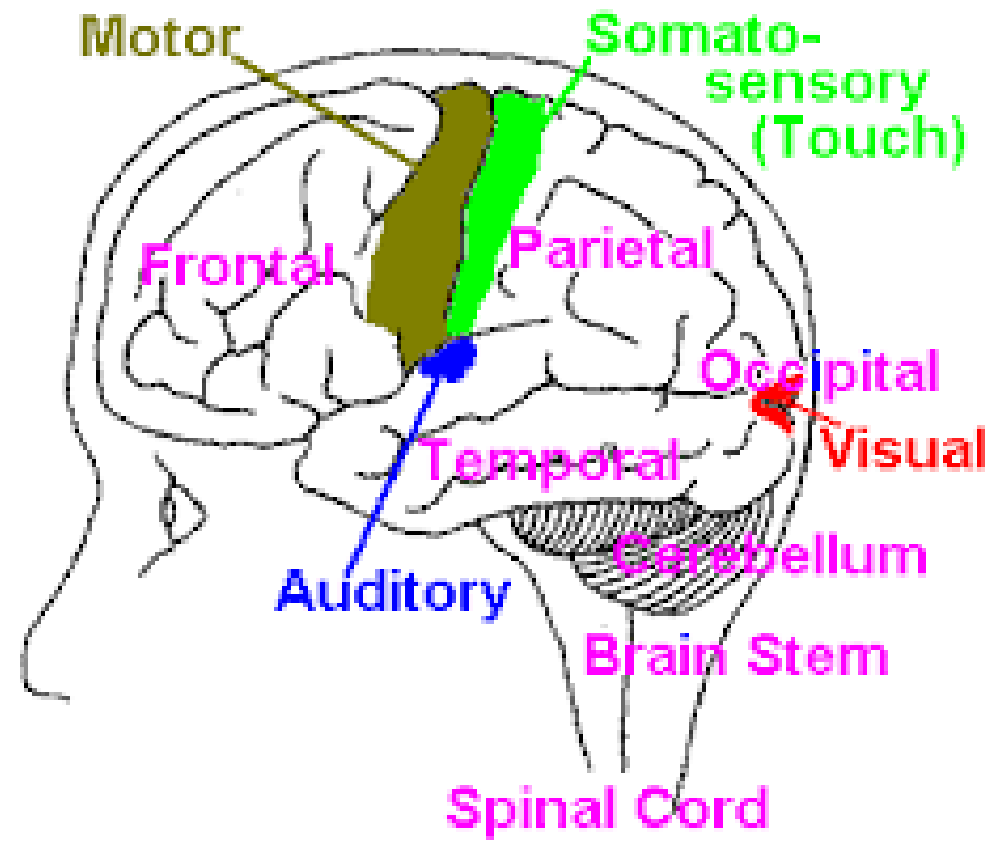
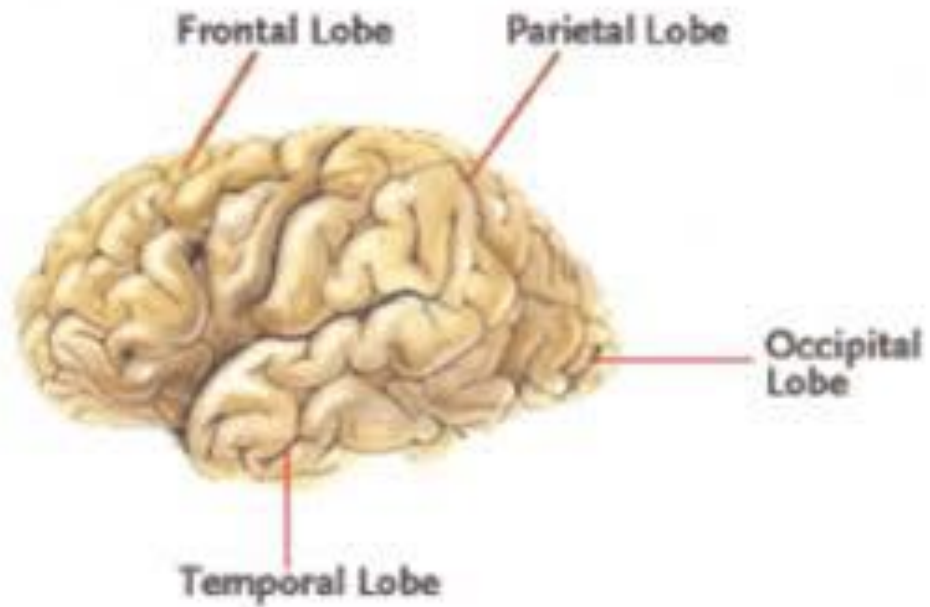
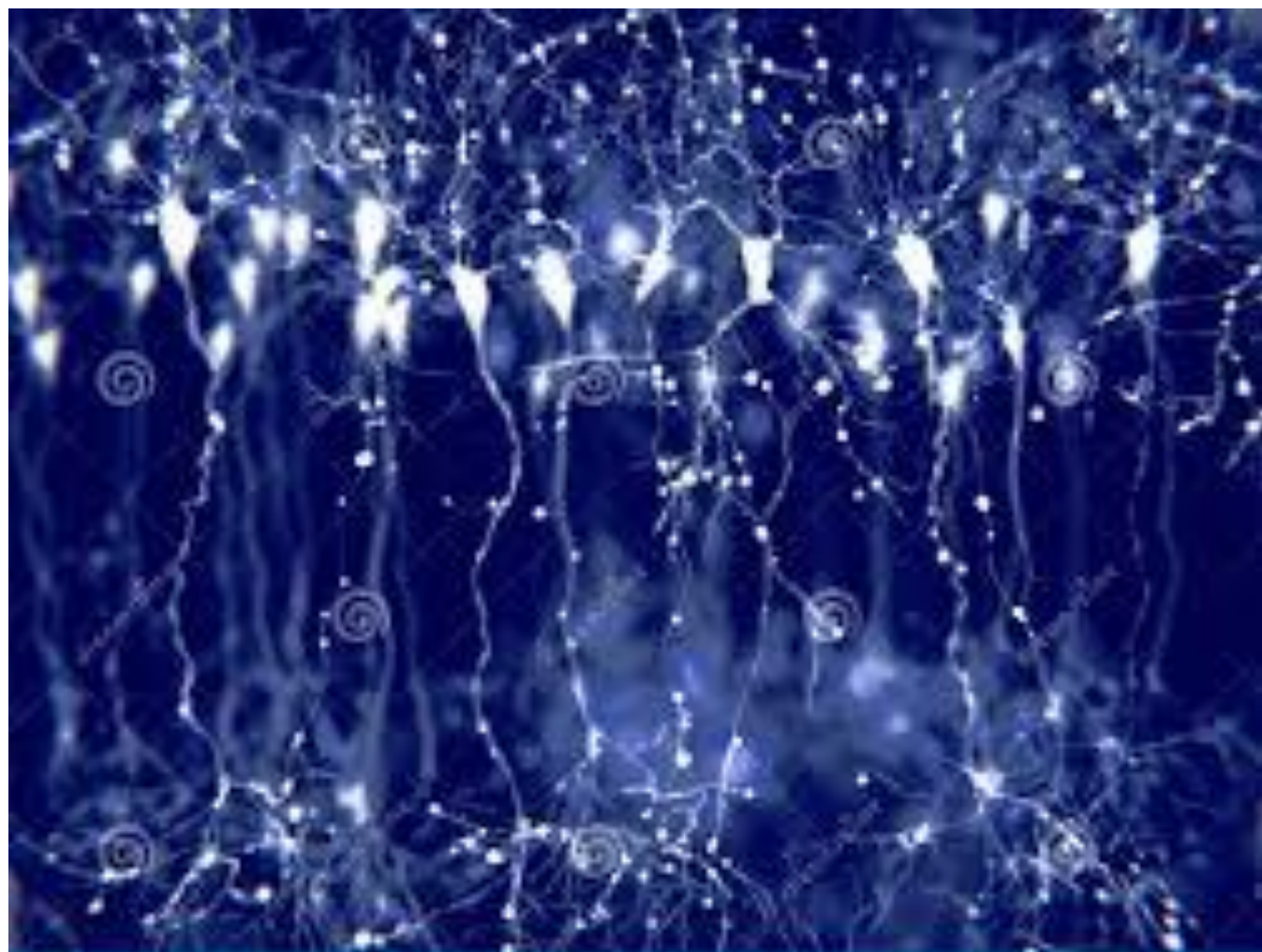
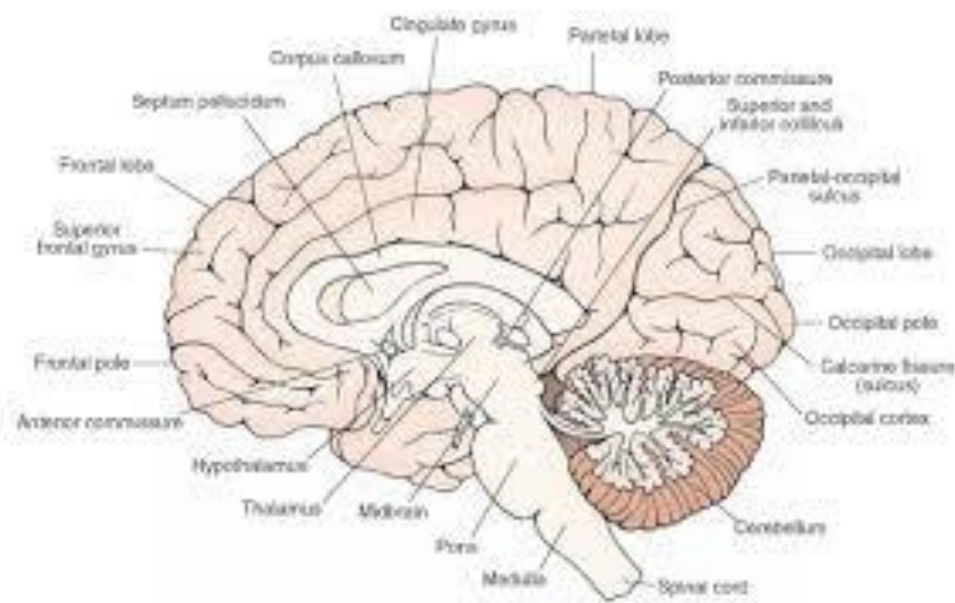


Some information on CNS  
for  
PharmacoEpigenomics







## Functional Areas of Cerebral Cortex 1

- Anatomically the cortex is divided into 6 lobes: frontal, parietal, temporal, occipital, limbic and insular
- Each lobe has several gyri
- Functionally the cortex is divided into numbered areas first proposed by Brodman in 1909
- Brodmann's areas were described based on cytoarchitecture; later they were found to be functionally significant



## Functional Areas of the Cerebral Cortex

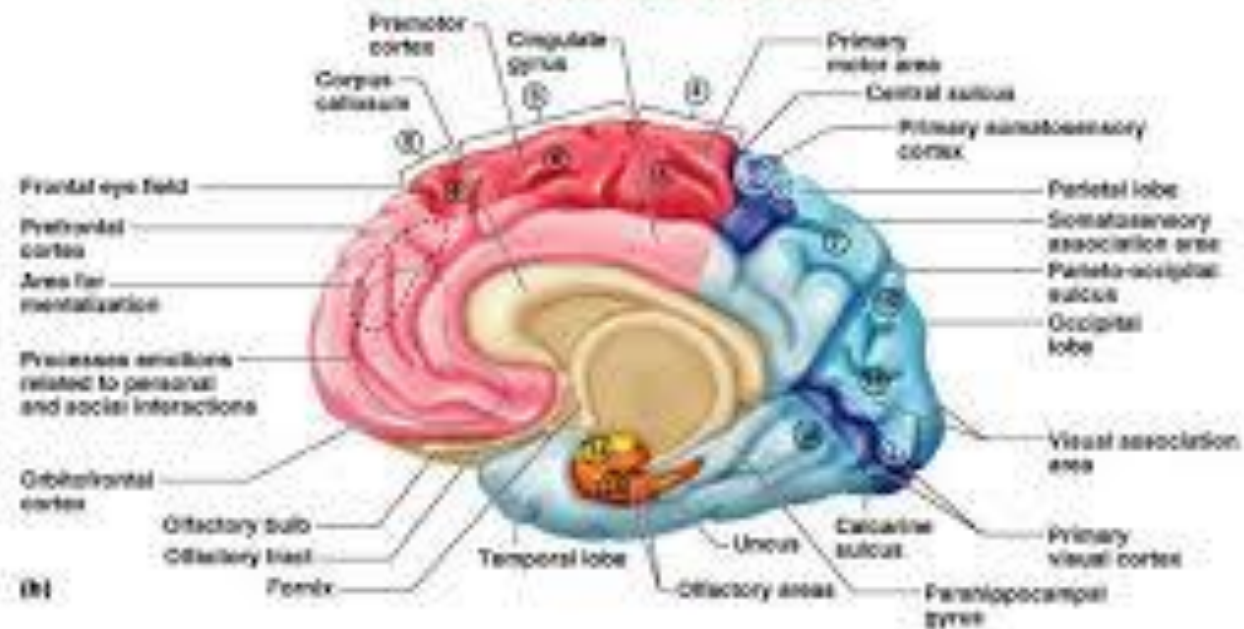
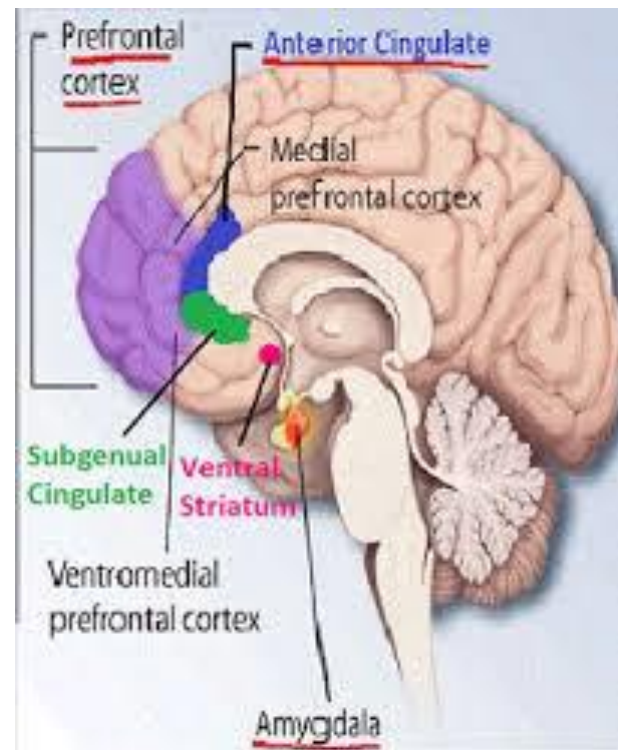
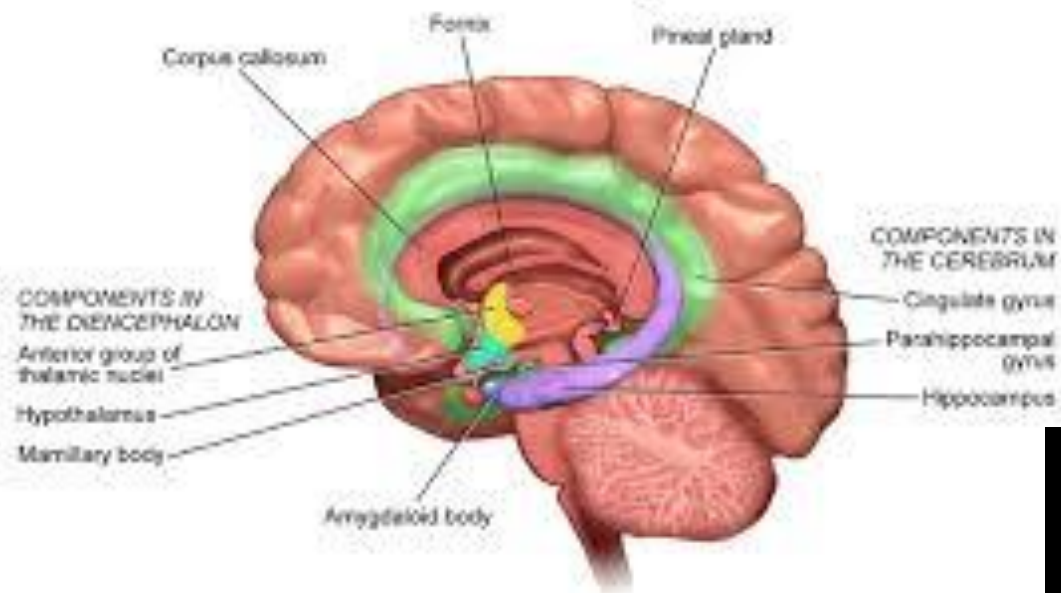
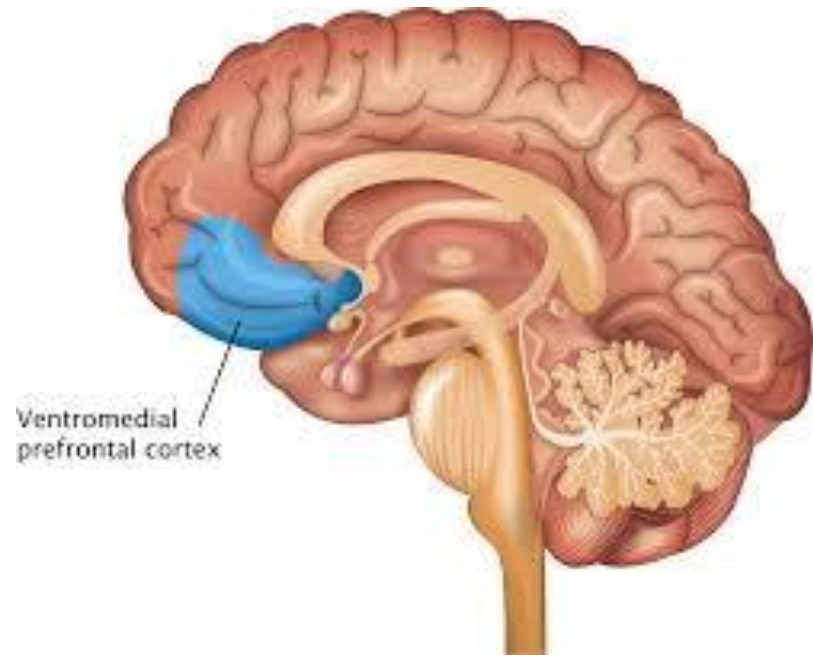


Figure 12.36

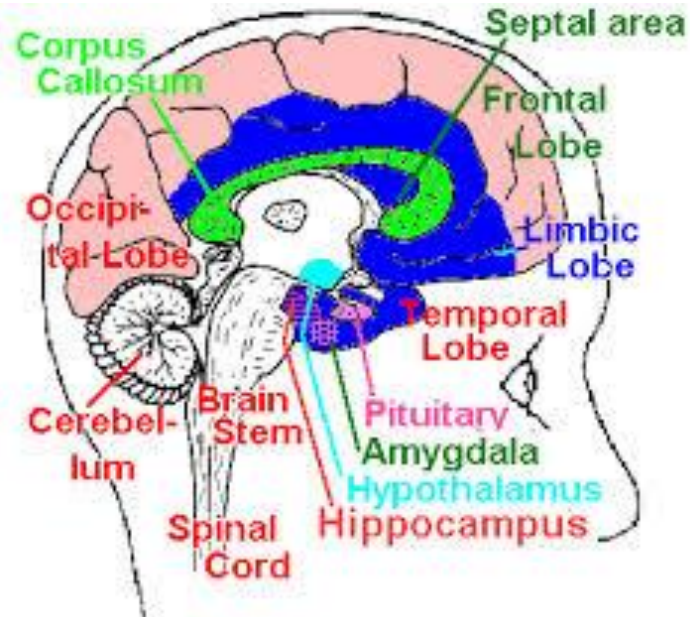
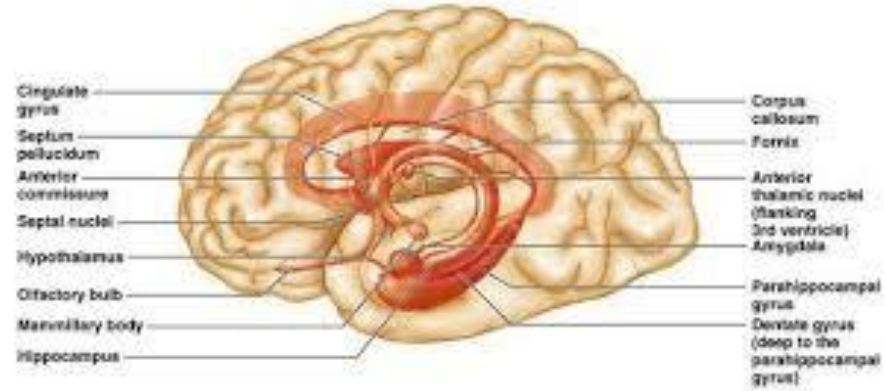


# The Limbic System





## THE LIMBIC SYSTEM



# Sistema limbico

corpo caloso

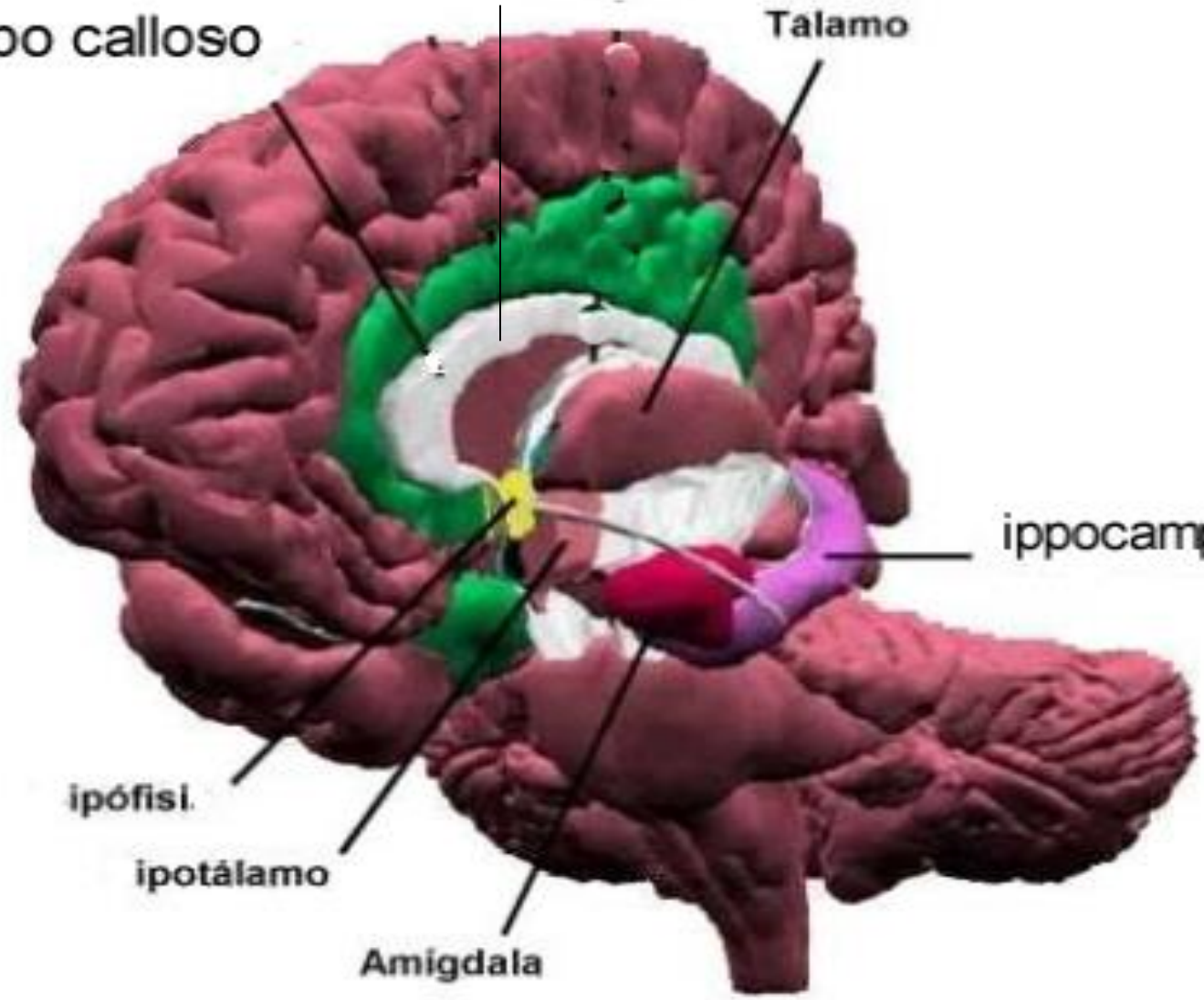
Talamo

ippocampo

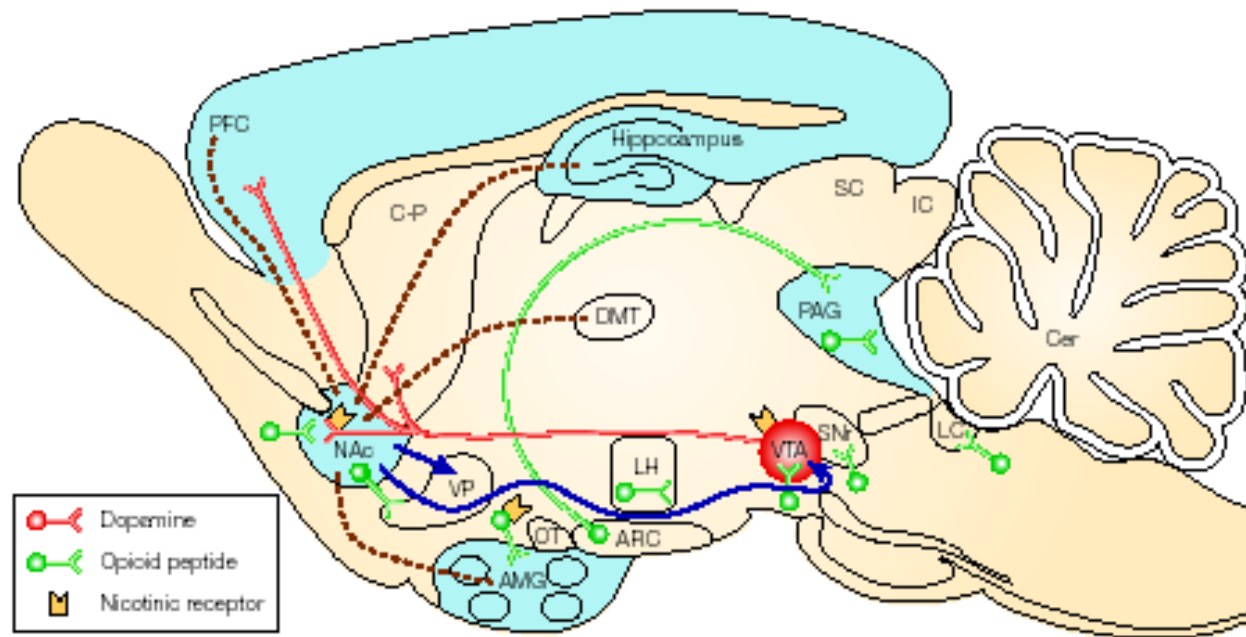
ipófisi.

ipotalamo

Amígdala

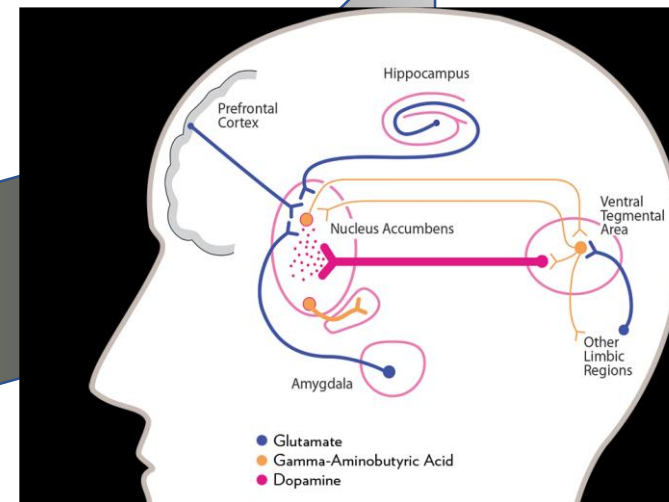
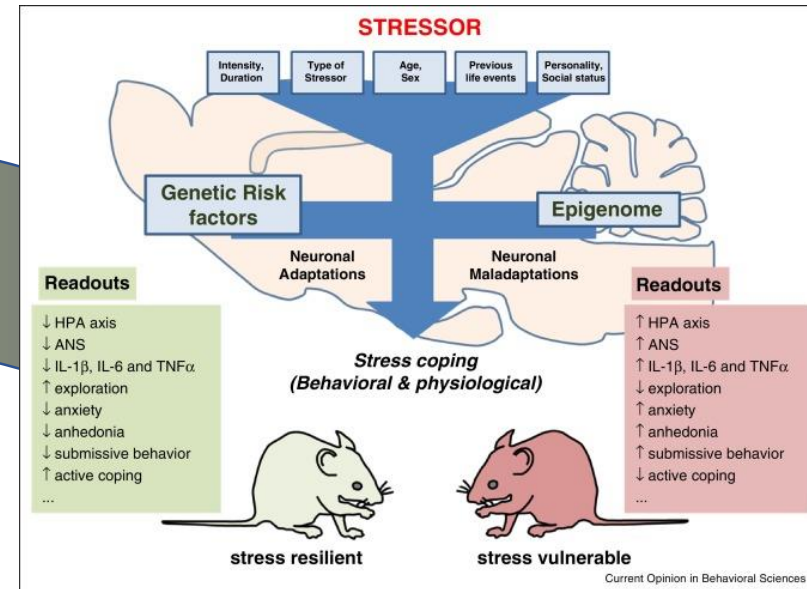
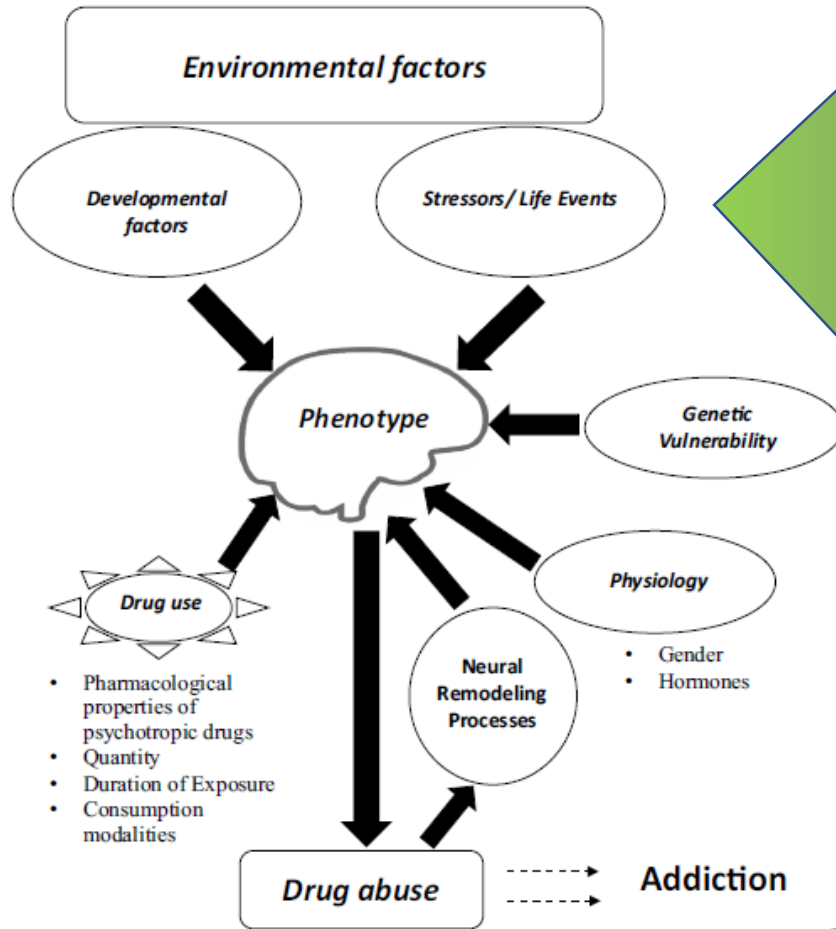




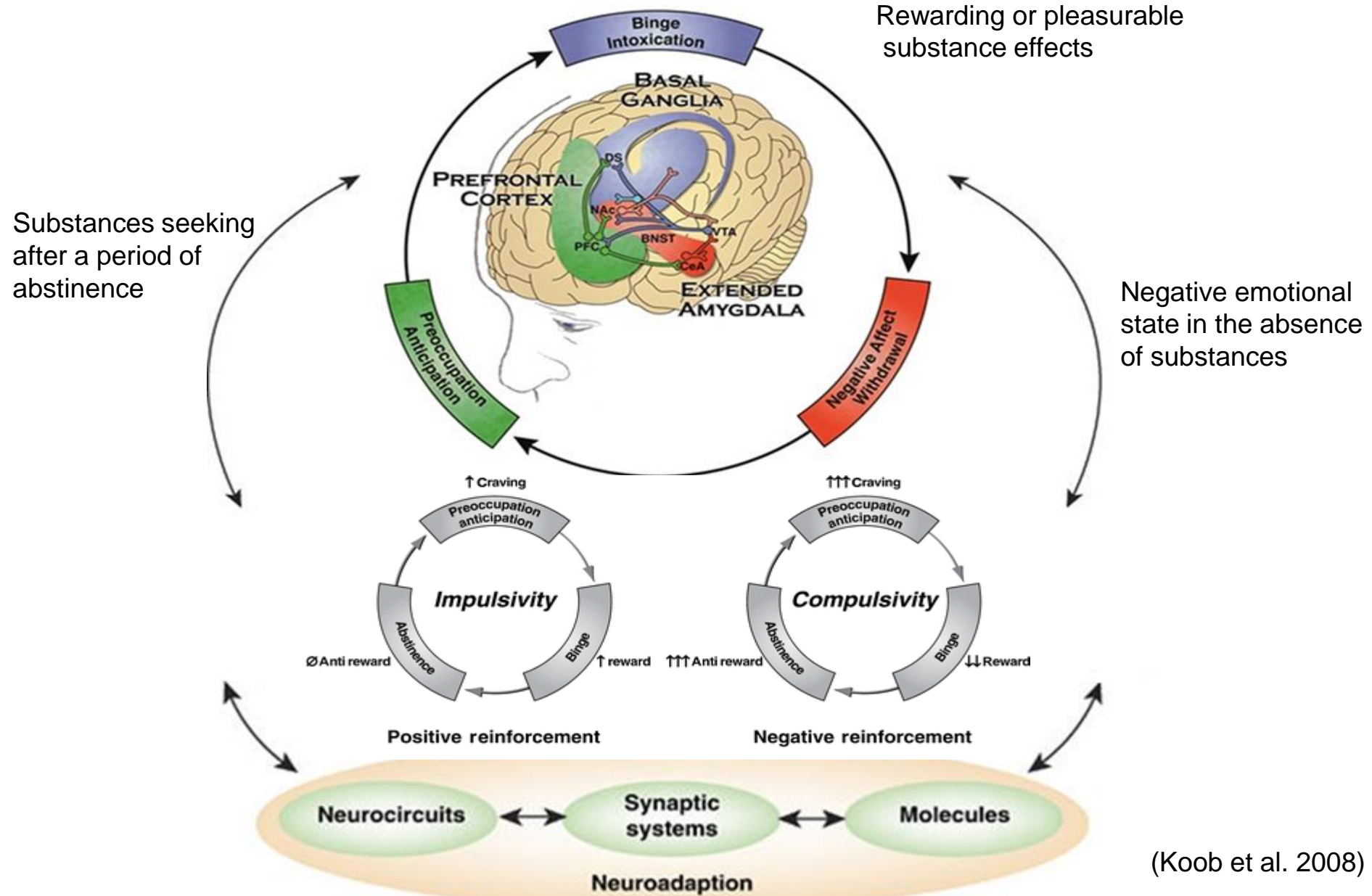


da: Nestler EJ, Nature Rev. Neurosci.,  
2, 119-128, 2001

# Environmental factor and Drug addiction



# Drug addiction defined as a **THREE-STAGE** **CYCLE**



(Koob et al. 2008)

# Factors Contributing to Vulnerability To Develop a Specific Addiction

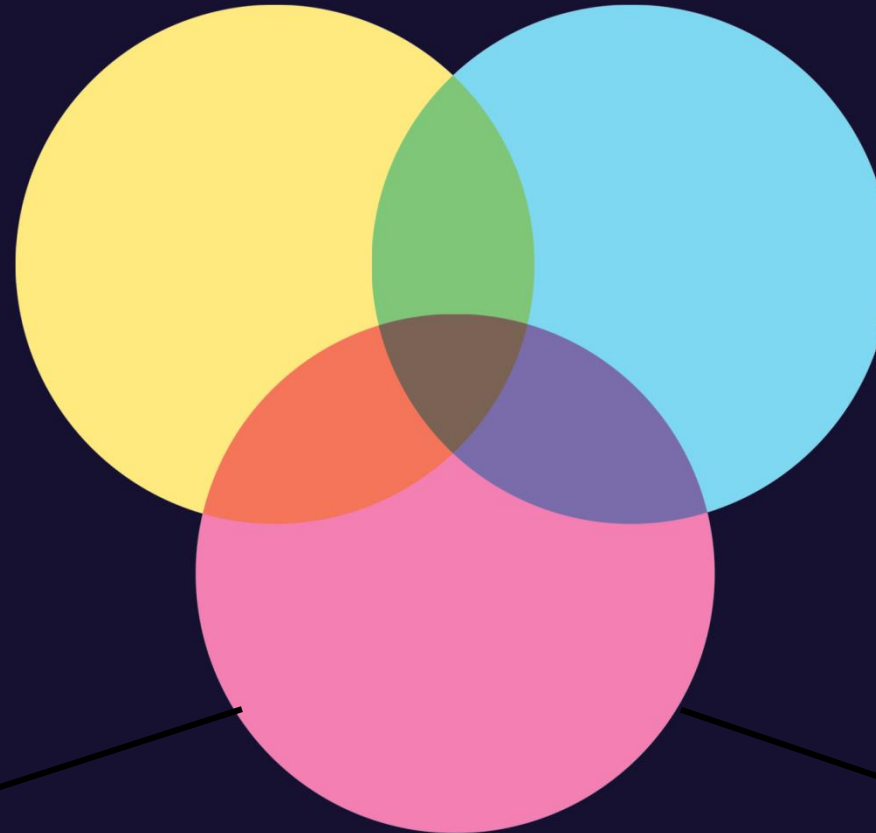
**Use of the drug of abuse essential (100%)**

## **Genetic (25-60%)**

- DNA
- SNPs
- other polymorphisms

## **Environmental (very high)**

- prenatal
- postnatal
- contemporary
- cues
- comorbidity
- stress-responsivity



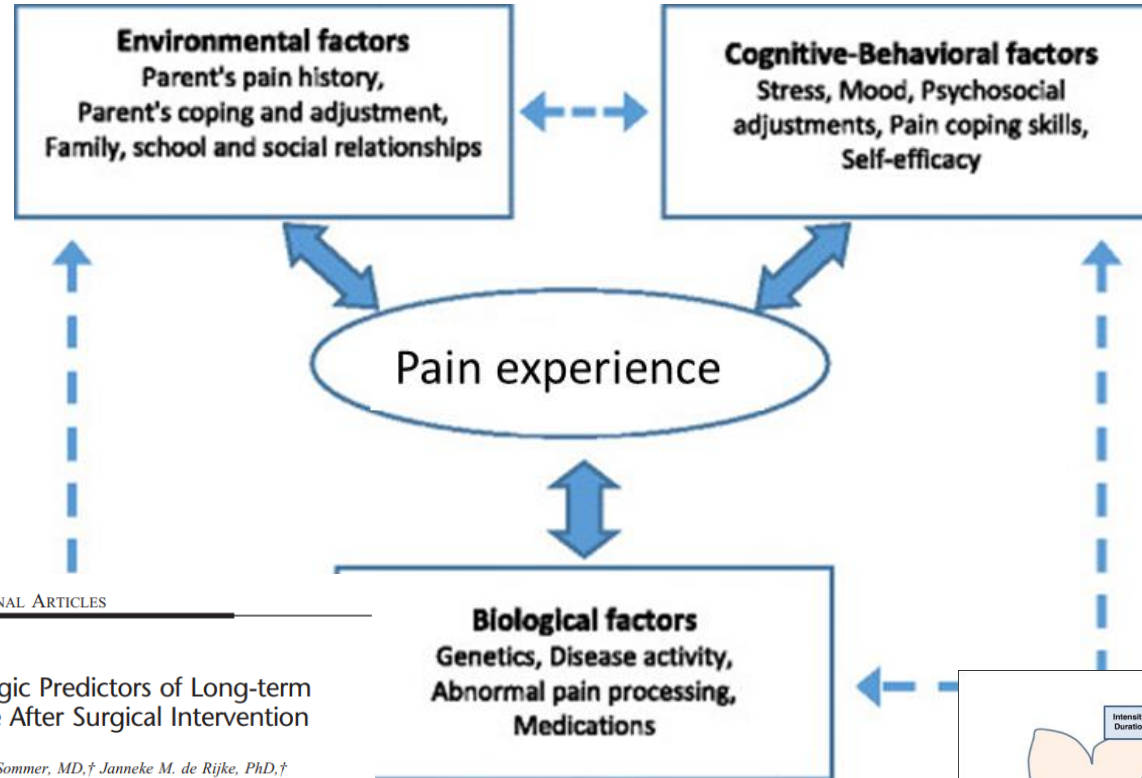
- mRNA levels
- peptides
- proteomics

## **Drug-Induced Effects (very high)**

- neurochemistry
- synaptogenesis
- behaviors

# Environmental factor and neuropathic pain

## ❖ Genes, environment and brain circuitry in neuropathic pain??



ORIGINAL ARTICLES

### Somatic and Psychologic Predictors of Long-term Unfavorable Outcome After Surgical Intervention

Madelon L. Peters, PhD,\* Micha Sommer, MD,† Janneke M. de Rijke, PhD,‡  
 Fons Kessels, MD, MSc,‡ Erik Heineman, MD, PhD,§ Jacob Patijn, MD, PhD,†  
 Marco A. E. Marcus, MD, PhD,† Johan W. S. Vlaeyen, PhD,\* and Maarten van Kleef, MD, PhD†

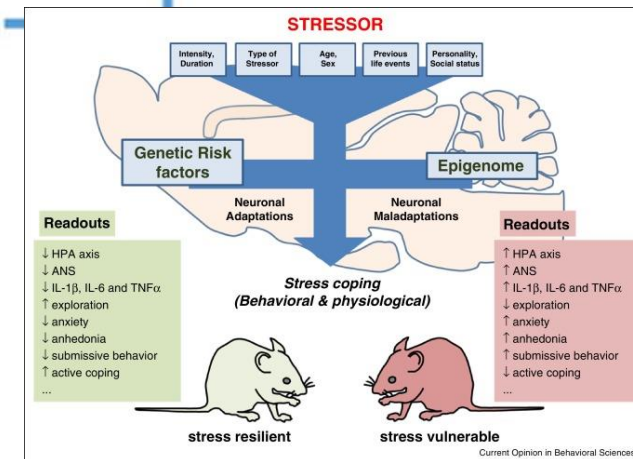


Review

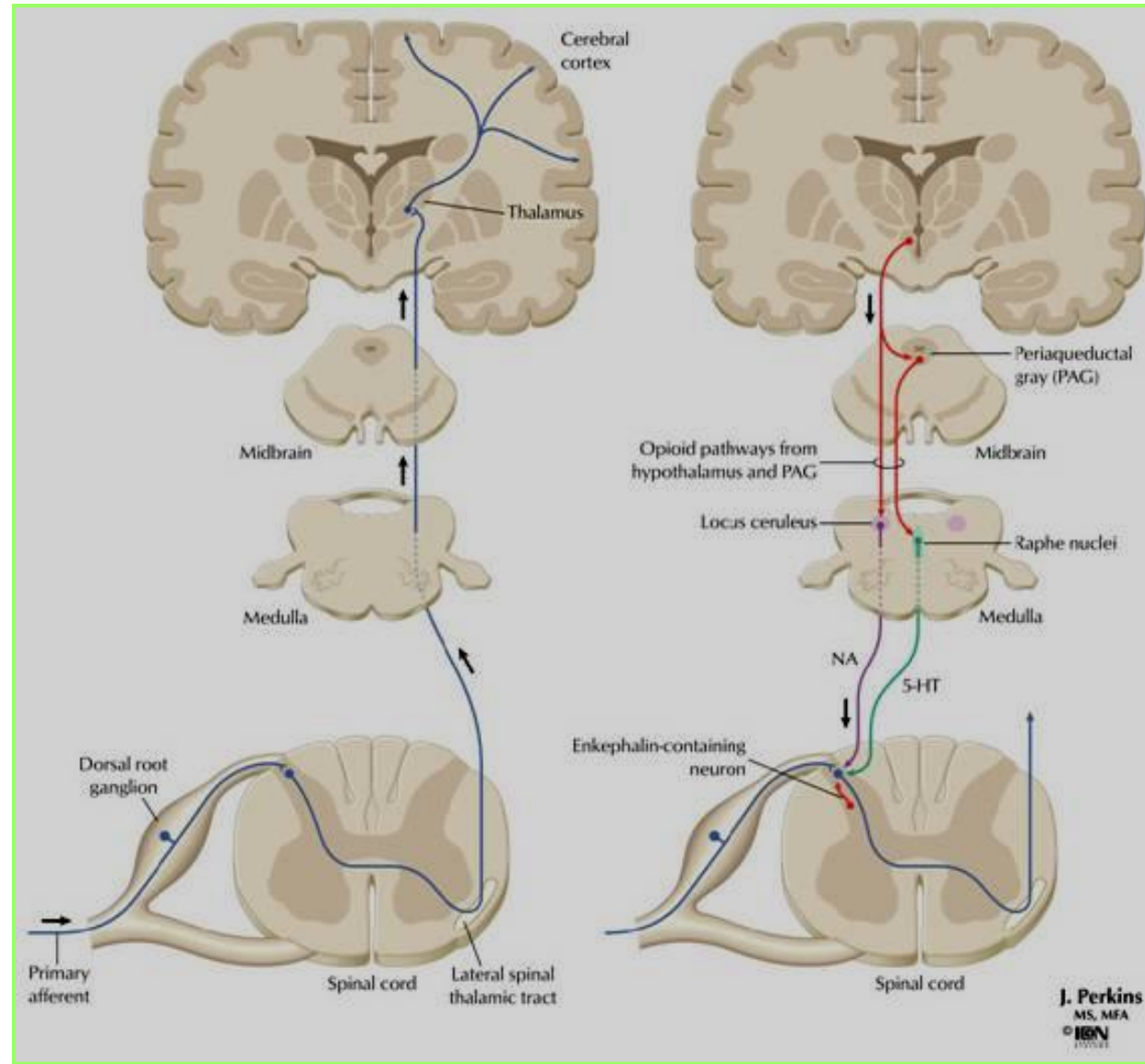
### Psychosocial predictors and correlates for chronic post-surgical pain (CPSP) – A systematic review

Anke Hinrichs-Rocker<sup>a</sup>, Kerstin Schulz<sup>a</sup>, Imke Järvinen<sup>a</sup>, Rolf Lefering<sup>a</sup>,  
 Christian Simanski<sup>b</sup>, Edmund A.M. Neugebauer<sup>a,b</sup>

<sup>a</sup>Institute for Research in Operative Medicine, Faculty of Medicine, Chair for Surgical Research, University of Witten/Herdecke, Ostmerheimer Strasse 200, 51109 Cologne, Germany  
<sup>b</sup>Department of Trauma and Orthopaedic Surgery Cologne-Merheim, Faculty of Medicine, University of Witten/Herdecke, Cologne, Germany



# Meccanismi di Analgesia centrale



Sistemi neuronali ascendenti e discendenti

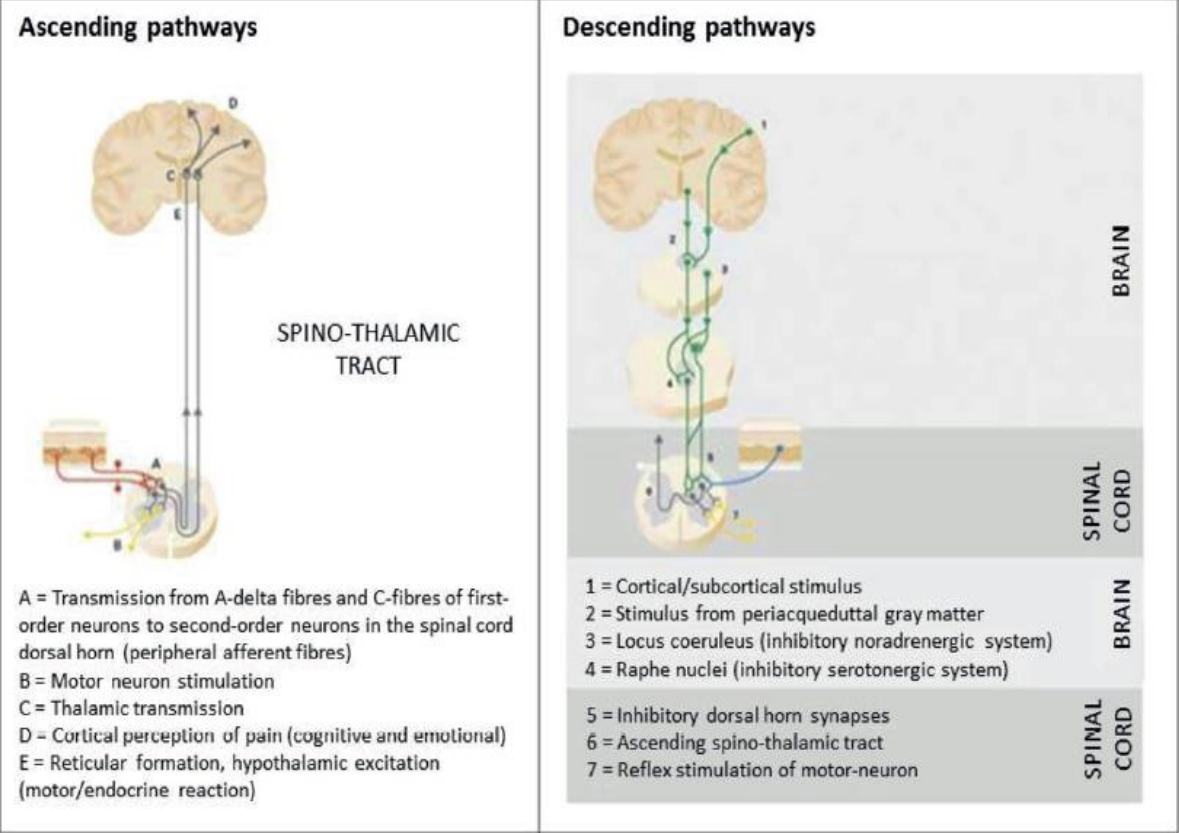
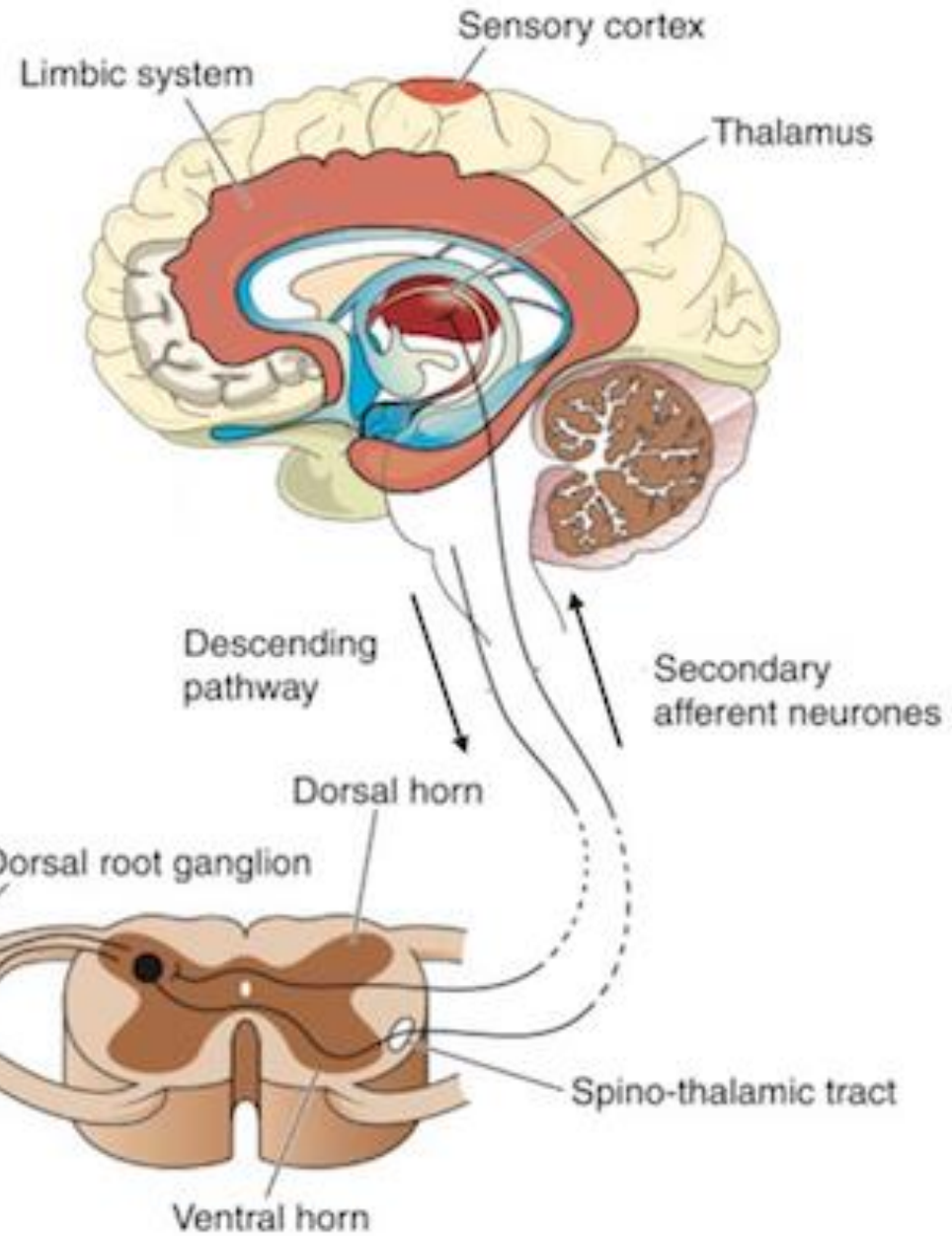
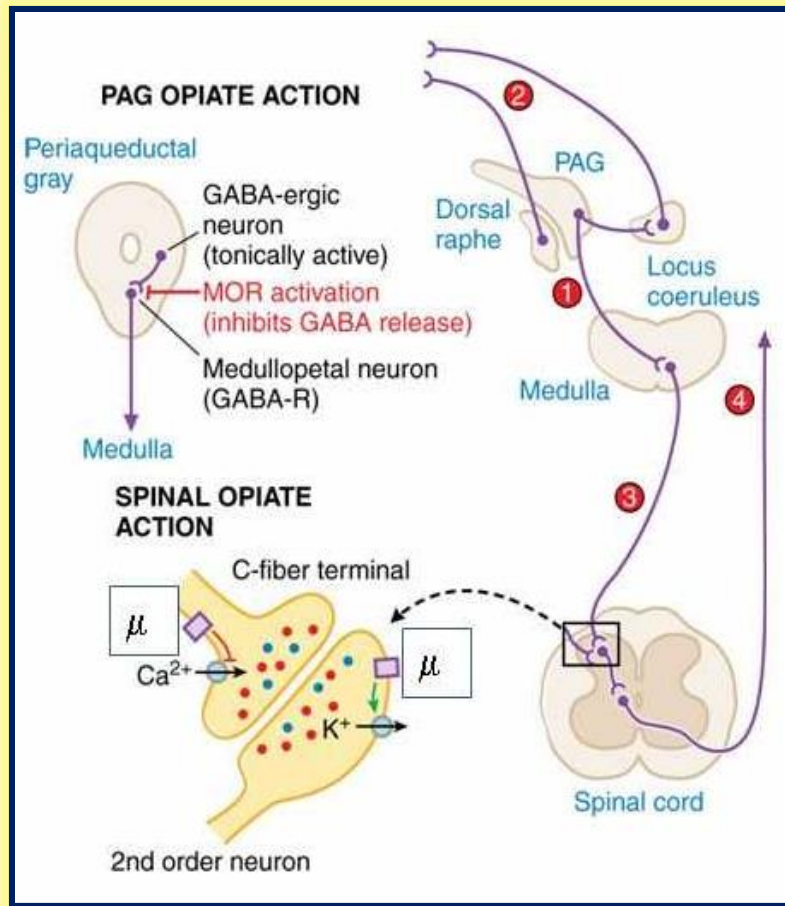


Figure 1. Ascending and descending pathways involved in pain transmission and modulation (modified from<sup>3</sup>).

# How Pain Works

©2007 HowStuffWorks

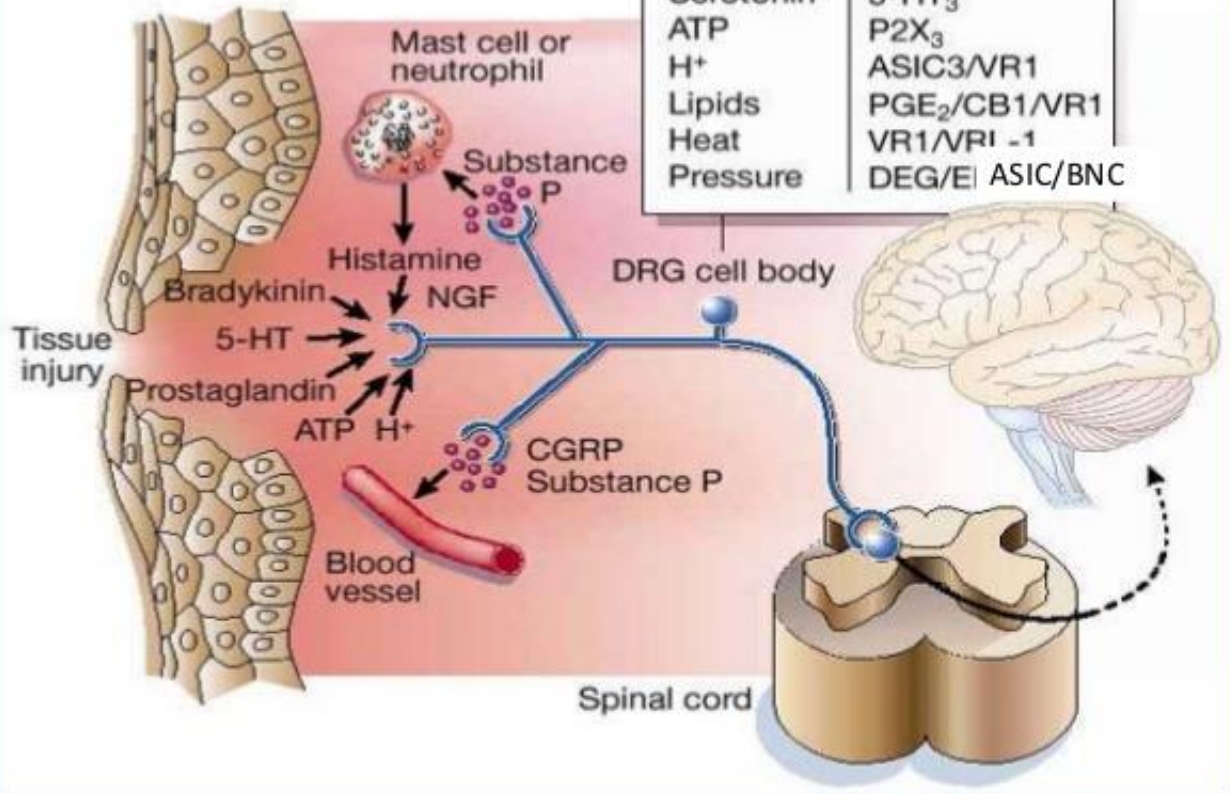


Primary afferent neurones (A $\delta$  and C fibres)

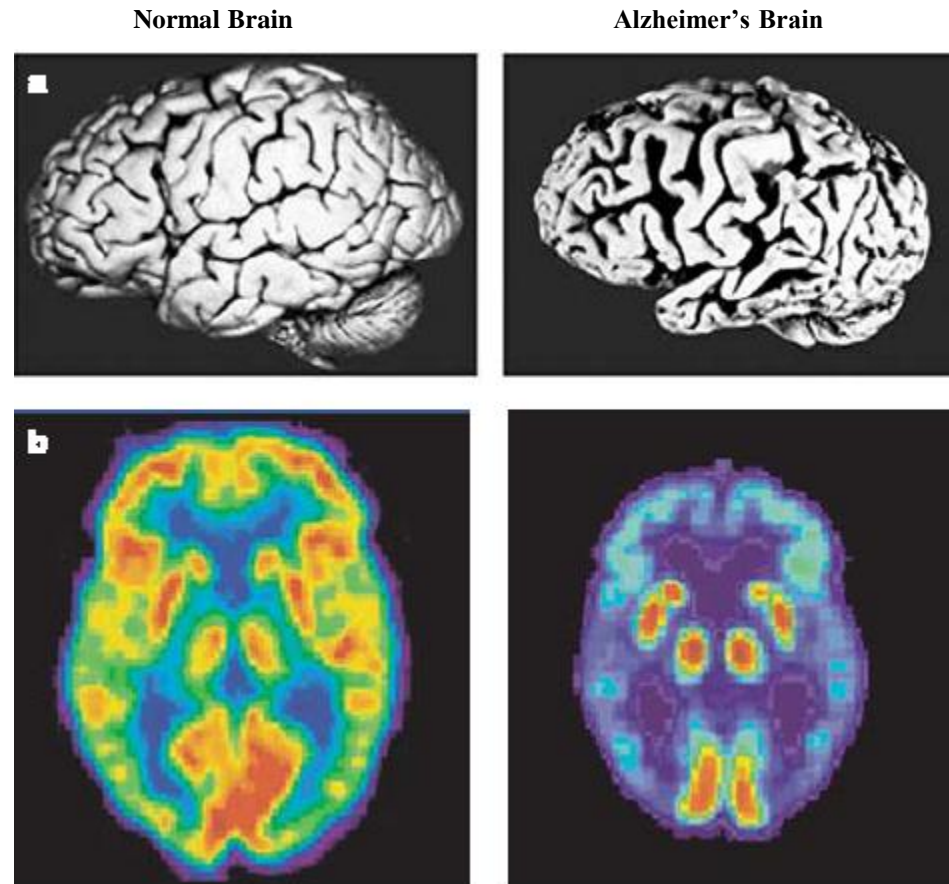


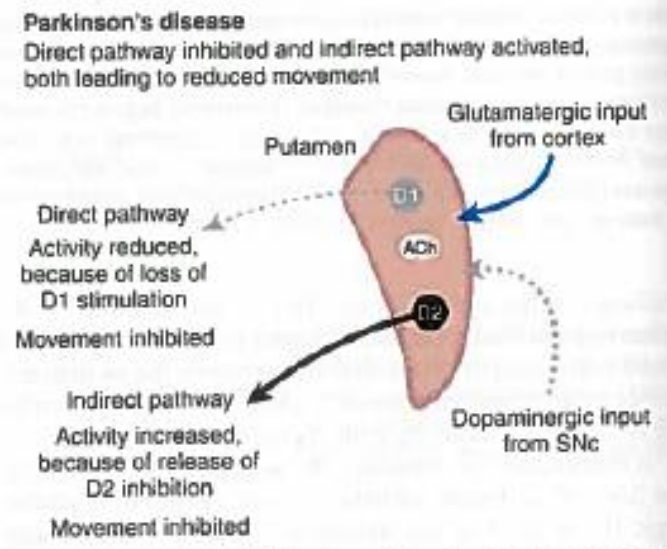
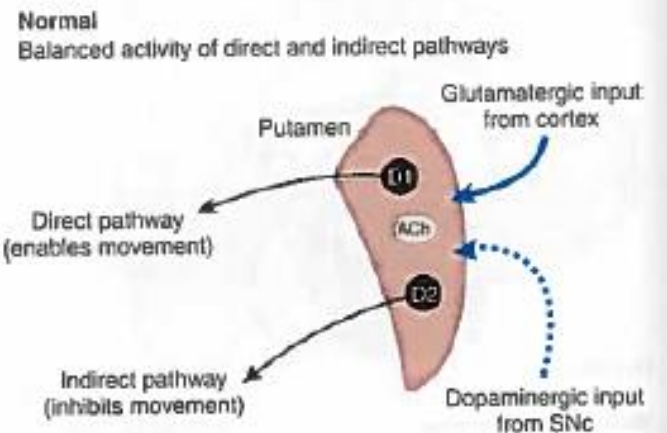
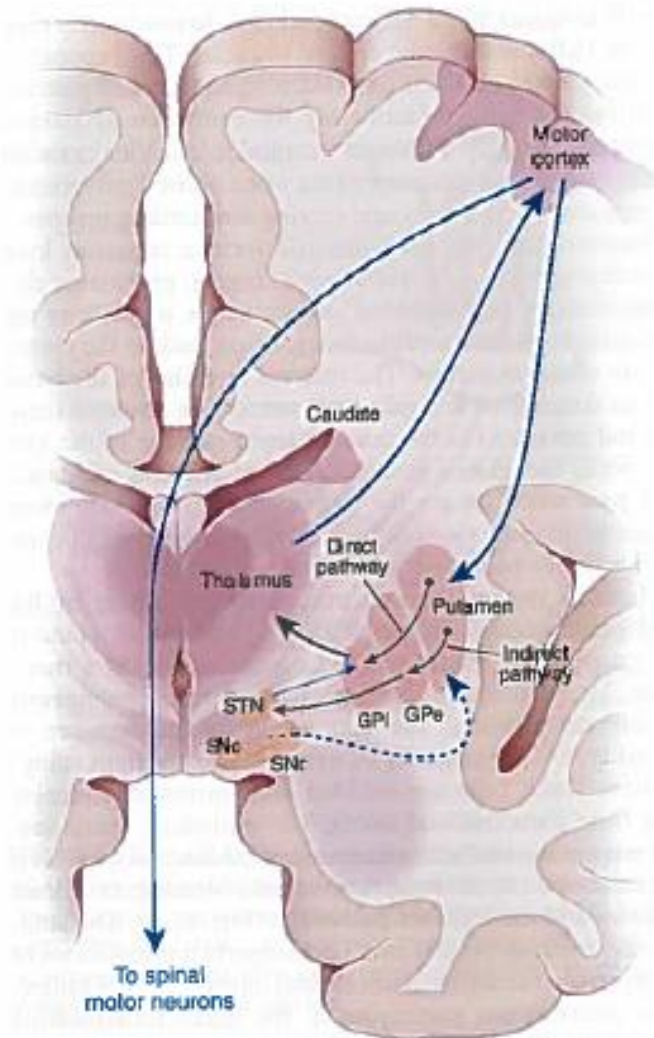
# 1. Peripheral sensitization

Stimulus	Representative receptor
NGF	TrkA
Bradykinin	BK <sub>2</sub>
Serotonin	5-HT <sub>3</sub>
ATP	P2X <sub>3</sub>
H <sup>+</sup>	ASIC3/VR1
Lipids	PGE <sub>2</sub> /CB1/VR1
Heat	VR1/VR1 -1
Pressure	DEG/E ASIC/BNC



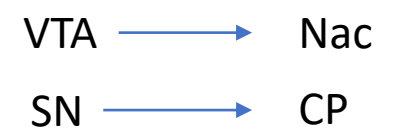
Neurodegenerative diseases as Alzheimer (AD) are characterized by a decrease of the size of specific cortical brain areas.





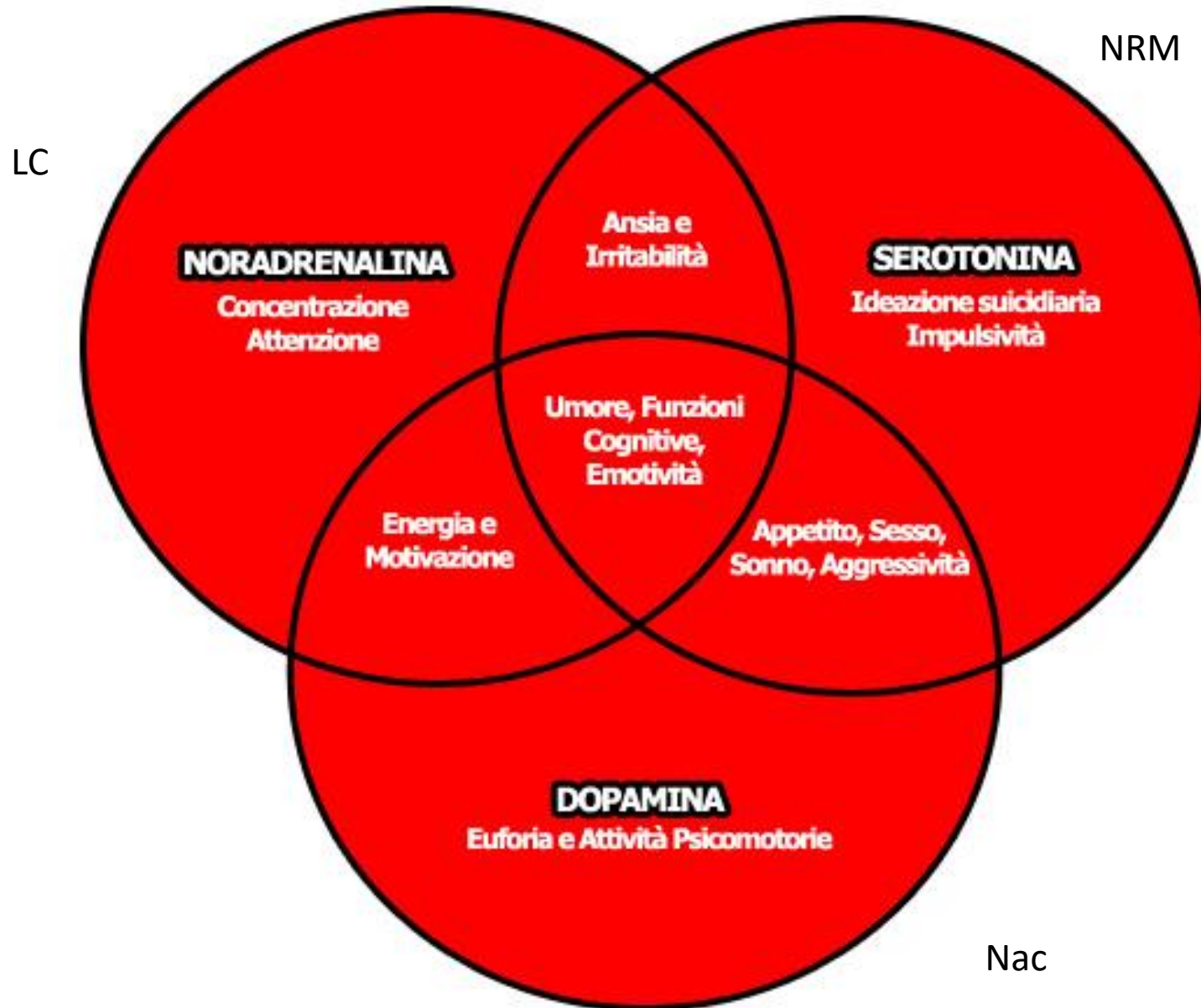
**FIGURE 13-7.** Effect of Parkinson's disease on dopaminergic pathways that regulate movement. Two principal pathways in the basal ganglia regulate movement: the indirect pathway, which inhibits movement, and the direct pathway, which enables movement. Dopamine inhibits the indirect pathway and stimulates the direct pathway, yielding a net bias that allows purposeful movement. Excitatory pathways are shown in blue, and inhibitory pathways are shown in black. The direct pathway signals from putamen to GPi to thalamus to cortex, while the indirect pathway signals from putamen to GPe to STN to GPi to thalamus to cortex. GPi, internal segment of the globus pallidus; GPe, external segment of the globus pallidus; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; STN, subthalamic nucleus. Inset: Both direct and indirect pathway neurons in the putamen receive inputs from the nigrostriatal dopaminergic system (dotted blue arrow) and from cortical glutamatergic systems (solid blue arrow). process these inputs in the context of local cholinergic influences (ACh), and transmit a GABAergic output (not shown). Degeneration of dopaminergic neurons in the substantia nigra results in understimulation of the direct (movement-enabling) pathway and underinhibition of the indirect (movement-inhibiting) pathway. Dotted gray arrow indicates decreased activity caused by understimulation, and thick black arrow indicates increased activity caused by underinhibition.

Parkinson



Nac is the ventral striatum  
CP is the dorsal striatum

## I Mediatori chimici coinvolti nella depressione



Depression

Is located in the limbic system