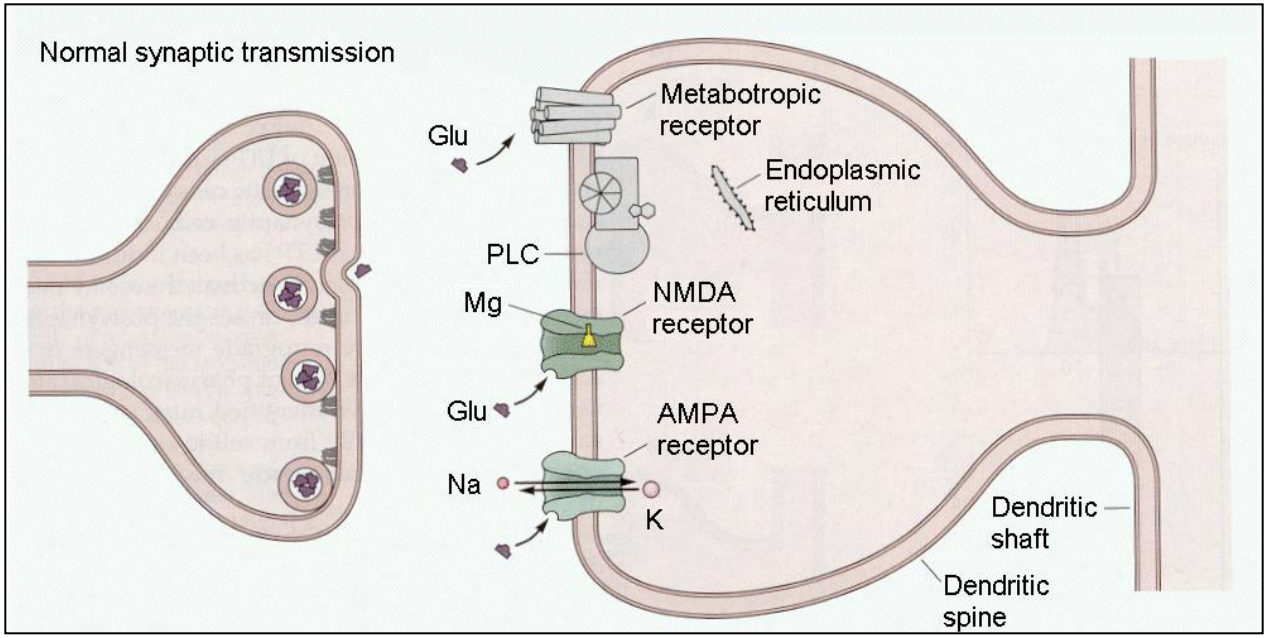
Sigma-RBI Product Numbers are shown in red; for detailed product information, visit the Sigma-RBI eHandbook at www.sigma-aldrich.com/sigma-rbiehandbook.

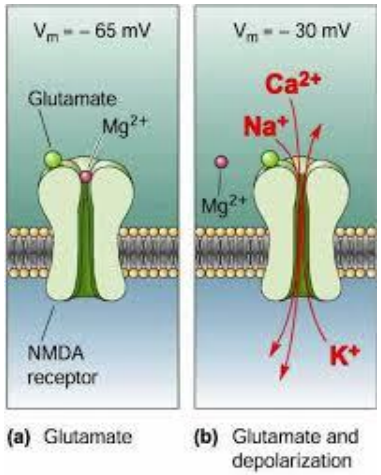
Abbreviations
AMPA: α-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
AP-5: 2-Amino-5-phosphonopentanoic acid
AP-7: 2-Amino-7-phosphonoheptanoic acid
ATPA: (RS)-2-Amino-3-(3-hydroxy-5-tert-butylisoxazol-4-yl)propanoic acid
D-CCPene: D-3-(2-Carboxypiperazin-4-yl)-propyl-1-phosphonene
CGP37849: D,L-(E)-2-Amino-4-methylphosphono-3-pentanoic acid
CGS19755: 4-Phosphonomethyl-2-piperidinecarboxylic acid (Selfotel)
CNQX: 6-Cyano-7-nitroquinoxaline-2,3-dione
CNS 1102: N-(1-Naphthyl)-N'-(3-ethylphenyl)-N'-methyl-guaniaine HCl
CP 101,606: (1S,2S)-1-(4-Hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol
CPP: 3-(2-Carboxypiperazin-4-yl)-propyl-1-phosphonic acid
CX-614: 2H,3H,6aH-Pyrolidino[2",1"-3',2']1,3-oxazino[6',5',-5,4]benzo[e]1,4-dioxan-10-one
DNQX: 6,7-Dinitroquinoxaline-2,3-dione
EAA-090: [2-(8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)-ethyl]phosphonic acid
GV 150526: 3-[2-(Phenylamino)carbonyl]ethenyl-4,6-dichloroindole-2-carboxylic acid
GYKI 52466: 1-(4-Aminophenyl)-4-methyl-7,8-methylenedioxy-5H-2,3-benzodiazepine
GYKI 53655: 1-(4-Aminophenyl)-3-methylcarbamyl-4-methyl-7,8-methylenedioxy-3,4-dihydro-5H-2,3-benzodiazepine
HA-966: 1-Hydroxy-3-aminopyrrolid-2-one
L-689,560: (±)-4-(trans)-2-Carboxy-5,7-dichloro-4-phenylaminocarbonylamino-1,2,3,4-tetrahydroquinoline
L-701,324: 7-Chloro-4-hydroxy-3-(3-phenoxy)phenyl-2(H)-quinolinone
LY-294486: (3SR,4aRS,6SR,8aRS)-6-((((1H-Tetrazol-5-yl)methyl)oxy)methyl)-1,2,3,4,4a,5,6,7,8,8a-decahydroisoquinoline-3-carboxylic acid
MNQX: 5,7-Dinitro-1,4-dihydro-2,3-quinoxalinedione
NBQX: 2,3-Dihydro-6-nitro-7-sulphamoyl-benzo(f)quinoxaline
NMDA: N-Methyl-D-aspartic acid
NS 102: 5-Nitro-6,7,8,9-tetrahydrobenzo[G]indole-2,3-dione-3-oxime
Ro 25-6981: R-(R*,S*)-α-(4-Hydroxyphenyl)-β-methyl-4-(phenylmethyl)-1-piperidine propanol
Ro 8-4304: 4-[3-[4-(4-Fluorophenyl)-3,6-dihydro-2H-pyridin-1-yl]-2-hydroxy-propoxy}-benzamide
Ro 48-8587: 9-(1H-Imidazol-1-yl)-8-nitro-[1,2,4]triazolo[1,5-c]quinazoline-2,5(3H,6H)-dione
SPD-502: 8-Methyl-5(4-(N,N-dimethylsulfamoyl)phenyl)6,7,8,9,-tetrahydro-1H-pyrrolo[3,2-h]-isoquinoline-2,3-dione-3-O-(4-hydroxybutyrate-2-yl)oxime
YM90K: 6-(1H-Imidazol-1-yl)-7-nitro-2,3(1H,4H)-quinoxalinedione

Footnotes

a Ion channel family is also referred to as ionotropic.
b Selectively inhibits low affinity [^{3}H]-kainate binding.
c Non-competitive antagonist.
d Allosteric potentiator.

RECETTORI IONOTROPI GLUTAMATERGICI





RECETTORI METABOTROPI GLUTAMATERGICI

Glutamate Receptors (G Protein Family) [a]

	Group I		Group II		Group III			
Currently Accepted Name	$mGluR_1$	$mGluR_5$	$mGluR_2$	$mGluR_3$	$mGluR_4$	$mGluR_6$	$mGLuR_7$	$mGluR_8$
Structural Information	1194 aa (human)	1212 aa (human)	872 aa (human)	879 aa (human)	912 aa (human)	853 aa (human)	915 aa (human)	908 aa (human)
Receptor Selective Agonists	S-DHPG	S-DHPG z-CBQA	2R,4R-APDC DCG-IV LY-354740 MGS 0028 LY-379268	NAAG (A 5930) 2R,4R-APDC DCG-IV LY-354740 MGS 0028 LY-379268	L-AP-4 (A 7929) L-SOP (P 0878) RS-PPG	L-AP-4 (A 7929) L-SOP (P 0878) RS-PPG S-homo-AMPA	L-AP-4 (A 7929)	L-AP-4 (A 7929) L-SOP (P 0878) RS-PPG S-3,4-DCPG
Receptor Selective Antagonists	LY-367385	MPEP (M 5435) [b] SIB-1757 (S 9186) [b] SIB-1893 (S 9311) [b]	LY-341495 [c] EGLU ADED	LY-341495 [c] EGLU ADED	MAP4 (M 5560)	MAP4 (M 5560)	MAP4 (M 5560)	None known
Signal Transduction Mechanisms	$G_{q/11}$ (increase IP_3/DAG)	$G_{q/11}$ (increase IP_3/DAG)	G_i (cAMP modulation)	G_i (cAMP modulation)	G_i (cAMP modulation)	G_i (cAMP modulation)	G_i (cAMP modulation)	G_i (cAMP modulation)
Radioligands of Choice	[^{3}H]-Quisqualate	[^{3}H]-Quisqualate	[^{3}H]-LY-354740 [^{3}H]-DCG IV [^{3}H]-LY-341495	[^{3}H]-LY-354740 [^{3}H]-DCG IV [^{3}H]-LY-341495	[^{3}H]-L-AP4	[^{3}H]-L-AP4 [^{3}H]-LY-341495 [d]	[^{3}H]-L-AP4 [^{3}H]-LY-341495 [d]	[^{3}H]-LY-341495 [d]

Sigma-RBI Product Numbers are shown in red; for detailed product information, visit the Sigma-RBI eHandbook at www.sigma-aldrich.com/sigma-rbiehandbook.

Abbreviations
ADED: (2S,4S)-2-Amino-4-(2,2-diphenylethyl)pentane-1,5-dioic acid
L-AP-4: 2-Amino-4-phosphonobutyric acid
(2R,4R)-APDC: (2R,4R)-Aminopyrrolidine-2,4-dicarboxylic acid
z-CBQA: (Z)-1-Amino-3-[2′-(3′,5′-dioxo-1′,2′,4′-oxadiazolidinyl-cyclobutane-1-carboxylic acid
DCG-IV: (2S,1′R,2′R,3′R)-2-(2,3 Dicarboxycyclopropyl)glycine
S-DHPG: (R,S)-3,5-Dihydroxyphenylglycine
S-3,4-DCPG: (*S*)-3,4-Dicarboxyphenylglycine
E-GLU: (S)-α-Ethylglutamic acid
S-Homo-AMPA: (RS)-2-Amino-4-(3-hydroxy-5-methylisoxazol-4-yl)butyric acid
LY-341495: (2S)-2-Amino-2-(1S,2S-2-carboxycyclopronan-1-yl-3-(xanth9-yl)propanoic acid
LY-354740: (+)-2-Aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid
LY-367385: (+)-2-Methyl-4-carboxyphenylglycine
LY-379268: (–)-2-Thia-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate
MAP4: (S)-2-Amino-2-methyl-4-phosphonobutyric acid
MGS 0028: (1R,2S,5S,6S)-2-Amino-6-fluoro-4-oxobicyclo[3.1.0]hexane-2,6-dicarboxylic acid
MPEP: 2-Methyl-6-(phenylethynyl)pyridine
NAAG: N-Acetyl-L-aspartyl-l-glutamic acid
RS-PPG: (RS)-4-Phosphonophenylglycine
SIB-1757: 6-Methyl-2-(phenylazo)-pyridinol
SIB-1893: (E)-2-Methyl-6-(2-phenylethenyl)pyridine
L-SOP: L-Serine-O-phosphate

Footnotes

a G Protein family is also referred to as metabotropic.
b Non-competitive.
c Also significant antagonism of Group I and group II receptors.
d In cell lines expressing recombinant receptor subtypes.

EFFETTI

- Stimolazione.
- Veglia.
- Aumento dell’attenzione.
- Pro-convulsivante.

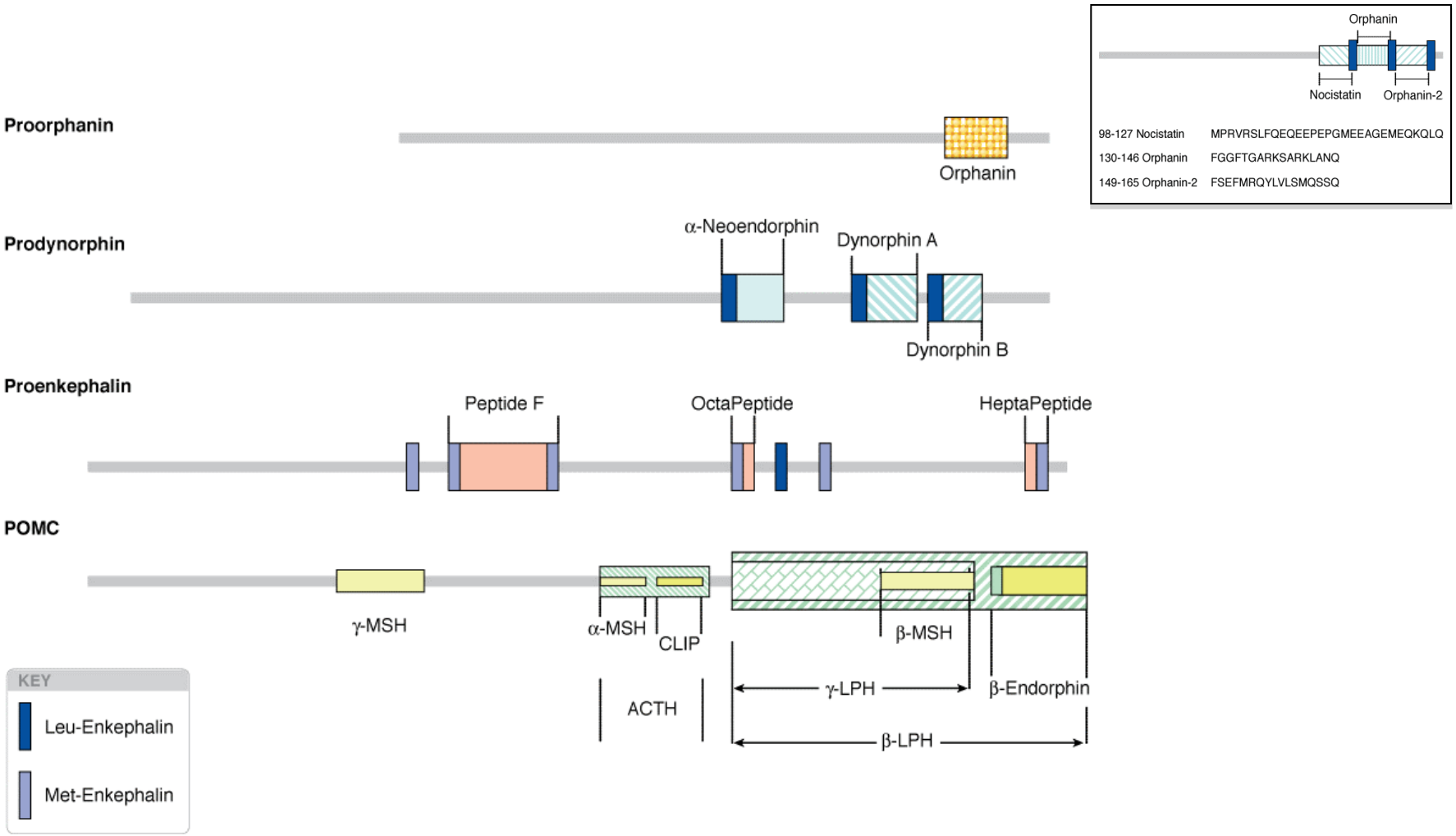
FARMACI

- Anti-epilettici
- Anti-Alzheimer: memantina, antagonista non competitivo NMDA
    - A concentrazioni fisiologiche il glutamato supporta la memoria; a concentrazioni elevate la può peggiorare per sovra-stimolazione e danno cellulare (eccito-tossicità)

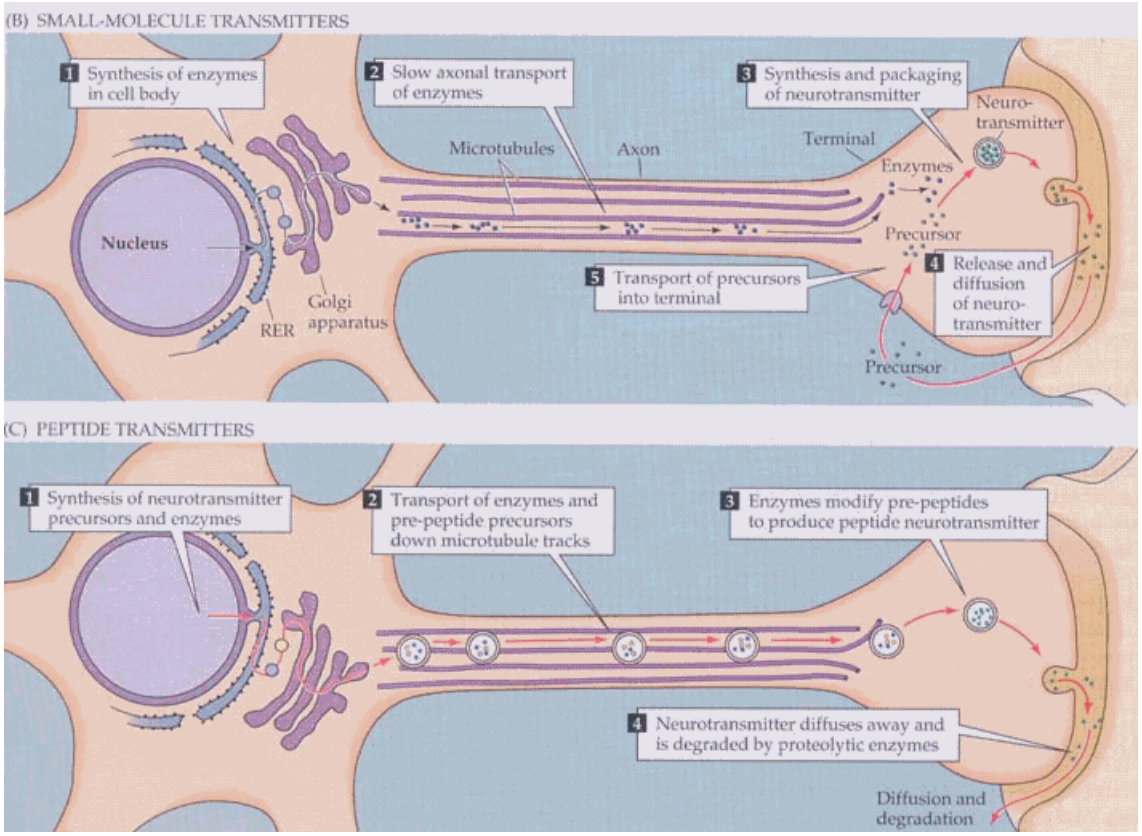
PEPTIDI

Oppioidi endogeni

SINTESI
quattro distinti sistemi neuronali



PACKAGING e RELEASE



DISTRIBUZIONE

- **beta-ENDORFINA**
  - nucleo arcuato dell'ipotalamo (proiezioni al sistema limbico, all'ipotalamo, al tronco, al midollo spinale)
  - ipofisi
  - cellule Langherans (pancreas)
- **ENCEFALINE**
  - lamina I e II del midollo spinale - nucleo spinale del trigemino – PAG
  - amigdala - ippocampo - accumbens - locus coeruleus – corteccia
  - midollo allungato – ipotalamo
  - plessi intestinali - midollare del surrene
- **ENDOMORFINE**
  - corno dorsale del midollo spinale - nucleo spinale del trigemino - talamo – PAG
  - accumbens - amigdala
- **DINORFINA**
  - corno dorsale del midollo spinale (lamina II) - nucleo spinale del trigemino
  - ippocampo - striato – corteccia
  - tronco – ipofisi
  - plessi intestinali
- **NOCICETTINA**
  - corno dorsale del midollo spinale - PAG – talamo
  - ippocampo - amigdala

DISTRIBUZIONE
anatomia funzionale

- Controllo del dolore
- Modulazione del tono affettivo
- Modulazioni di funzioni vegetative

RECETTORI

- **SOTTOTIPI**

  μ, δ, κ, ORL-1 (MOP, DOP, KOP, NOP)

- **STRUTTURA**

  7TM

- **LOCALIZZAZIONE**

  simile a quella degli oppioidi endogeni

- **AGONISTA ENDOGENO**

  NOP per nocicettina

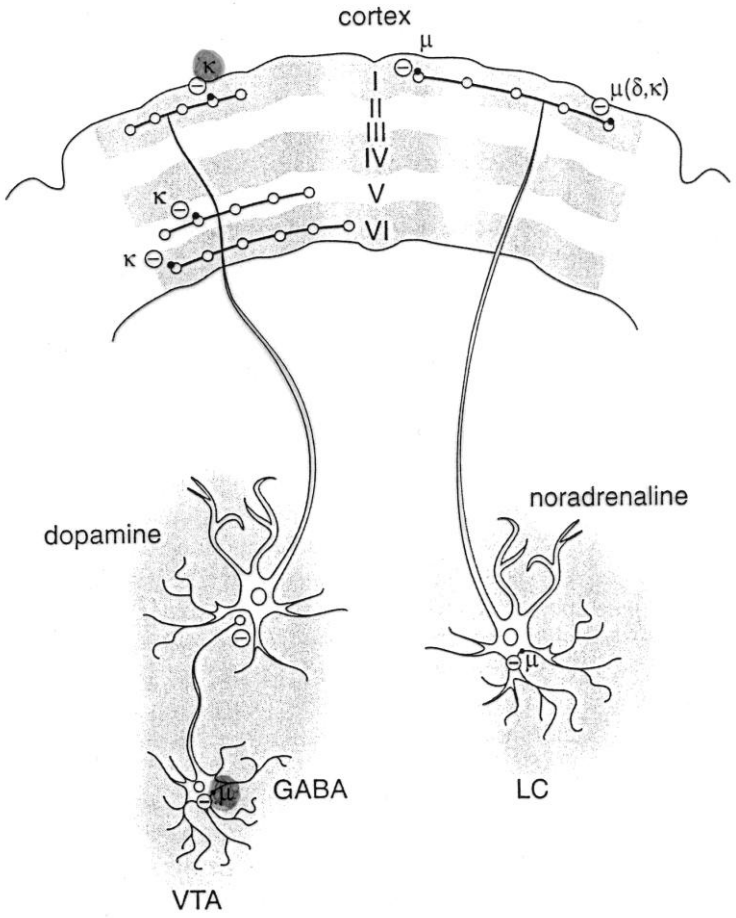
	μ	δ	κ
Endogenous peptides			
β-Endorphin	+++	+++	+++
Leu-enkephalin	+	+++	-
Met-enkephalin	++	+++	-
Dynorphin	++	+	+++

RECETTORI
trasduzione del segnale

- Gi/o
  - Inibizione dell'adenilato ciclasi
  - Inibizione dei flussi del calcio
  - Aumento dei flussi del potassio

- QUINDI INIBIZIONE

NB: è possibile la disinibizione, per inibizione di neuroni inibitori



AZIONI

- **SUL SISTEMA NERVOSO CENTRALE**
  - ANALGESIA **(analgesici)**
    - senza modificazioni degli altri input sensitivi
    - ridotta componente affettiva (μδ), spinale (μδκ), vegetativa (μ)
  - DISFORIA (κ) o EUFORIA (effetto indiretto dopaminergico) **(sostanze di abuso)**
  - MIOSI (stimolazione III paio nervi cranici)
  - EFFETTI IPOTALAMO-IPOFISARI (effetti μ e/o indiretti)
    - dim. CRF (e ACTH), GRF (e LH e FSH)
    - aum. prolattina, ADH
  - DEPRESSIONE DELL'ATTIVITA' RESPIRATORIA (μ2)
  - INIBIZIONE DEL RIFLESSO DELLA TOSSE (via recettori non naloxone-sensibili) **(antitussivi)**
  - INDUZIONE DEL VOMITO (stimolazione CTZ)

AZIONI

- **SUL SISTEMA CARDIOCIRCOLATORIO**
  - IPOTENSIONE ORTOSTATICA (istamino-mediata?)
- **SULL'APPARATO DIGERENTE** (effetti prevalentemente periferici)
  - DIMINUZIONE SECREZIONI E ATTIVITA' PROPULSIVA **(antidiarroici)**
  - AUMENTO TONO COLON E SFINTERI (inc. ODDI)
- **SULL'APPARATO URO-GENITALE**
  - CONTRAZIONE DELLA DIURESI (dim. produzione urina, aum. tono detrusore e sfintere vescicale)
  - DIMINUZIONE MOTILITA' UTERINA
- **SULLA CUTE**
  - ROSSORE, SUDIRAZIONE, ORTICARIA (istamina)
- **SUL SISTEMA IMMUNITARIO**
  - DIMINUZIONE NUMERO E ATTIVITA' DI LEUCOCITI

- **TOLLERANZA E DIPENDENZA**

CONCLUSIONI GENERALI SULLA NEUROTRASMISSIONE

- Un insieme di sistemi complessi sia a livello periferico che (molto di più) centrale.
- Possibilità di manipolazione farmacologica a vari livelli (sintesi, rilascio, interazione con recettori, ricaptazione, degradazione), con vari livelli di specificità e selettività d'azione.
- Spettro di indicazioni amplissimo (shock, ipertensione, aritmie, infarto, disturbi gastro-intestinali e genito-urinari, miastenia gravis, glaucoma, depressione, schizofrenia, ansia, induzione del sonno, epilessia, Parkinson, …).
- Spettro di controindicazioni e di effetti collaterali altrettanto vasto ➔ individualizzare la terapia.
- Elementi ancora poco esplorati (non trattati in questo modulo di lezioni): altri sistemi trasmettitoriali peptidici (NPY, somatostatina, galanina, sostanza P, bradikinine, …); neuromodulatori, neurotrasmettitori retrogradi, autacoidi (NO, purine, …); fattori neurotrofici.

…the future's so bright, I gotta wear shades… (o no?)