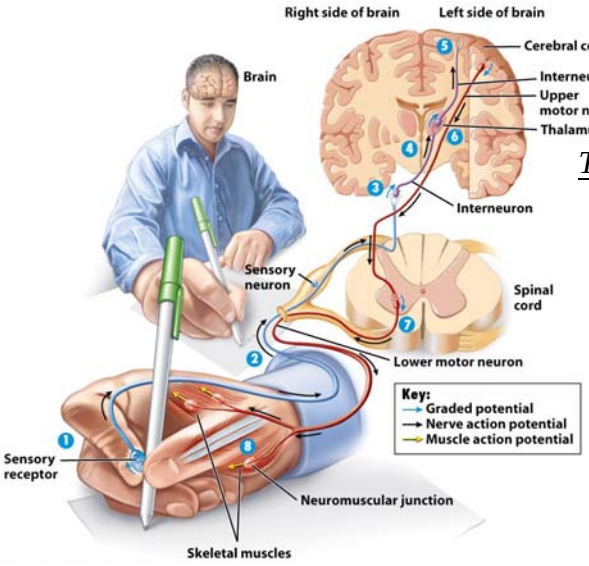
Nervous System



Three basic functions

- **Sensing changes** with sensory receptors
- **Interpreting and remembering** those changes
- **Reacting** to those changes with effectors

1

Major Structures of the Nervous System

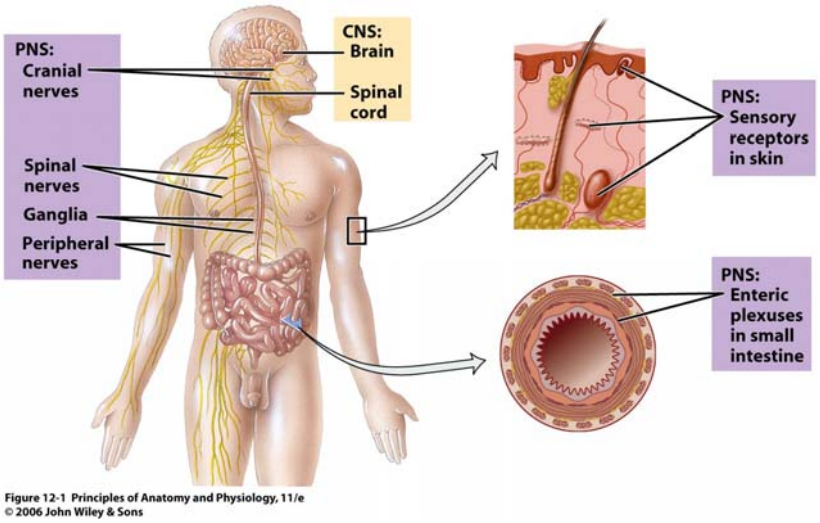


Figure 12-1 Principles of Anatomy and Physiology, 11/e
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2

Functions of the Nervous Systems

- The sensory *function* of the nervous system is to sense changes in the internal and external environment through sensory receptors.
  Sensory (afferent) neurons serve this function.
- The integrative *function* is to analyze the sensory information, store some aspects, and make decisions regarding appropriate behaviors.
  Association or *interneurons* serve this function.
- The motor *function* is to respond to stimuli by initiating action.
  Motor(efferent) neurons serve this function.

3

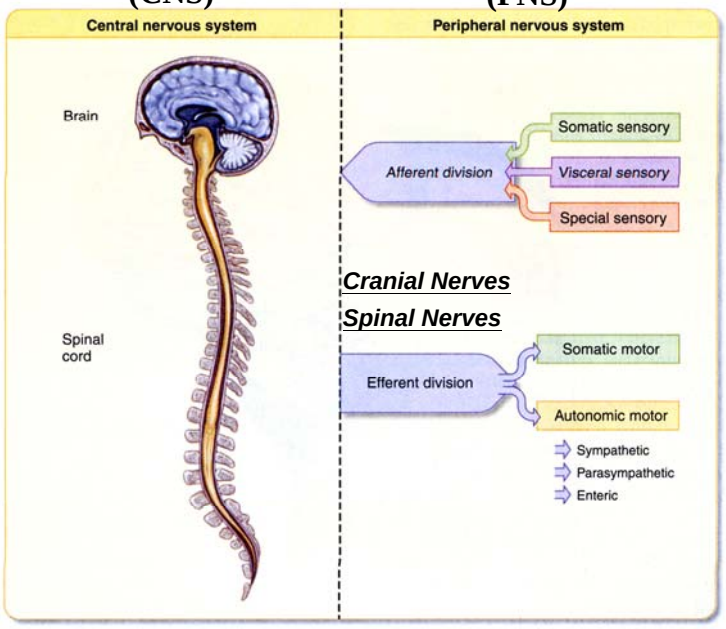
Nervous System Divisions

Neuron & Glia (Neuroglia)

- Central Nervous System (CNS)
  -- Brain & Spinal Cord
- Peripheral Nervous System (PNS)
  Output: Motor Nerves
  -- Cranial Nerves & Spinal Nerves
  （1） Autonomic Nervous System (ANS)
  （2） Somatic Nervous System (SNS)
  （3） Enteric Nervous System (ENS)
  Input: Sensory Nerves

4

(CNS) **(PNS)**



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Organization of the Nervous System

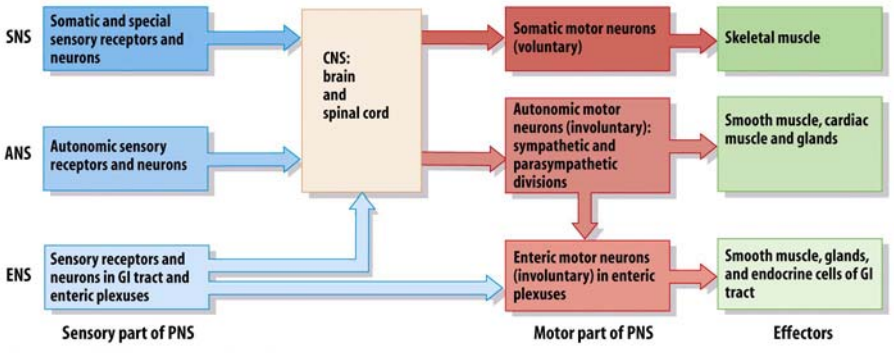


Figure 12-2 Principles of Anatomy and Physiology, 11/e

6

Neuron

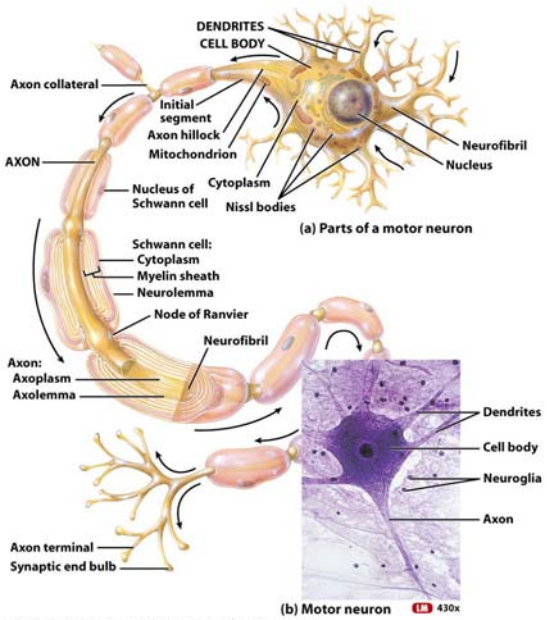


Figure 12-3 Principles of Anatomy and Physiology, 11/e

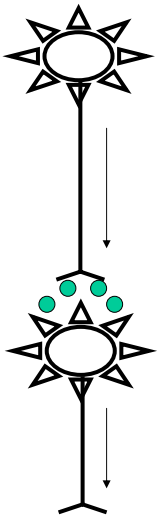
7

Structure of Neurons

名稱	特性
細胞體 (soma or cell body)	內有細胞核及胞器(如內質網、粒線體…等)，因此細胞內可以合成許多酵素及蛋白質、類固醇、醣類…等
樹突 (dendrites)	主要功能為接受訊號的地方
軸突 (axon)	主要功能為「運送物質的地方」或者傳遞電訊號
軸突末(終)端或神經末梢 (axon terminals)	位於軸突最末端有許多細細長長的肥大結構，主要功能為分泌神經傳導物質
起始段(軸突丘) (axonal hillock or initial segment)	位於軸突與細胞體的連接處，主要功能為產生動作電位(電訊號)的地方

8

Cellular Communication



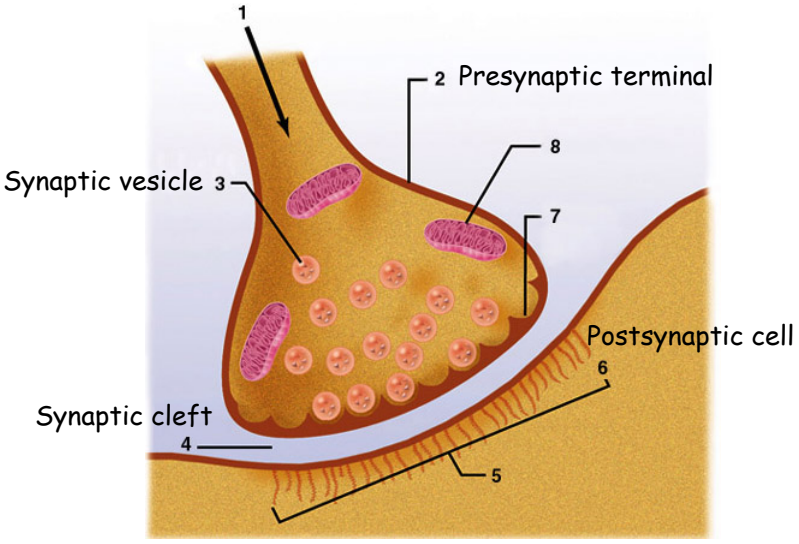
Intracellular communication
動作電位(電訊號)

Synapses
Chemical synapses
Electrical synapses

Intercellular communication
Chemical messengers

9

Chemical Synapse



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Functional Classes of Neurons

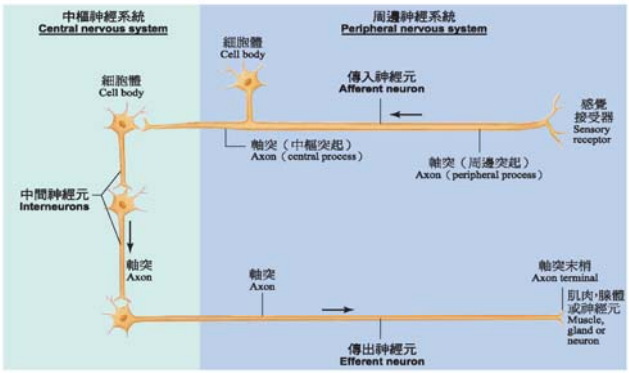
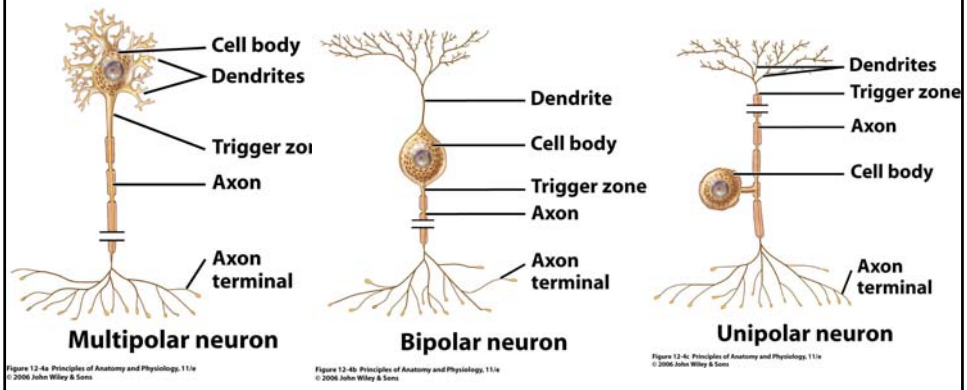


圖 4-3
三種類型的神經元。箭頭顯示神經活性傳遞的方向。位於周邊神經系統的傳入神經元通常從感覺接受器接受傳入訊息。周邊神經系統的傳出神經元終止於肌肉、腺體或神經元等作用器。傳入與傳出的成員可能由兩個神經元組成，而不是像這裡所顯示的只有一個神經元。

Functional Classes of Neurons

名稱	特性
感覺神經元(sensory neurons) **傳入神經元(afferent neurons)**	a. 接受器接收到訊號後，會經由刺激把訊號傳到中樞。 b. 大部份的傳入神經元位在CNS之外，只有少數在CNS（只有少部份的軸突；神經末梢進入到CNS。大部份的軸突、cell body 在 PNS）。 c. 傳入神經元通常沒有樹突。
中間神經元(interneurons) **聯絡神經元(association neurons)**	a. 訊號整合。 b. 所有的中間神經元皆落在 CNS 內。
運動神經元(motor neurons) **傳出神經元(efferent neurons)**	a. 把訊號從中樞傳出，傳到作用器 cell (如腺體，骨骼肌or其他神經cell）。 b. 傳出神經元的cell body 位於 CNS內，但神經末梢和大多數的軸突都在 PNS 內。

Structural Classes of Neurons



13

神經相關名稱	定義
神經 (Nerves)	成束的神經纖維
神經纖維 (Nerve fibers)	包括—(1) 感覺神經纖維；(2) 運動神經纖維 總稱為混合神經纖維 (mixed nerves)
神經節 (Ganglia)	中樞神經以外（周邊）細胞本體聚集在一起
神經核 (Nucleus)	中樞神經內的細胞本體聚集在一起
神經徑 (Nerve tract)	中樞神經相連區域的神經纖維聚集處

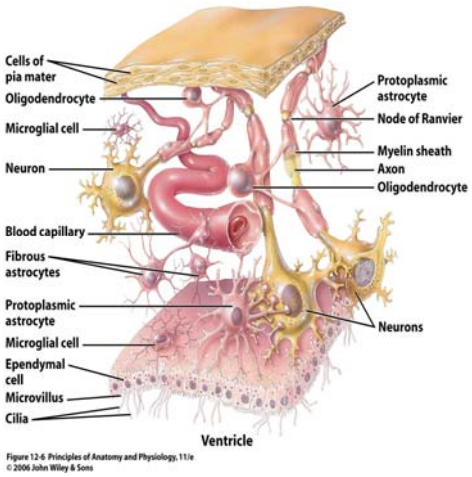
14

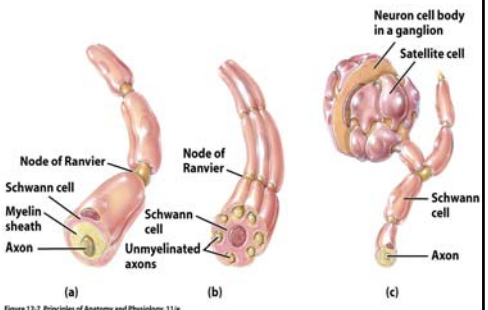
Functional Classes of Glia Cells

支持細胞	位置	功能
許旺氏細胞 (Schwann cells)	周圍神經	環繞所有周圍神經軸突，形成神經鞘膜，或稱為許旺氏鞘；環繞周圍神經形成髓鞘
寡樹突細胞 (Oligodendrocytes)	中樞神經	形成中樞神經軸突的髓鞘，為中樞神經的白質
衛星細胞 (Satellite cells)	周圍神經	支持感覺及自律神經節中的神經元
星形細胞 (Astrocytes)	中樞神經	環繞血管並覆蓋腦微血管形成血腦障壁 (Blood Brain Barrier, BBB)
小神經膠細胞 (Microglial cells)	中樞神經	中樞神經的阿米巴狀細胞，有吞噬功能
室管膜細胞 (Ependymall cells)	中樞神經	形成腦腔(室)及脊髓腔的內襯，覆蓋微血管叢形成分泌腦脊髓液的脈絡叢

15

Functional Classes of Glia Cells





Neuroglia of the CNS

Neuroglia of the PNS

16

Membrane Potential

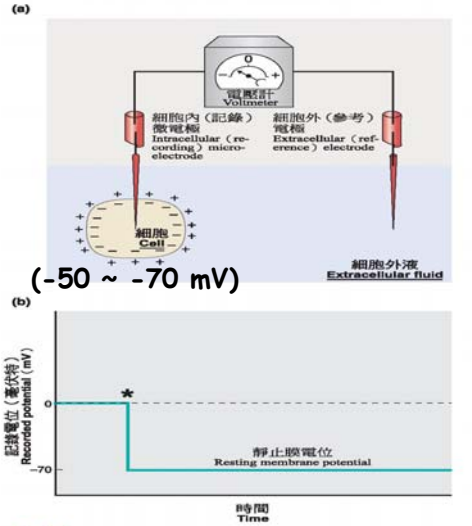


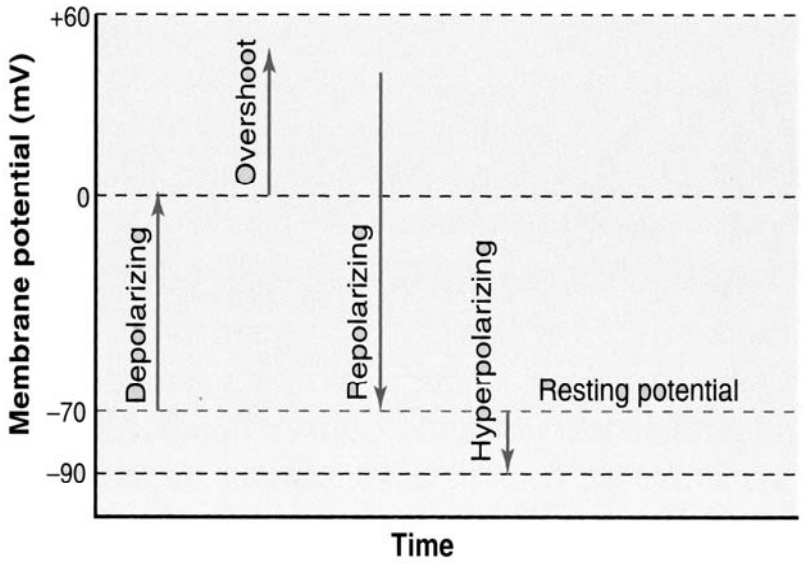
圖 4-6
(a)測量膜電位的裝置。電壓計可以測得細胞外與細胞內電極間的電壓差。(b)細胞內微電極所測得細胞膜內外的電位差。星狀標誌顯示電極剛剛插入細胞的那一瞬間。

17

膜電位相關名稱	定義
Potential (Potential difference)	The voltage difference between two points
Membrane potential (Transmembrane potential)	The voltage difference between the inside and outside of a cell
Equilibrium potential	The voltage difference across a membrane that produces a flux of a given ion species that is equal but opposite the flux due to the concentration gradient affecting that same ion species
Resting membrane potential (Resting potential)	The steady transmembrane potential of a cell that is not producing an electric signal
Graded potential	A potential change of variable amplitude and duration that is conducted decrementally; it has no threshold or refractory period
Action potential	A brief all-or-none depolarization of the membrane, reversing polarity in neurons; it has a threshold and refractory period and is conducted without decrement
Synaptic potential	A graded potential change produced in the postsynaptic neuron in response to release of a neurotransmitter by a presynaptic teminal; it may be depolarizing (an excitatory postsynaptic potential or EPSP)or hyperpolarizing (an inhibitory postsynaptic potential or IPSP)

18

Change in MP



Two Types of Ion Channels

- **Leakage (nongated) channels** are always open
  - -nerve cells have more K+ than Na+ leakage channels
  - -as a result, membrane permeability to K+ is higher
  - -explains resting membrane potential of -70mV in nerve tissue
- **Gated channels** open and close in response to a stimulus
  - -results in neuron excitability

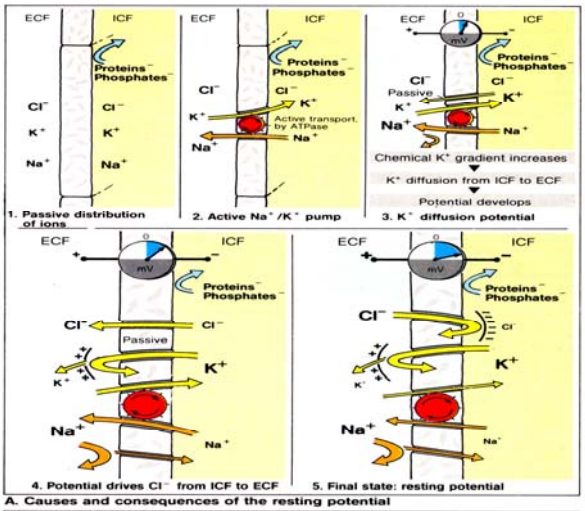
20

Ion Channels

- *Gated ion channels* respond to voltage changes, ligands (chemicals), and mechanical pressure.
  - ***Voltage-gated channels*** respond to a direct change in the membrane potential.
  - ***Ligand-gated channels*** respond to a specific chemical stimulus.
  - ***Mechanically gated ion channels*** respond to mechanical vibration or pressure.

21

Ionic Basis of RMP



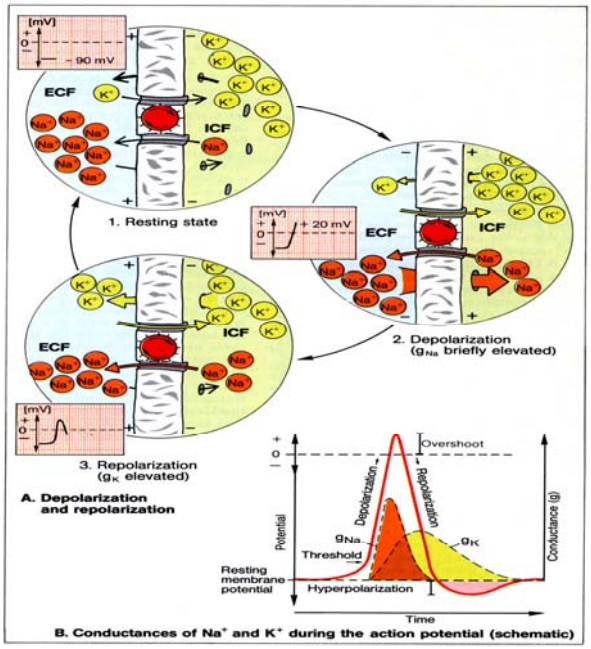
A. Causes and consequences of the resting potential

	"Effective" concentration (mmol/kg H_2O)		Equilibrium potential
	Interstitium (ECF)	Cell (ICF)	
K^+	4.5	160	− 95 mV
Na^+	144	7	+ 80 mV
H^+	$4 \cdot 10^{-5}$ (pH 7.4)	10^{-7} (pH 7.0)	− 24 mV
Cl^-	114	7	− 80 mV
HCO_3^-	28	10	− 27 mV

B. Typical "effective" concentrations and equilibrium potentials of important ions in skeletal muscle (37°C) (after Conway)

22

Ionic Basis of AP



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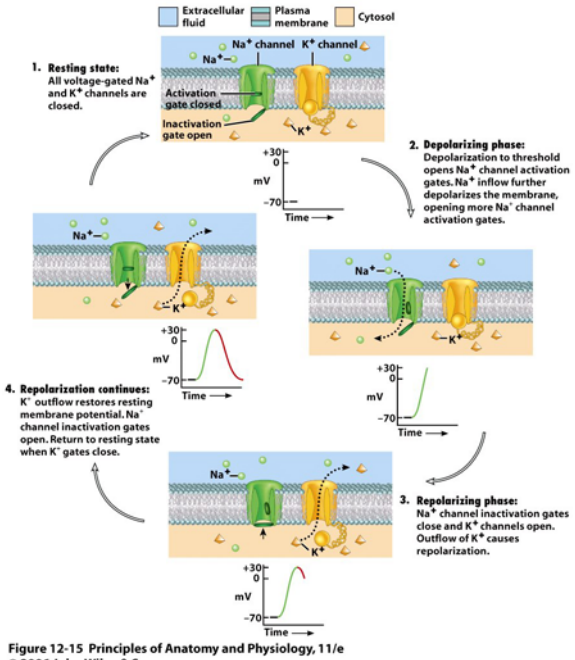
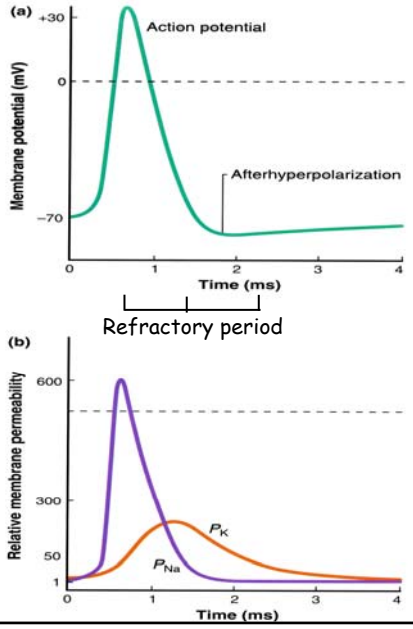


Figure 12-15 Principles of Anatomy and Physiology, 11/e

24

Ionic Basis of AP



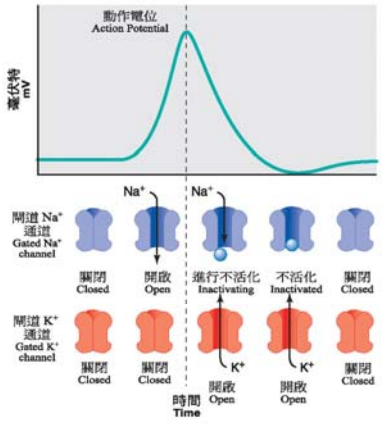
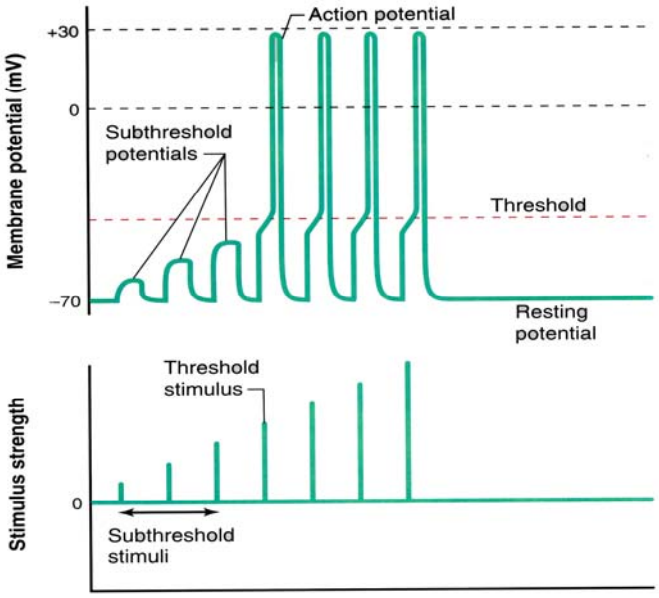


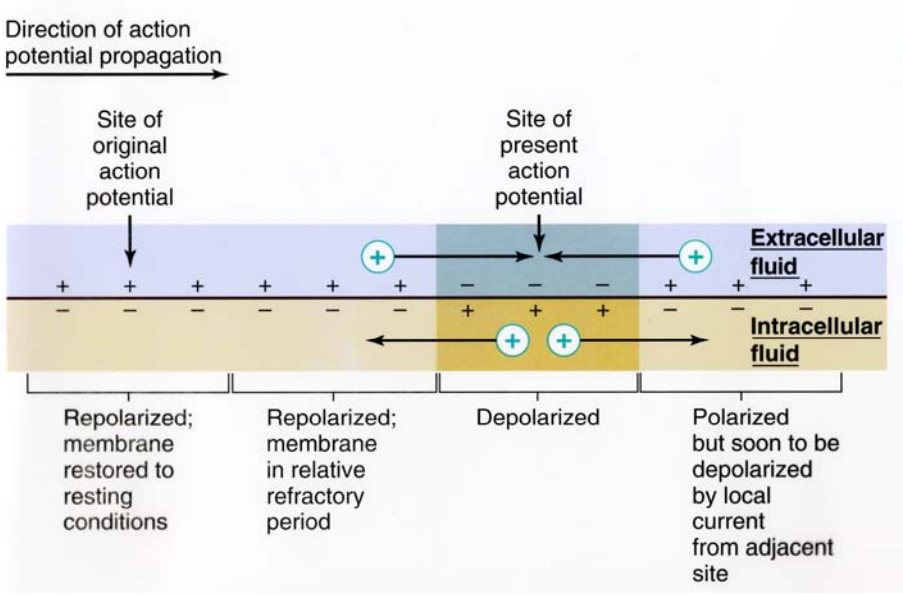
圖 4-18

在動作電位期間鈉與鉀離子通道功能之變化。電位變化都可以使這兩種通道開啟及活化，鈉離子通道有不活化閘（淡藍色），它可以暫時阻止離子流通。但是鉀離子通道沒有此不活化閘。電位感知性鉀離子通道比鈉離子通道還慢打開。本圖中沒有繪出鈉與鉀離子的漏流通道，細胞在靜止狀態時它們才會開啟。

All-or-None Law (AP)



Propagation of AP



Propagation of AP

Saltatory Conduction

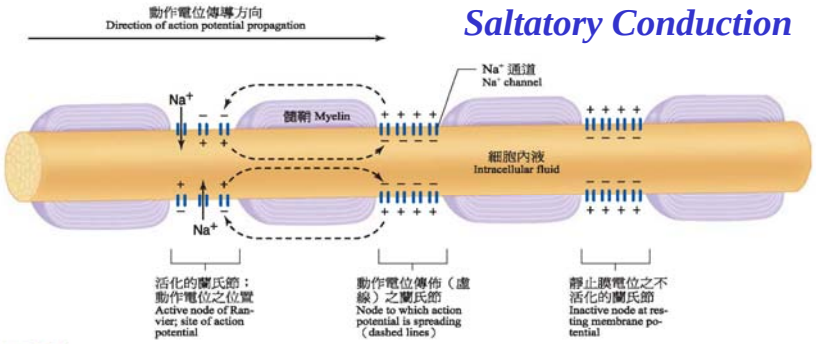


圖 4-21
髓鞘與動作電位之跳躍傳導。並未標示出鉀離子通道。

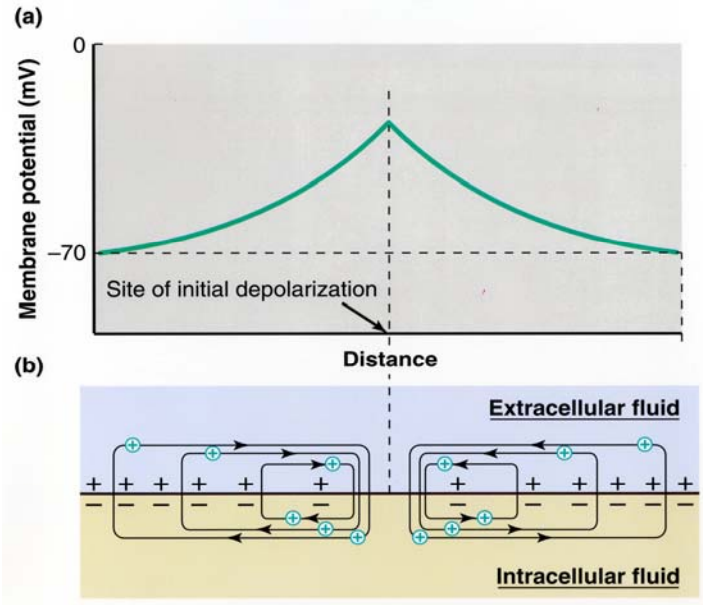
28

Speed of Impulse Propagation

- The propagation speed of a nerve impulse is not related to stimulus strength.
  - larger, myelinated fibers conduct impulses faster due to size & saltatory conduction
- Fiber types
  - A fibers largest (5-20 microns & 130 m/sec)
    myelinated somatic sensory & motor to skeletal muscle
  - B fibers medium (2-3 microns & 15 m/sec)
    myelinated visceral sensory & autonomic preganglionic
  - C fibers smallest (0.5-1.5 microns & 2 m/sec)
    unmyelinated sensory & autonomic motor

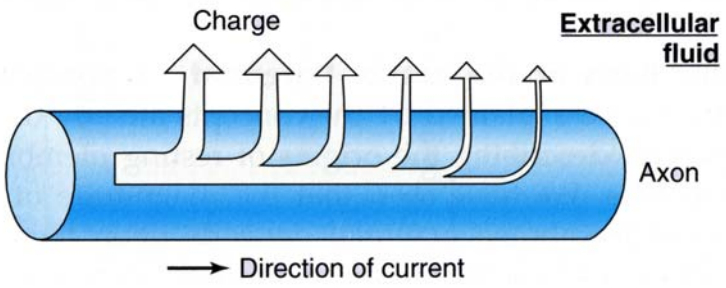
29

Graded Potential



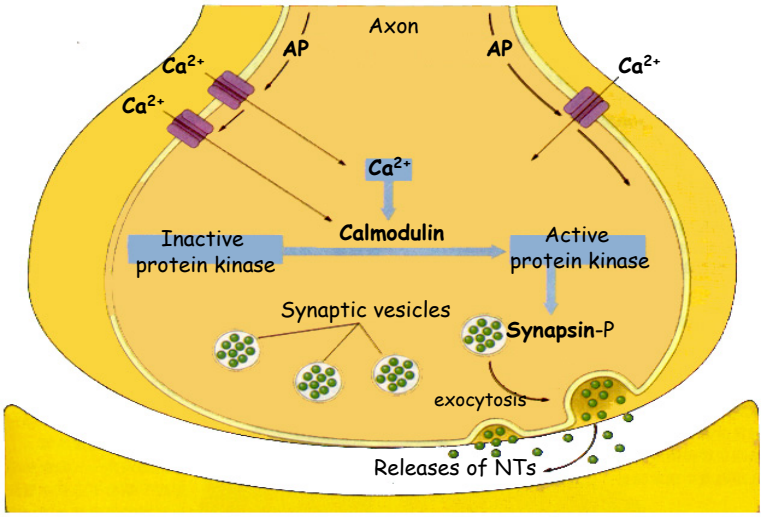
30

Axon = Cable



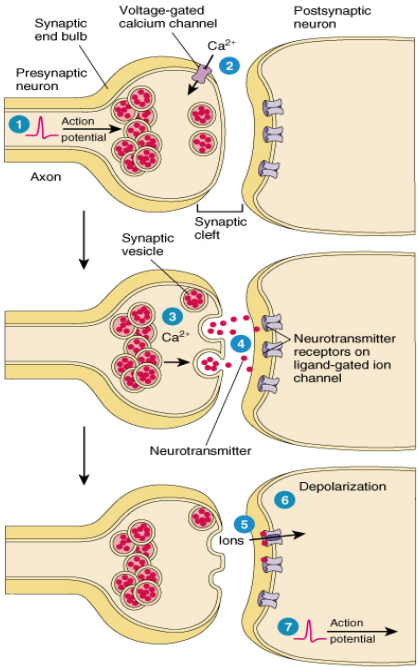
31

Release of NTs/Chemical Synapse



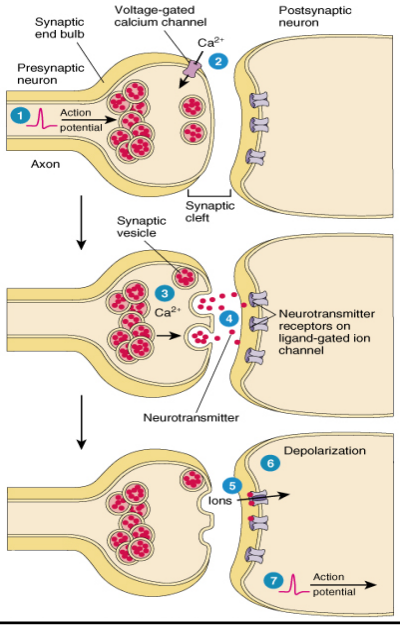
32

- Action potential reaches end bulb and voltage-gated Ca^{+2} channels open
- Ca^{+2} flows inward triggering release of NTs
- NTs crosses synaptic cleft & binding to ligand-gated receptors
- Synaptic delay is 0.5 msec
- One-way information transfer



Removal of Neurotransmitter

- Diffusion
  - move down concentration gradient
- Enzymatic degradation
  - acetylcholinesterase
- Uptake by neurons or glia cells
  - neurotransmitter transporters
  - Prozac = serotonin reuptake inhibitor



Three Possible Responses

- **Small EPSP occurs**
  - potential reaches -56 mV only
- **An impulse is generated**
  - threshold was reached
  - membrane potential of at least -55 mV
- **IPSP occurs**
  - membrane hyperpolarized
  - potential drops below -70 mV

35

Neurotransmitters

分類	化學分子
Amines	乙醯膽鹼(acetylcholine)、組織胺(histamine)、 血清張力素(serotonin, 5-hydroxytryptamine; 5-HT)
Catacholamines	多巴胺(dopamine)、腎上腺素(epinephrine)、正腎上腺素(norepinephrine)
Amino acids	天門冬胺酸(aspartic acid) 、γ-胺基丁酸(GABA)、麩胺酸(glutamic acid)、甘胺酸(glycine)
Polypeptide	昇糖激素(glucagon)、胰島素(insulin)、生長激素釋放抑制因子(somatostatin)、P物質(substance P)、促腎上腺皮質分泌激素 (ACTH)、血管收縮素 II (angiotensin II)、腦內啡(endorphins)、促甲狀腺激素釋放激素 (TRH)、血管加壓素（抗利尿激素, ADH）、膽囊收縮素 (CCK)

36

Endorphins

- 平常有在運動的人，對疼痛的指數比較高，也就是對疼痛的耐受性較高。運動時，腦內嗎啡(內源性嗎啡；endorphins)分泌會增加。Endorphins被分泌出來，其具有止痛的效果、會使人有快樂的感覺，所以當你適度運動流完汗後，會感到很舒服，這就是和endorphins增加有關。像運動員和劇烈運動的人，都曾說會感到一種與endorphins劑量提高有關的特殊陶醉感或快感。

37

Synaptic Potential

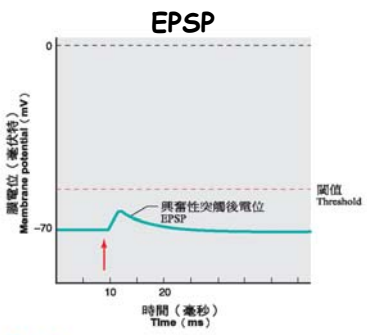


圖 4-26
興奮性突觸後電位（EPSP）。箭頭指出在突觸前神經元之刺激。

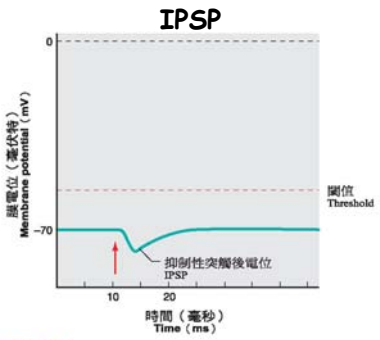


圖 4-27
抑制性突觸後電位（IPSP）。箭頭指出在突觸前神經元之刺激。

38

Spatial & Temporal Summation

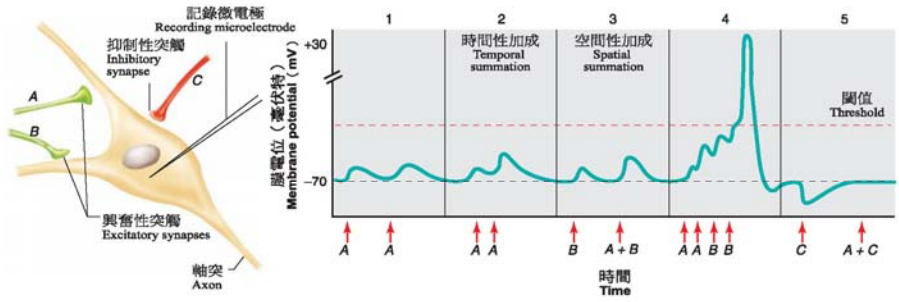
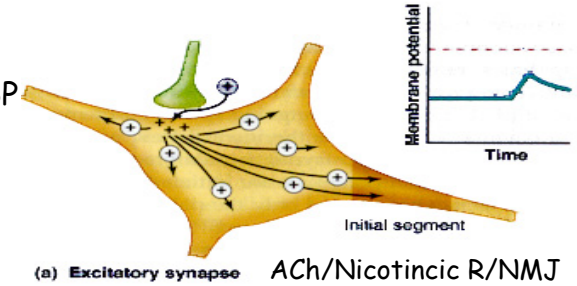


圖 4-29

EPSP與IPSP在突觸後細胞體上之交互作用。傳入信息的神經元（A-C）分別在箭頭所標示的時間被刺激，突觸後細胞上有微電極記錄所生成的膜電位。

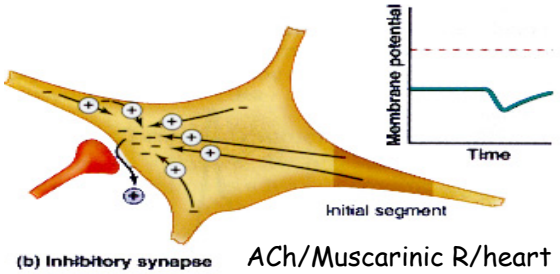
Synaptic Potential

EPSP



(a) Excitatory synapse ACh/Nicotincic R/NMJ

IPSP



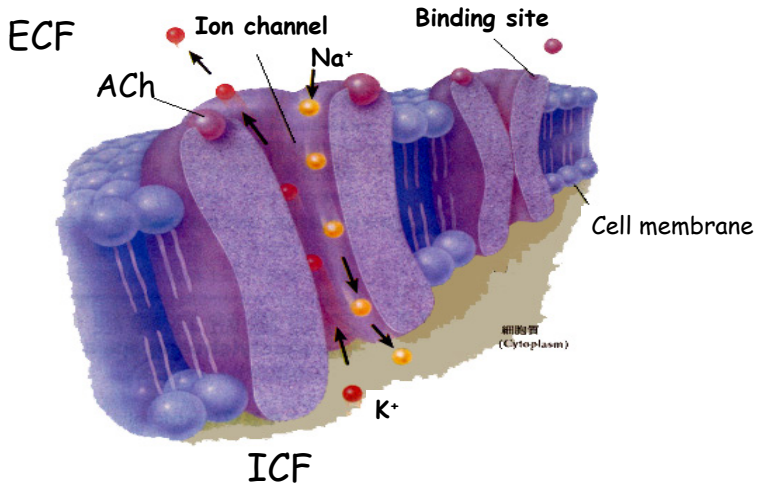
(b) Inhibitory synapse ACh/Muscarinic R/heart

AP & EPSP

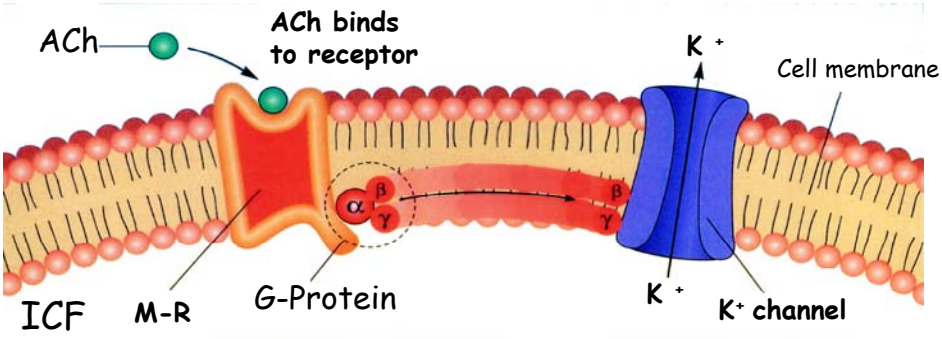
特性	動作電位(AP)	興奮性突觸後電位(EPSP)
開啟離子閘門的刺激	去極化	乙醯膽鹼
刺激所產生的初期效果	Na channels開啟	Na及 K channels開啟
再極化的產生	K channels開啟	胞內正電荷隨時間及距離消失
傳導距離	沿著軸突產生	1-2 mm , 為局部的電位
去極化及Na channels	有	無
最大去極化	+40mV	接近零
加成(summation)作用	無加成 ,遵循全或無定律	EPSPs 的加成， 產生有等級的去極化
不反應期	有	無
藥物的作用	可被河豚毒素(tetrodotoxin)抑制 ,但不被南美箭毒(curare)抑制	可被南美箭毒抑制, 但不被河豚毒素抑制

41

Nicotinic ACh Receptor/NMJ

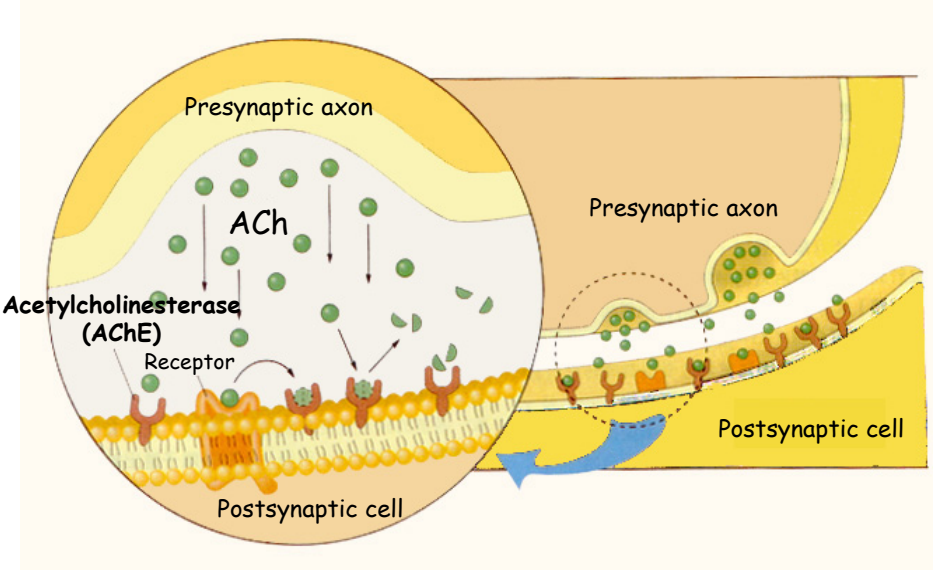


Muscarinic ACh Receptor/Heart

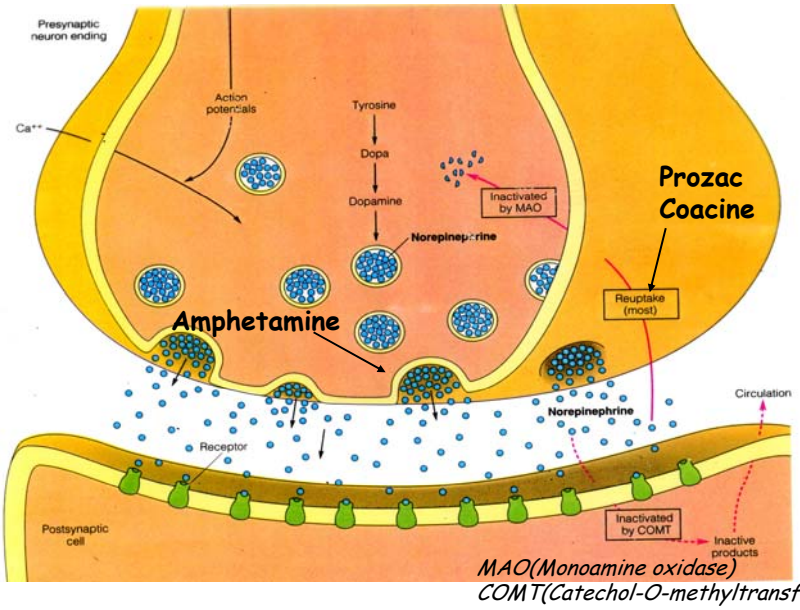


43

AChE/Postsynaptic Cell Membrane



Release & Inactivation of NE



MAO(Monoamine oxidase)
COMT(Catechol-O-methyltransferase)

Catecholamine Biosynthetic Pathway

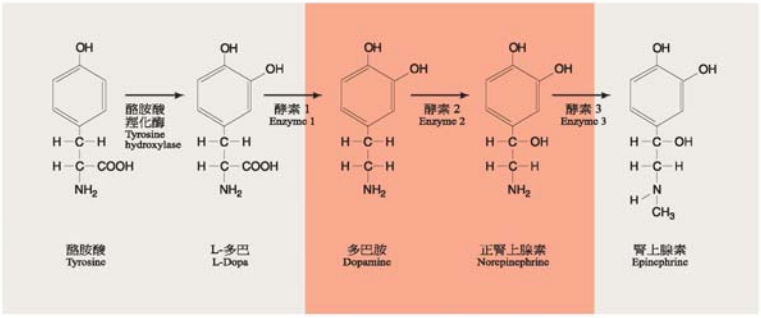
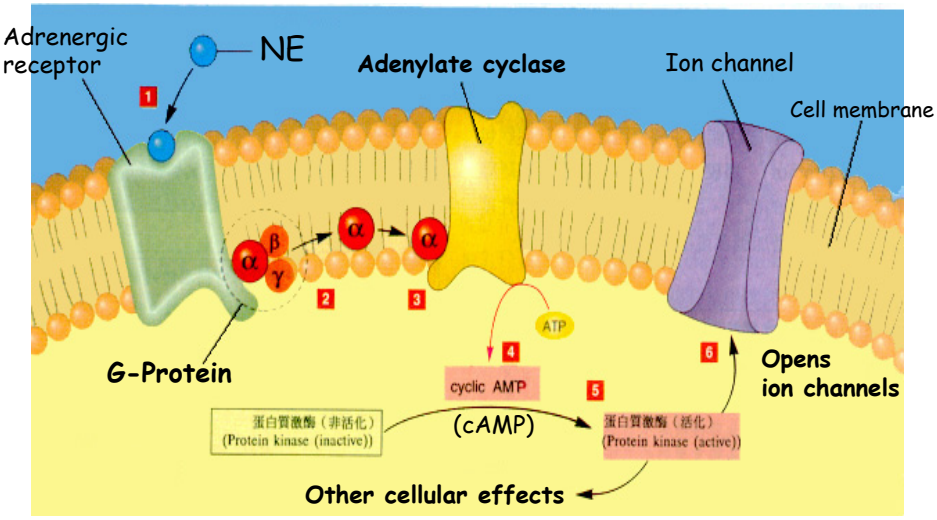


圖 4-33
兒茶酚胺之生物合成路徑。速率限制酵素-酪胺酸羥化酶（tyrosine hydroxylase）是作用在生物合成的第一步。神經元最後會釋放哪一種物質作為神經傳遞物質，端視神經元還具有其他三種酵素中的哪幾種酵素而定。有色區塊顯示在中樞神經系統較常見的兒茶酚胺類之神經傳遞物質。

46

Effect of NE

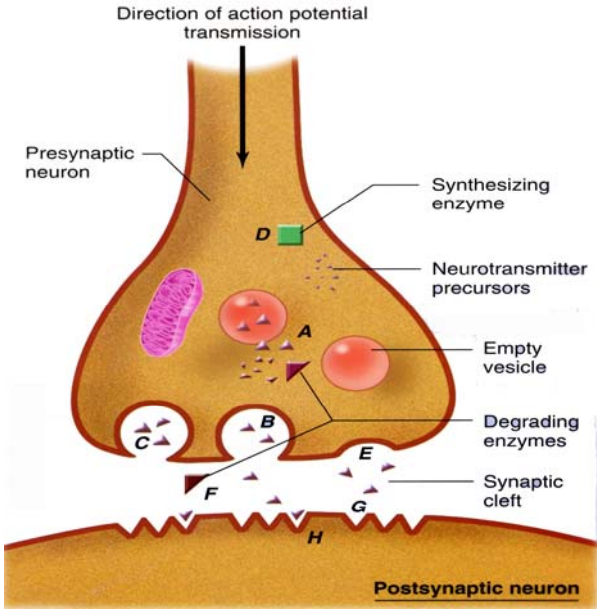


47

Condition	Symptoms	Imbalance of Neurotransmitter in brain
Alzheimer's disease	Memory loss, depression , disorientation, dementia, hallucinations, death	Deficient ACh
Clinical depression	Debilitating, inexplicable sadness	Deficient NE and/or 5-HT
Epilepsy	Seizures, loss of consciousness	Excess GABA leads to excess NE and DA
Huntington disease	Personality changes, loss of coordination, uncontrollable dancelike movements, death	Deficient GABA
Hypersomnia	Excessive sleeping	Excess 5-HT
Insomnia	Inability to sleep	Deficient 5-HT
Mania	Elation, irritability, overtalkativeness, increased movements	Excess NE
Myasthenia gravis	Progressive muscular weakness	Deficient ACh receptors at neuromuscular junctions
Parkinson's disease	Tremors of hands, slowed movements, muscle rigidity	Deficient DA
Schizophrenia	Inappropriate emotional responses, hallucinations	Deficient GABA leads to excess DA
Sudden infant death syndrome (''crib death'')	Baby stops breathing , dies if unassisted	Excess DA
Tardive dyskinesia	Uncontrollable movements of facial muscles	Deficient DA

48

Drug Actions at Synapses



49

Drug	Neurotransmitter	Affected Mechanism of Action	Effect
Tryptophan	Serotonin	stimulates neurotransmitter synthesis	Sleepiness
Reserpine	Norepinephrine	Decrease packaging neurotransmitter into vesicles	Decreases blood pressure
Curare	Acetylcholine	Decreases neurotransmitter in synaptic cleft	Muscle paralysis
Botulinus toxin	Acetylcholine	decrease neurotransmitter release	Muscular weakness
Tertodotoxin	Acetylcholine….	Block Na channels	Muscle paralysis
Nerve gas	Acetylcholine	Blocks enzymatic degradation of neurotransmitter in postsynaptic cell (AChE)	Spastic paralysis
Neostigmine	Acetylcholine	Blocks enzymatic degradation of neurotransmitter in postsynaptic cell (AChE)	Muscle contraction
Nicotine	Acetylcholine	Stimulates synthesis of enzyme that degrades neurotransmitter	Increases alertness

50

Drug	Neurotransmitter	Affected Mechanism of Action	Effect
Valium	GABA	Enhances receptor binding	Decrease anxiety
Cocaine	Norepinephrine	Blocks reuptake	Euphoria
Tricyclic antidepressants	Norepinephrine	Blocks reuptake	Mood elevation
Monoamine oxidase inhibitors	Norepinephrine	Blocks enzymatic degradation of neurotransmitter in presynaptic cell	Mood Elevation
Prozac and related drugs	Serotonin	Blocks reuptake	Mood Elevation

51

古柯鹼(Cocaine)

是一種和安非它命(amphetamines)作用相似的中樞興奮劑，在美國有濫用此藥物的趨勢。服用此藥早期會有快樂並且較世故的感覺，但長期持續服用則造成退縮、憂慮，對高劑量藥物的依賴、並會引起嚴重心血管及腎臟疾病而導致心臟及腎衰竭 。古柯鹼對中樞神經的作用導致抑制突觸前軸突末梢對單胺類的再吸收作用而造成對使用多巴胺及其它單胺類神經傳導物質之神經路徑的過度刺激 。

52

Benzodiazepines

是一種鎮靜安眠類藥物,可加強 GABA在腦及脊髓的作用。GABA是一種神經傳導物質，可抑制脊髓支配骨骼肌神經元的活性。所以靜脈注射該類藥可抑制癲癇持續狀態(status epilepticus)時的肌肉收縮及藥物過量和中毒時所產生的徵狀。由於GABA對大腦有廣泛的抑制作用，所以似乎也參與情緒的表現。因此二氯平(Valium)等benzodiazepines類藥劑也用來作為安眠劑

53

肉毒桿菌
(Clostridium botulinum)

是非常毒的菌，可分為七種亞型: A~G ，一般臨床用A型肉毒桿菌毒素， 1897年開始有許多眼科醫生用A型來治療斜視、不自主的抽動、顏面神經痙攣，而且還具有除皺的功能。A型肉毒桿菌毒素的除皺作用機轉：一種位於神經末梢可分解突觸蛋白的酵素，使突觸小泡無法與突觸前細胞膜融合,則神經傳導物質(ACh)就無法被釋放出去，便造成肌肉無力(使過度收縮的肌肉可以放鬆，減緩皺紋產生)。

54

神經毒氣 (nerve gas)

可抑制骨骼肌中AChE的活性使ACh不被分解，也就是在突觸間隙的ACh濃度相對增高，相對的作用於突觸後接受器也會增加，骨骼肌就一直會產生收縮。而持續刺激突觸後細胞導致痙攣性癱瘓(spastic paralysis)。而神經肌肉傳達就會減弱，用AChE抑制劑如: neostigmine 與神經毒氣很相似，主要抑制AChE作用，還可以治療重症肌無力。

55

Alzheimer's disease

是最常見的老年痴呆症；其病程常於中年開始，造成進行性的智力退化。阿茲海默氏疾病的原因並不清楚，但證據顯示和膽鹼激導性神經元 (cholinergic neuron) (用ACh為神經傳導物質)的減少有關。這些神經元終止於海馬迴 (hippocampus)及腦皮質(和記憶儲存有關的區域)。 因為乙醯膽鹼是由 acetyl coenzyme A和choline構成，所以有人利用攝食大量卵磷脂 (lecithin)含有膽素來增加腦部的 ACh。到目前為止，這種營養治療及利用藥物抑制 AChE 以增加乙醯膽鹼的方法只有一點點成效。

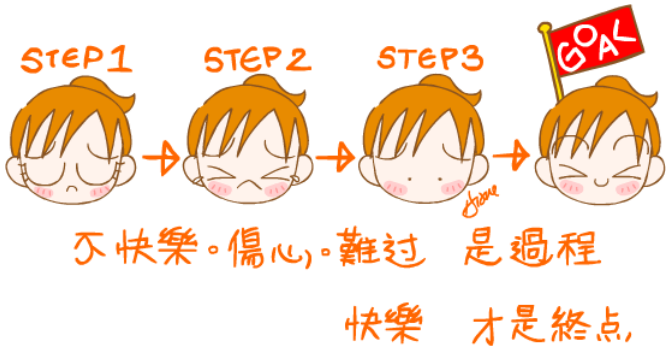
56

重症肌無力 (myasthenia gravis)

ACh接受器被免疫系統的抗體摧毀， so即使有ACh也是無法作用， so骨骼肌無法有利的收縮，肌肉就會無力。可利用neostigmine來作治療，雖然骨骼肌上的ACh接受器被破壞，但還有少許接受器存在，如果分泌出來的ACh很容易被破壞，也是沒辦法作用到接受器，所以為了增加ACh的濃度，因此利用neostigmine抑制AChE ，使ACh沒辦法代謝，則ACh濃度就會變高，容易作用到稀少的ACh接受器上，讓骨骼肌稍微收縮。

57

快樂才是終點



58