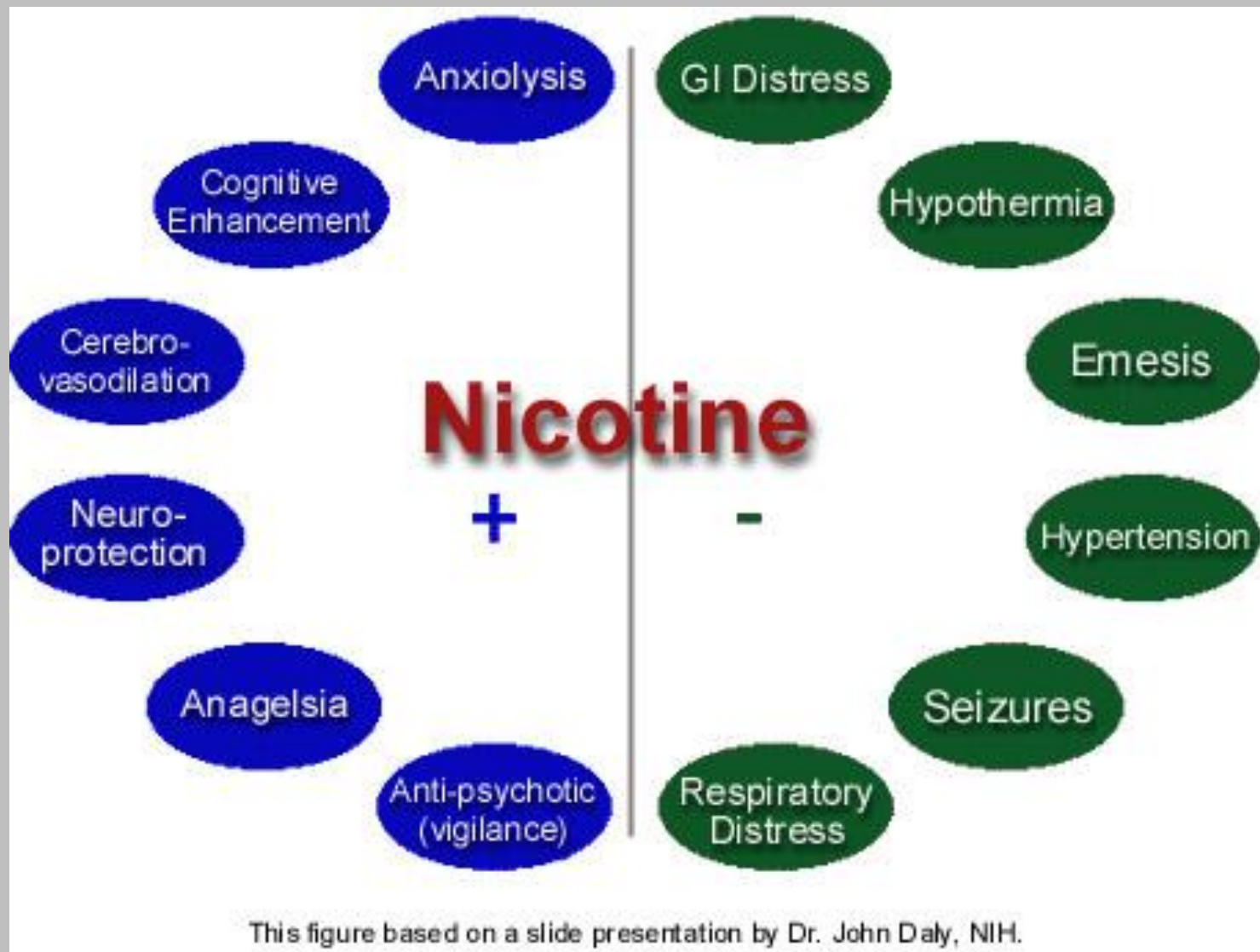


NICOTINE





Effects on the (+) side are considered beneficial, while those on the (-) side are considered detrimental

Plasmatic Concentrations of Nicotine

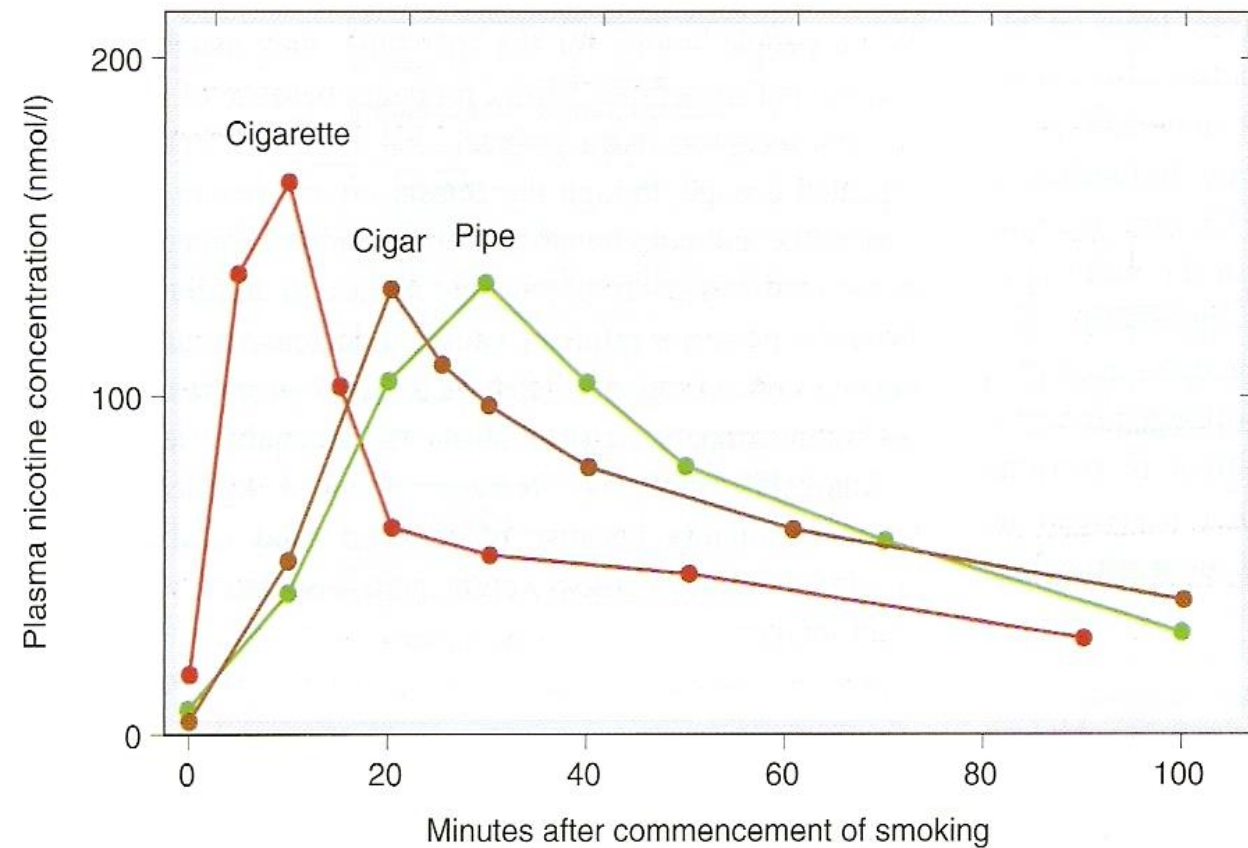
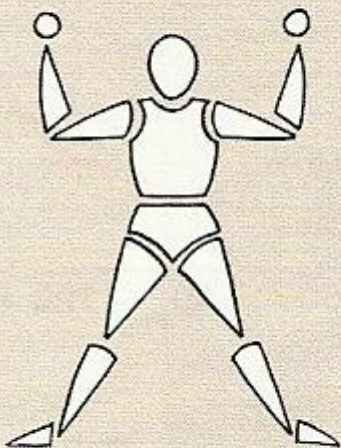


Fig. 42.5 Nicotine concentration in plasma during smoking. The subjects were habitual smokers who smoked a cigarette, cigar or pipe according to their usual habit. (From: Bowman W C, Rand M 1980 Textbook of pharmacology. Blackwell, Oxford, ch. 4.)

NICOTINE

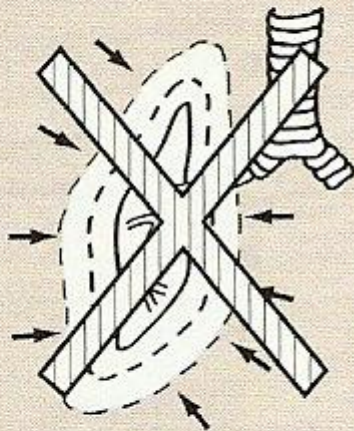
Dosi basse
di *nicotina*



ATTIVAZIONE
E RILASSAMENTO

**Ganglionic
Stimulation**

Dosi alte
di *nicotina*



PARALISI
RESPIRATORIA
Hypotension

**Ganglionic
Blokade**

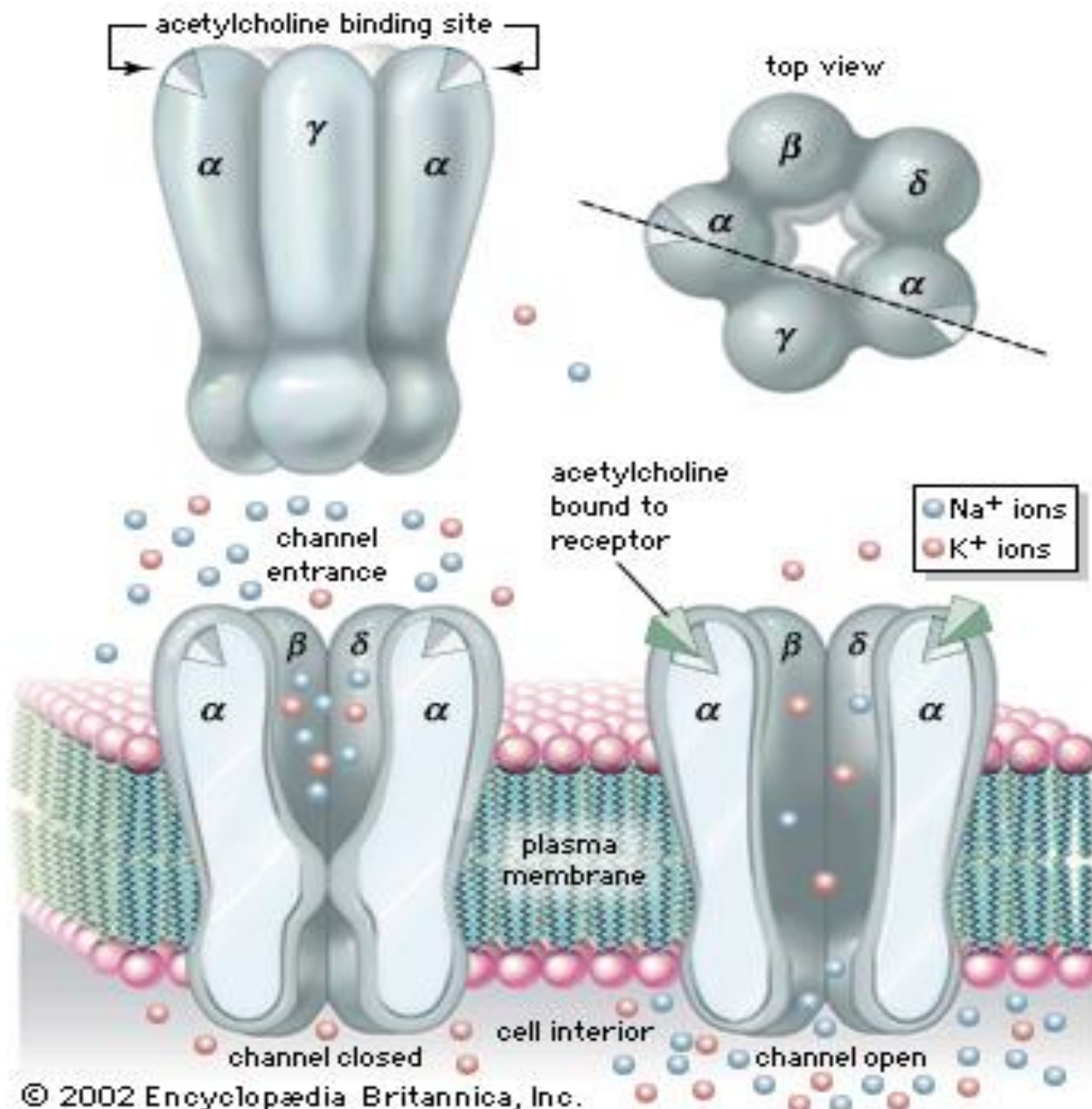
**POTENZIALE DI
TOSSICODIPENDENZA**

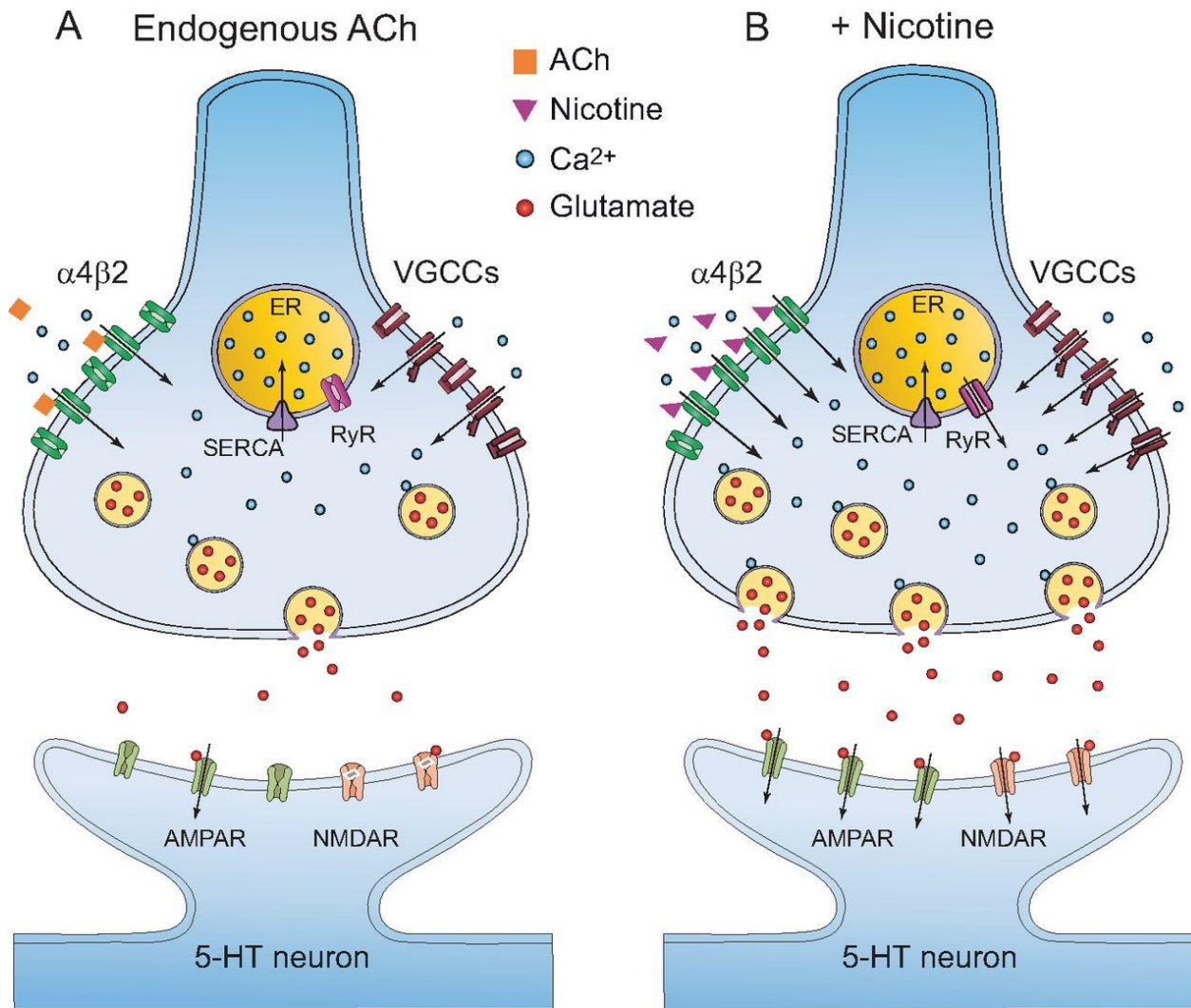


Nicotina

Pharmacology of NICOTINE

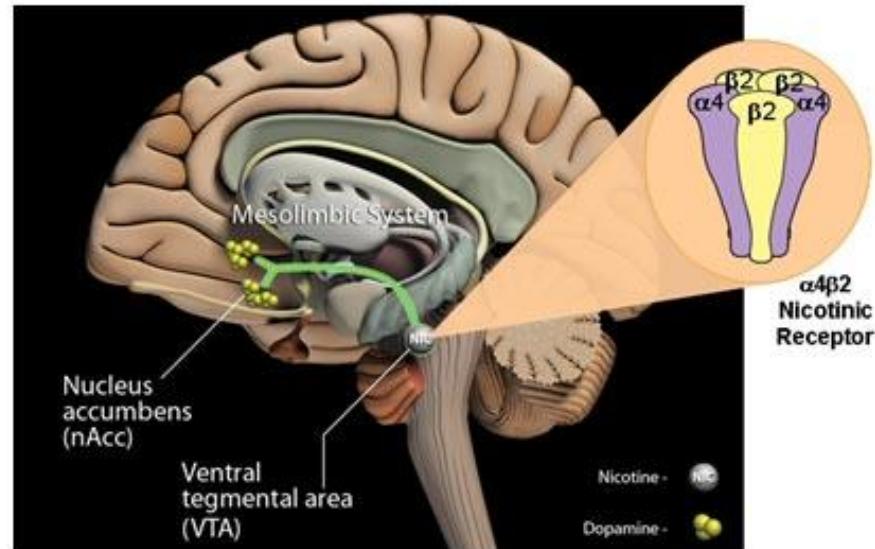
- At a cellular level, nicotine acts on nicotinic acetylcholine receptors, mainly of the $\alpha 4\beta 2$ subtype, to cause neuronal excitation. Its central effects are blocked by receptor antagonists such as mecamylamine.
- At the behavioural level, nicotine produces a mixture of inhibitory and excitatory effects.
- Nicotine shows reinforcing properties, associated with increased activity in the mesolimbic dopaminergic pathway, and self-administration can be elicited in animal studies.
- Electroencephalography changes show an arousal response, and subjects report increased alertness, accompanied by a reduction of anxiety and tension.
- Learning, particularly under stress, is facilitated by nicotine.
- Peripheral effects of nicotine result mainly from ganglionic stimulation: tachycardia, increased blood pressure and reduced gastrointestinal motility. Tolerance develops rapidly to these effects.
- Nicotine is metabolised, mainly in the liver, within 1–2 hours. Its inactive metabolite, cotinine, has a long plasma half-life and can be used as a measure of smoking habits.
- Nicotine gives rise to tolerance, physical dependence and psychological dependence (craving); it is highly addictive. Attempts at long-term cessation succeed in only about 20%.
- Nicotine replacement therapy (chewing gum or skin patch preparations) improves the chances of giving up smoking, but only when combined with active counselling.





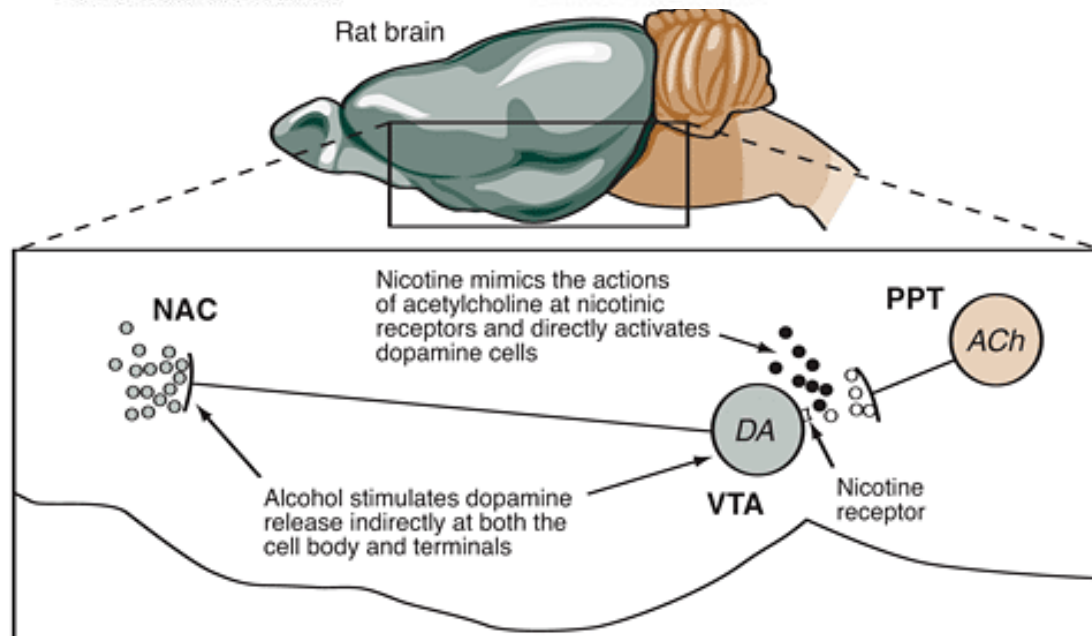
Presynaptic $\alpha 4\beta 2$ Nicotinic Acetylcholine Receptors Increase Glutamate Release and Serotonin Neuron Excitability in the Dorsal Raphe Nucleus

Nicotine effects on limbic areas



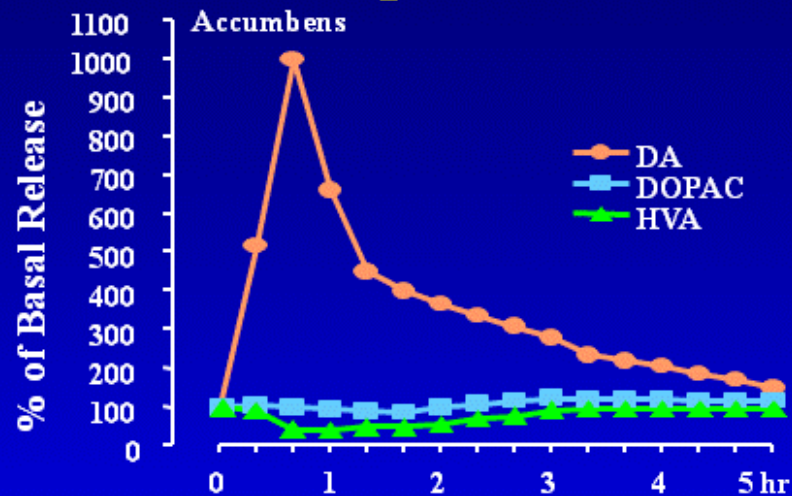
■ Nicotine binds predominantly to nicotinic acetylcholine (nACh) receptors in the CNS; the primary is the $\alpha 4 \beta 2$ nicotinic receptor in the Ventral Tegmental Area (VTA)

■ After nicotine binds to the $\alpha 4 \beta 2$ nicotinic receptor in the VTA, it results in a release of dopamine in the Nucleus Accumbens (nAcc) which is linked to reward

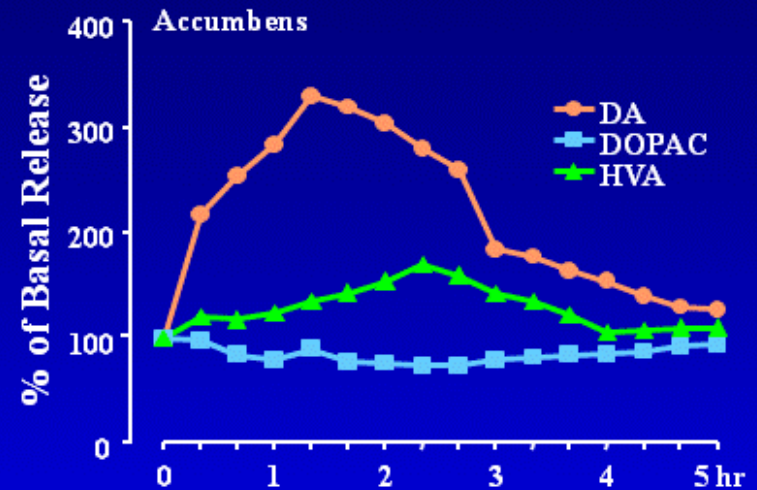


Effects of Drugs on Dopamine Release

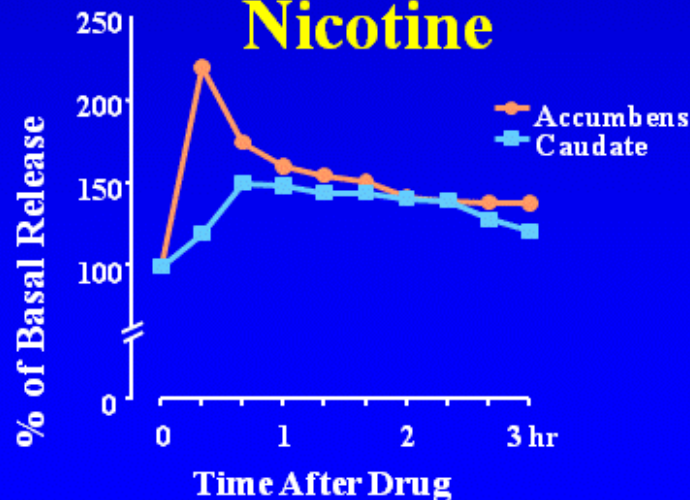
Amphetamine



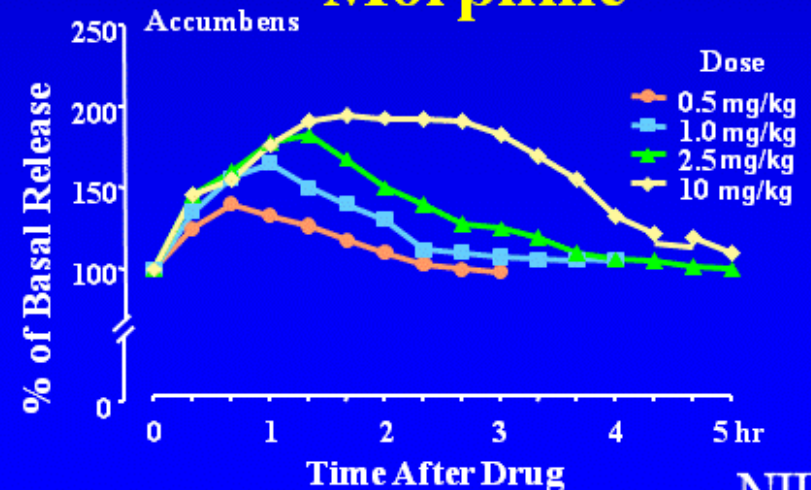
Cocaine



Nicotine



Morphine



Nicotine

One cigarette 6-8 mg nicotine. Lethal acute dose 60 mg

- **Pharmacokinetic**

SNC and all organs

Placenta, maternal milk

Metabolism in lung, liver, excretion in urine

Tolerance

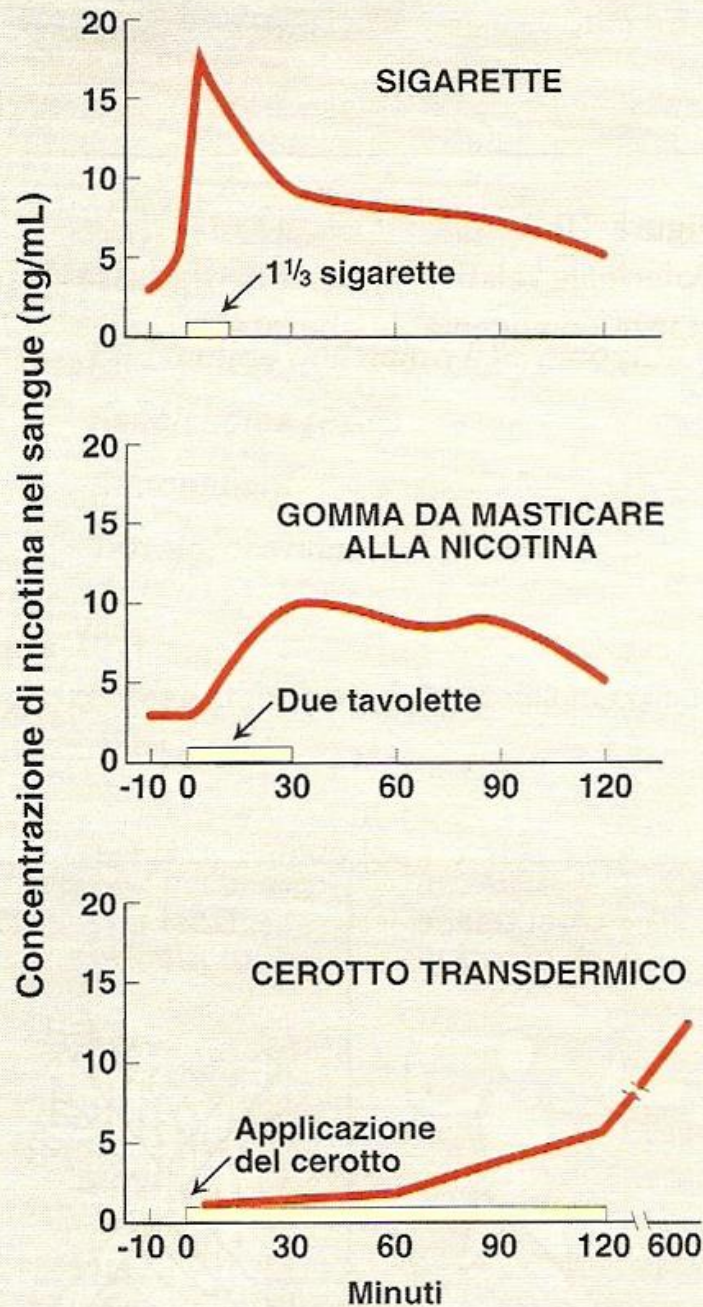
- **Side Effects**

Irritability, tremor

Increase in heart rate and blood pressure, intestinal contractions, diarrhea

Induction of CYP 450, increase in drug metabolism

Withdrawal syndrome: irritability, anxiety, agitation, difficulty in concentration, cephalgia, insomnia



**Plasmatic concentration of nicotine
after different supports
against withdrawal**

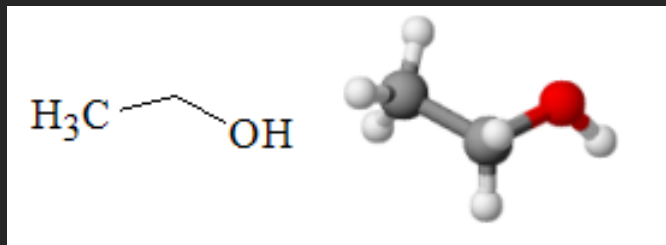
Bupropione (DAT)

■ Criteri diagnostici per F17.3 Astinenza da Nicotina [292.0]

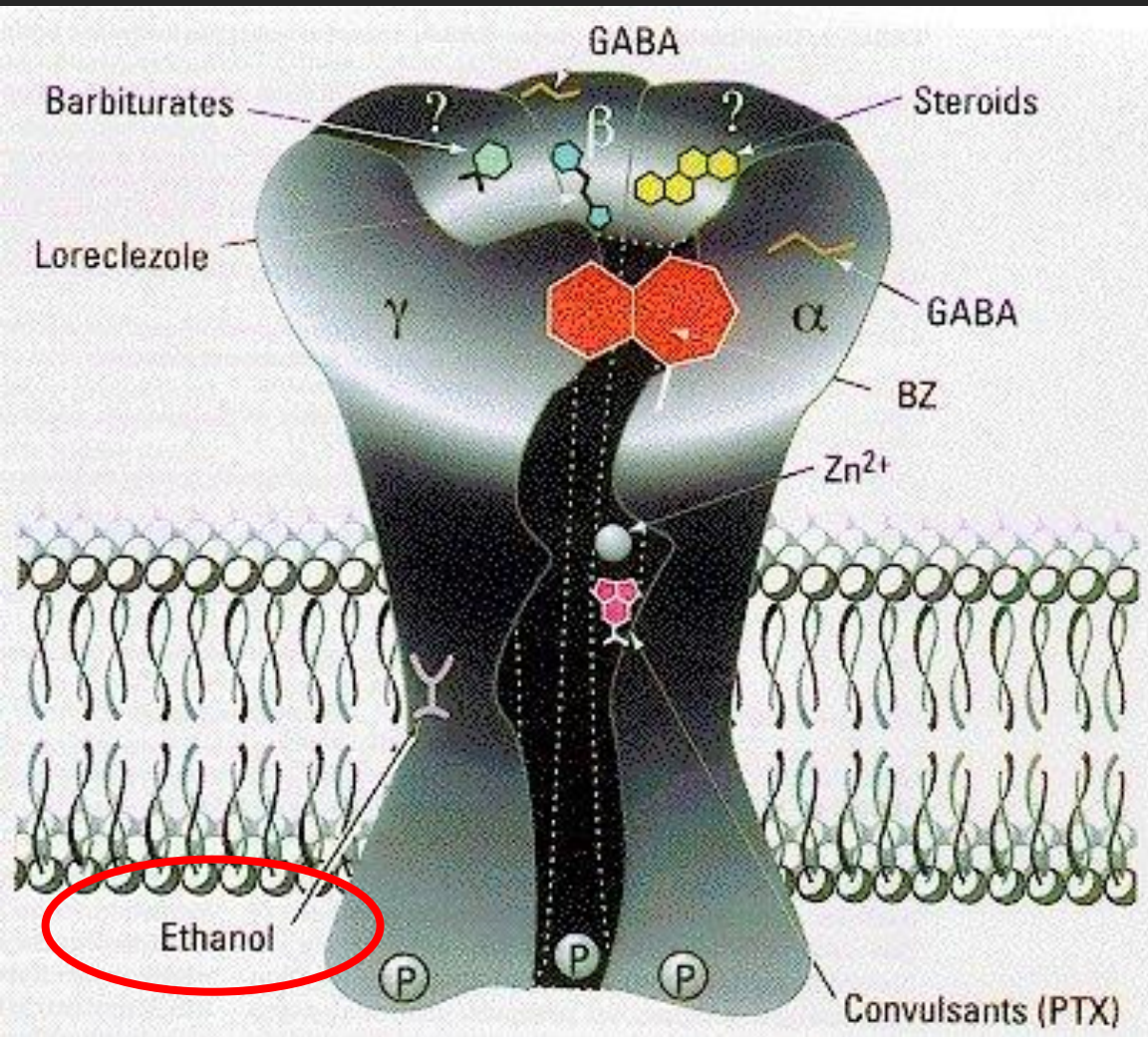
- A. Uso giornaliero di nicotina per almeno alcune settimane.
- B. Brusca cessazione dell'uso di nicotina, o riduzione della quantità di nicotina usata, seguita entro 24 ore da quattro (o più) dei segni seguenti:
 - 1) umore disforico o depresso
 - 2) insonnia
 - 3) irritabilità, frustrazione o rabbia
 - 4) ansia
 - 5) difficoltà di concentrazione
 - 6) irrequietezza
 - 7) diminuzione della frequenza cardiaca
 - 8) aumento dell'appetito o del peso.

- C. I sintomi del Criterio B provocano disagio clinicamente significativo o menomazione del funzionamento sociale, lavorativo o di altre aree importanti.
- D. I sintomi non sono dovuti a una condizione medica generale, e non sono meglio spiegati con un altro disturbo mentale.

Ethanol



GABA



Receptors

↓ **NMDA & KA**

↑ ↓ **Nicotinic**

↑ **5-HT₃**

↑ **Ca⁺ activated K channel**

↓ **oxytocin, vasopressin**

Ethanol



Three wine glasses: 60-90 mg / dl
Motor slowing down: 20-30 mg / dl
Intoxication: 150 mg / dl
A glass: metabolized in 60-90 min
Men-women

Ethanol

alcohol
dehydrogenase (ADH)

Acetaldehyde

~~aldehyde
dehydrogenase
(ADH)~~

disulfiram

migraine, vomiting,
sweating, confusion,
tachycardia

Effects of low and high doses of ethanol

Acute EFFECTS

Anxiolytics, sedatives (low doses)
Disinhibition, violent behavior
Motor incoordination

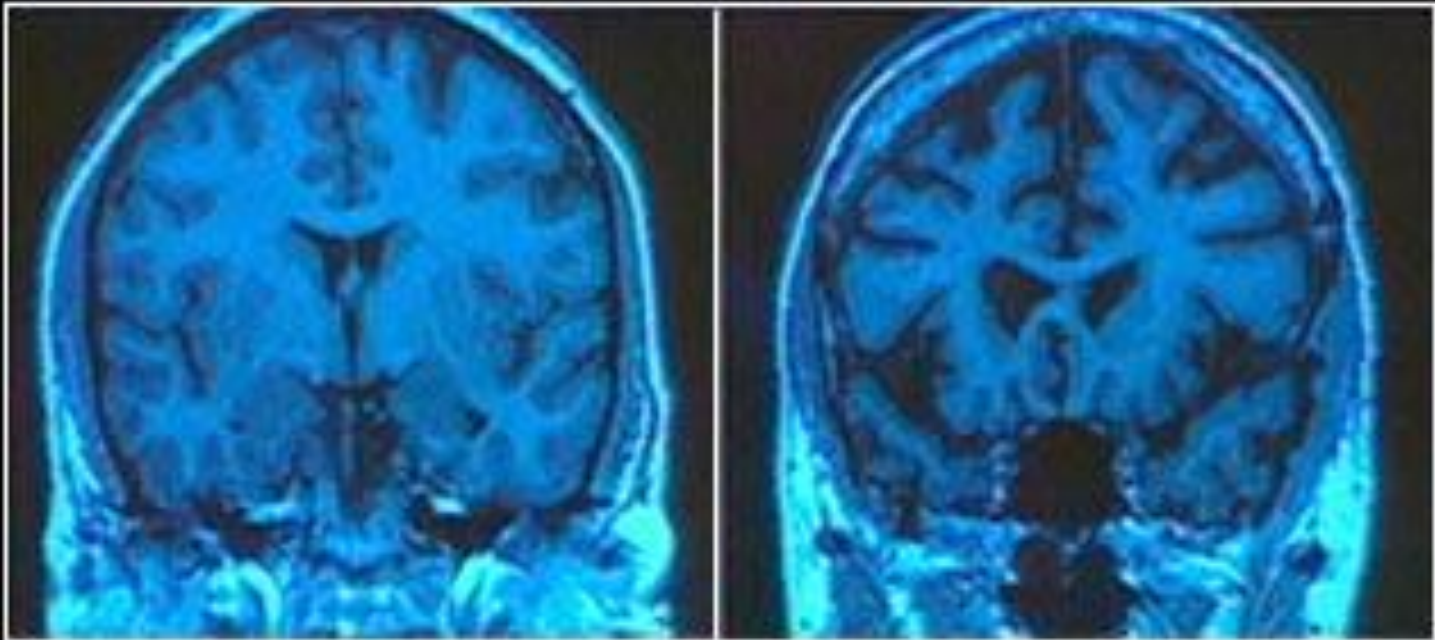
Long term EFFECTS

Tolerance
Addiction
Compulsive alcohol research
Cognitive deficits, dementia, delirium tremens
Interference with other drugs
Gastritis (destroys mucosa), cirrhosis, teratogenesis

Alcohol withdrawal: benzodiazepines, carbamazepine

*Alcohol dependence: disulfiram, acamprosate (GABA & NMDA), ondansetron (5HT3 ant.)
gamma-hydroxy-butyrate (GHB)*

Ethanol Neurotoxicity



Normal
43-year-old

Alcoholic
43-year-old

Substances that interact with alcohol

Sedatives: GHB, roipnol (flunitrazepam), ketamine

Marijuana: decreases motor control, mental concentration (driving) and inhibits swallowing reflex

Opiates: inhibition of brain function and respiratory reflex

Prescription or over-the-counter medications: anxiolytics, hypnotics, antihistamines, antidepressants

Aspirin (↑ bioavailability ↓ ADH)

Criteria diagnostici per F10.00 Intossicazione Alcoolica [303.00]

- A. Recente ingestione di alcool.
- B. Comportamento maladattivo clinicamente significativo o modificazioni psicologiche (per es., comportamento sessuale o aggressivo inappropriato, labilità d'umore, deficit delle capacità critiche, compromissione del funzionamento sociale o lavorativo) che si sviluppano durante, o poco dopo, l'ingestione alcoolica.
- C. Uno (o più) dei segni seguenti, che si sviluppano durante, o poco dopo, l'assunzione di alcool:
 - 1) pronuncia indistinta
 - 2) incoordinazione
 - 3) marcia instabile
 - 4) nistagmo
 - 5) deficit di attenzione o di memoria
 - 6) stupor o coma.
- D. I sintomi non sono dovuti a una condizione medica generale, e non possono essere meglio spiegati con un altro disturbo mentale.

**STIMOLANTI
DEL SNC**

Caffeina

Nicotina

Cocaina

Amfetamina

ALLUCINOGENI

LSD

Cannabis

Fenciclidina

**DEPRIMENTI
DEL SNC**

Etanolo

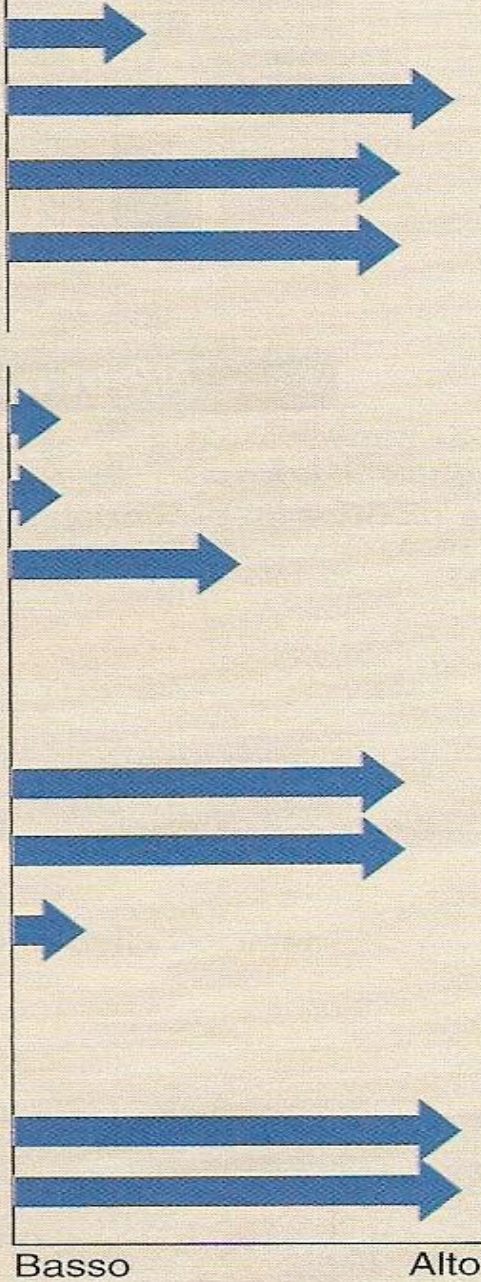
Barbiturici

Benzodiazepine

**OPPIACEI
STUPEFACENTI**

Morfina

Eroina



Dependency potential

