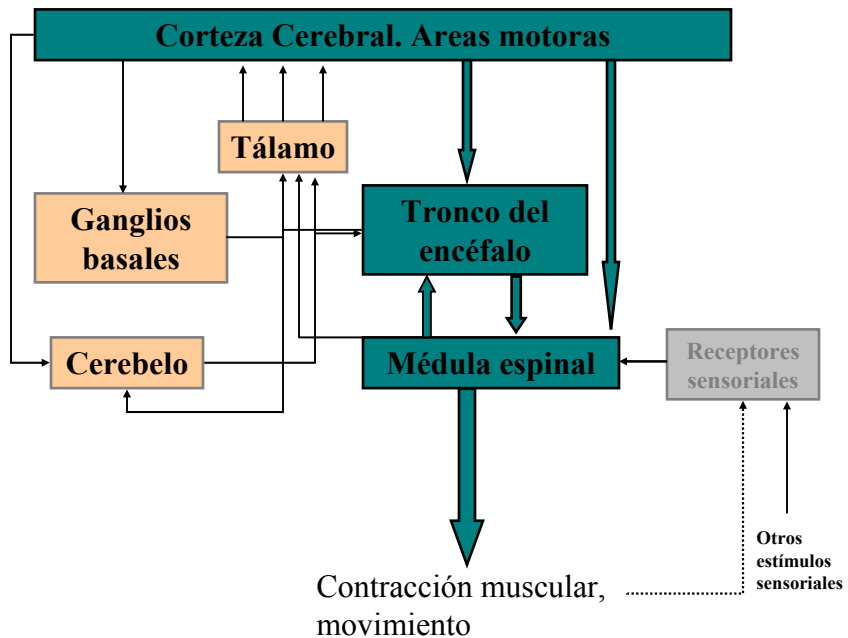


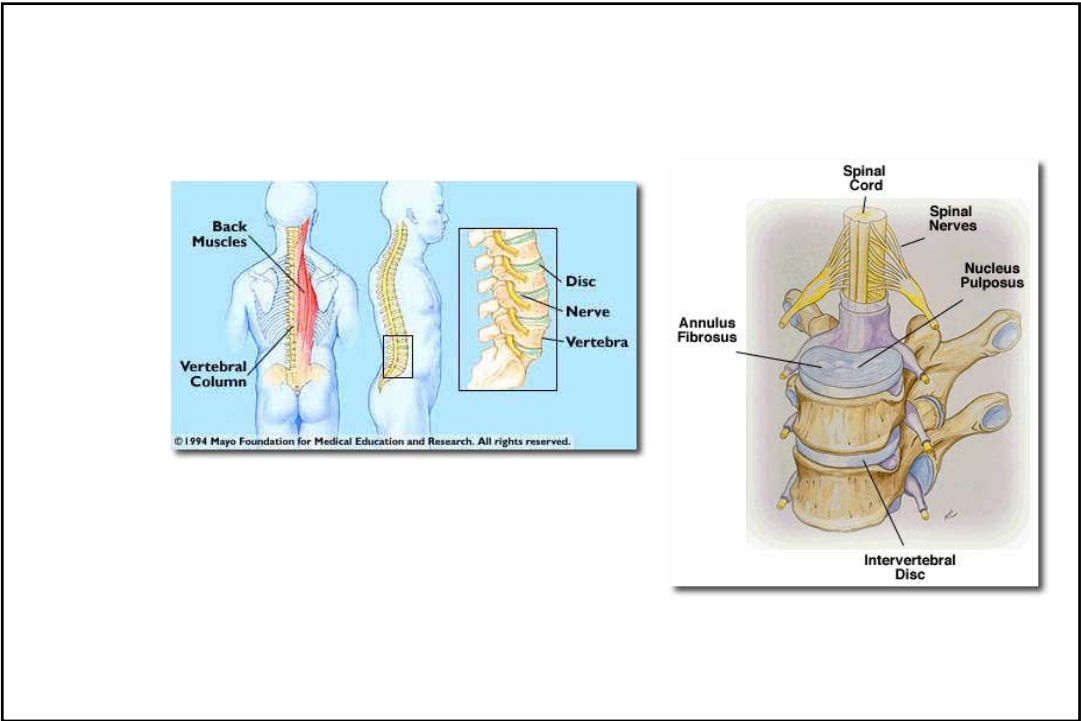
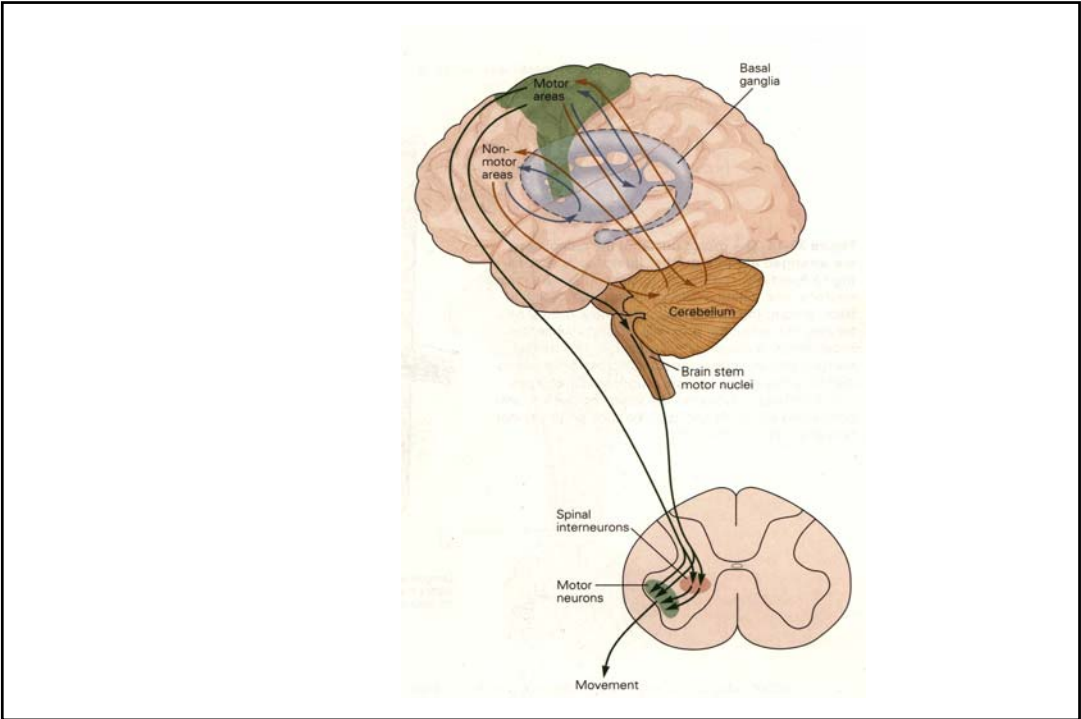


Sistema motor

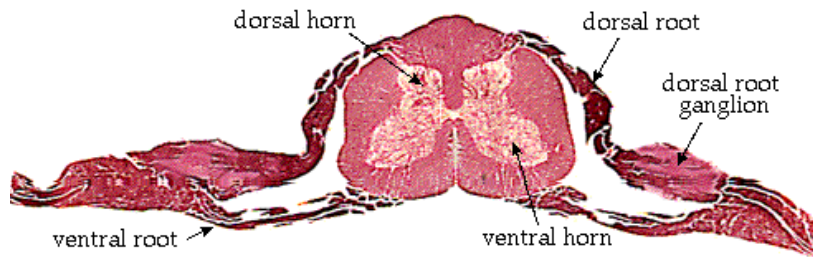
Pablo Caviedes

Programa de Farmacología
Molecular y Clínica

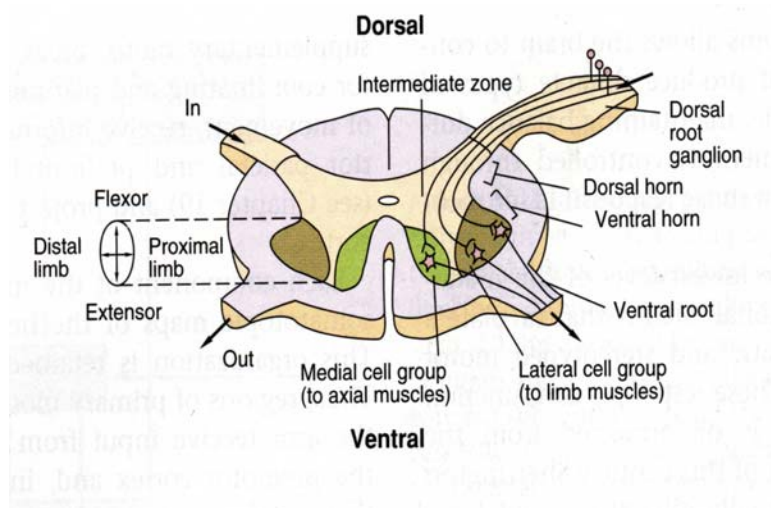




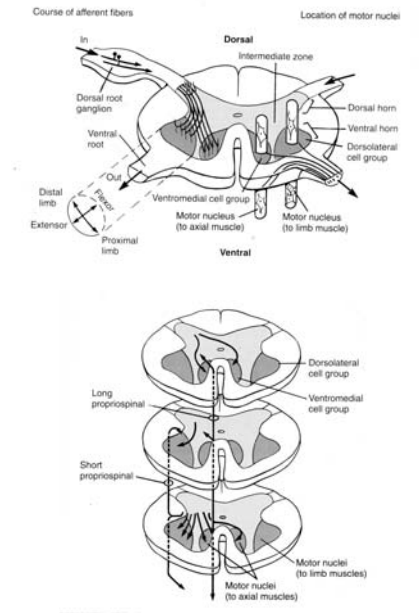
Médula espinal



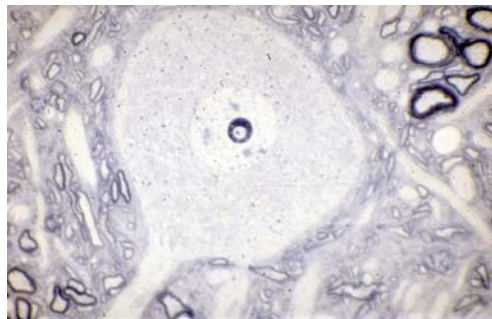
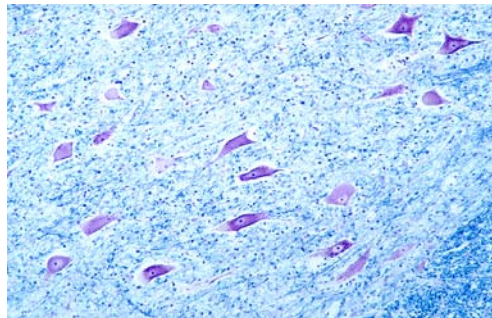
Médula espinal



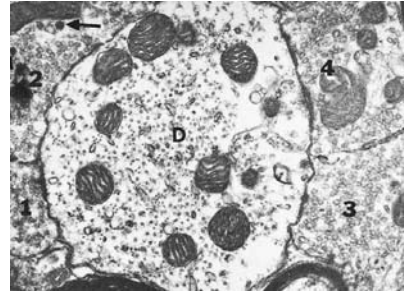
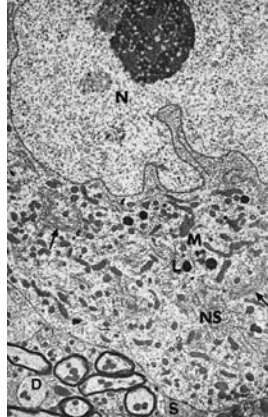
Médula espinal



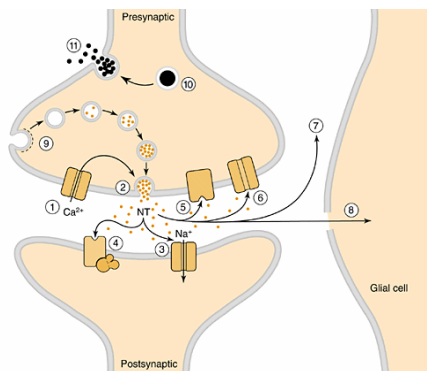
Médula espinal



Médula espinal

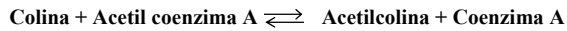
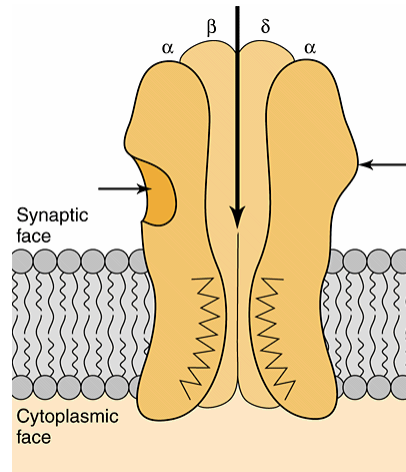
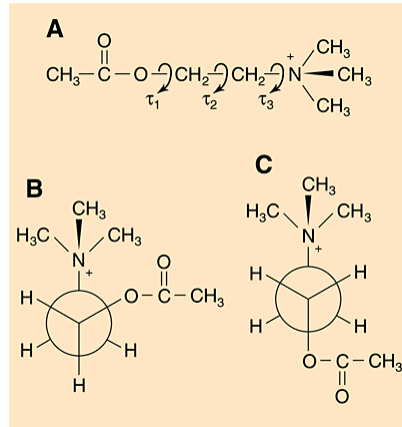


Acetilcolina: Receptores

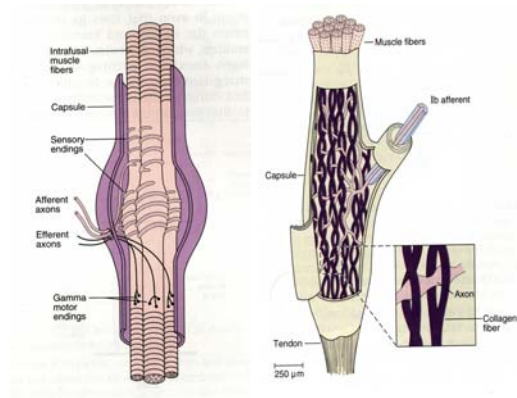
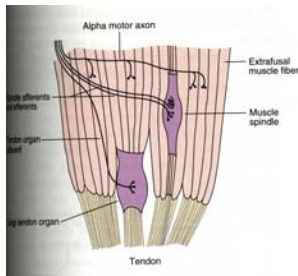


Stage	Cholinergic	
	Nicotinic	Muscarinic
Stage 1	Agonist: Nicotine Antagonist: α -Tubocurarine	Agonist: Muscarine, Pilocarpine Antagonist: Atropine
Stage 2	Nicotinic muscle Agonist: Phenyltrimethylammonium Antagonist: Elapid α -toxins, α -Tubocurarine	Nicotinic neuronal (α + β) Agonist: Dimethylphenylpiperazinium, Cytisine Antagonist: Trimethaphan, Neuronal bungarotoxin
	Nicotinic Junctional [(α 1) β 2] Nicotinic Embryonic [(α 1) β 3] Nicotinic neuronal [(α 1) β 4] Nicotinic neuronal [(α 1) β 5]	Nicotinic neuronal α 2 (α -toxin insensitive) α 3 (α -toxin insensitive) α 4 (α -toxin insensitive) α 5 (non-functional without other α subunits) α 6 (α -toxin insensitive) α 7 (α -toxin sensitive) α 8 (α -toxin sensitive) α 9
Stage 3		Muscarinic $m_1 - M_1$ Antagonist: Pirenzepine $m_2 - M_2$ Antagonist: Methoctramine $m_3 - M_3$ Antagonist: Hexahydro-siladifenidol $m_4 - M_4$ Antagonist: Himbacine $m_5 - M_5$

Acetilcolina: Estructura, Receptores

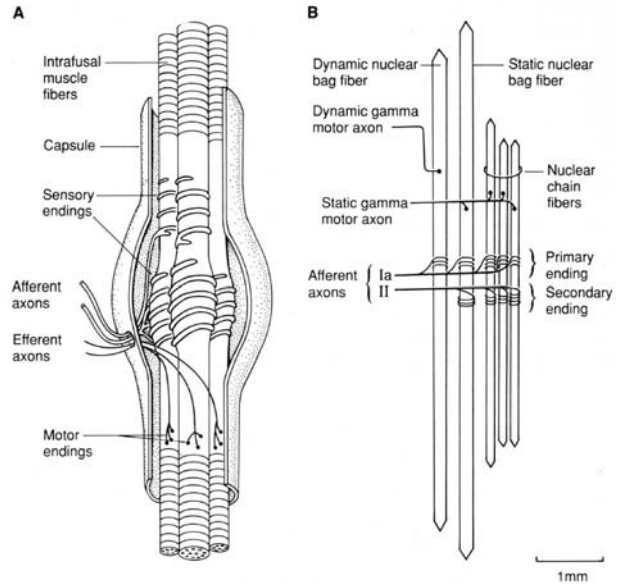


Reflejo miotático, antimiotático: Receptores

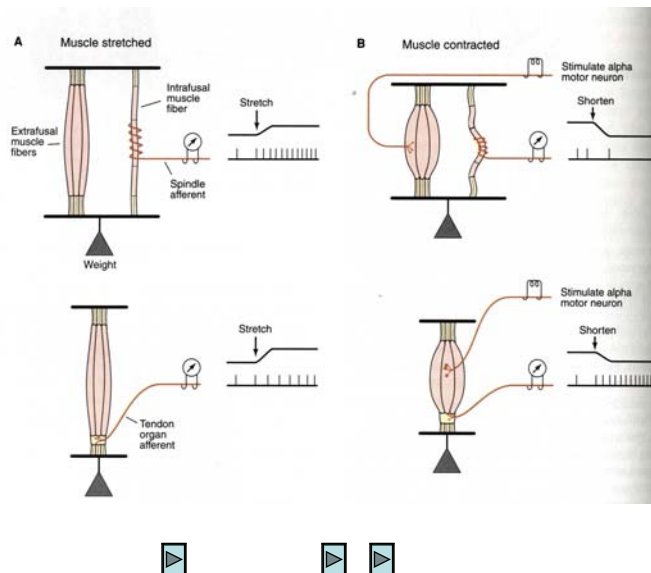


Reflejo miotático:

Huso neuromuscular



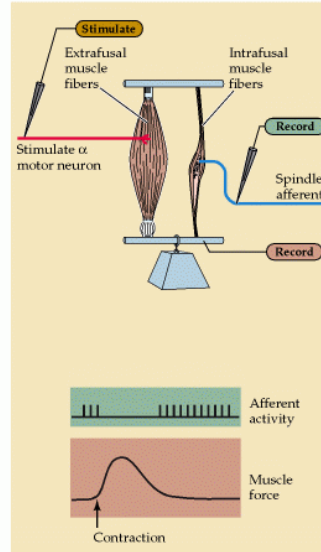
Reflejo miotático, antimiotático: Receptores



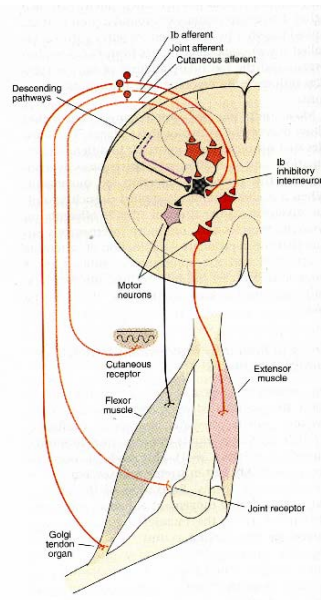
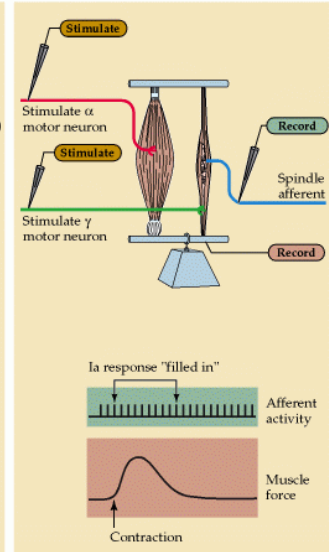
Coactivación

α - γ

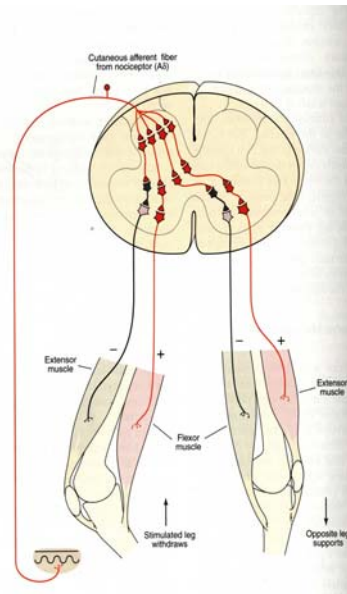
(A) α Motor neuron activation without γ



(B) α Motor neuron activation with γ

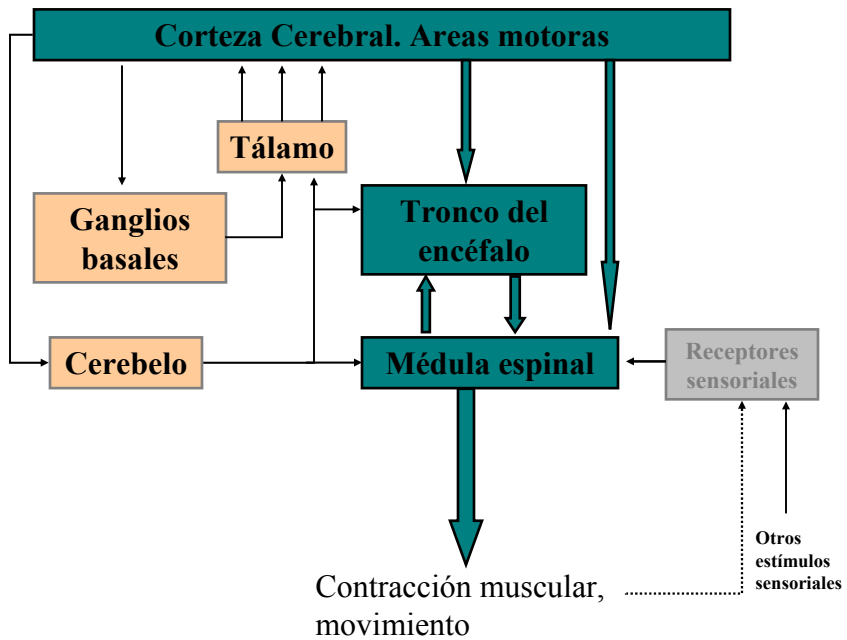
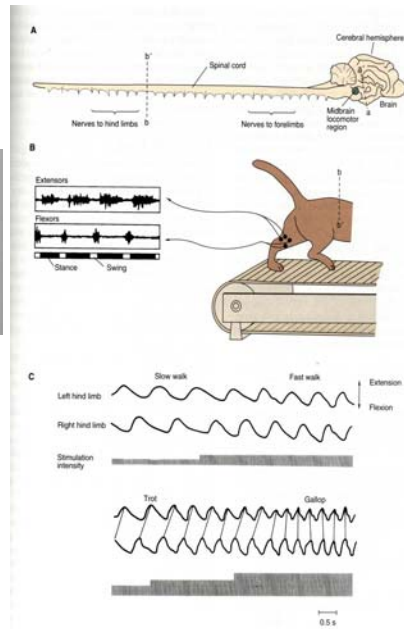
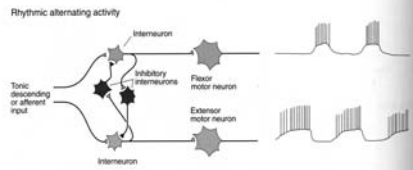


Reflejo flexor

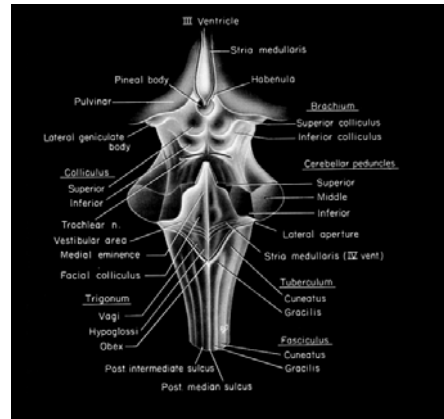
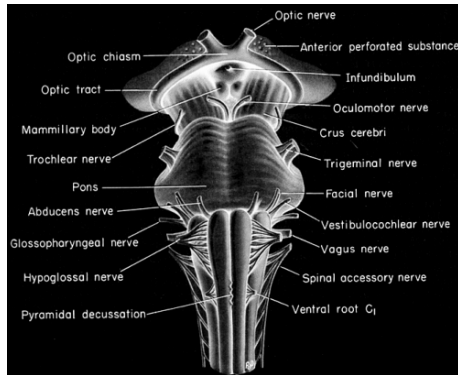


Extensión cruzada

Circuitos medulares

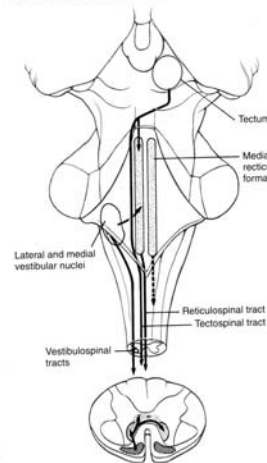


Tronco del encéfalo



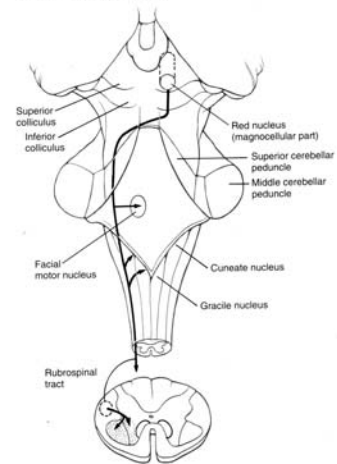
Tronco del encéfalo

A Medial brain stem pathways



Proximal
Extensor > Flexor

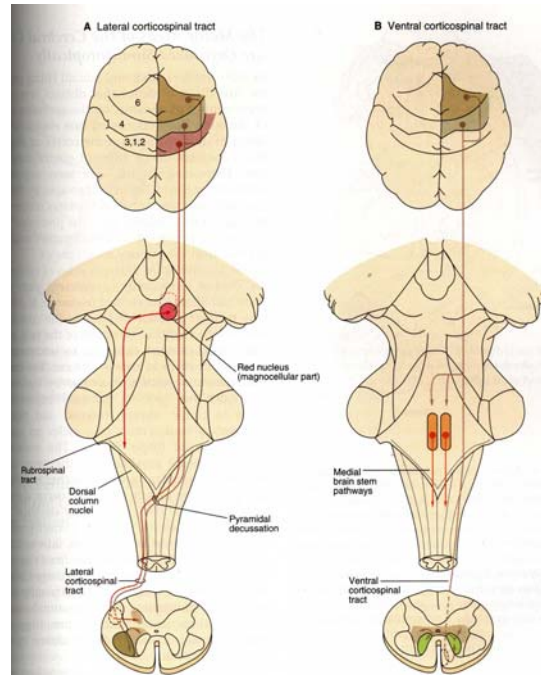
B Lateral brain stem pathways



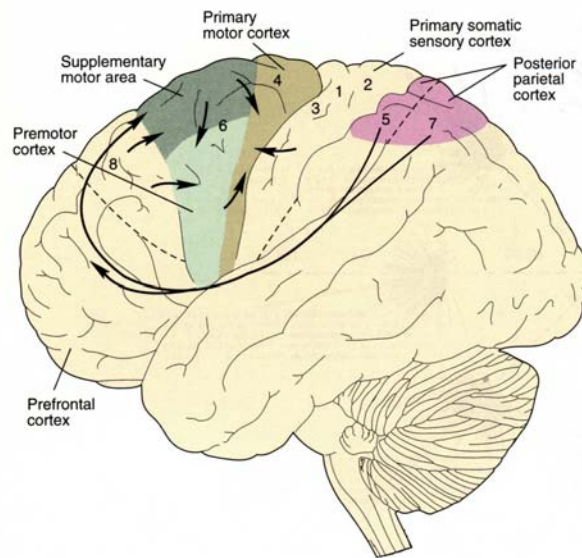
Distal
Extensor < Flexor



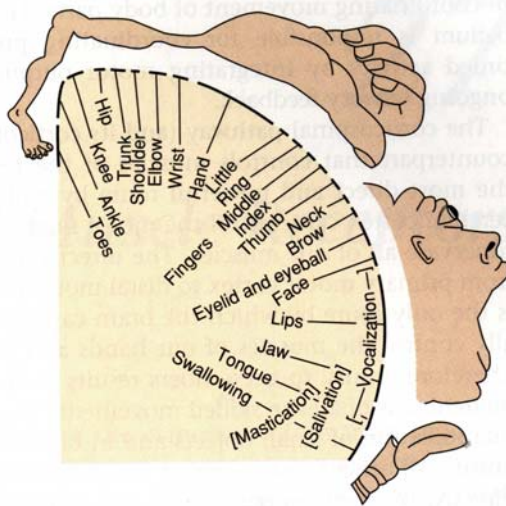
Corteza cerebral: Vía corticoespinal



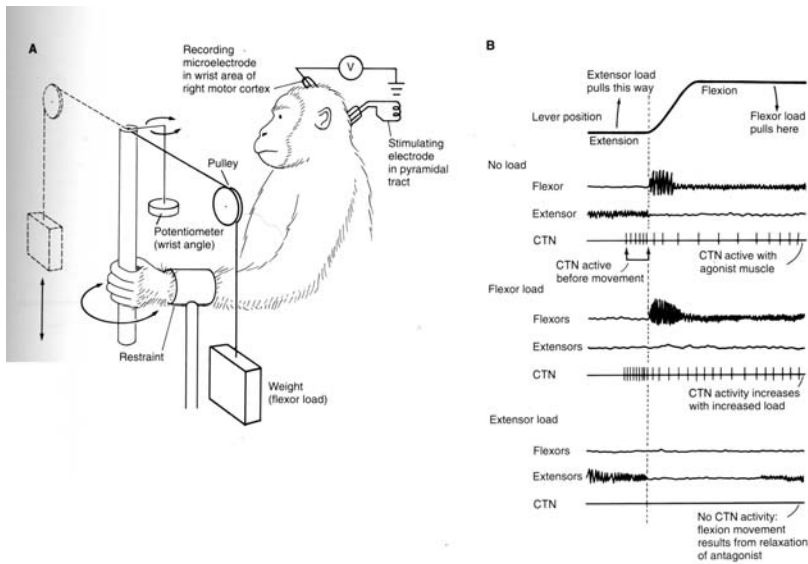
Corteza cerebral



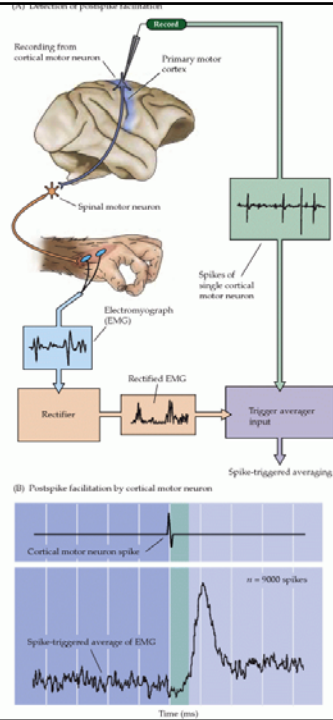
Corteza cerebral: Homúnculo



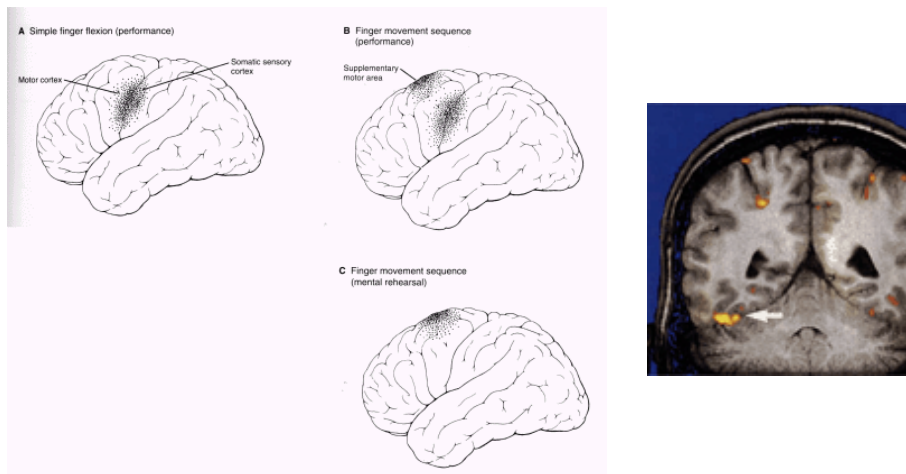
Monos entrenados (Evarts)



Facilitación post espiga



Estudios de flujos regionales



Neurona superior vs. Neurona inferior:

PARALISIS

Límite dado por la α motoneurona

MN Superior:

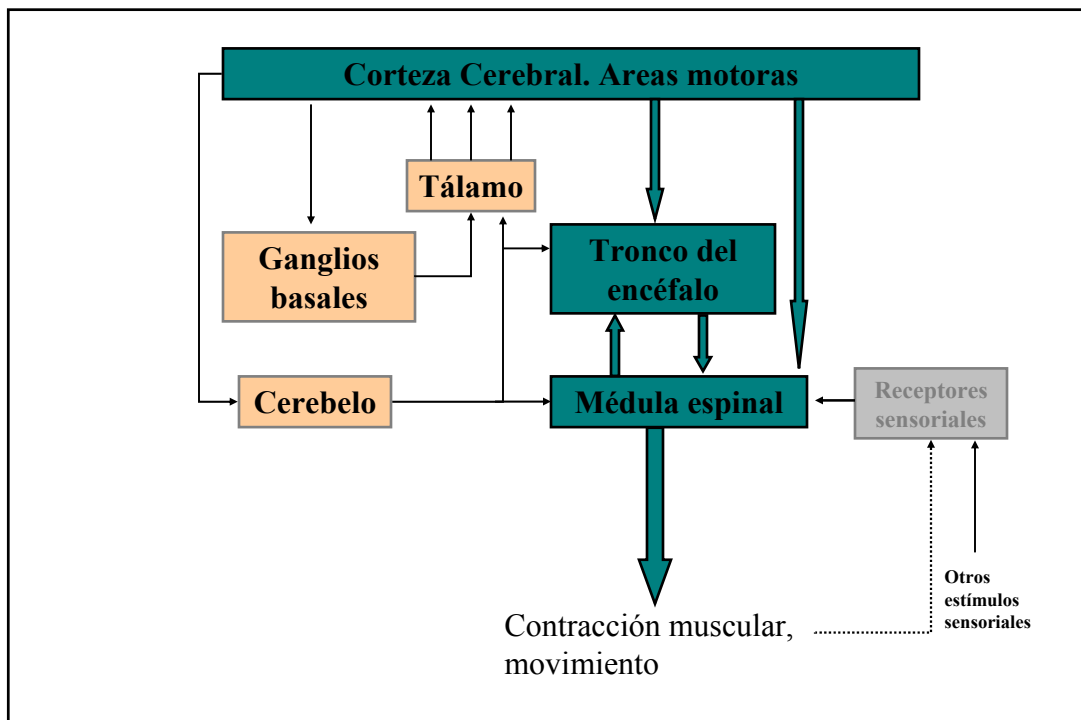
- ♦ Exacerbación de respuesta.
Espasticidad
- ♦ Simetría/asimetría
- ♦ Signos positivos (Babinski)

Ej.: AVE cápsula interna, sección medular

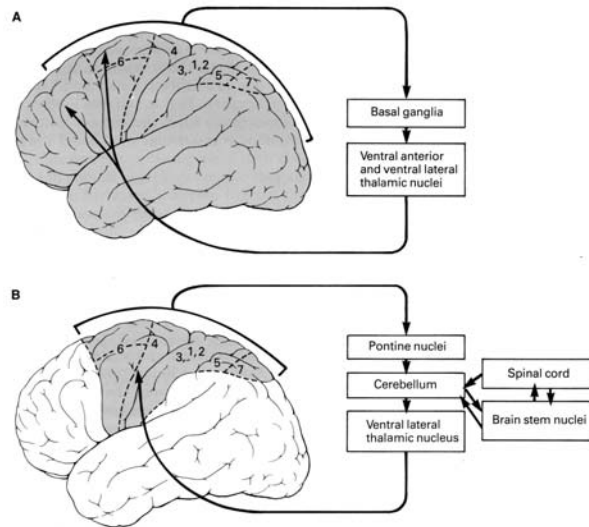
MN Inferior:

- ♦ Flaccidez
- ♦ Simetría/asimetría
- ♦ Hiporreflexia/arreflexia
- ♦ Marcada atrofia

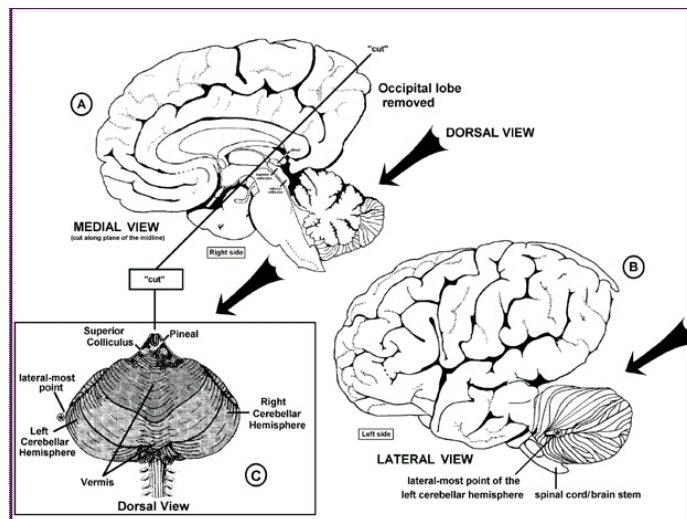
Ej.: Poliomiелitis



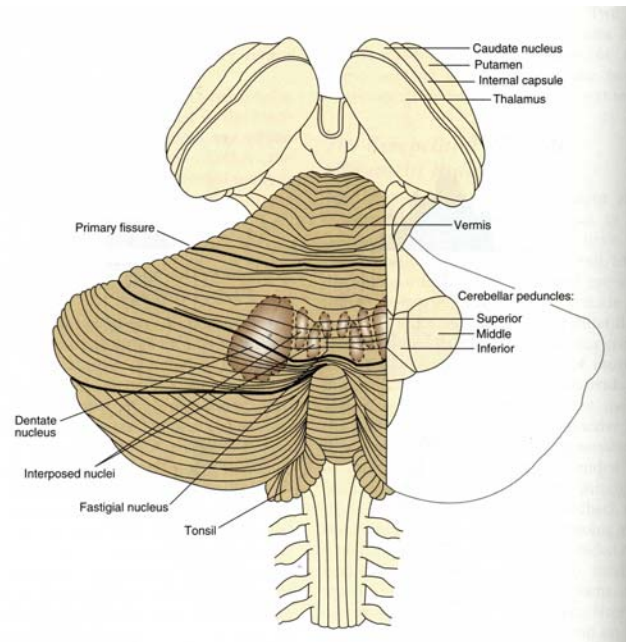
Ganglio basales - Cerebelo



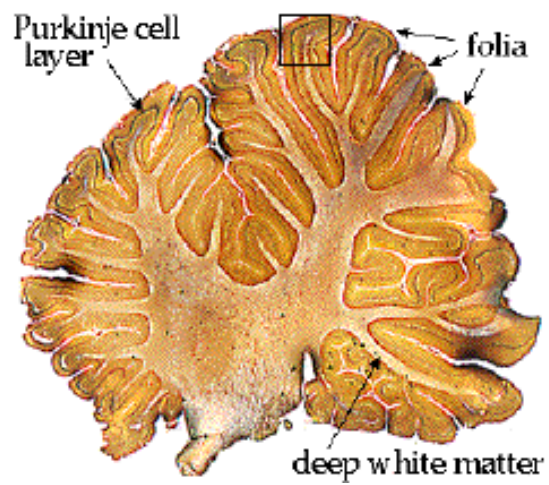
ANATOMIA



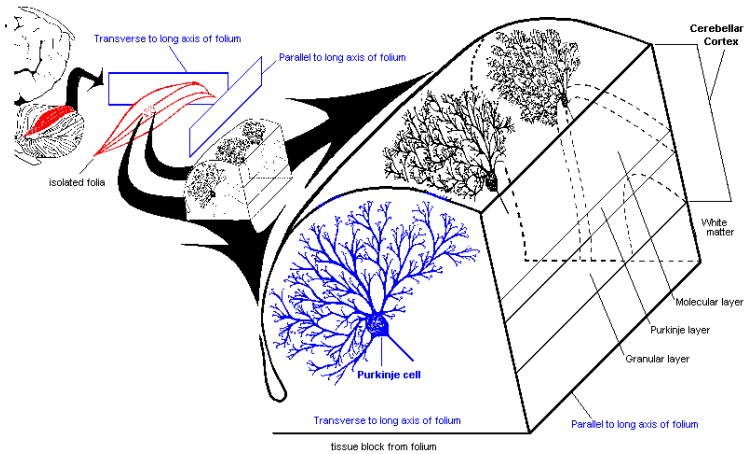
ANATOMIA



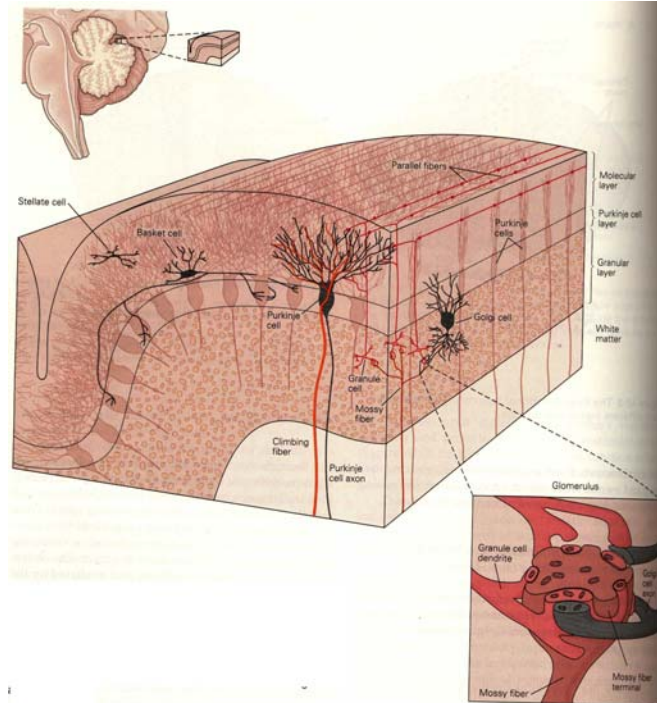
ANATOMIA



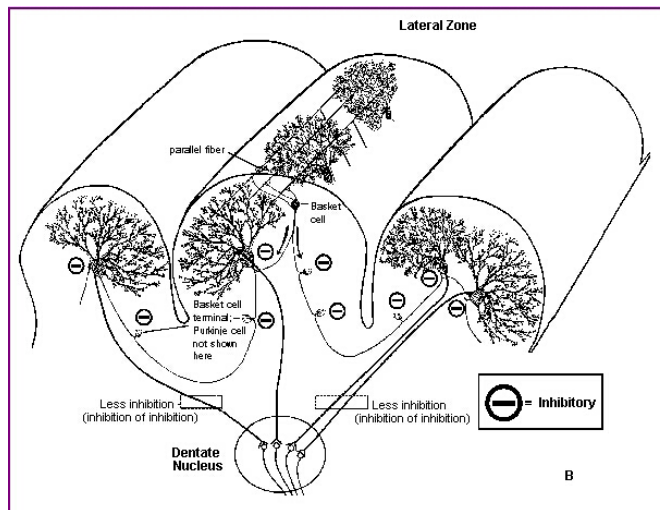
CORTEZA



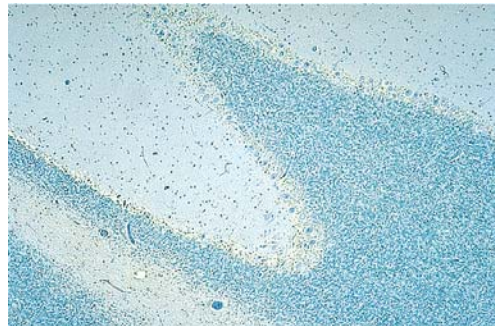
CORTEZA



CORTEZA



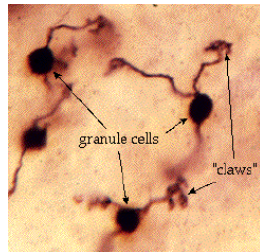
Corteza



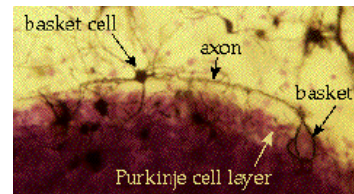
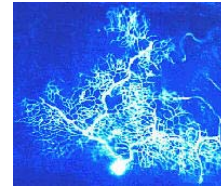
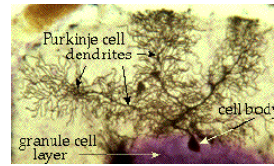
**Cels. Cesta,
Purkinje**



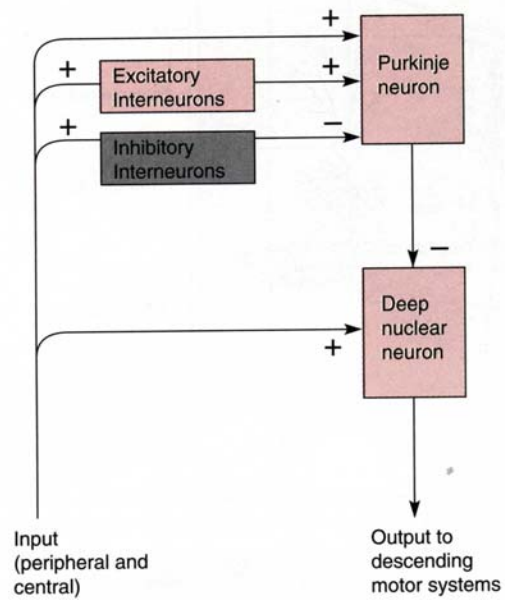
Capa granular



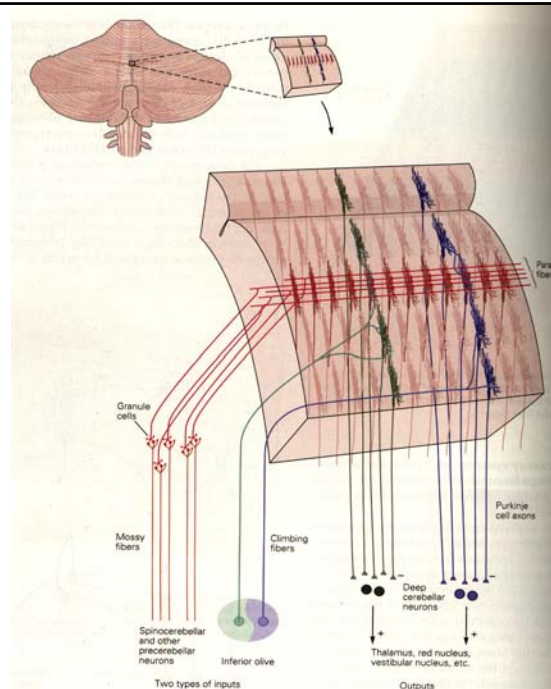
Capa Purkinje



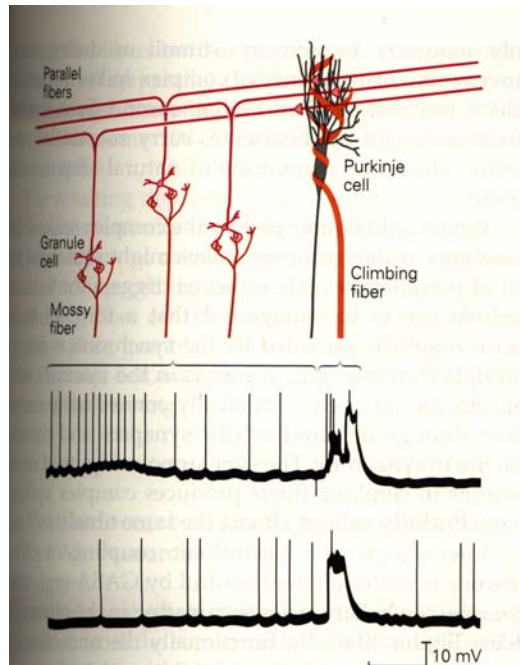
CIRCUITO BASICO



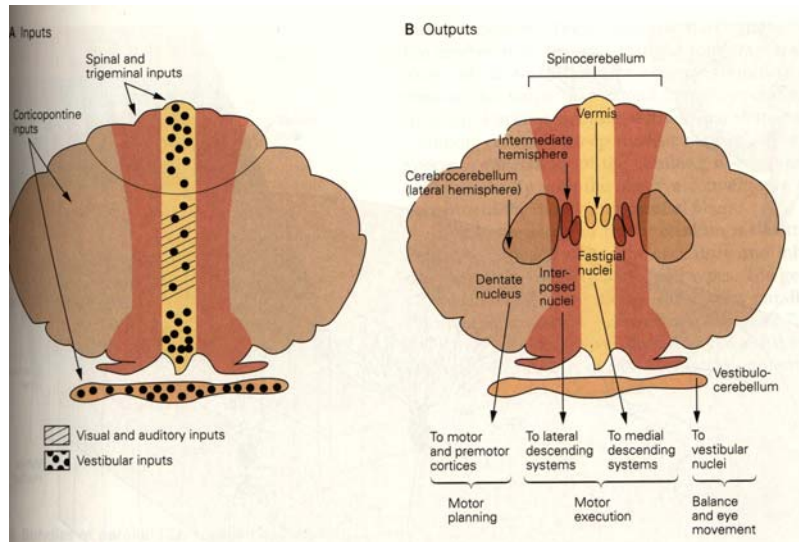
CORTEZA



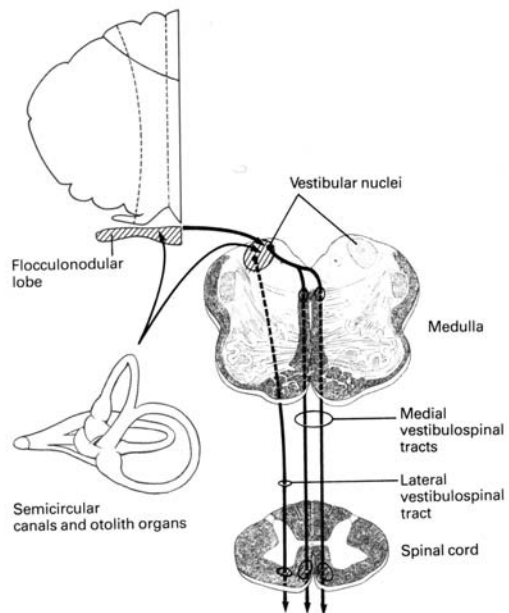
RESPUESTAS NEURONALES



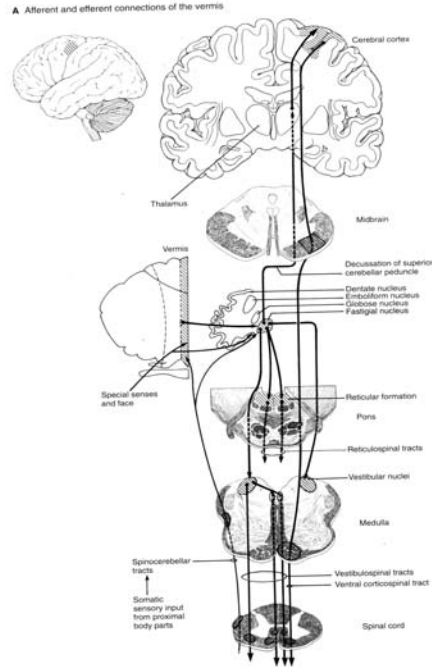
ANATOMIA - FUNCIÓN



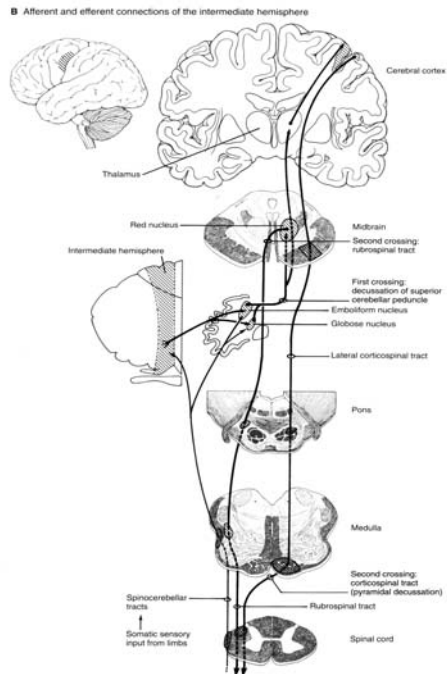
VESTIBULO CEREBELO



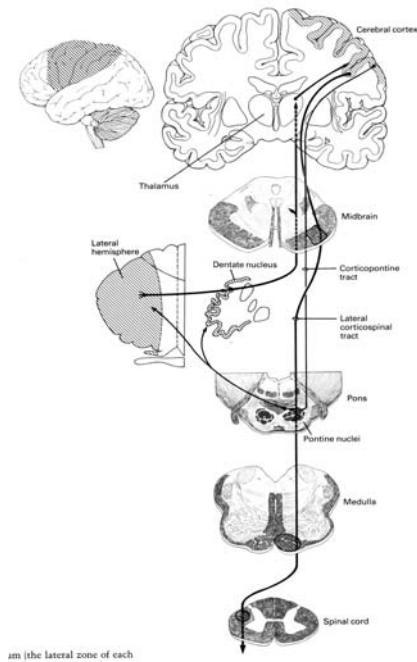
ESPINO CEREBELO MEDIAL



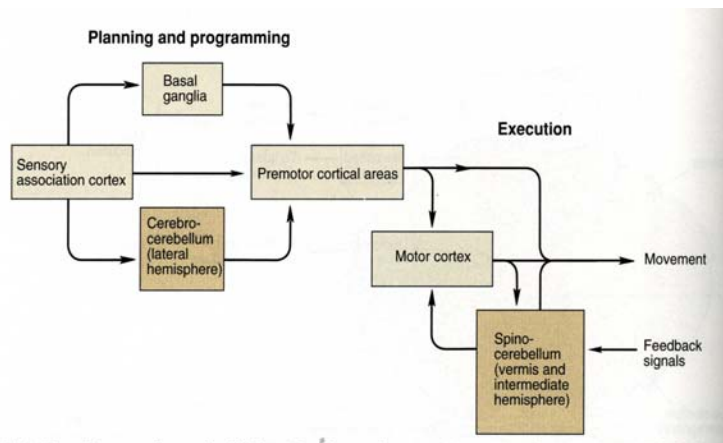
ESPINO CEREBELO LATERAL



CEREBRO CEREBELO

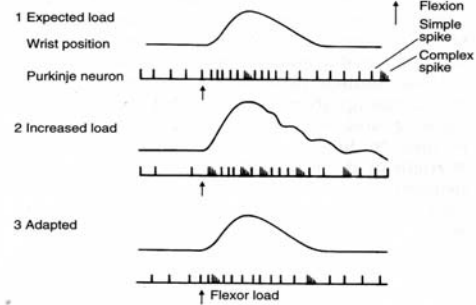


ESQUEMA FUNCION

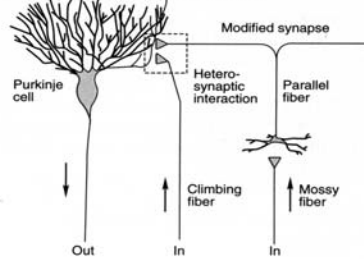


APRENDIZAJE MOTOR

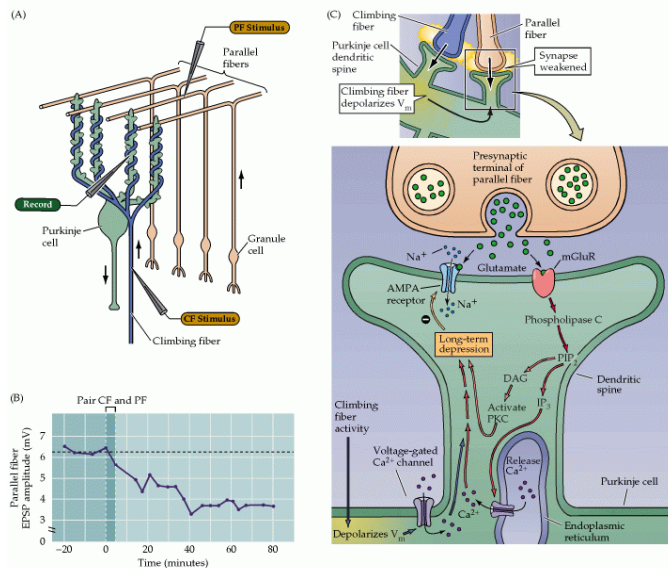
A Neural activity during motor adaptation



B Modification of inputs during adaptation

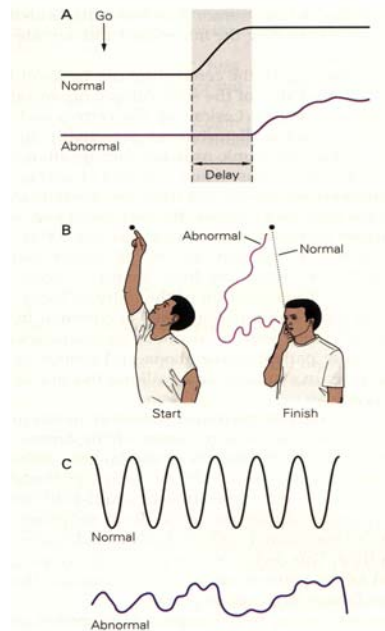


APRENDIZAJE MOTOR

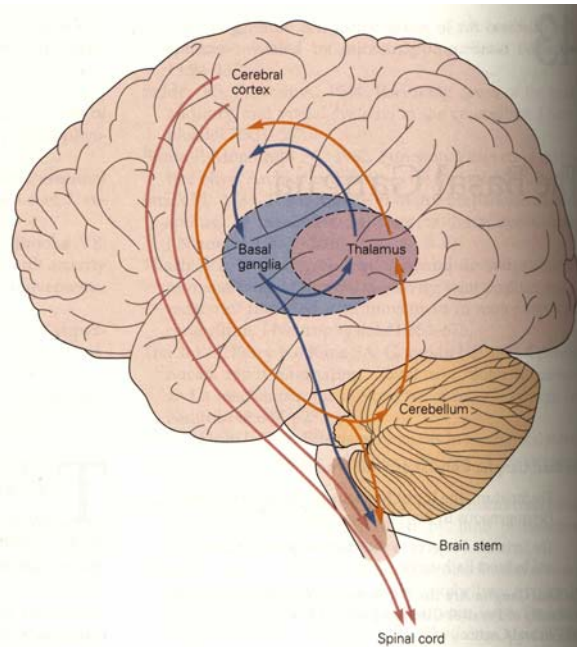


DEFICIT

- Retardo en inicio de movimientos
- Ataxia, temblor de intención
- Disdiadocosinesia
- Hipotonía, sin déficit motor.
- Sin deterioro intelectual



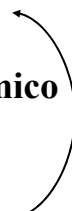
Ganglios basales



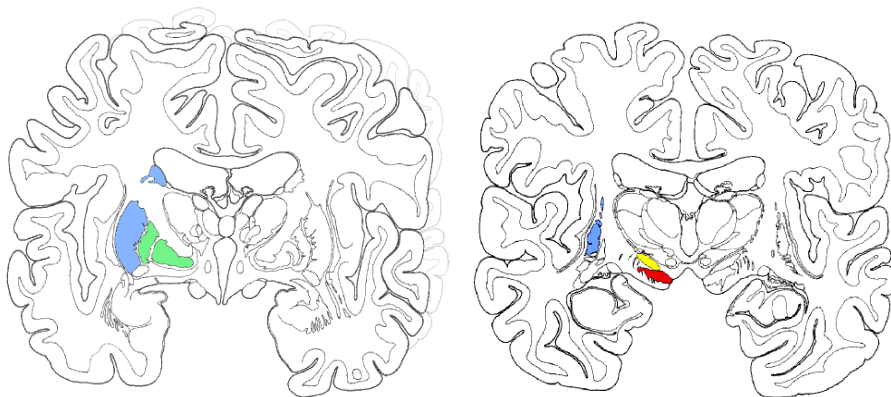
Ganglios basales

- Caudado
- Putámen
- Globus pallidus
- Núcleo subtalámico
- Sustantia nigra:
 - Pars reticulata
 - Pars compacta

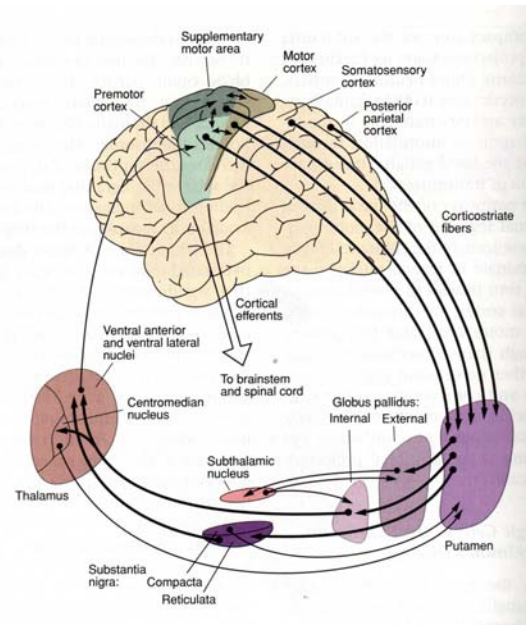
} Cuerpo estriado



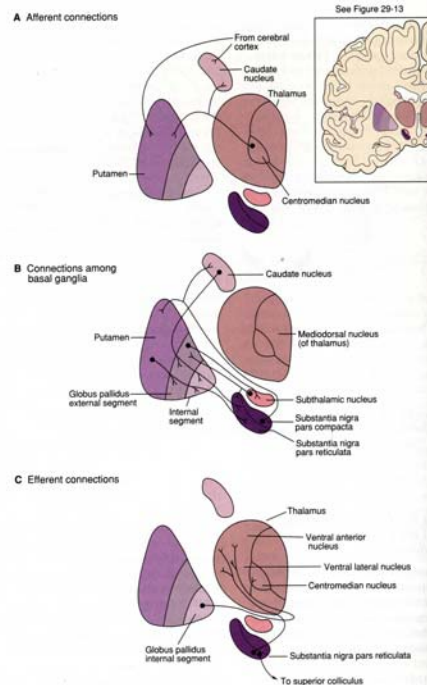
Ganglios basales



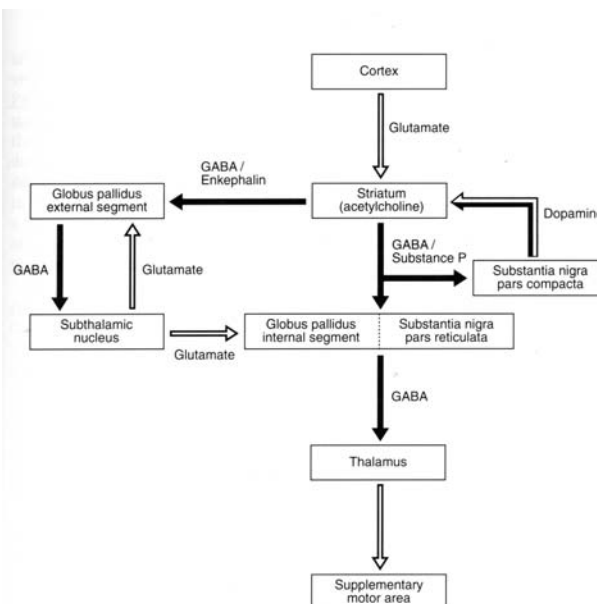
Ganglios basales



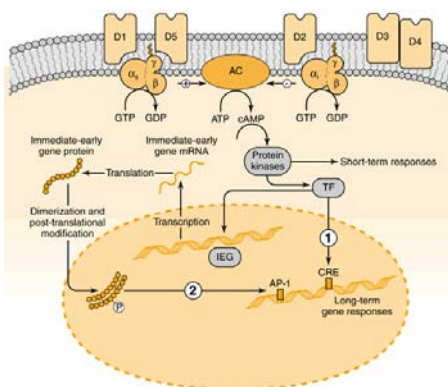
Ganglios basales



Ganglios basales: circuito básico



Ganglios basales: Receptores Dopamina



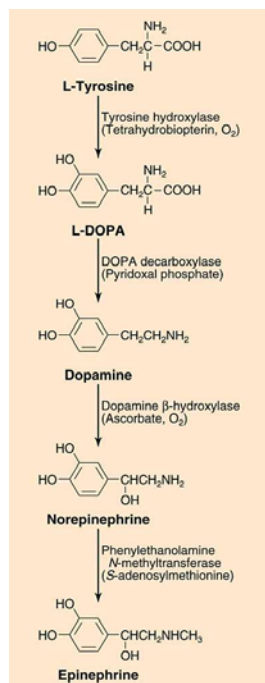
PROPIEDADES DE RECEPTORES DE DOPAMINA CLONADOS

	D1	D5	D2S/D2L	D3	D4
Aminoácidos (hum)	446	477	415/444	400	387
Cromosoma	5	4	11	3	11
Vías efectoras	↑cAMP	↑cAMP	↓cAMP ↑canal K ⁺ ↓canal Ca ²⁺	↓cAMP	↓cAMP ↑canal K ⁺
Distribución mRNA	Caudado putámen, nucleus accumbens, hipotálamo Tub. olfatorio	Hipocampo, nucleus accumbens, hipotálamo	Caudado putámen, nucleus accumbens, Tub. olfatorio	Tub. olfatorio	Corteza frontal hipotálamo bulbo, tronco nucleus accumbens

CONCENTRACION DE DOPAMINA ESTRIATAL EN PARKINSON, PARKINSONISMO

Patología	% Control normal	
	Caudado	Putámen
Parkinson	31	22
	10	4
	18	2
Parkinsonismo postencefalitis	6	6
	1.5	0.6
Síndromes Parkinsonianos		
Degeneración Nigroestriatal	<0.4	<0.4
Steele-Richardson-Olszewski	20	27
Hallervorden-Spatz	1.4	0.9
Atrofia olivopontocerebelosa	0.3	0.01
SIDA	43	—
Huntington	86 (NS)	99 (NS)
Alzheimer	61 (NS)	50 (NS)

Parkinson: Base neuroquímica



CAMBIOS NEUROBIOQUIMICOS EN LA VIA DOPAMINERGICAS NIGROSTRIATAL EN PARKINSON

	Región	% control normal
<i>Dopamina, metabolitos</i>		
Dopamina	Substantia nigra	17
	Caudado	10
	Putámen	4
DOPAC	Substantia nigra	2
	Putámen	10
HVA	Substantia nigra	48
	Putámen	29
<i>Enzimas</i>		
Tirosina hidroxilasa	Substantia nigra	46
	Caudado	60
	Putámen	16
Decarboxilasa aminoácidos aromáticos	Caudado	9
	Putámen	4
Catecol-O-metil transferasa	Substantia nigra	82
	Caudado	70
	Putámen	78
Monoamino oxidasa-B	Substantia nigra	125
DAT	Caudado	32
	Putámen	16

Parkinson. Clínica

Fase “Off”



Fase “On”



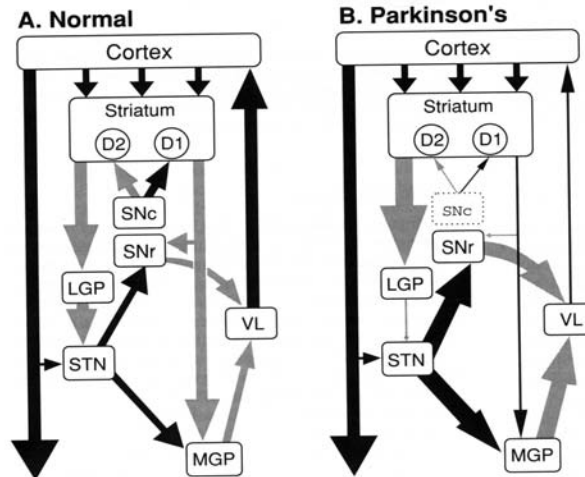
Diskinesia



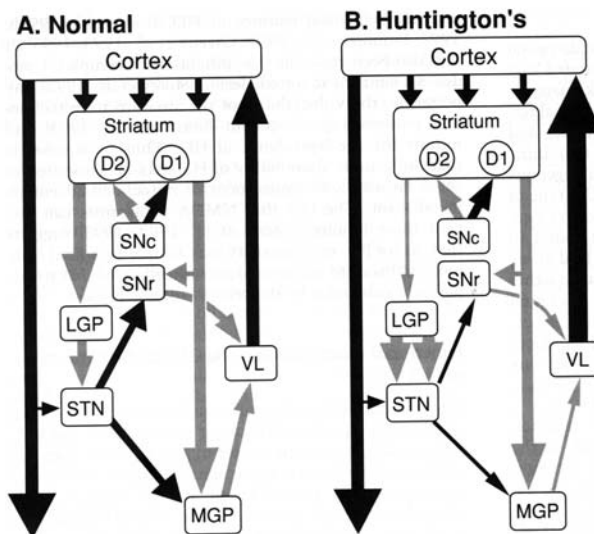
Inestabilidad
postural



Parkinson. Fisiopatología



Huntington. Fisiopatología



Normal

Parkinson's

Pre-Transplant

Post-Transplant

