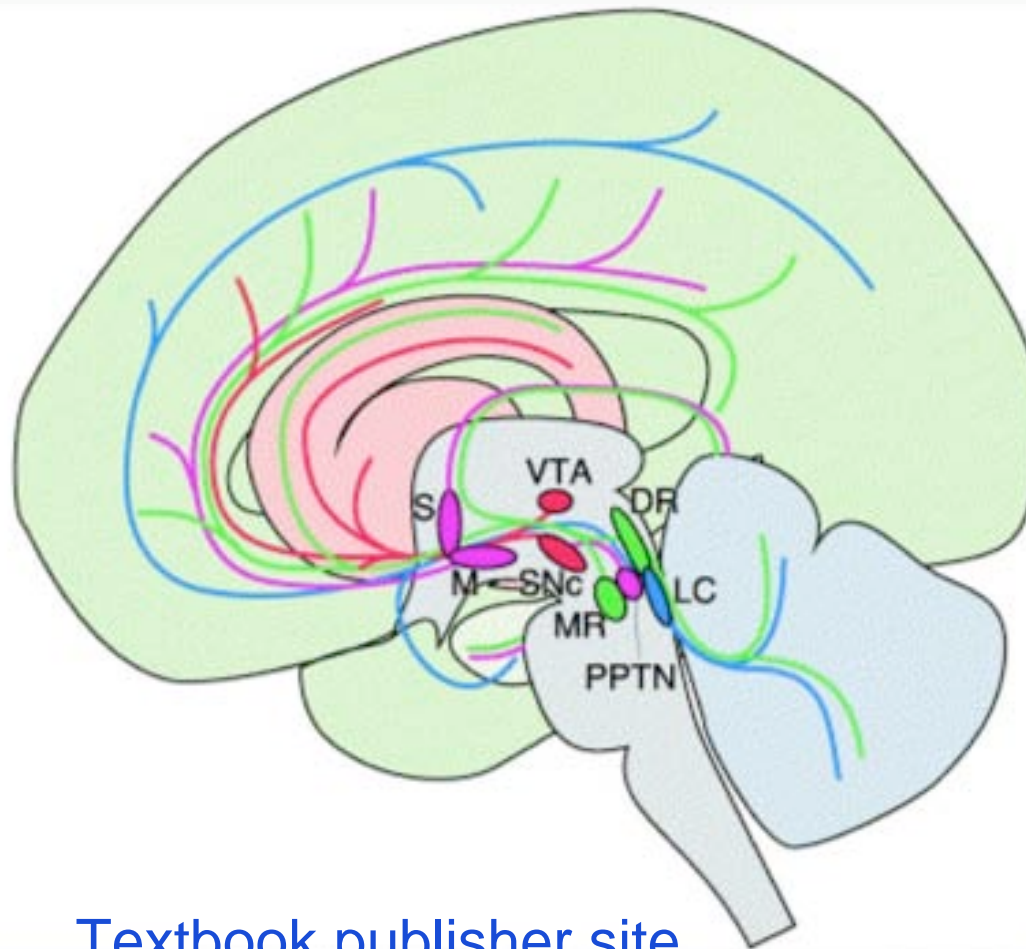


Psychopharmacology



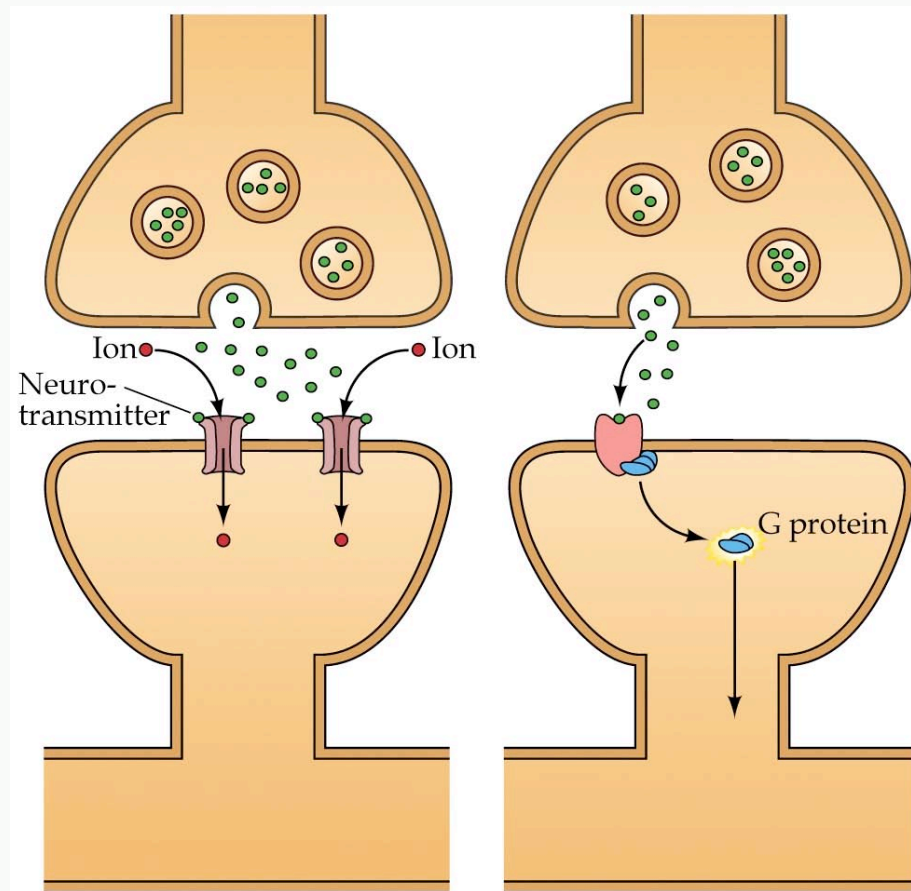
Exam is multiple choice (~80%) and short answers (~20%)

includes:
pages 7-9 &
Chpt 2 to 4

Textbook publisher site
<http://ablongman.com/carlsonpob9e>

A quick review of synaptic action

- receptor types (ionotropic and metabotropic)



Being a neurotransmitter: What does it take?

- Exists pre-synaptically
- Released in response to action potential
- Application at synapse produces response
 - post-synaptic membrane has receptors
- Blocking release stops synaptic function

Psychopharmacology: The study of the effects of drugs on the nervous system and on behaviour

Drug effects: The changes a drug produces in an animal's physiological processes and behavior

What is a 'drug'?

- a very vague term
- all ingested substances alter bodily function
- 'drug' is reserved for things that have pronounced effects when ingested in small quantities

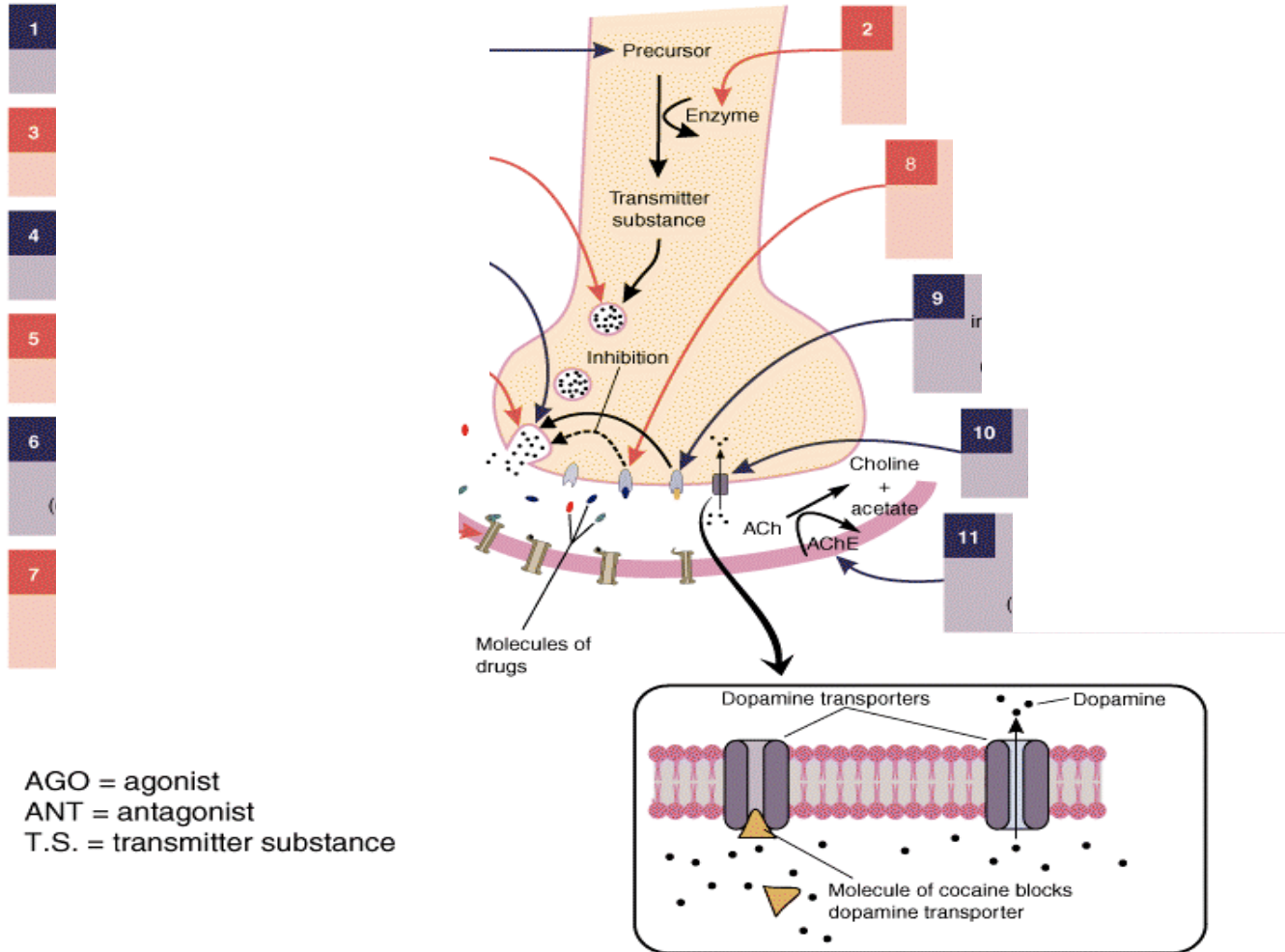
Sites of Action: The locations at which drugs interact with cells of the body, thus affecting some biochemical processes of these cells

Basic classification of drug actions

Agonist: A drug that facilitates the effects of a particular neurotransmitter on the postsynaptic cell

Antagonist: A drug that *opposes* or inhibits the effects of a particular neurotransmitter on the postsynaptic cell

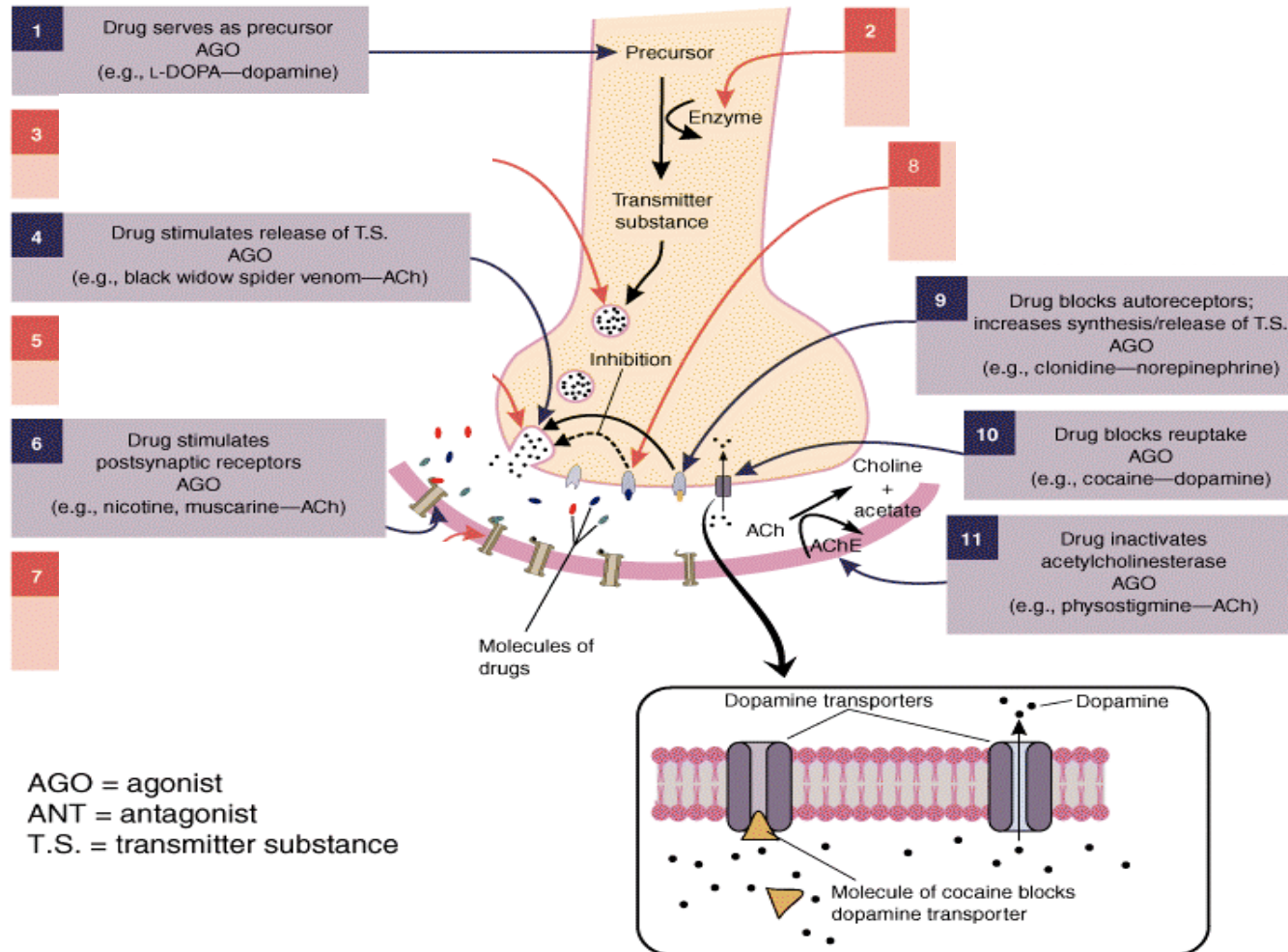
► Summary of the Ways Drugs Affect the Synaptic Transmission



AGO = agonist
 ANT = antagonist
 T.S. = transmitter substance

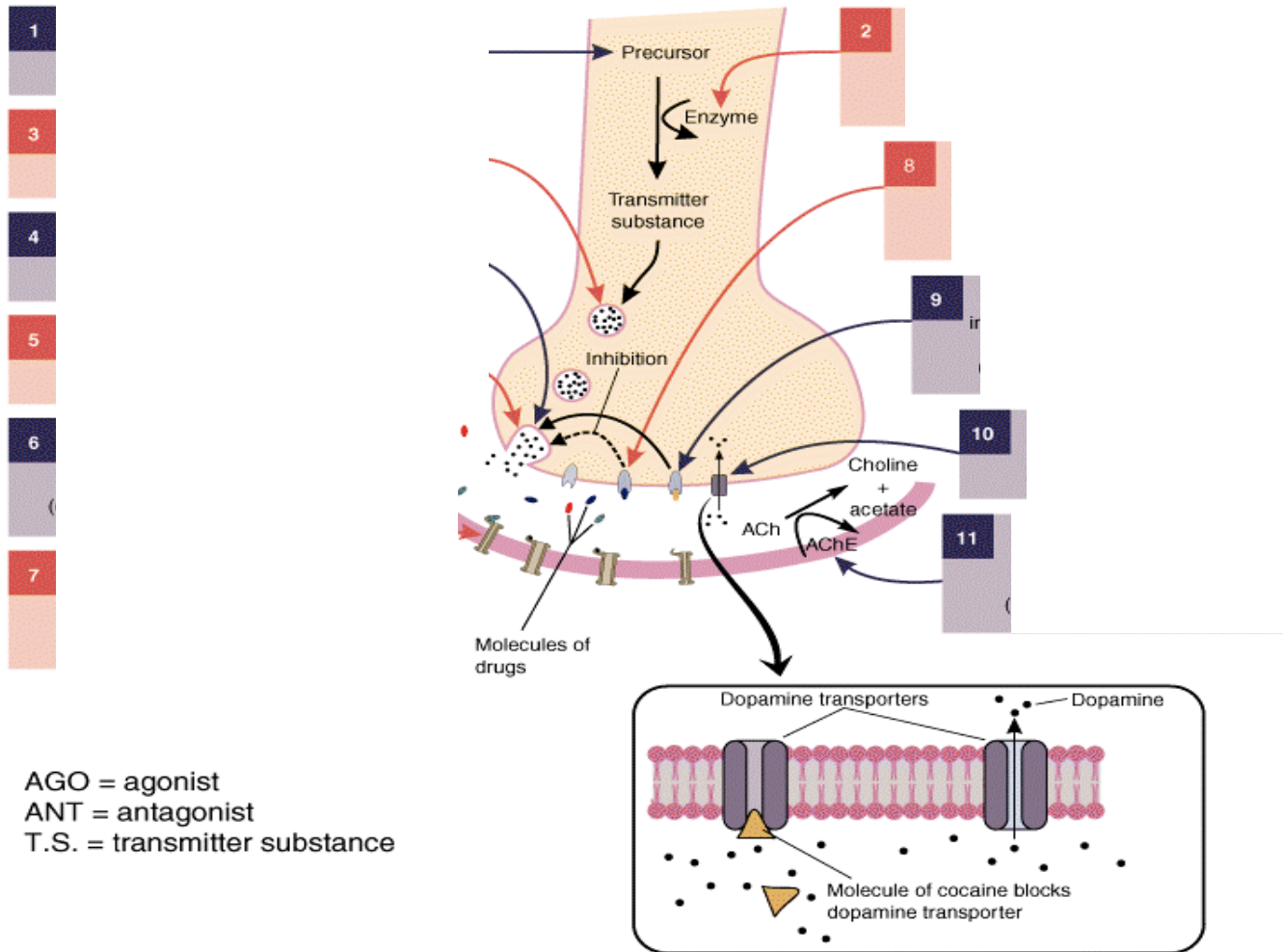
Ways that drugs can agonize

► Summary of the Ways Drugs Affect the Synaptic Transmission



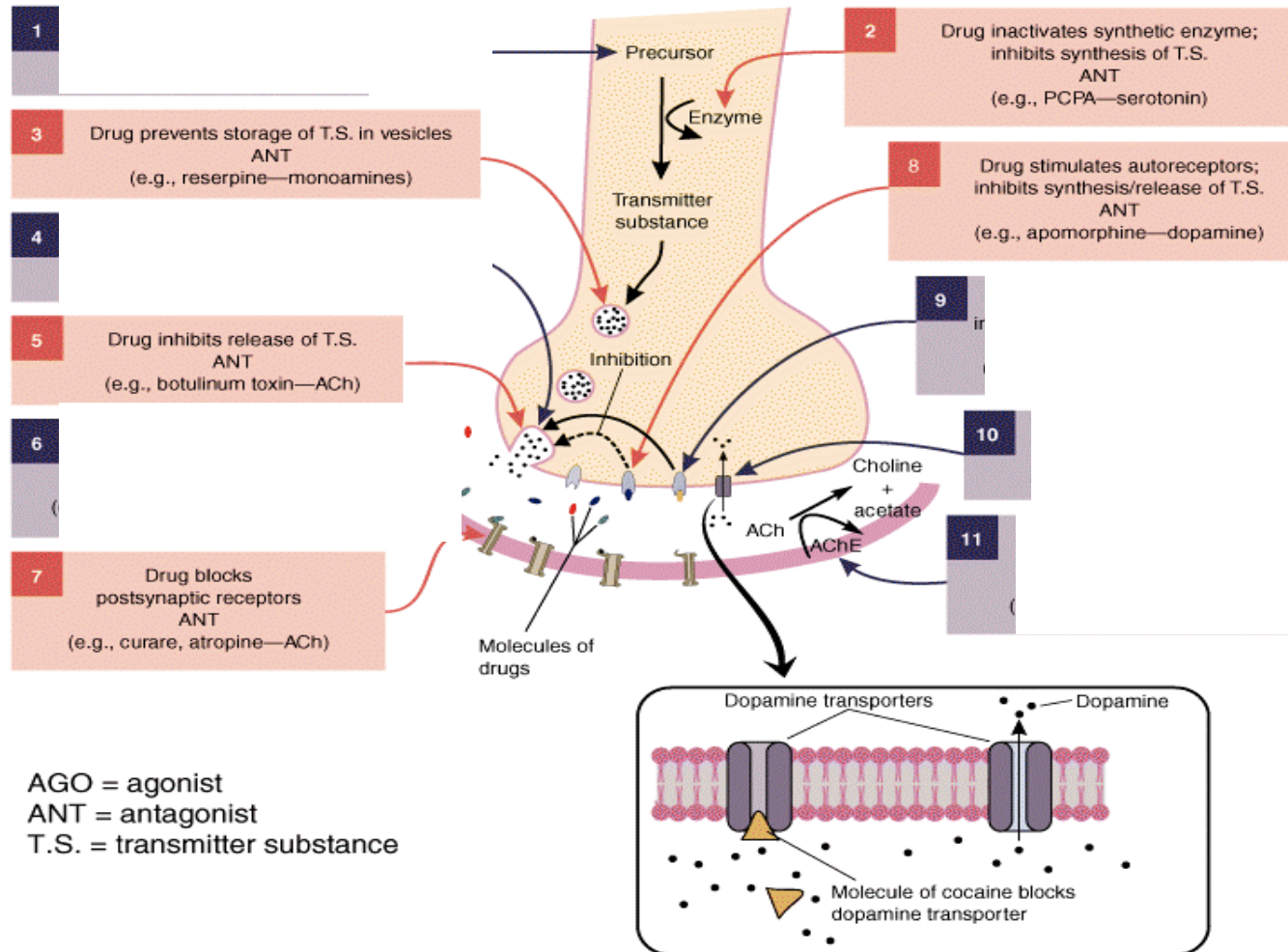
- precursor to neurotransmitter
- stimulate release
- receptor binding
- block autoreceptors
- inhibition of reuptake
- inhibition of deactivation

► Summary of the Ways Drugs Affect the Synaptic Transmission



Ways that drugs can
antagonize

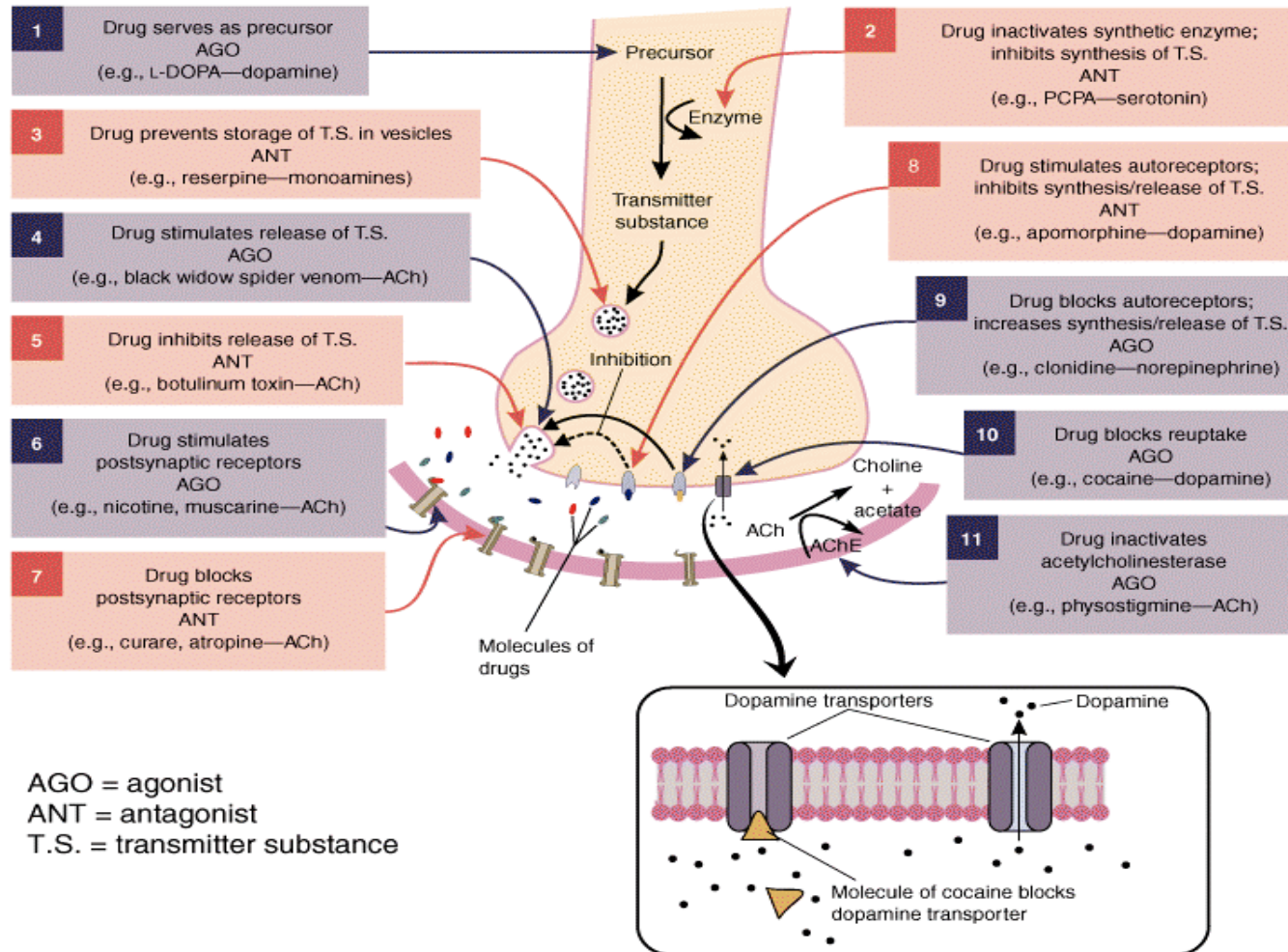
► Summary of the Ways Drugs Affect the Synaptic Transmission



- prevent synthesis
- prevents storage
- block release

- receptor blocker
- stimulates autoreceptors

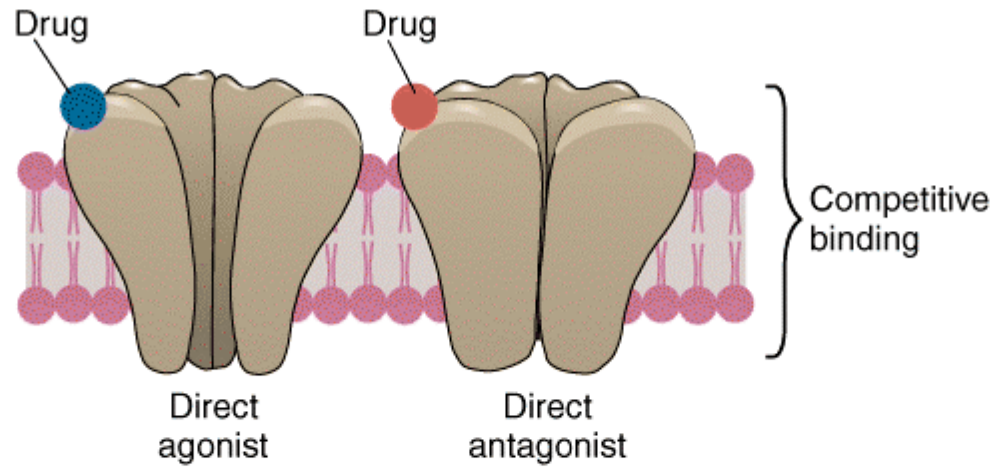
► Summary of the Ways Drugs Affect the Synaptic Transmission



Your text's CD provides a very good review of these mechanisms

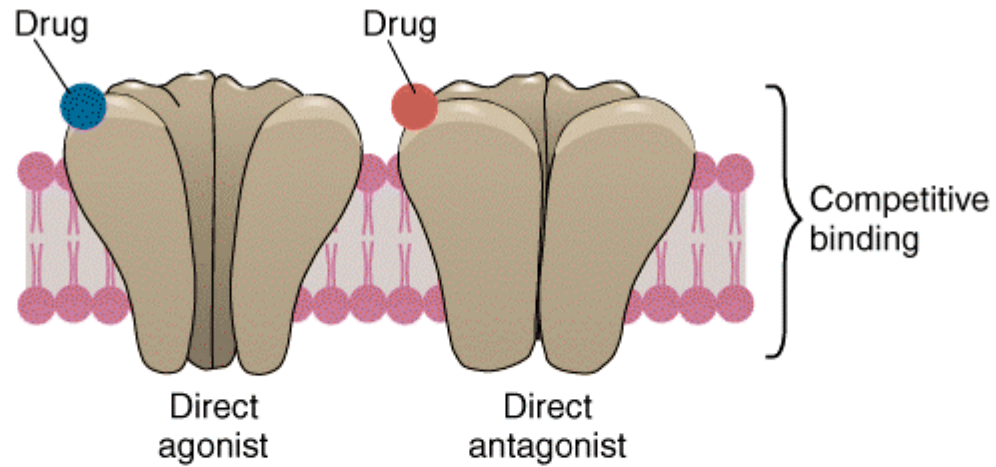
► Actions of Drugs at Binding Sites on Receptors

Binds at same site
neurotransmitter
would



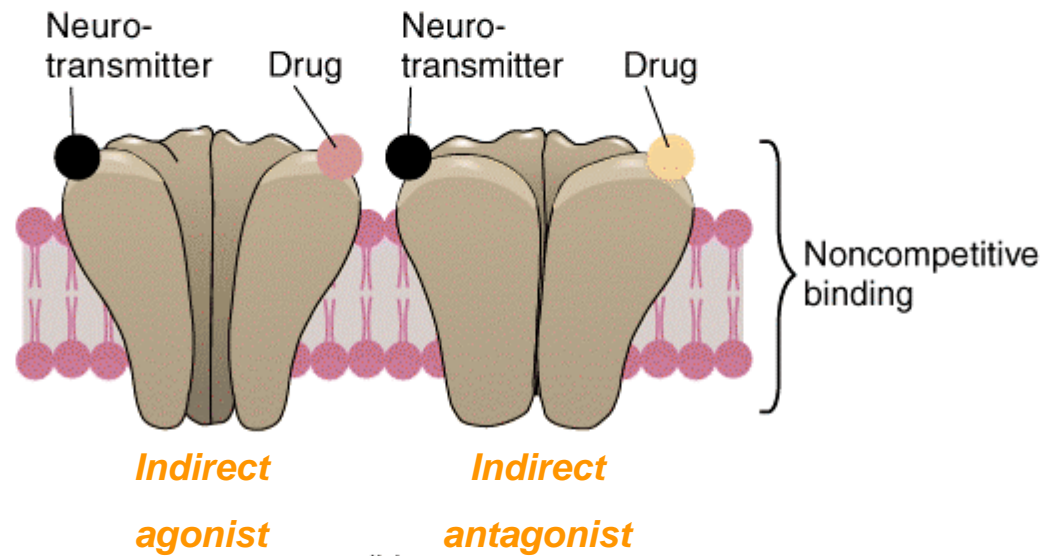
► Actions of Drugs at Binding Sites on Receptors

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(a)

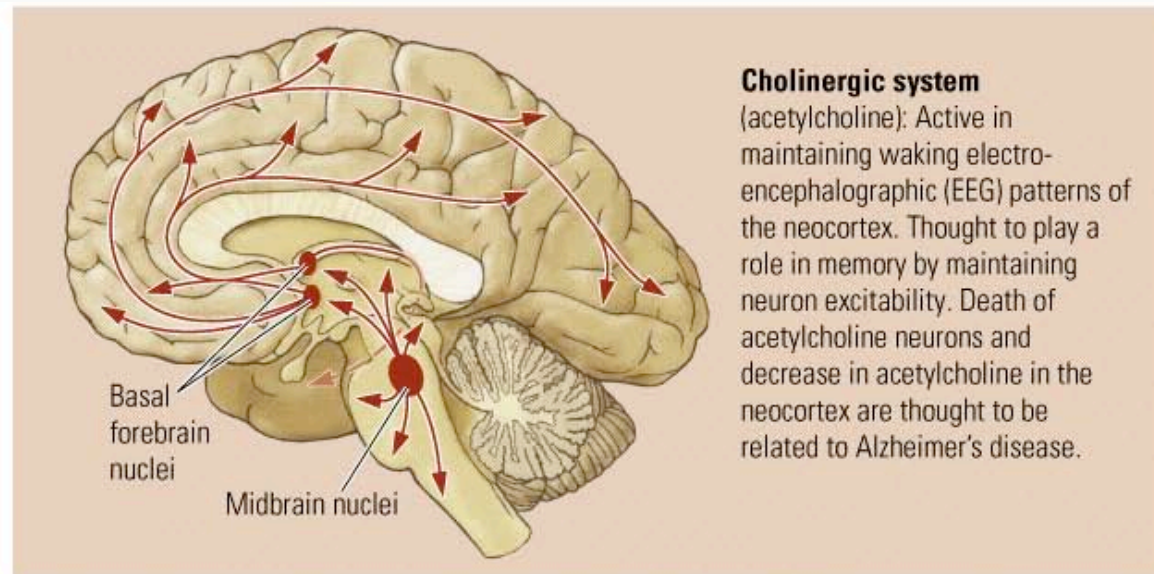
Binds at different site



(b)

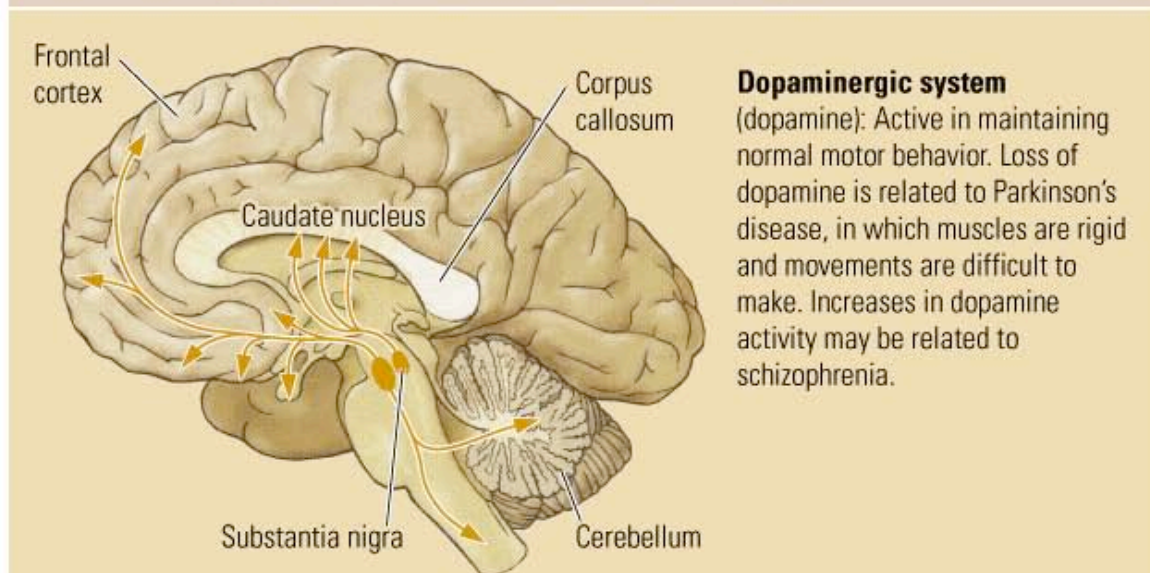
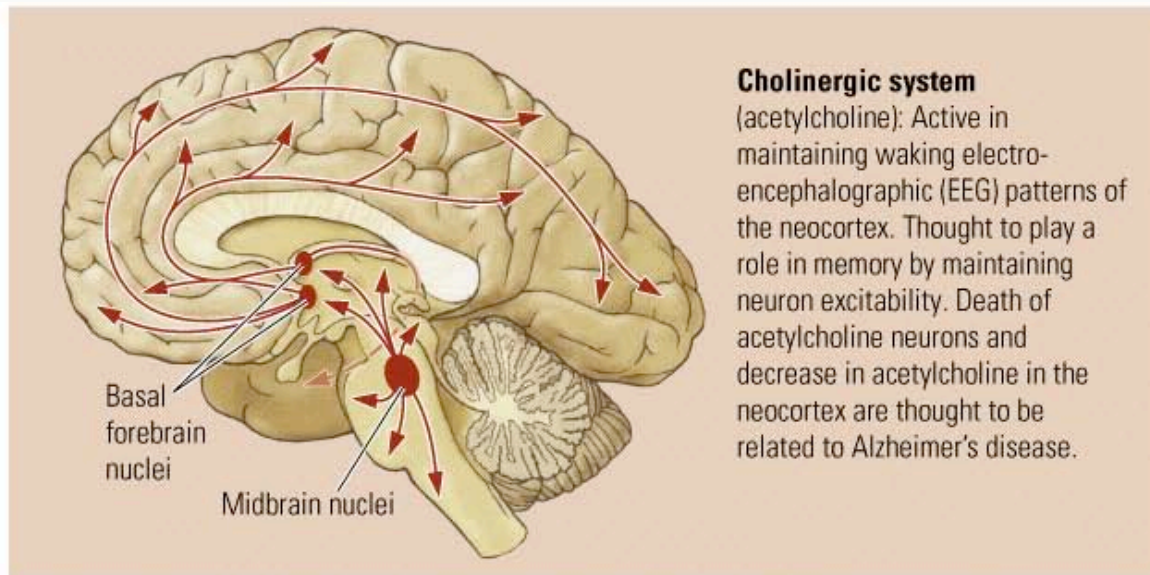
Neurotransmitters

- four major neurotransmitter systems
- Acetylcholine, Dopamine, Norepinephrine, Serotonin (5HT)



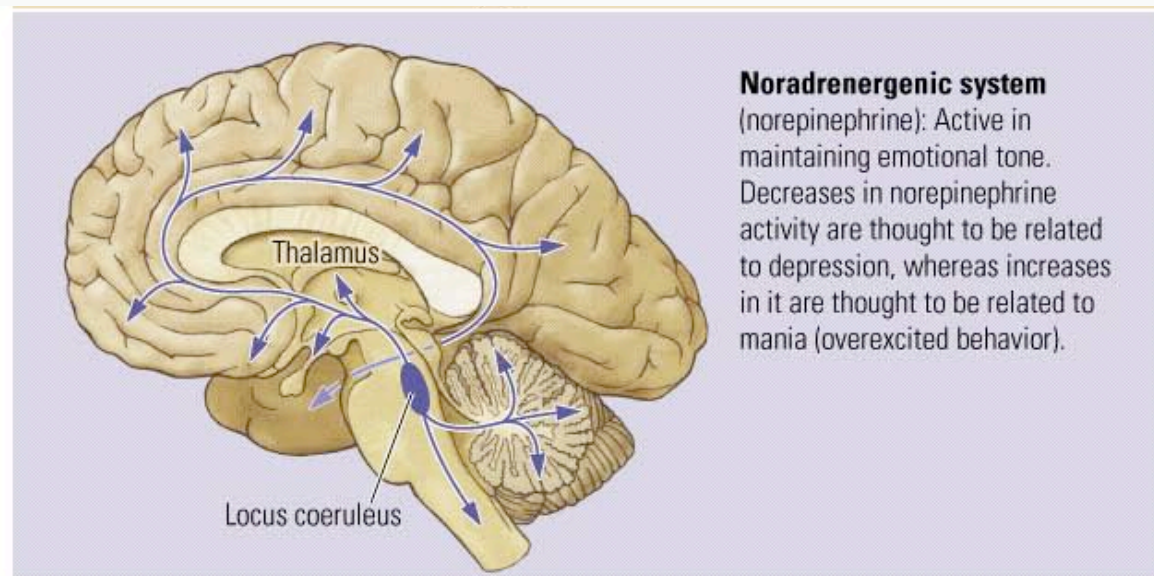
Neurotransmitters

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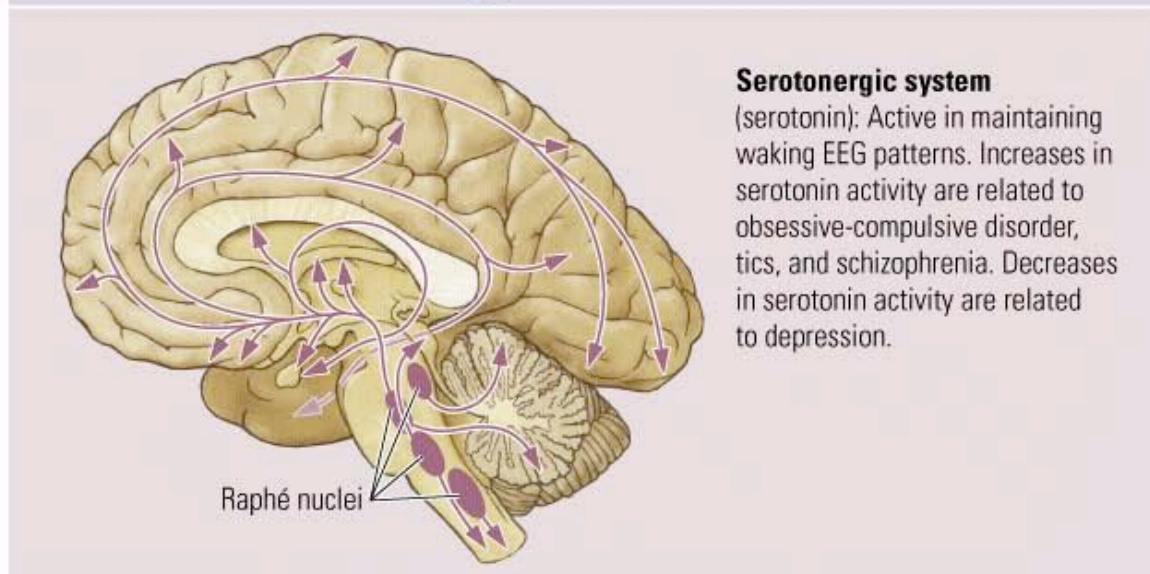
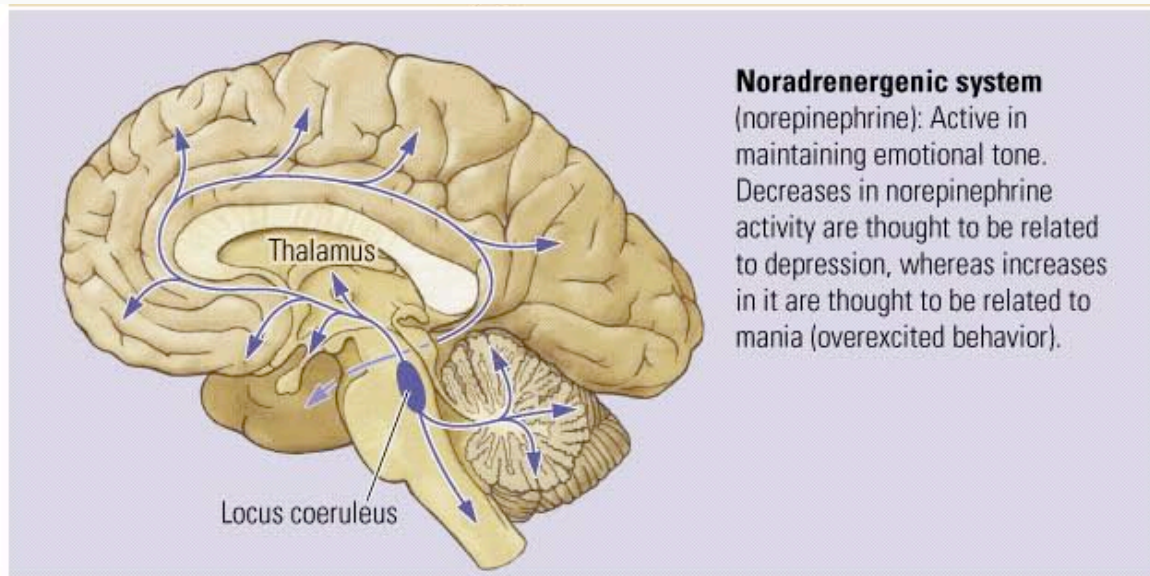
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Neurotransmitters

- 4 major neurotransmitter systems
- Acetylcholine, Dopamine, Norepinephrine, Serotonin (5HT)



The classical neurotransmitters

- Amines – Modulatory effect on systems

Monoamines

- catecholamines (dopamine, noradrenaline)
- indoleamines (serotonin, melatonin)

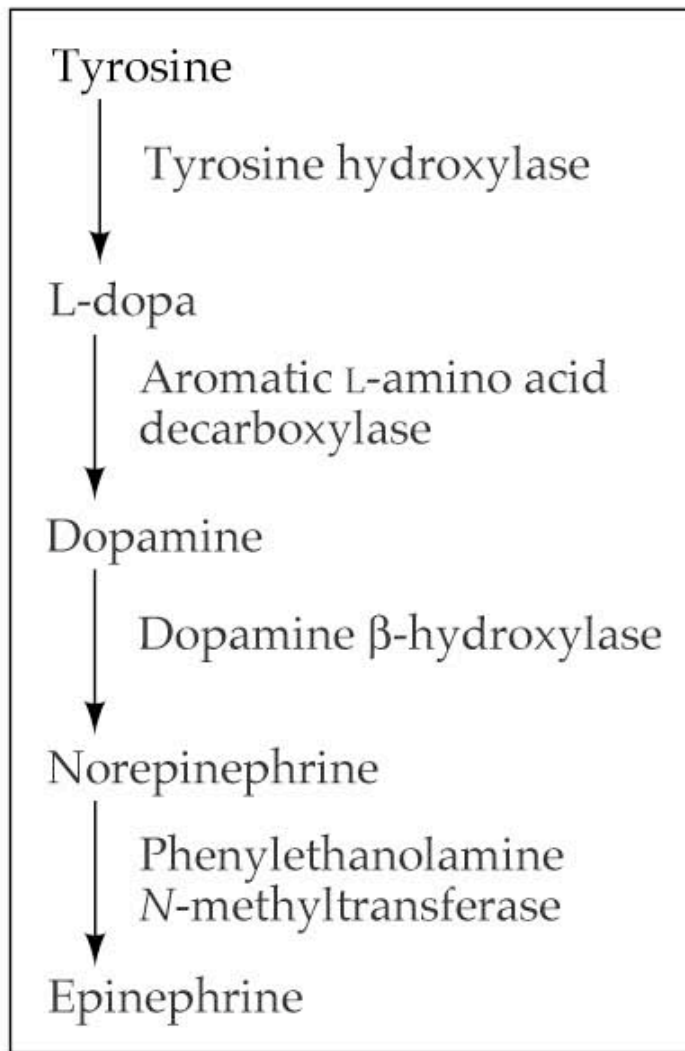
Quaternary amines

- Acetylcholine

Information transmitters

- amino acids (glutamate, GABA)

Catecholamine synthesis

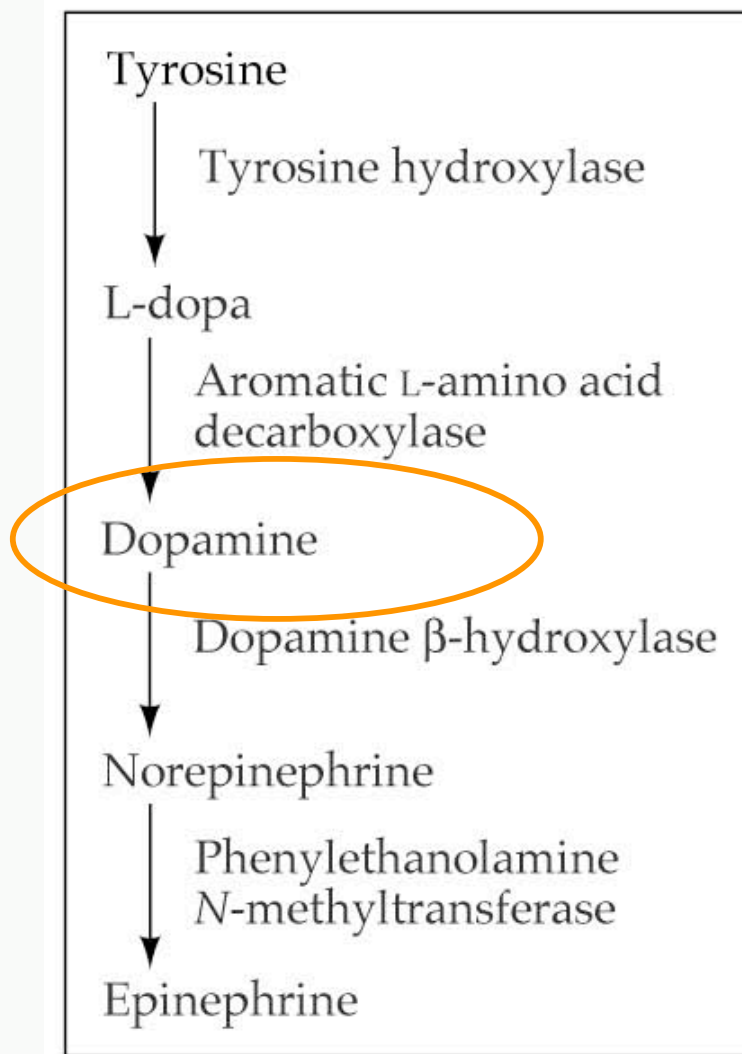


- understanding synthesis can be important for understanding drug action

Neurotransmitters

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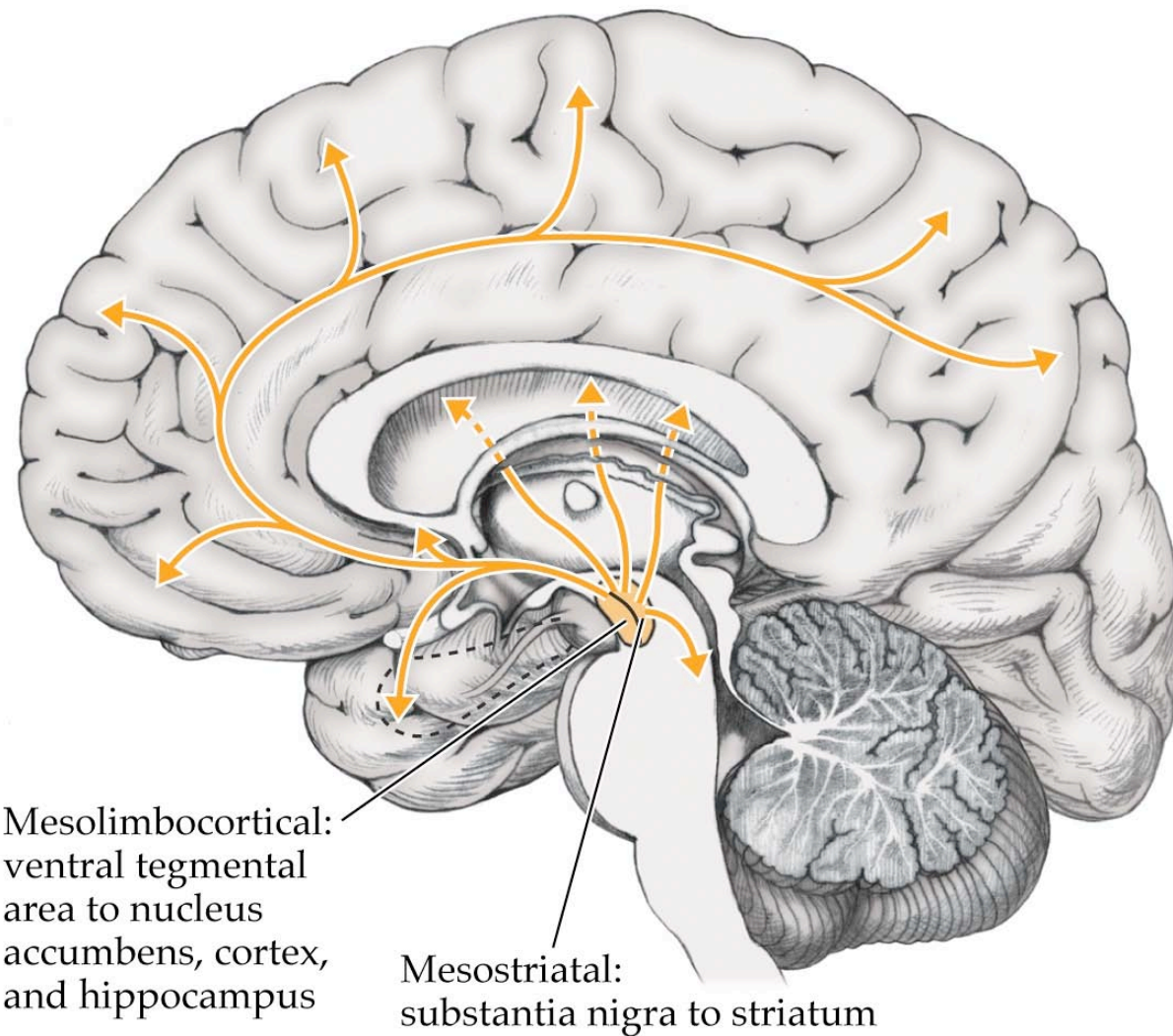
Catecholamine synthesis



- understanding synthesis can be important for understanding drug action

Catecholamines

Dopamine

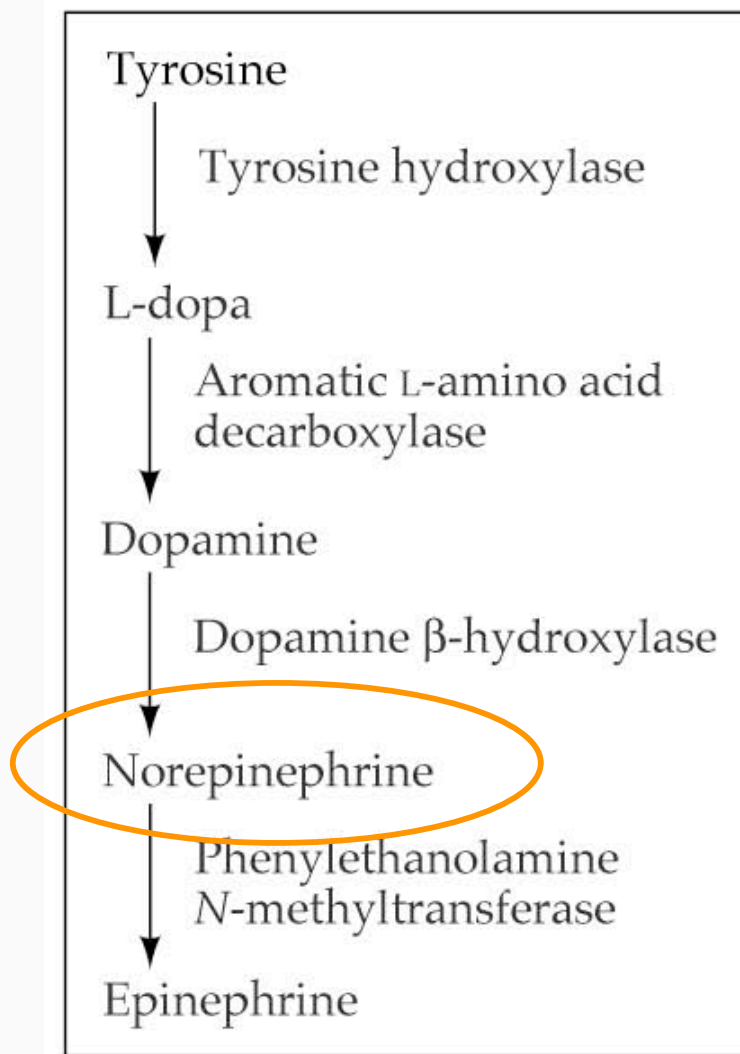


- receptor specificity
- can produce both EPSP and IPSP depending on receptor
- Amphetamines can alter dopamine uptake and produce schizophrenic-like delusions
- can see similar effects with cocaine use

Mesocorticolimbic system
and schizophrenia

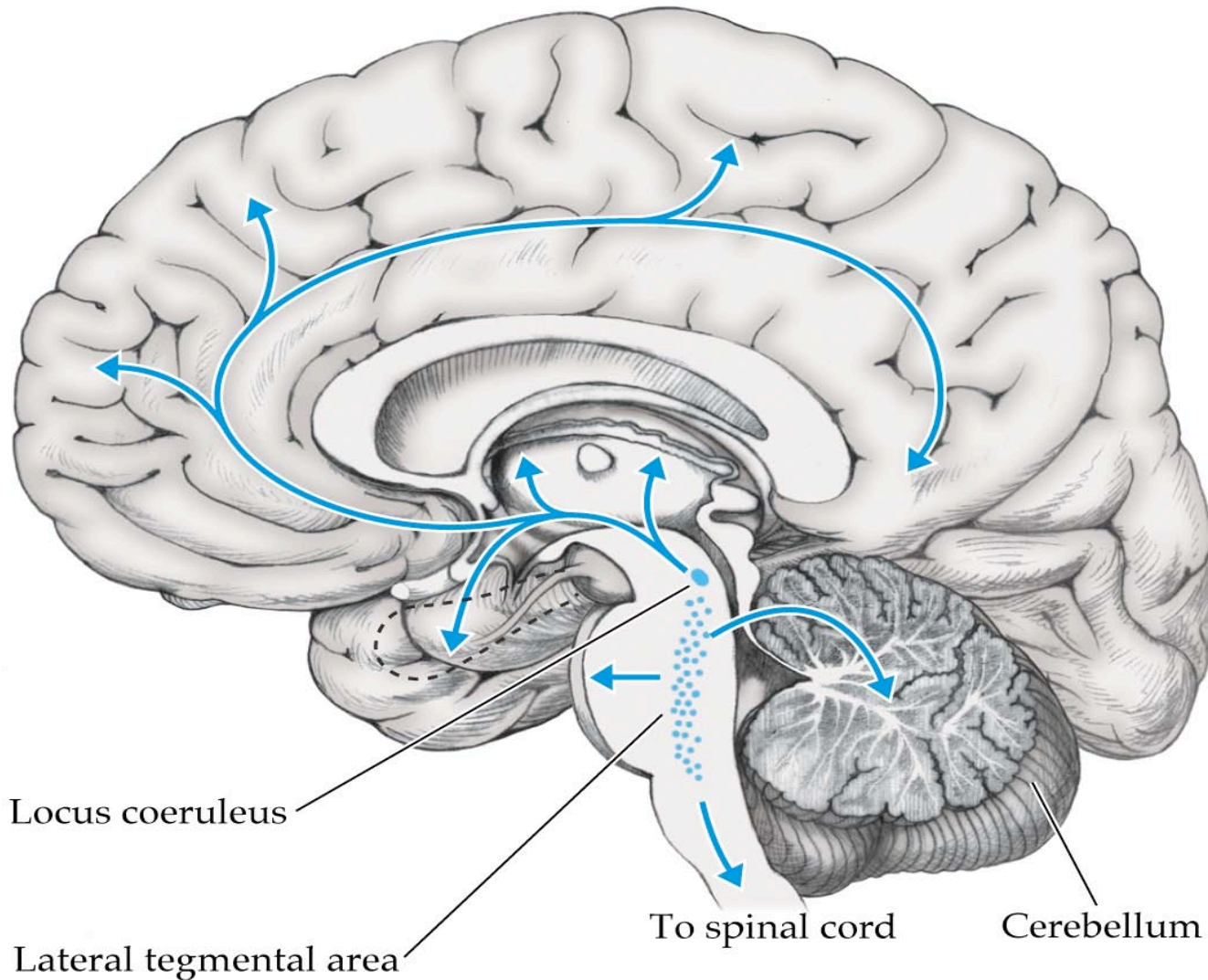
Substantia nigra and
Parkinson's disease -
movement

Catecholamine synthesis



- understanding synthesis can be important for understanding drug action

Catecholamines



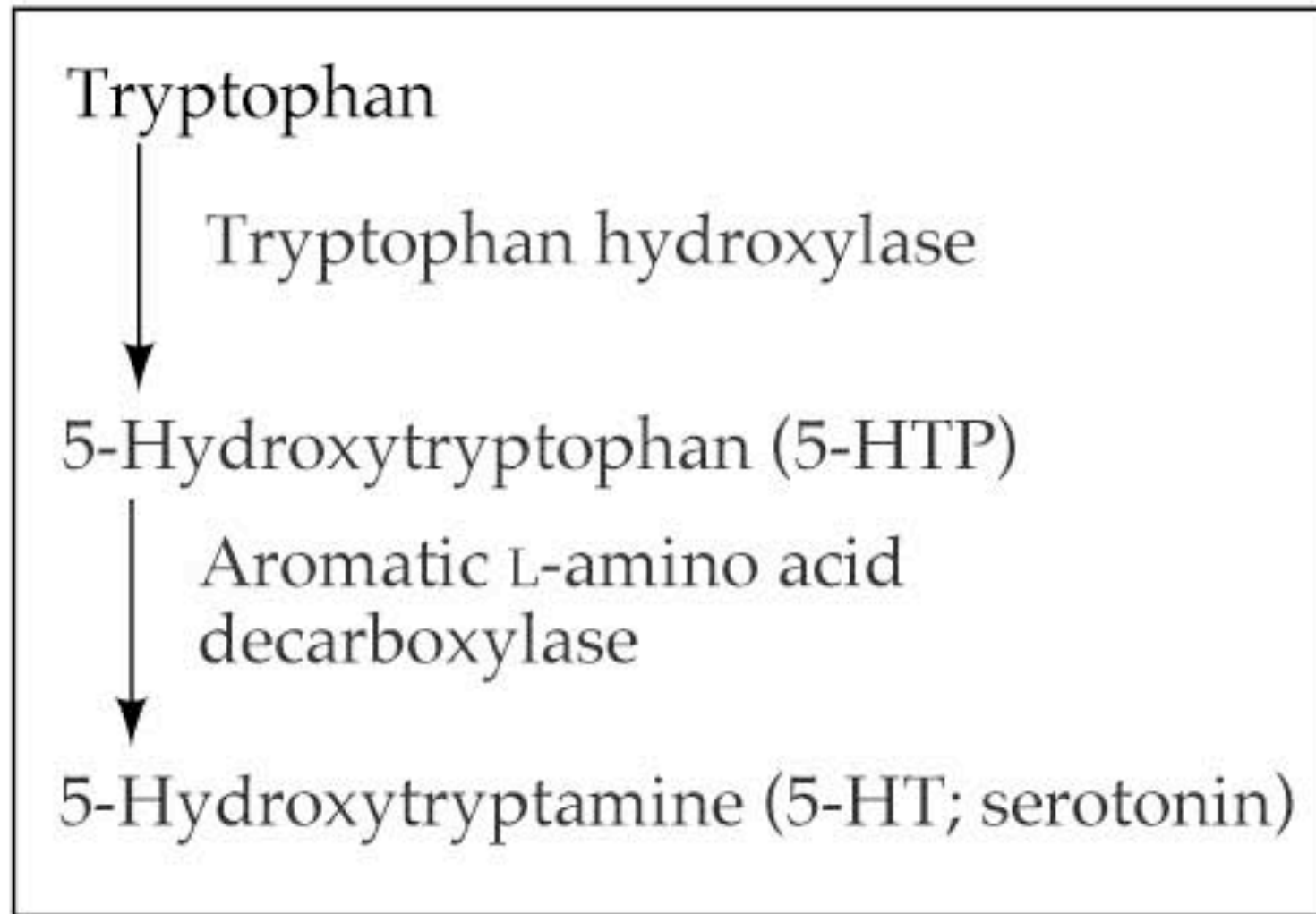
Norepinephrine/ Noradrenalin

- increase in vigilance
- attention
- sexual behaviour
- appetite

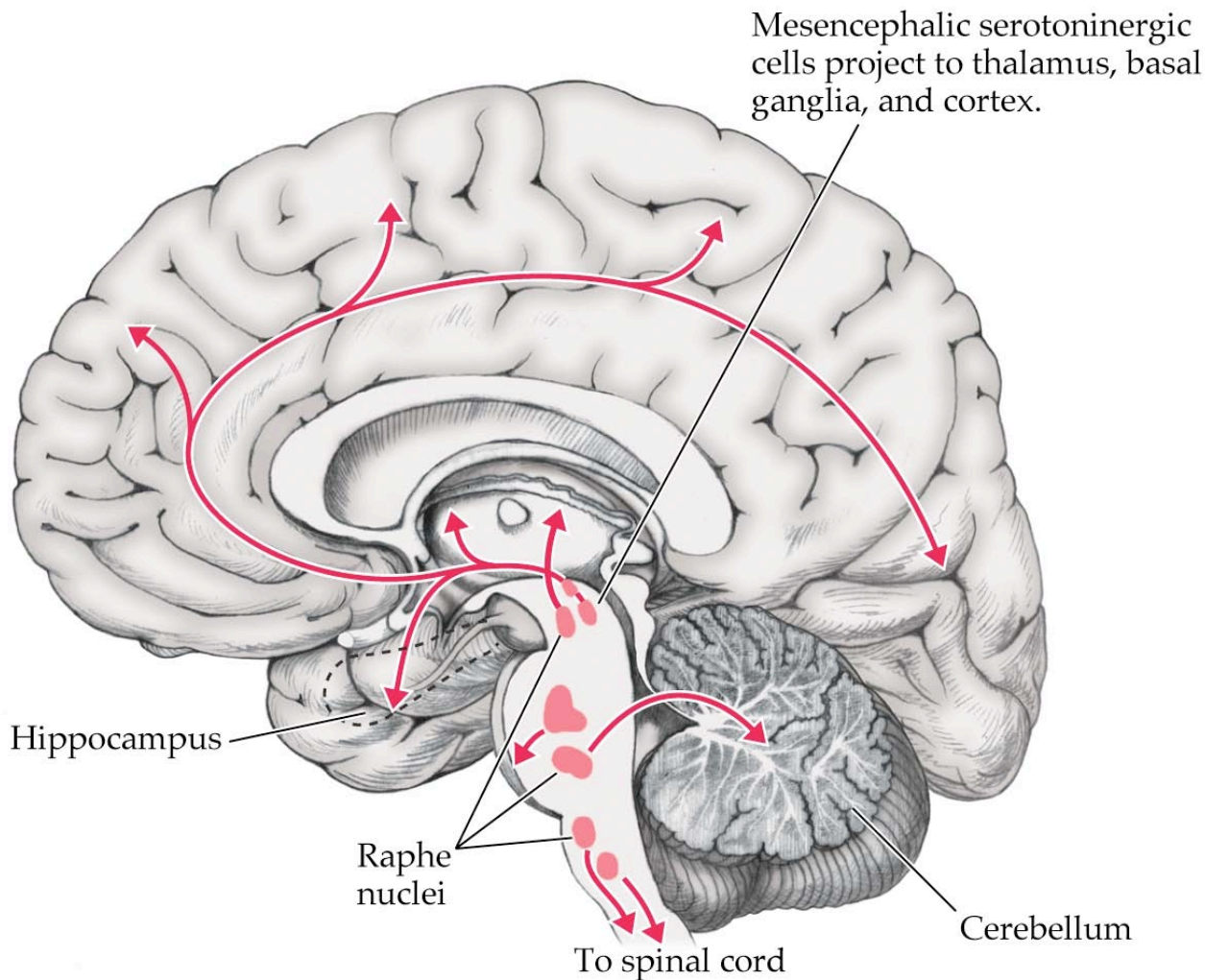
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Noradrenergic pathways in the brain - locus coeruleus

Serotonin synthesis



Serotonin



- regulation of mood
- control of eating, sleeping and arousal
- regulation of pain
- dreaming

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Serotonergic pathways in the brain – raphe nuclei, 15 subtypes of serotonin, Prozac and depression

The classical neurotransmitters

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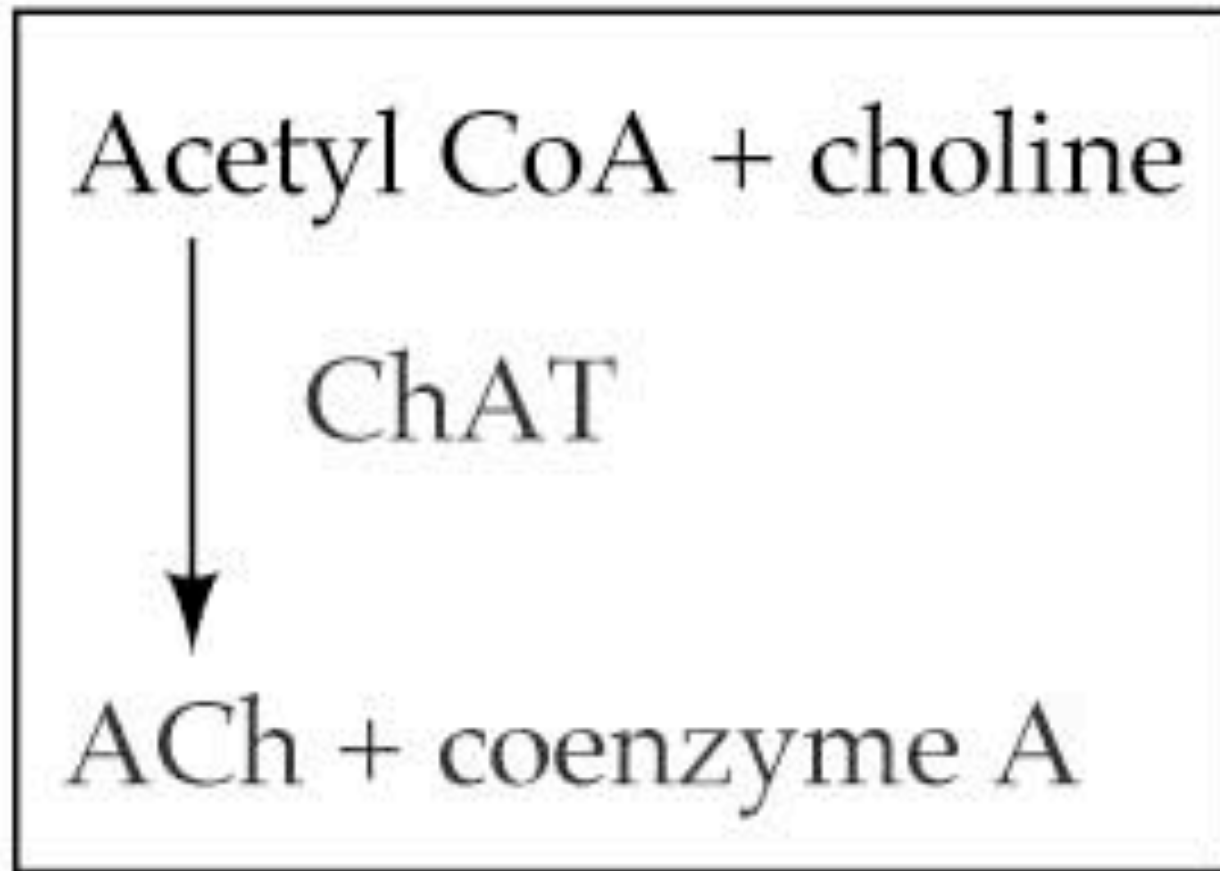
Quaternary amines

- Acetylcholine

Information transmitters

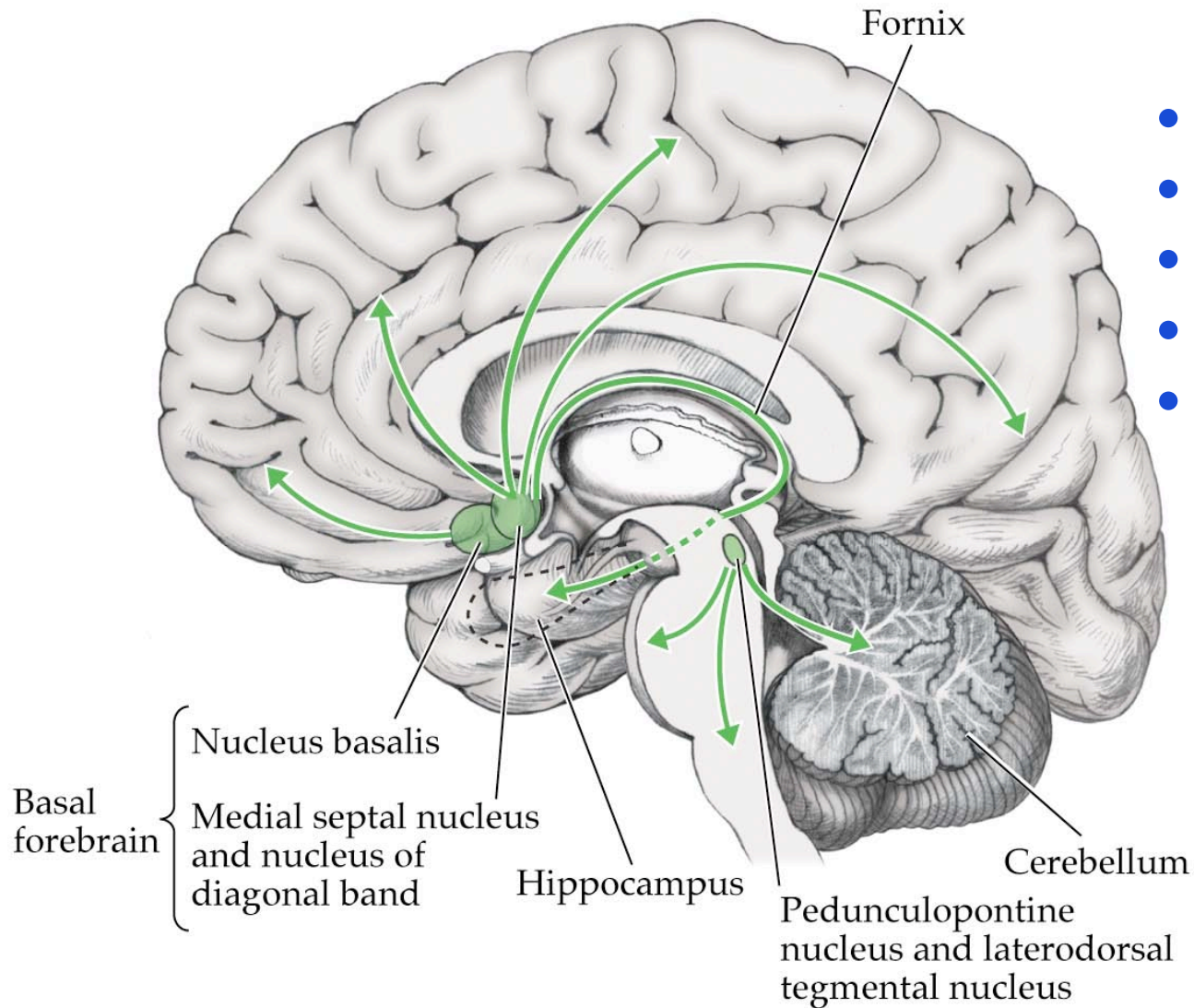
- amino acids (glutamate, GABA)

Acetylcholine synthesis



ChAT = Choline acetyltransferase

Acetylcholine

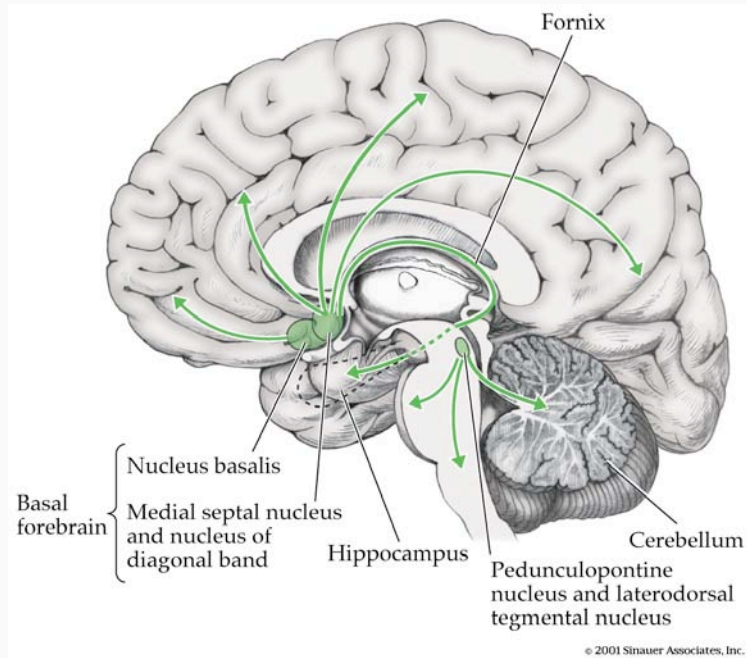


- muscular movement
- facilitatory effect
- REM sleep
- learning
- memories

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Cholinergic pathways in the brain - basal forebrain, dorsolateral pons, medial septum

Acetylcholine blockers



- block muscular movement



The classical neurotransmitters

- Amines – Modulatory effect on systems

Monoamines

- catecholamines (dopamine, noradrenaline)
- indoleamines (serotonin, melatonin)

Quaternary amines

- Acetylcholine

Information transmitters

- amino acids (glutamate, GABA)

Amino acids: The workhorses of the neurotransmitter family

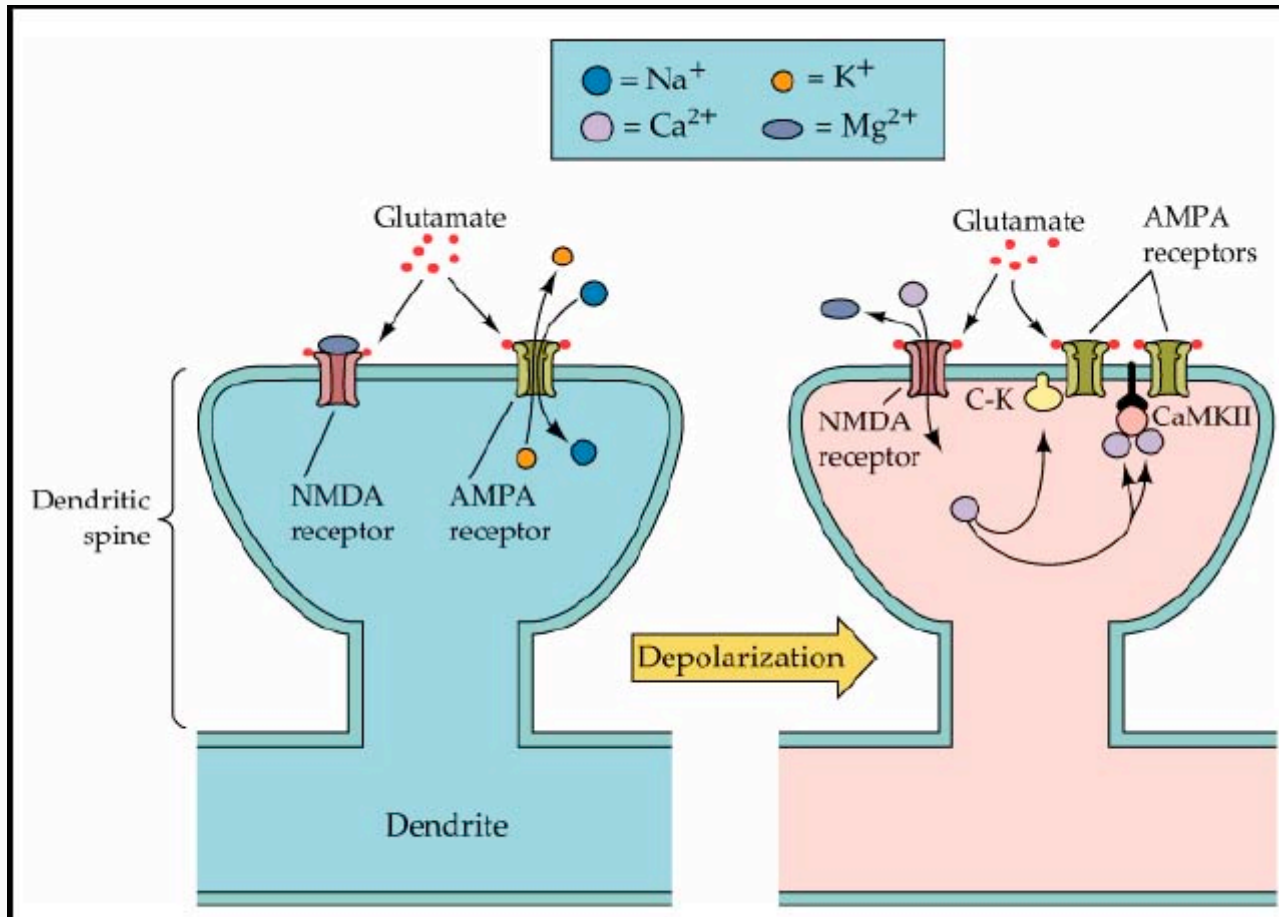
Glutamate - the primary excitatory neurotransmitter in brain

GABA (Gamma-amino-butyric-acid) - the primary inhibitory neurotransmitter

Other neurotransmitters have more of a modulatory effect – rather than an information transmitting effect

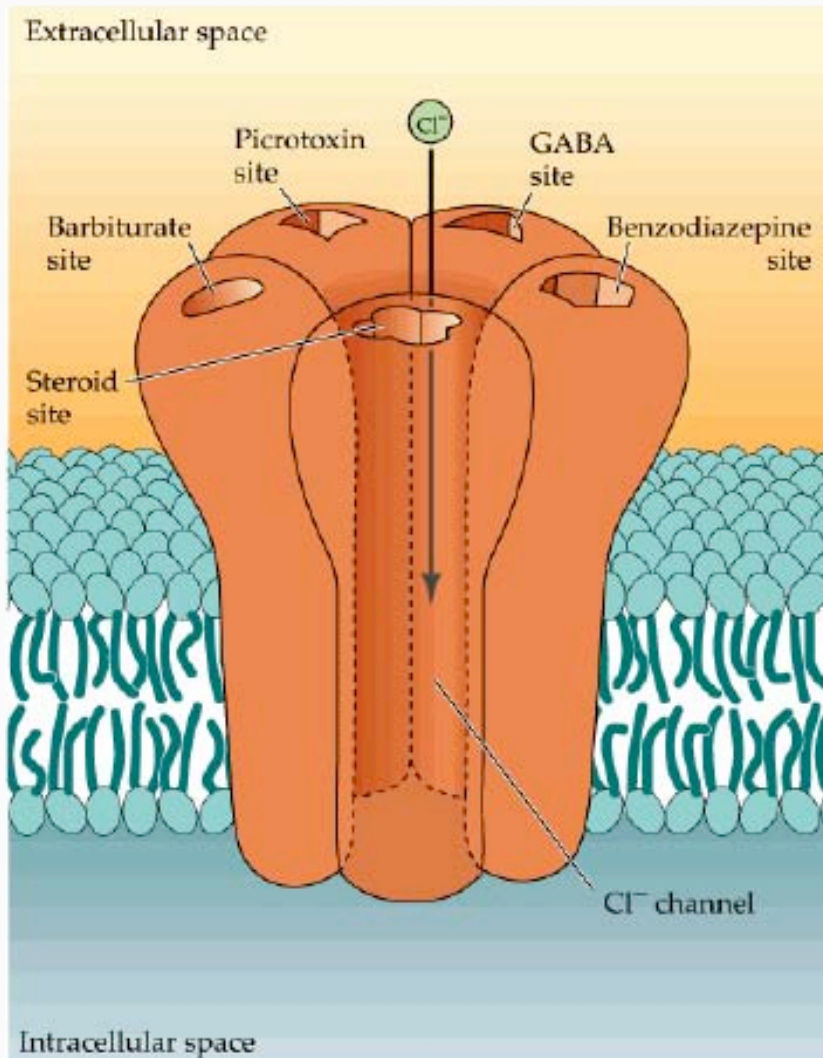
Information that is learned and remembered is transmitted by neurons secreting glutamate and GABA

The glutamate receptor



Activation of NMDA receptor can cause entry of calcium and changes in the numbers of AMPA receptors – a mechanism for learning? Building blocks of a new formed memory?

The GABA receptor



- inhibitory synapses
- necessary for brain stability
- Epilepsy may be related to an abnormality in this process

Barbiturates: gaba agonists

- anxiety drugs
- sleep medication
- seizure treatments

Multiple binding sites

Peptides

- produced in minute quantities
- often substances that are also found in areas of body other than brain (vasoactive intestinal polypeptide)
- tremendously potent and long-acting (neuromodulatory)
- opiates

The opiate story

- Opiates have been used for centuries to relieve pain
- Pert and Snyder found that opiates bind to receptors in several areas
- not until 1975 did we know of endogenous (produced from within) opioids
- several varieties of receptors

Schizophrenia

Affects about 1/100 people

Begins in 20's

Often triggered by stress, illness, etc. but there's also a genetic predisposition

Symptoms of schizophrenia

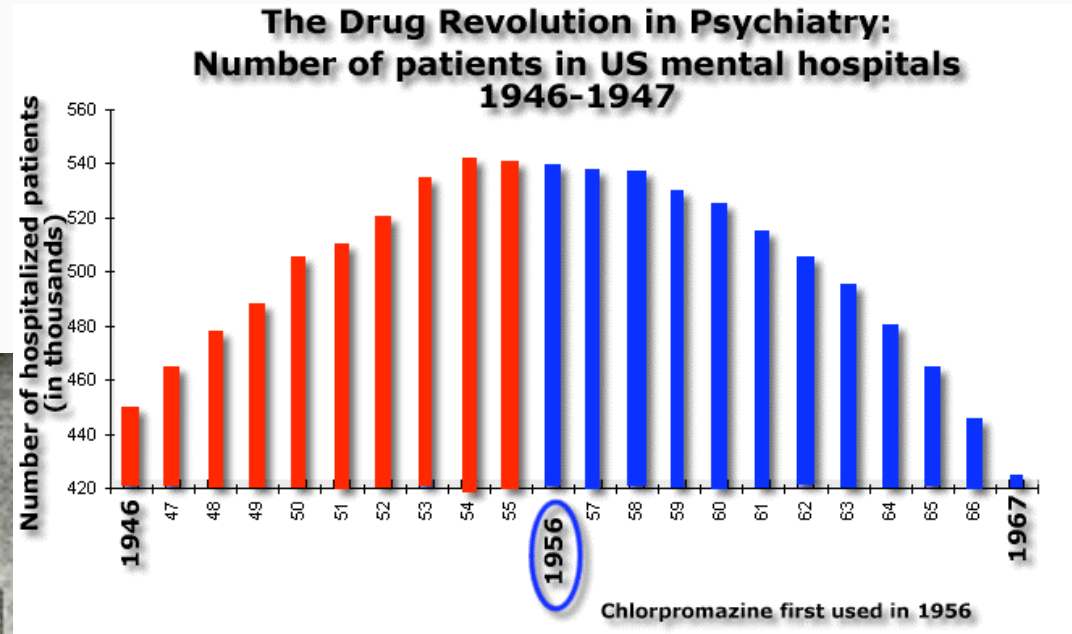
Positive symptoms

- hallucinations, delusions, paranoia

Negative symptoms

- lack of emotion, energy, directedness

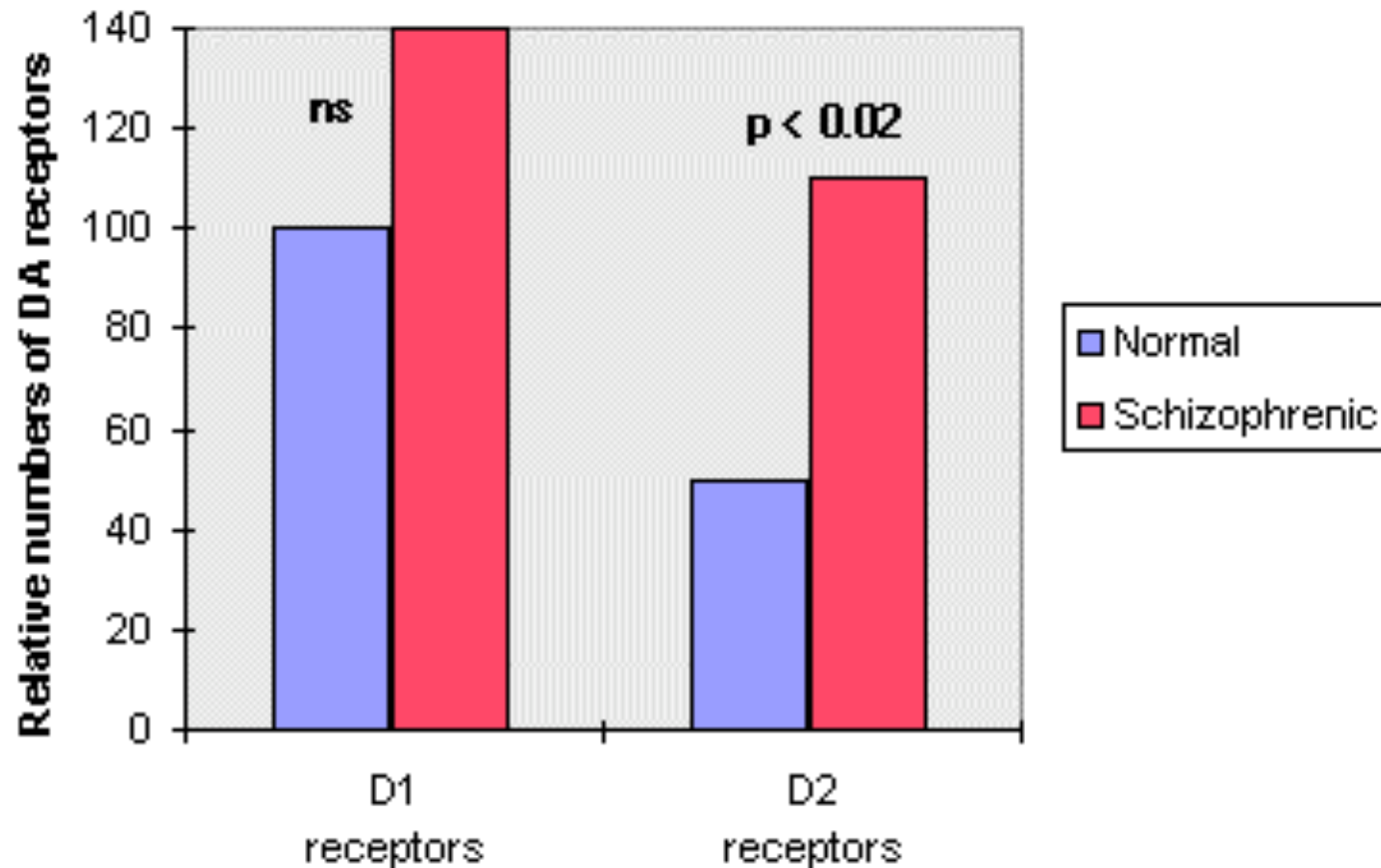
The dopamine theory of schizophrenia



Dopamine antagonist

Dopamine receptors in normal and schizophrenic individuals

Dopamine receptors in the brains of deceased schizophrenics and nonschizophrenic controls



Beyond dopamine

New generation antipsychotics affect serotonin as well

Glutamate agonists can help with negative symptoms

- But they can cause seizures
 - Glycine agonists are usually given that facilitate glutamate but don't have the dangerous side-effects.

Schizophrenia likely affects a host of systems perhaps by disturbing a fundamental balance among neurotransmitters

Alzheimer's Disease

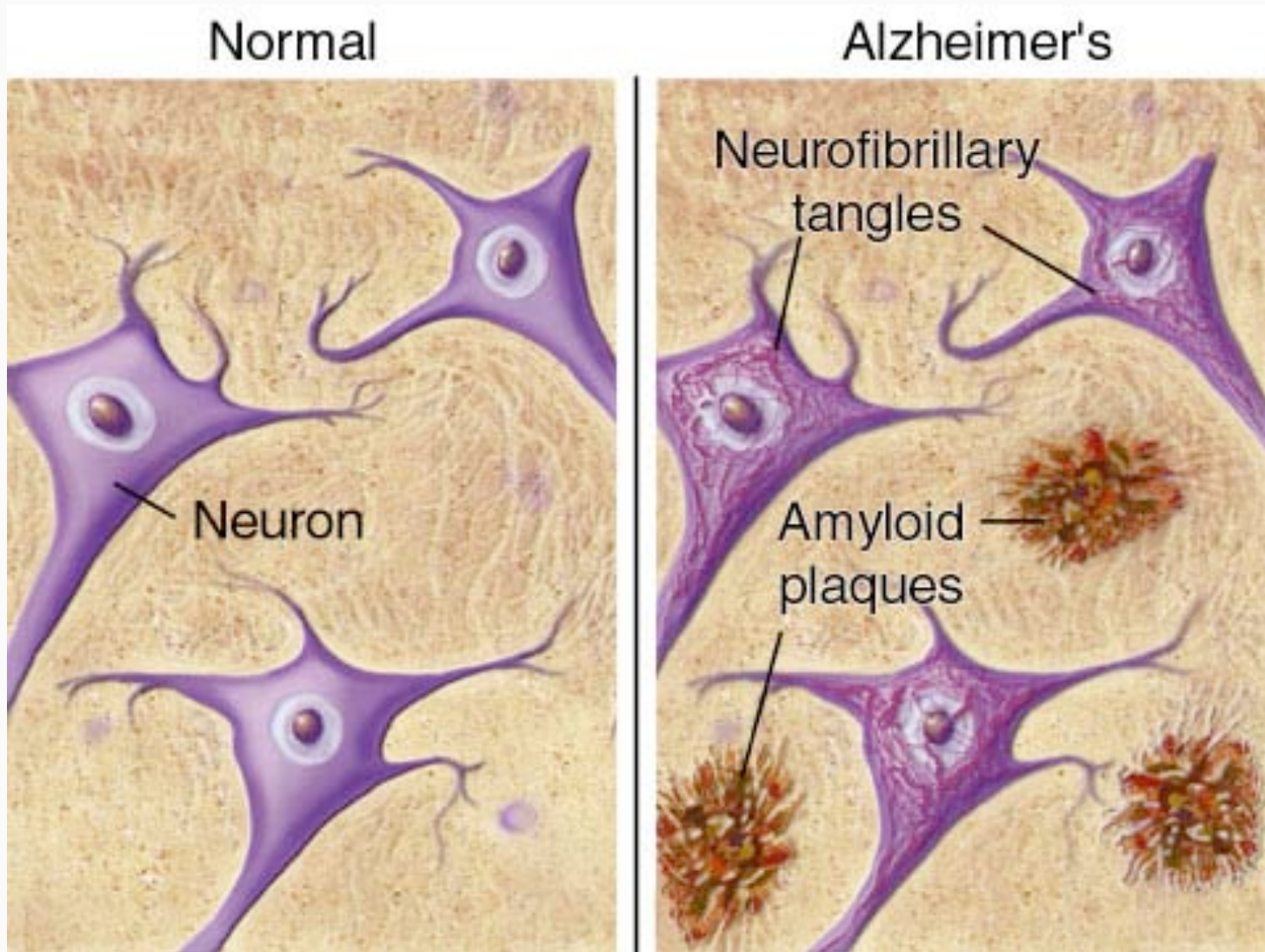
First described by [Alois Alzheimer](#) in 1907

Course of disease:

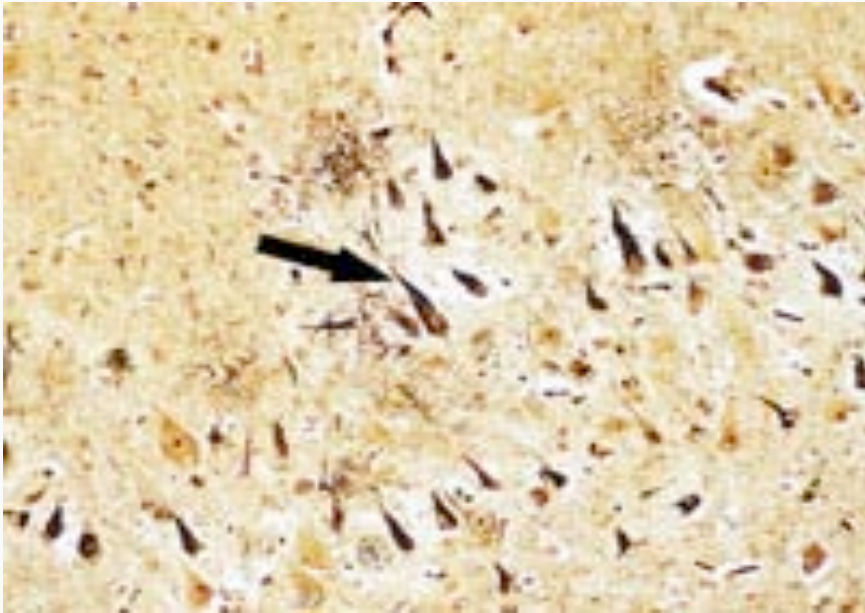
- initially, some memory loss (new memories and disorientation)
- relentlessly progressive until one loses identity

Toronto Star [Alzheimers](#)

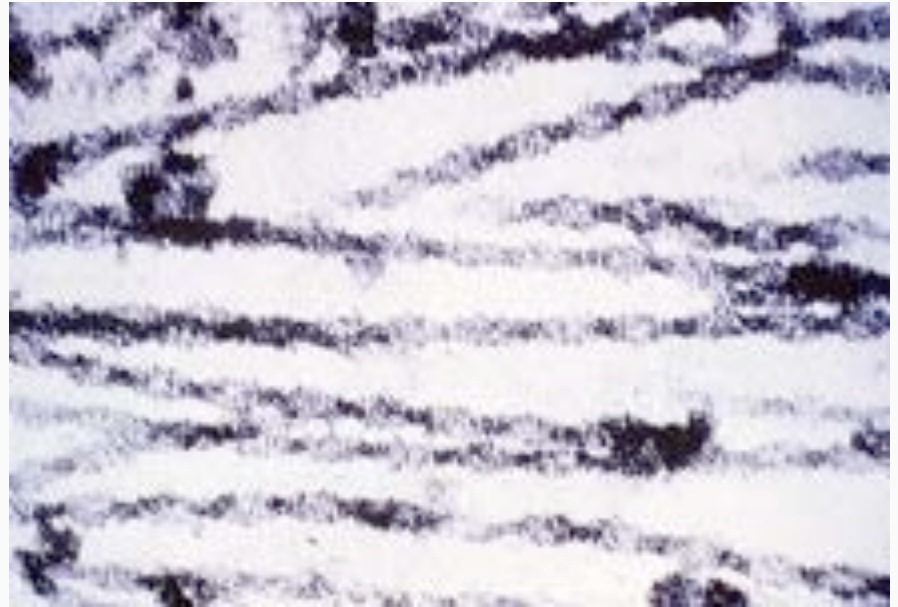
Neuropathology in Alzheimer's disease



Neurofibrillary tangles

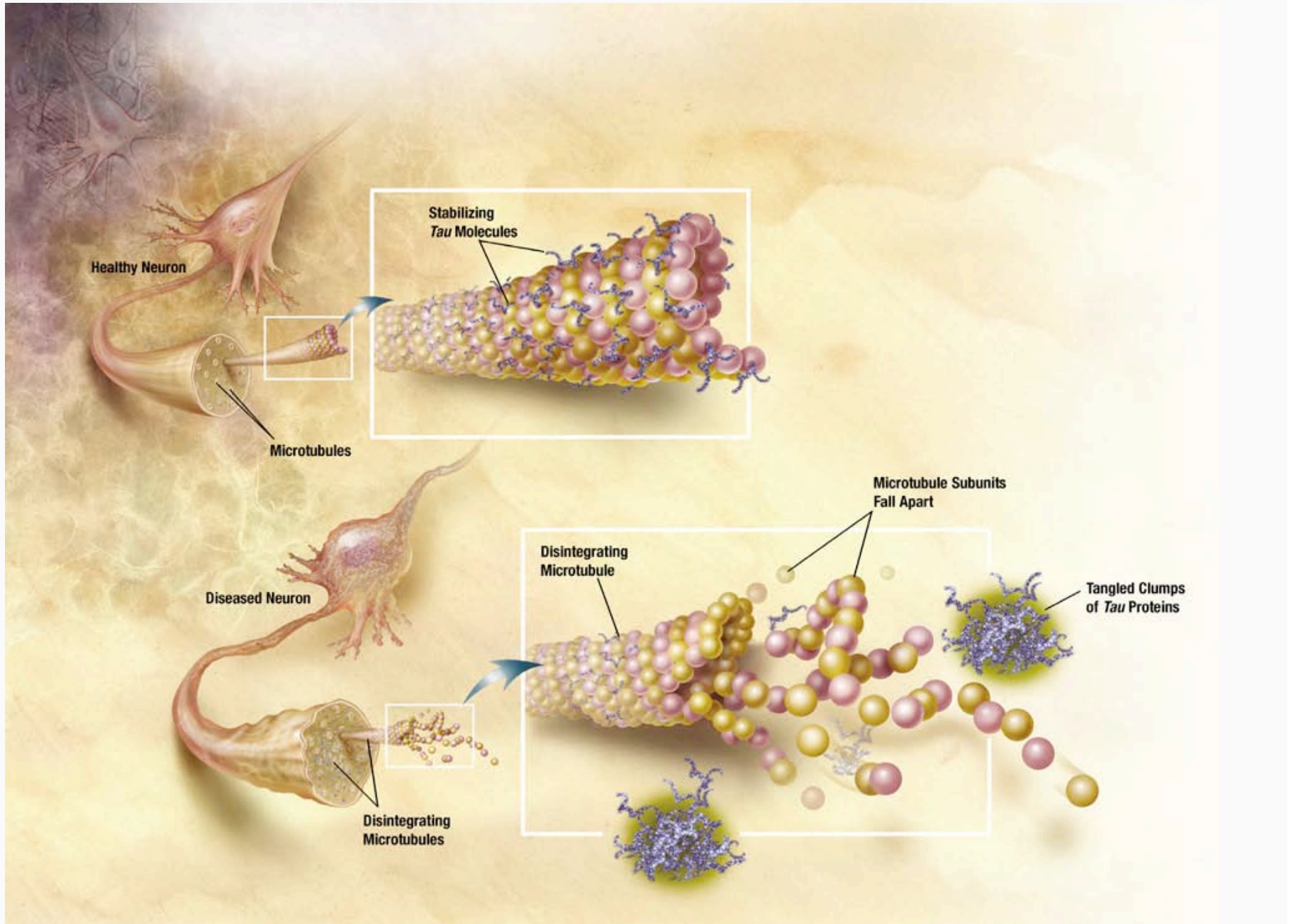


Silver stain

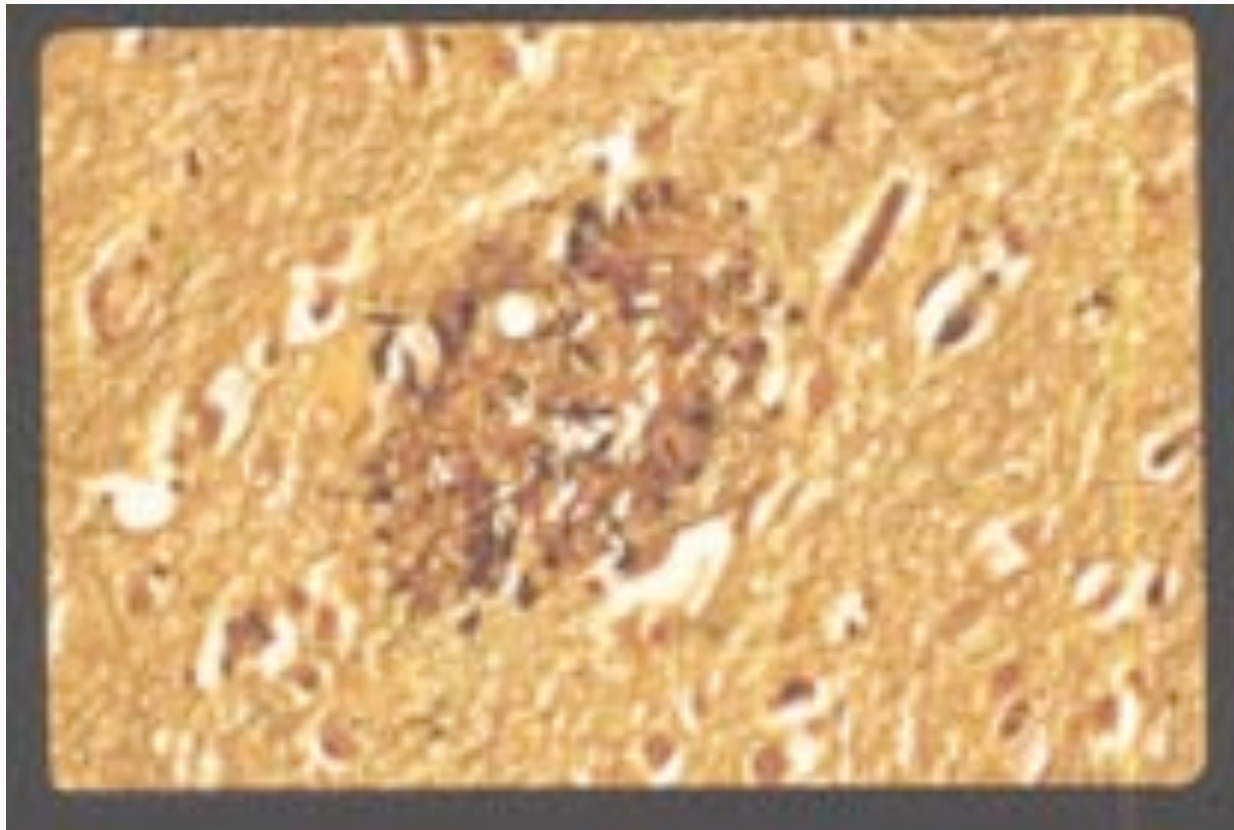


Paired helical filaments

Formation of NFT's



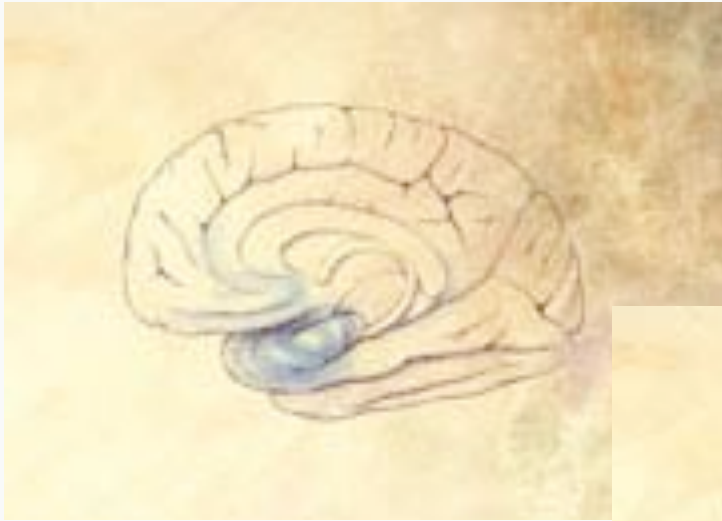
Amyloid plaques



New Information! (Feb 1, 2005)

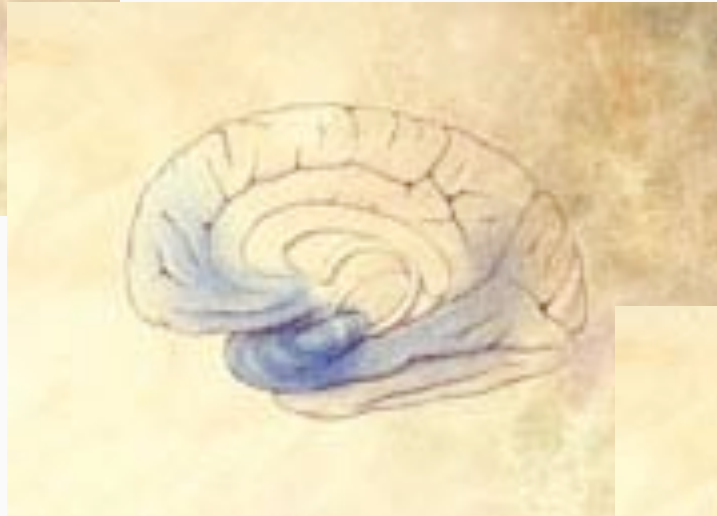
- can see amyloid plaques in virtually every older person – they don't all get AD
- sensitive test for AD demonstrated on patients that could identify the disease long before symptoms appear
- detects minute protein molecules called ADDLs (amyloid beta-driven diffusible ligand) – present in CSF
- ADDLs attack and disrupt synapses
- process is thought to be reversible – opening up the possibility of early treatments that can halt the disease

In addition....



Mild

Massive loss of synapses in cortex

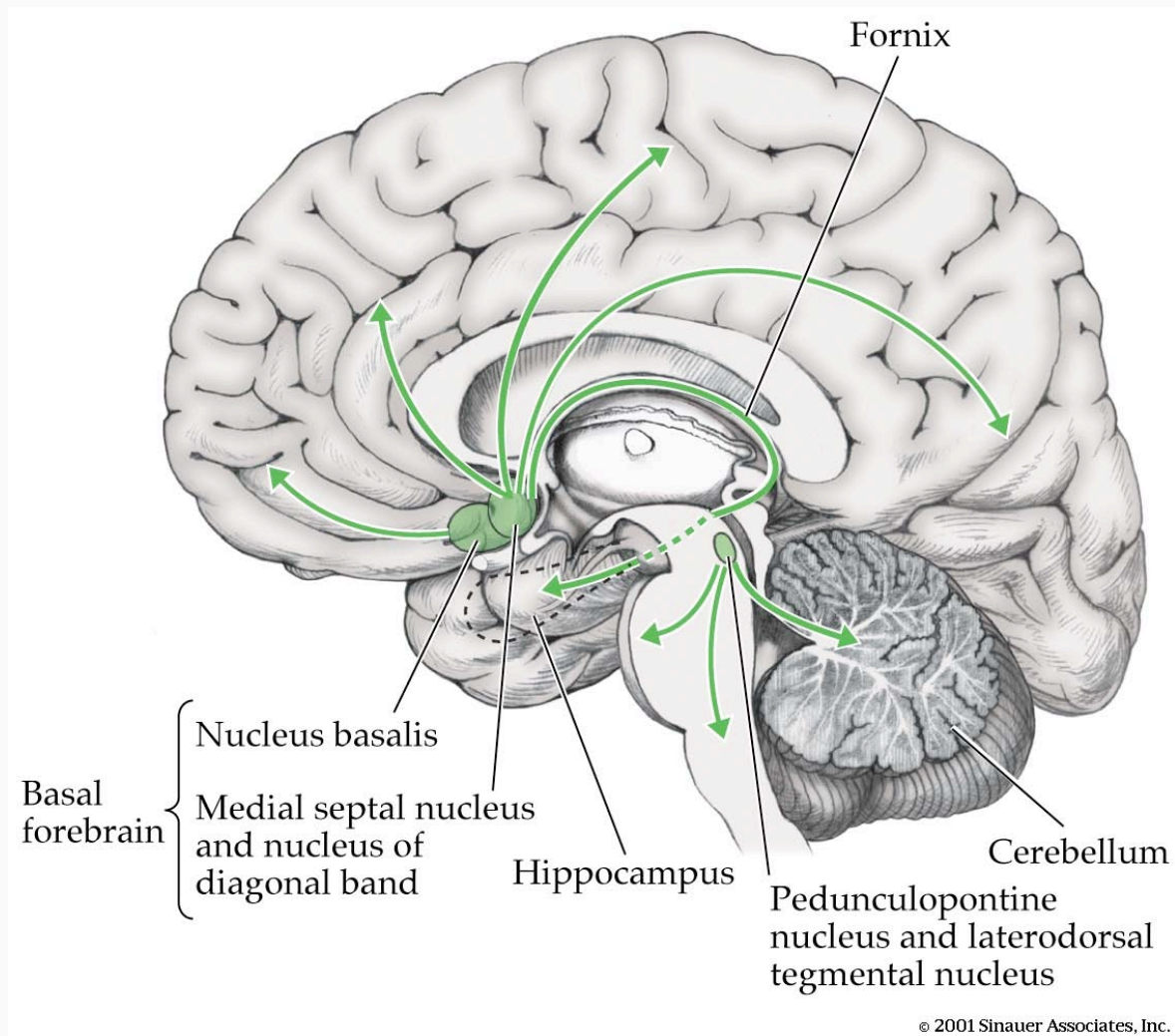


Moderate



Severe

Cholinergic involvement Basal forebrain



Nucleus basalis of Meynert – cell loss seen in AD

Causes

Largely unknown

- Down's syndrome link
- but strongly inherited forms account for only small proportion
- plaques seen in wide variety of disorders acquired by disease (encephalitis, CJD) and accident (punch-drunk syndrome)

Treatments

1. 'Cognitive enhancers'

- Acetylcholinesterase inhibitors to offset loss of cholinergic neurons
- stops ACE from destroying synaptic ACH
- allowing it to keep working

- NMDA antagonists

- Memantine

- idea here is that part of problem in AD is that chronic release of glutamate prevents NMDA receptors from working properly