

PSYC304:

Neural communication II

(between cells)

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Overview

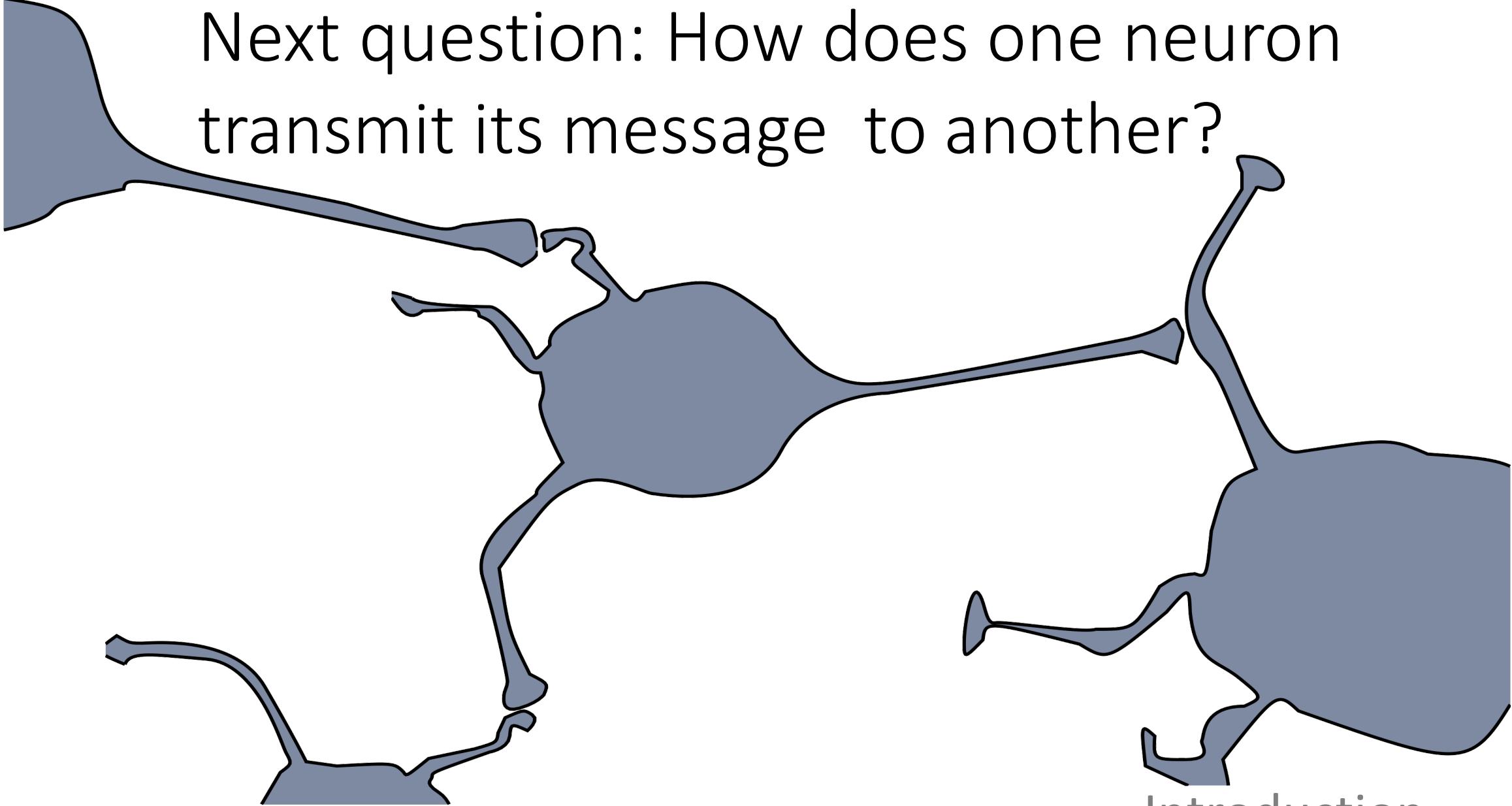
- A. Receptors
- B. Types of neurotransmitters



Learning objectives

1. Name and describe the two basic types of receptors. Why have both?
2. Describe receptors by their locations. Describe the relationship between receptor location and its function.
3. Name three types of neurotransmitter clean-up.
4. Name the major groups of neurotransmitters, and some examples within each group.
5. Describe the two primary types of drug action.
6. Describe the roles of glutamate, GABA, dopamine, norepinephrine, serotonin, acetylcholine, endocannabinoids, adenosine, and the endogenous opioids.
7. Describe some drugs that affect these systems, including their drug action.
8. Is dopamine the pleasure molecule? Is serotonin the mood molecule? Is norepinephrine the memory molecule? Support your answers with evidence.

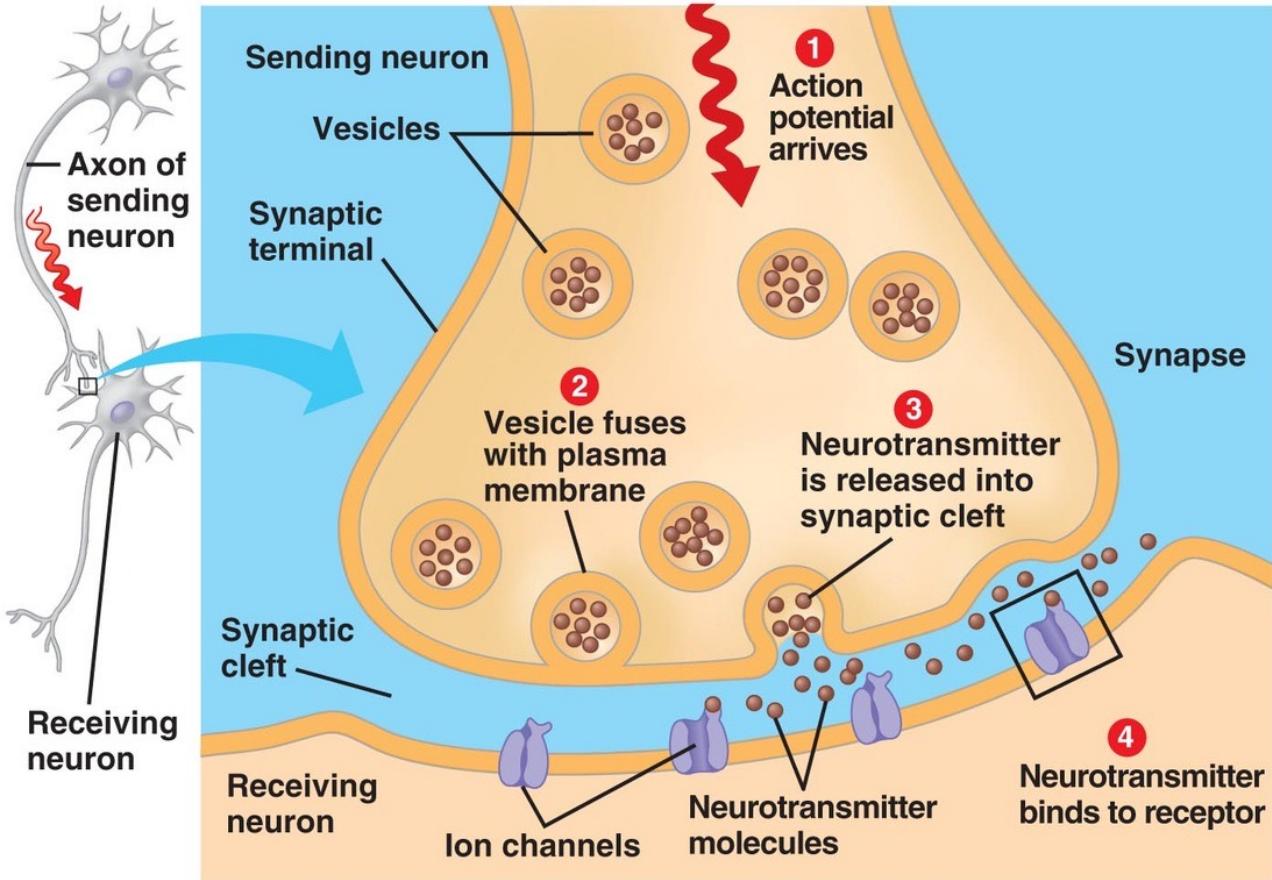




Next question: How does one neuron transmit its message to another?

Introduction

End of the line

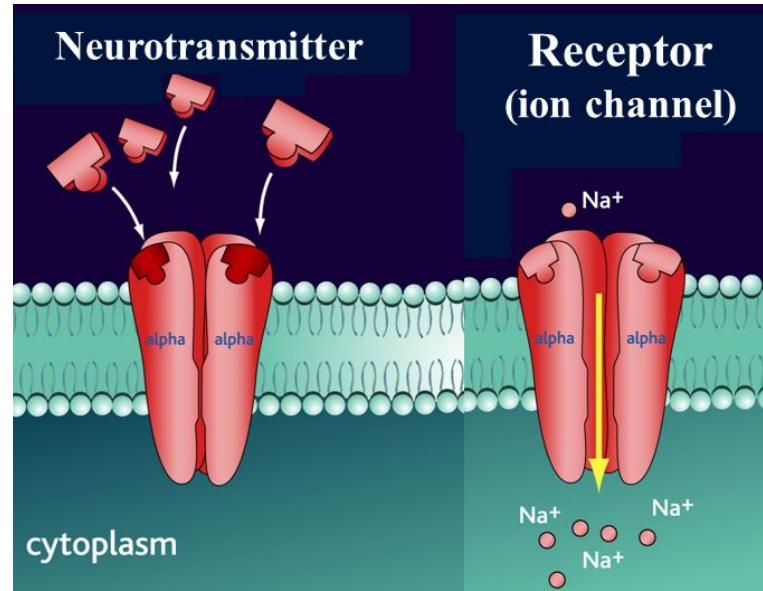
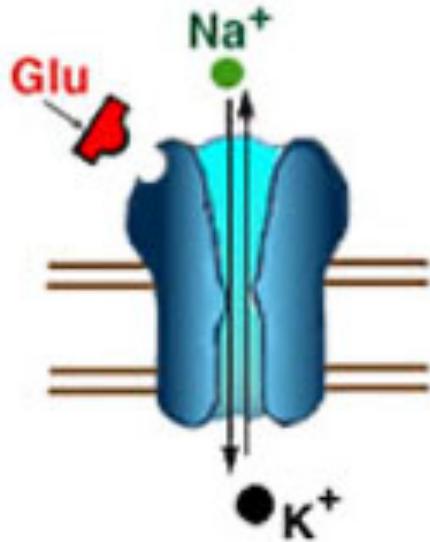


- Axon ends in terminal *boutons* ("buttons")
- Bouton has *vesicles* ("bubbles"?) filled with *neurotransmitters*
- Action potential depolarizes bouton
 - Vesicles fuse with membrane
 - Neurotransmitters released into synapse

Introduction

Welcome to the synapse

- Dendrite membrane has special *receptors* that fit, like lock and key, with the neurotransmitters
- Receptors are often just (closed) channels that open when they bind with neurotransmitter!
 - i.e. *ligand-gated ion channels*

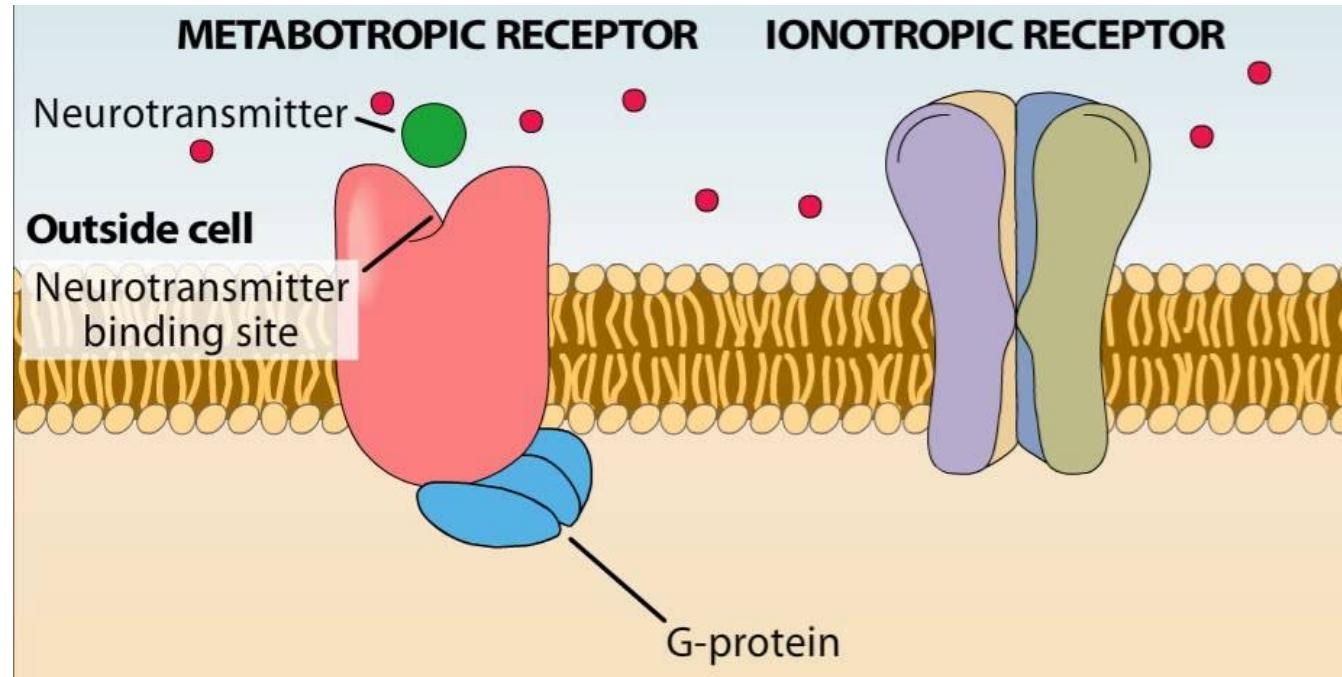


Glu: glutamate, most common excitatory neurotransmitter

Introduction

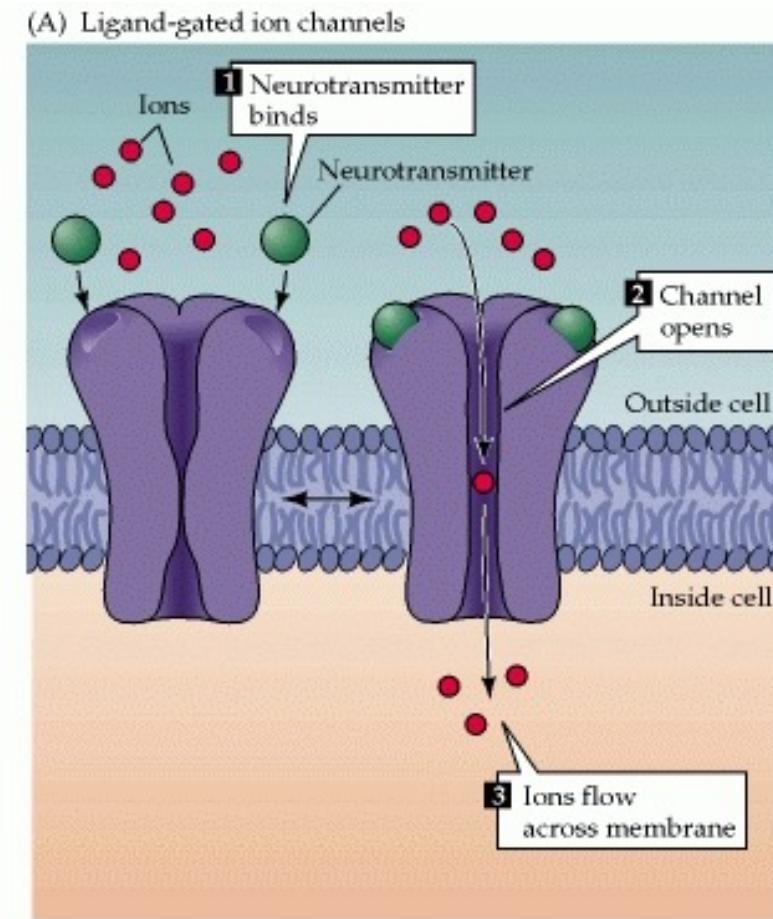
Receptor types

- Ionotropic (channels)
- Metabotropic (signalling proteins)



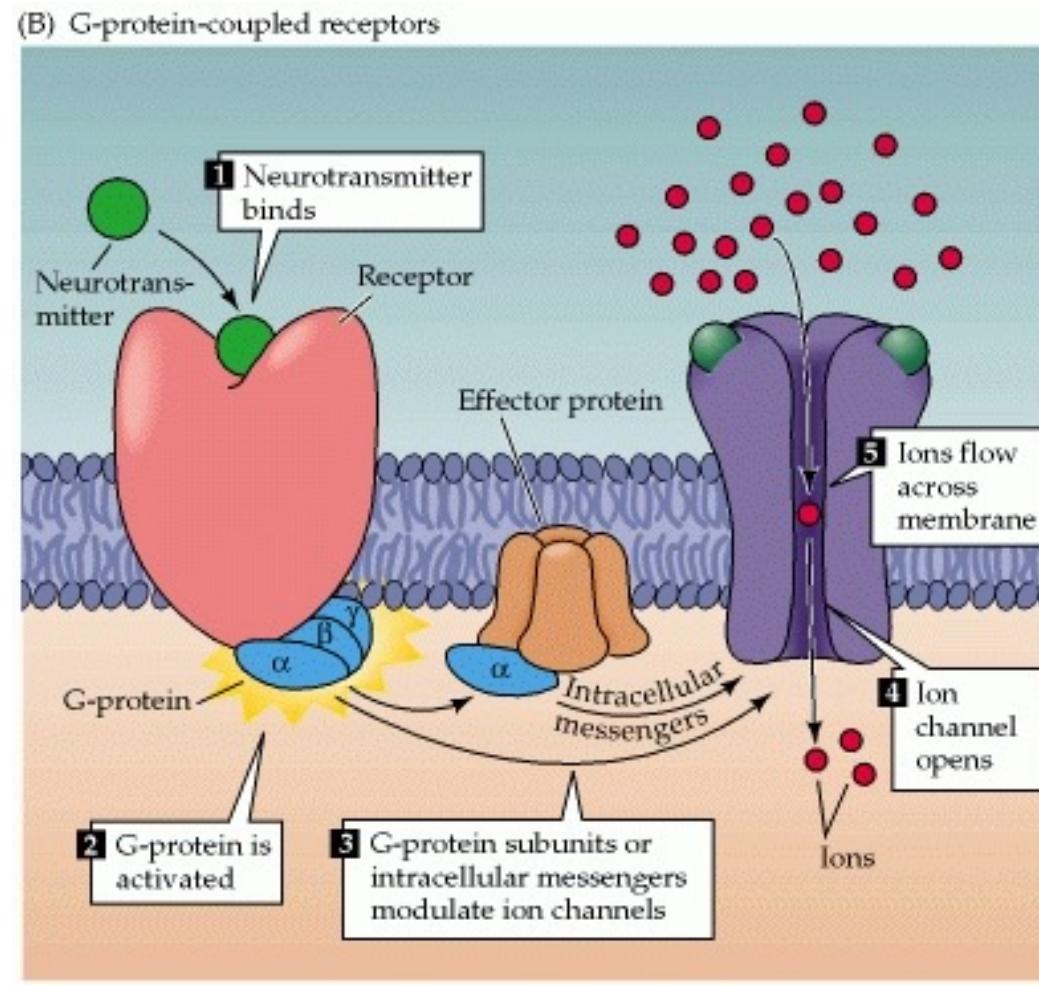
Receptor types

- Ionotropic
 - AKA ligand-gated ion channels
 - Excitatory (depolarize)
 - Inhibitory (hyperpolarize)
 - Fast, transient effect



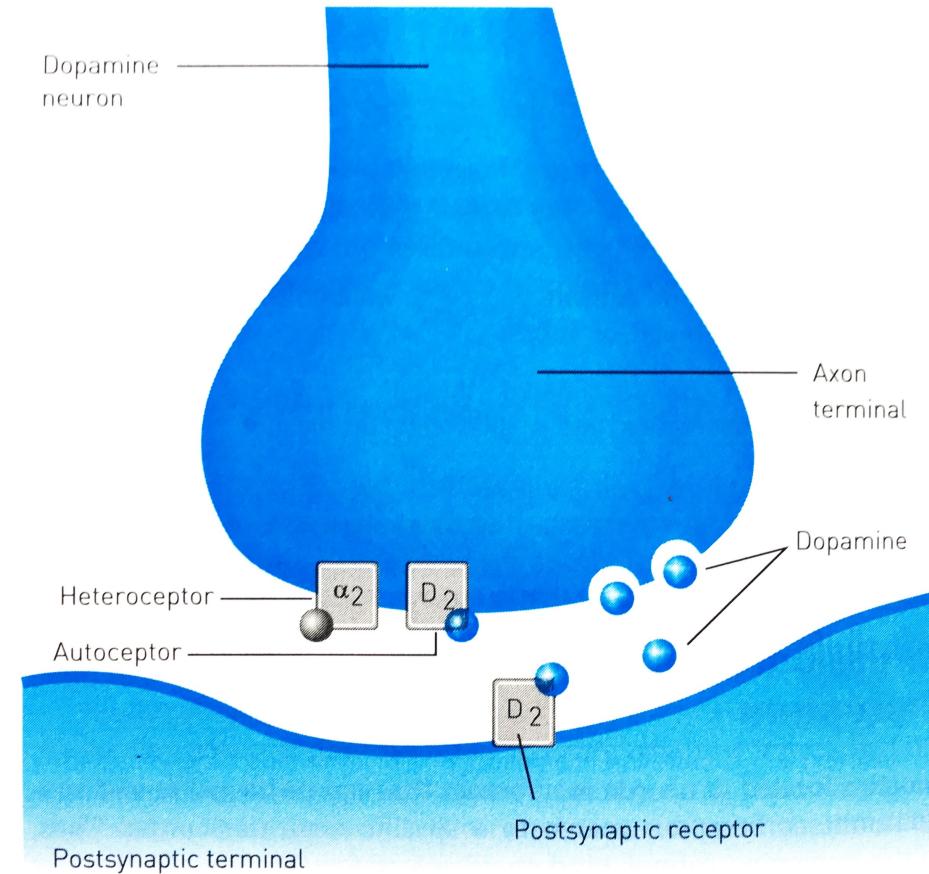
Receptor types

- Metabotropic
 - AKA G-protein-coupled receptors
 - Modulate cell
 - Modulate signals
 - Slow, longer lasting effect
 - Cause *signal cascades*



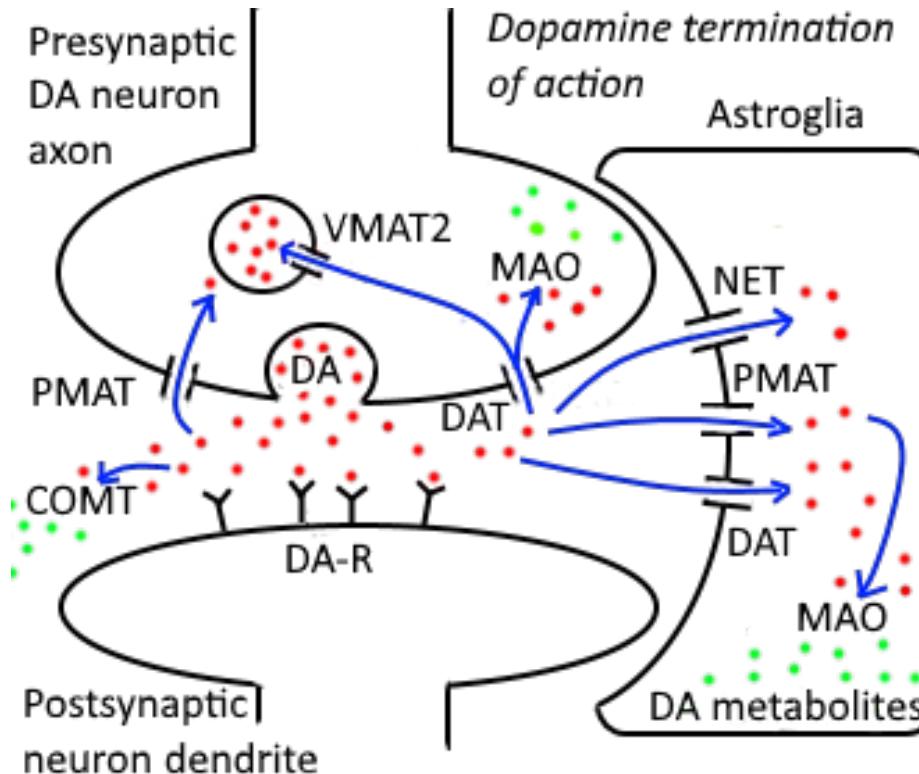
Receptor locations

- Postsynaptic
- Presynaptic
 - Autoreceptors
 - Heteroreceptors



Neurotransmitter clean-up

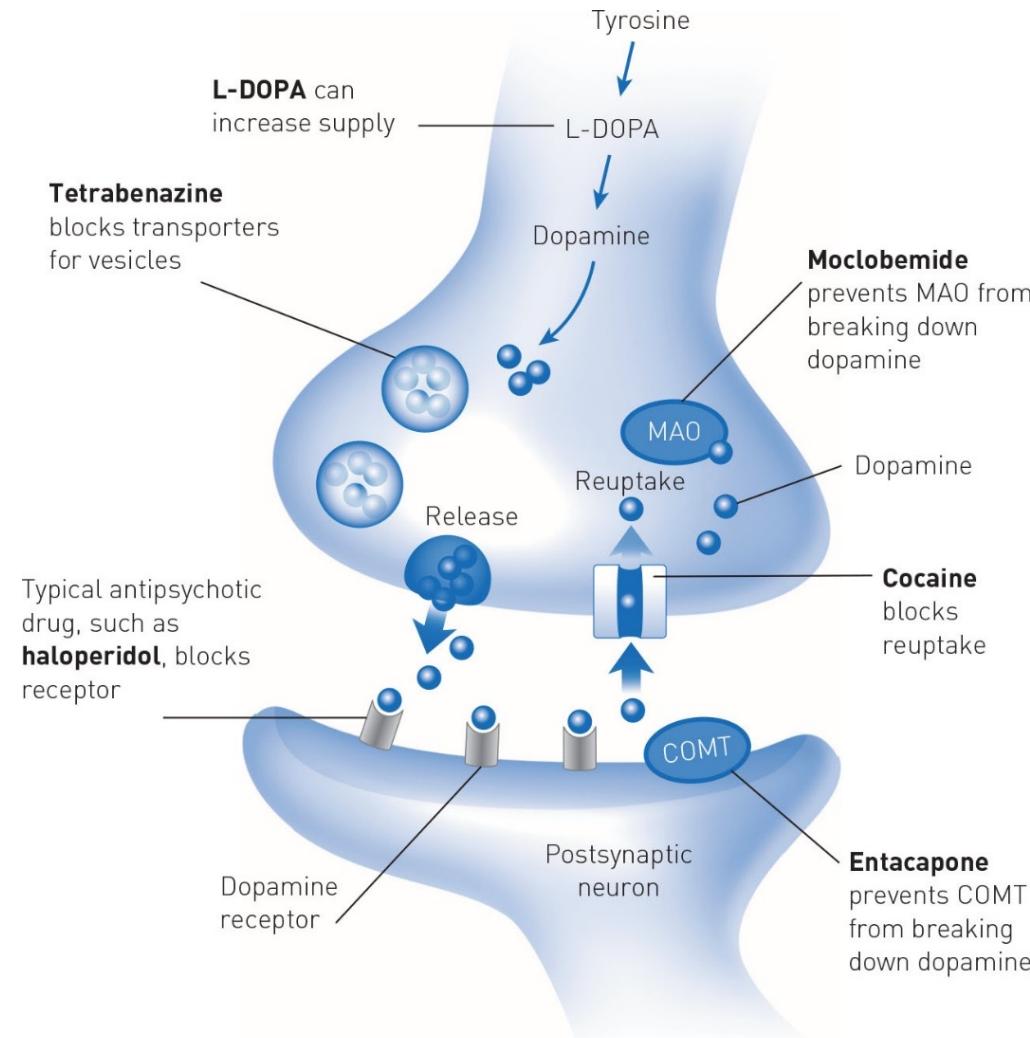
- Diffusion
- Enzymatic degradation
- Re-uptake
 - Pre-synaptic
 - Astrocytes



End of neurotransmission

Drug types

- Agonist
- Antagonist
- Other
 - e.g. transporter blocker, reuptake inhibitor, enzyme inhibitor



Onto our specific neurotransmitter systems!



Small-Molecule Neurotransmitters

Amino acids		Glutamate GABA
Monoamines	Catecholamines	Dopamine Epinephrine Norepinephrine
	Indolamines	Serotonin
Acetylcholine		Acetylcholine
Unconventional neurotransmitters		

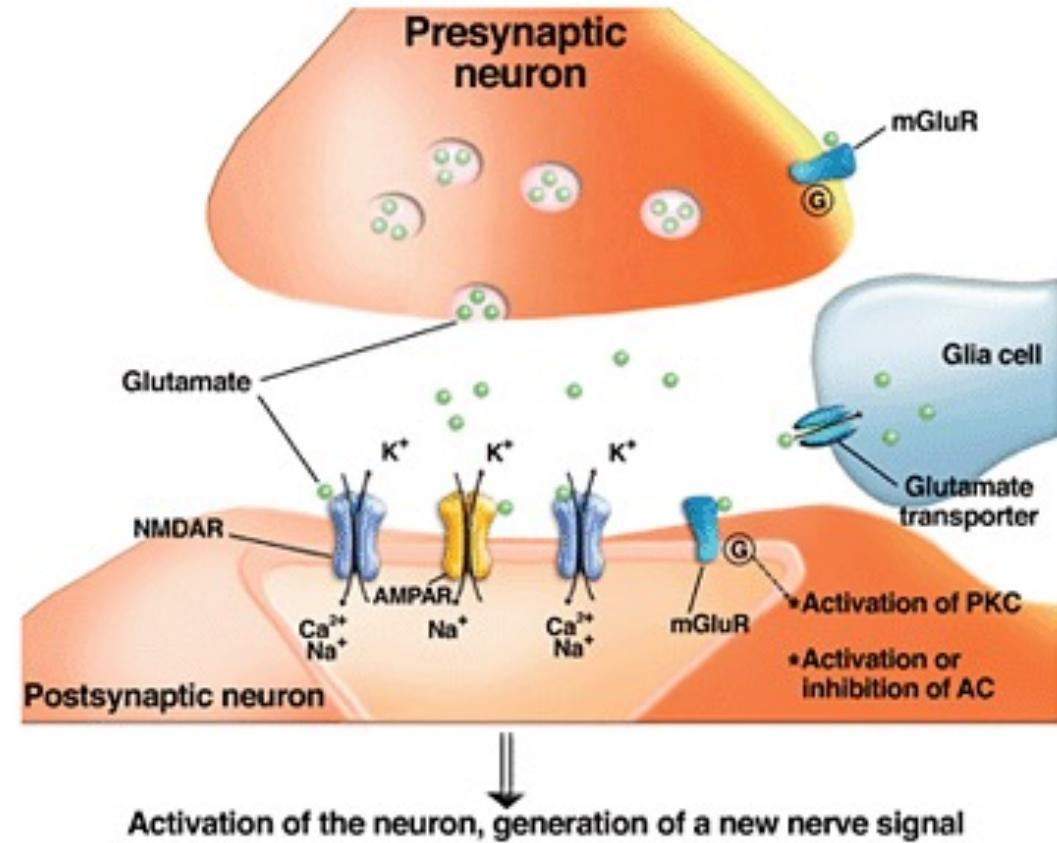
Large-Molecule Neurotransmitters



Types of neurotransmitters

Glutamate

- Primary excitatory neurotransmitter
- Used throughout the brain
- Ionotropic
 - AMPAR
 - NMDAR
 - Kainate
- Metabotropic
 - mGluR
- Often not a great target for drugs—why?



Types of neurotransmitters

Drugs: Glutamate (all antagonists)

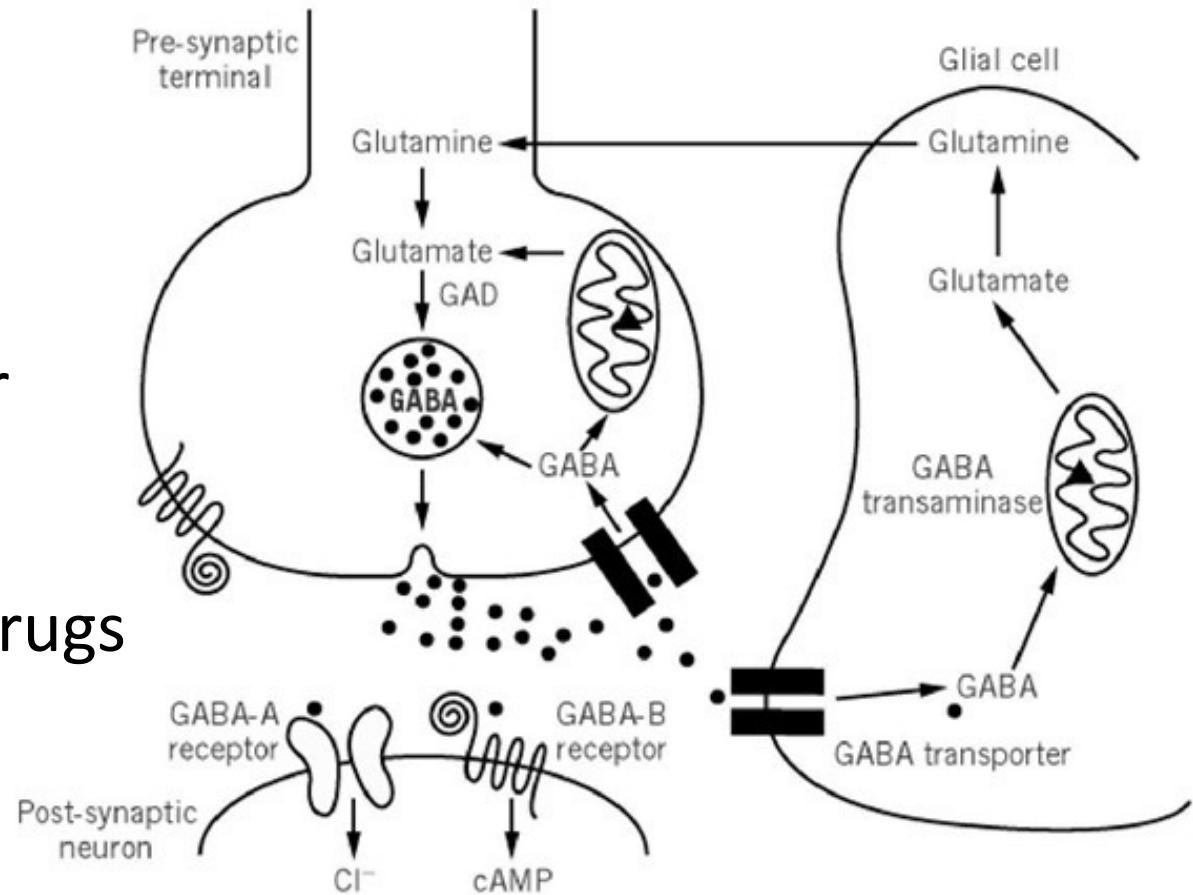
- Barbiturates
- Nitrous oxide
- Ketamine
- Ethanol



- Pattern?
- Agonists?

GABA

- aka gamma-Aminobutyric acid
- Primary inhibitory neurotransmitter
- Used throughout brain
- Ionotropic and metabotropic
- Again, often not a great target for drugs



Types of neurotransmitters

Drugs: GABA (all agonists)

- Benzodiazepines
- Ethanol
- Chloroform
- Ether

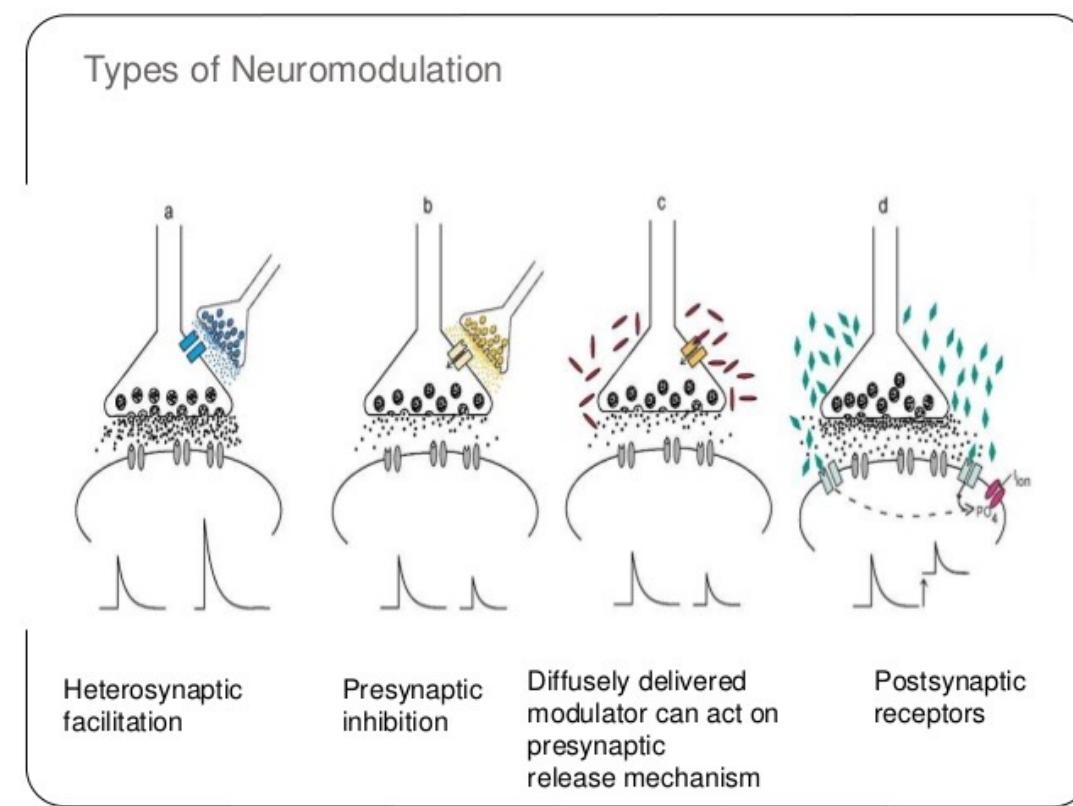


- Pattern?
- Antagonists?

Types of neurotransmitters

The amines

- Dopamine
- Epinephrine (Adrenaline)
- Norepinephrine (Noradrenaline)
- Histamine
- Serotonin

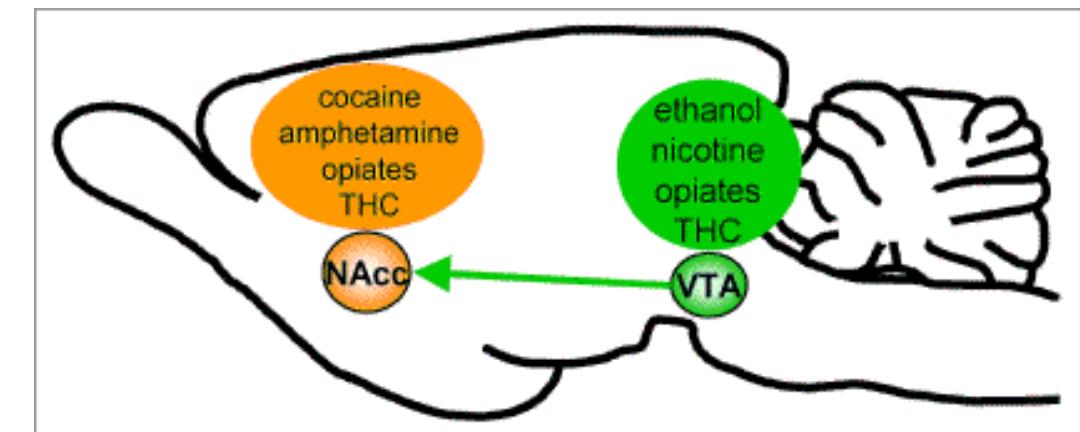
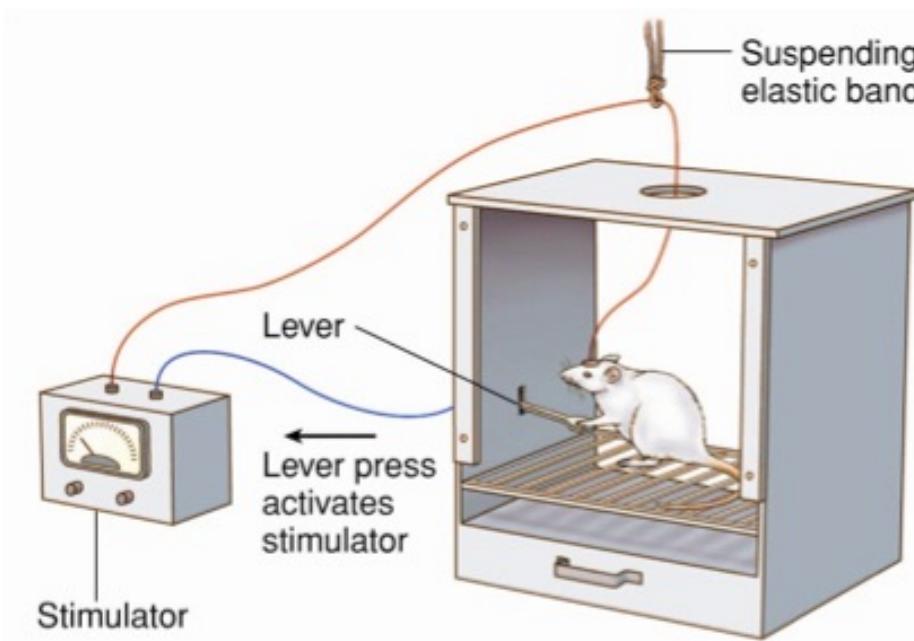


- All metabotropic—play a modulatory role

Types of neurotransmitters

Motivation for... Brain Stimulation?

- Olds and Milner (1954)
- Dopamine: pleasure?
- Dopamine projects from Ventral Tegmental Area (VTA) to Nucleus Accumbens (NAcc)



Types of neurotransmitters

Drugs: dopamine

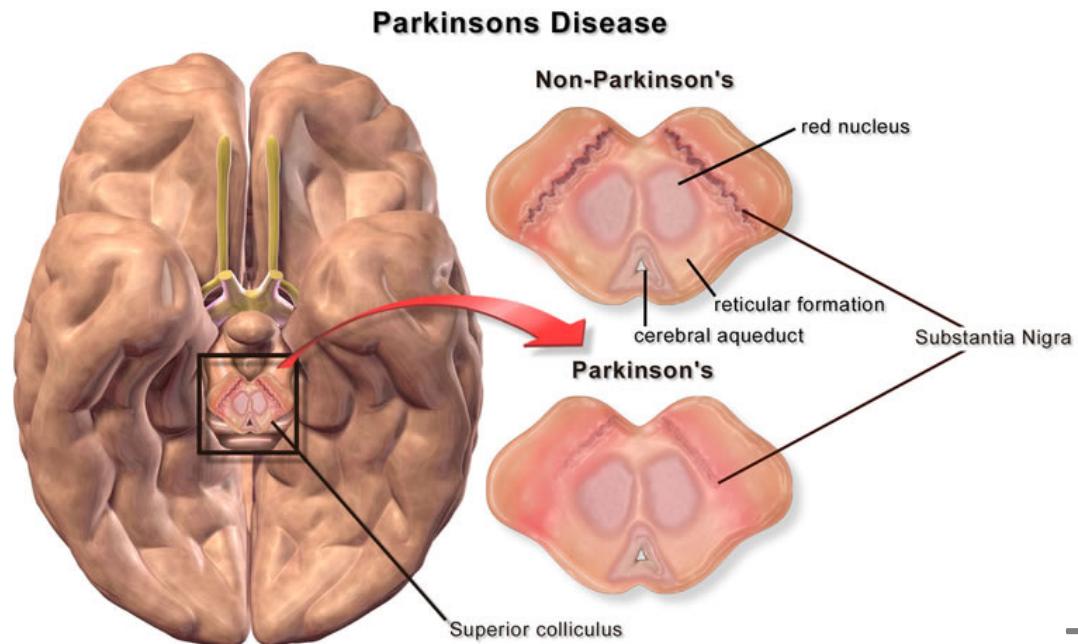
- All addictive drugs directly or indirectly increase dopamine transmission
 - Implication?
- Amphetamine*, cocaine*, heroin, nicotine, oxycodone, ethanol, and on and on and on



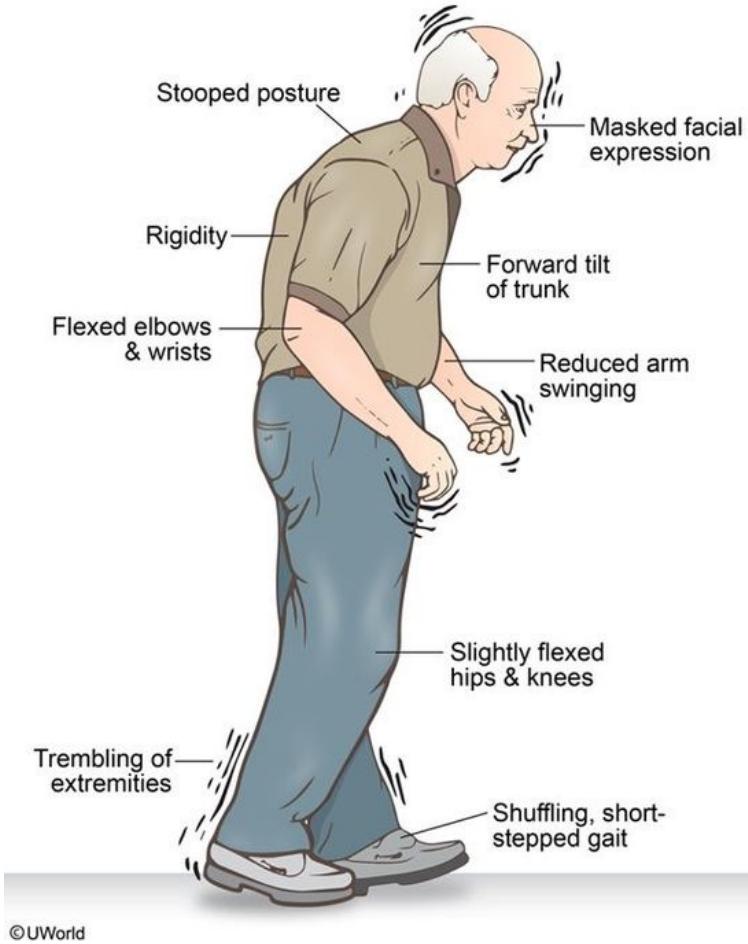
Types of neurotransmitters

Dopamine and Parkinson's Disease

- Substantia nigra pars compacta (SNc)
 - One of two major dopamine-producing regions
- L-DOPA as PD treatment



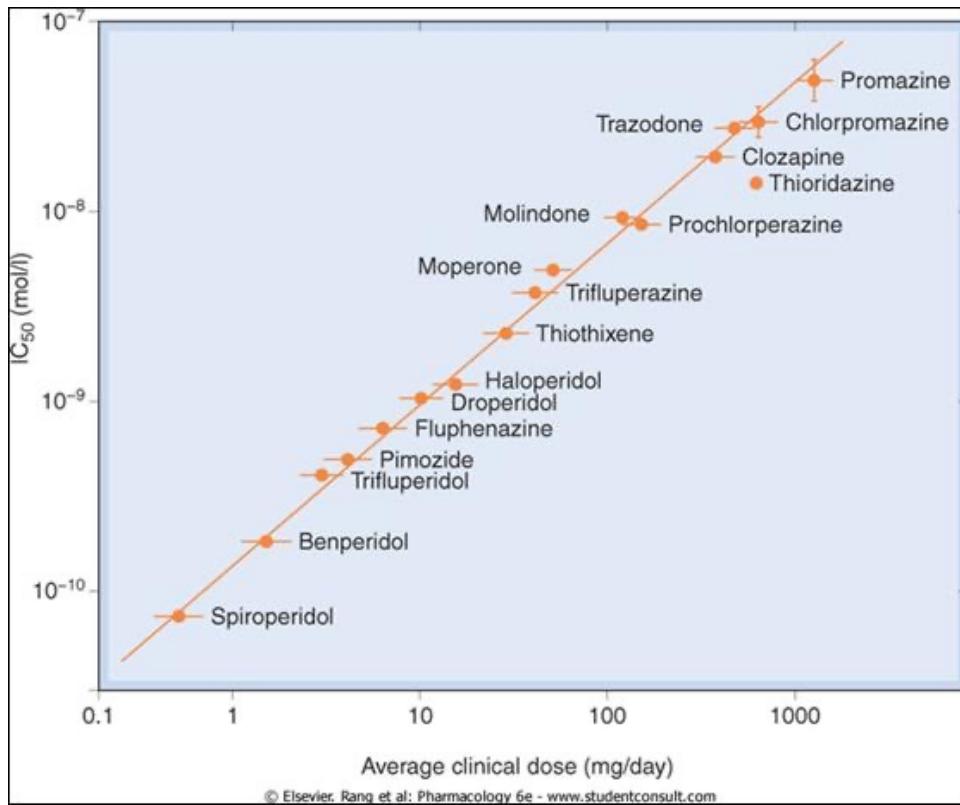
Typical appearance of Parkinson's disease



Types of neurotransmitters

Drugs: dopamine (antagonists)

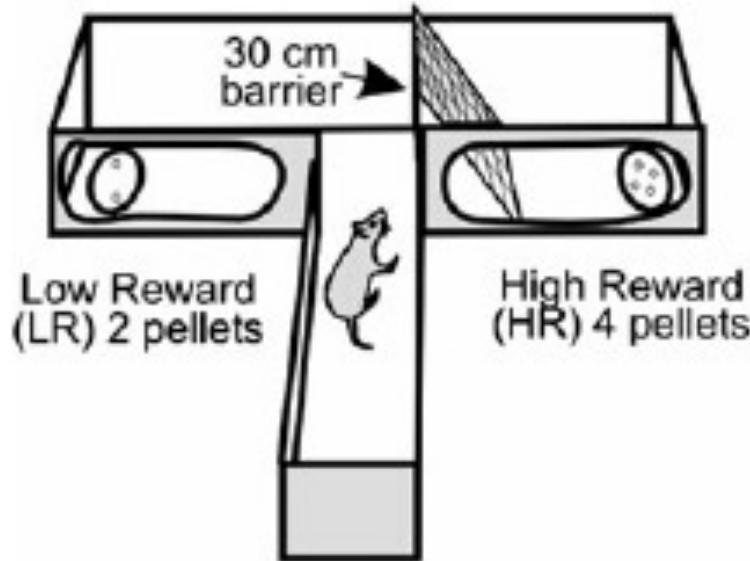
- Schizophrenia medications
 - Do individuals with schizophrenia have higher baseline pleasure?



Types of neurotransmitters

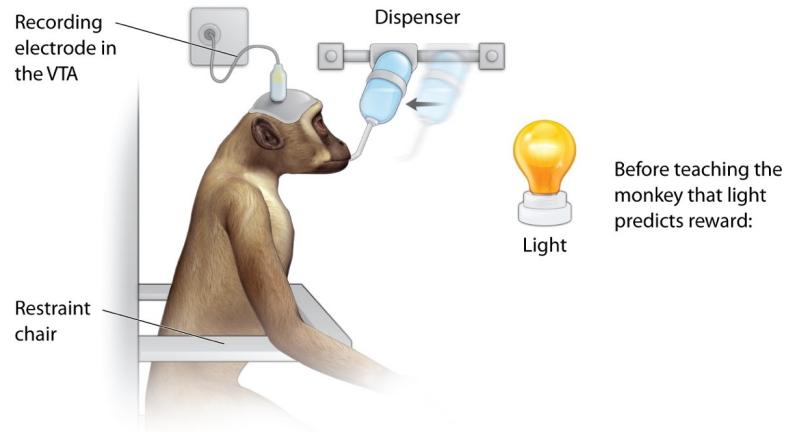
Separating Pleasure from Motivation

- Salamone (1990s)
 - Low effort, low reward vs. high effort, high reward
- Dopamine antagonists
 - Decrease motivation but not pleasure
 - Can be systemic or directly injected into VTA or NAcc

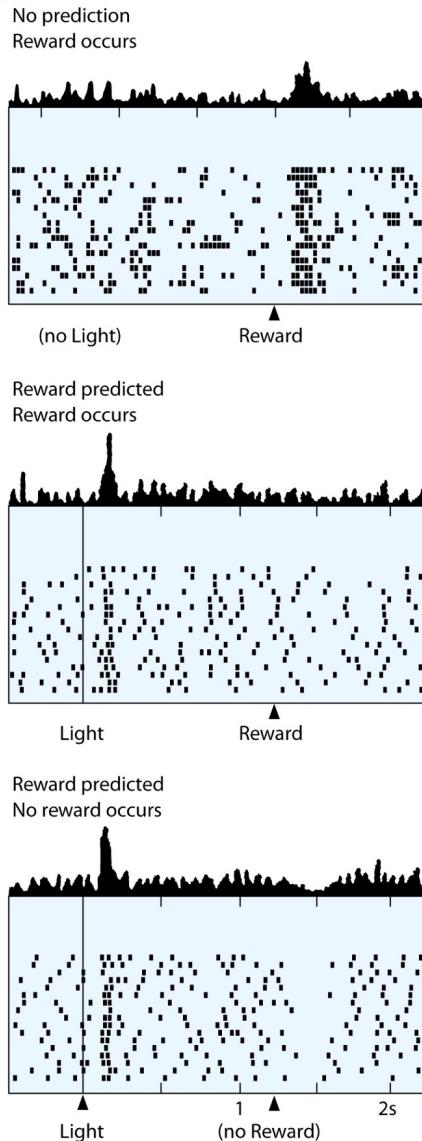


Types of neurotransmitters

Dopamine and reward prediction error



Before teaching the monkey that light predicts reward:



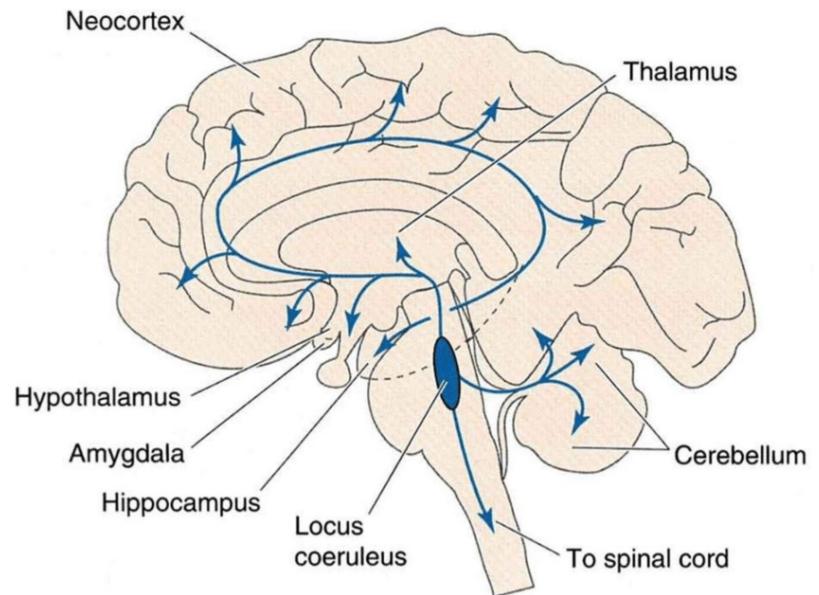
After teaching the monkey that light predicts reward:

- **Schultz *et al.* (1990s)**
 - Pavlovian learning
 - VTA (DA) neurons
 - Fire at first for unexpected reward
 - Shift their firing to stimuli that predict reward
 - Go silent when predicted reward not delivered (RPE)
 - Can be chained forward in time

Dopamine

Norepinephrine (aka noradrenaline)

- Originates in brain stem region called the **locus coeruleus**
- Causes *heterosynaptic facilitation* (via heteroceptors)
- Enhancement of memory by stress/emotion
- Evolutionarily useful



Types of neurotransmitters

Propranolol (norepinephrine receptor antagonist)

- Propranolol (norepinephrine receptor antagonist, aka noradrenergic receptor antagonist)
- Potential PTSD treatment via **reconsolidation**
- *Eternal Sunshine of the Spotless Mind?*
Not quite, but not entirely unlike



The image shows a screenshot of a CBC Radio news article. The header includes the CBC logo, a "MENU" button, and links for "radio", "Top Stories", "All Shows", "Podcasts", "Schedules", and "LISTEN LIVE". The main headline reads: "It may be possible to 'alter' memories of heartbreak so they hurt less, research finds". Below the headline, a subtext states: "Researcher calls it 'a big step forward' for mental health — but critics warn it could have downsides". At the bottom, it says "CBC Radio · Posted: Dec 02, 2019 5:33 PM ET | Last Updated: December 2". A decorative footer banner features various icons related to mental health and productivity.

Types of neurotransmitters

Serotonin

- Primarily from the raphe nuclei (brain stem)
- Precursor: tryptophan
- Serotonin depletion



red blue orange purple

orange blue green red

blue purple green red

orange blue red green

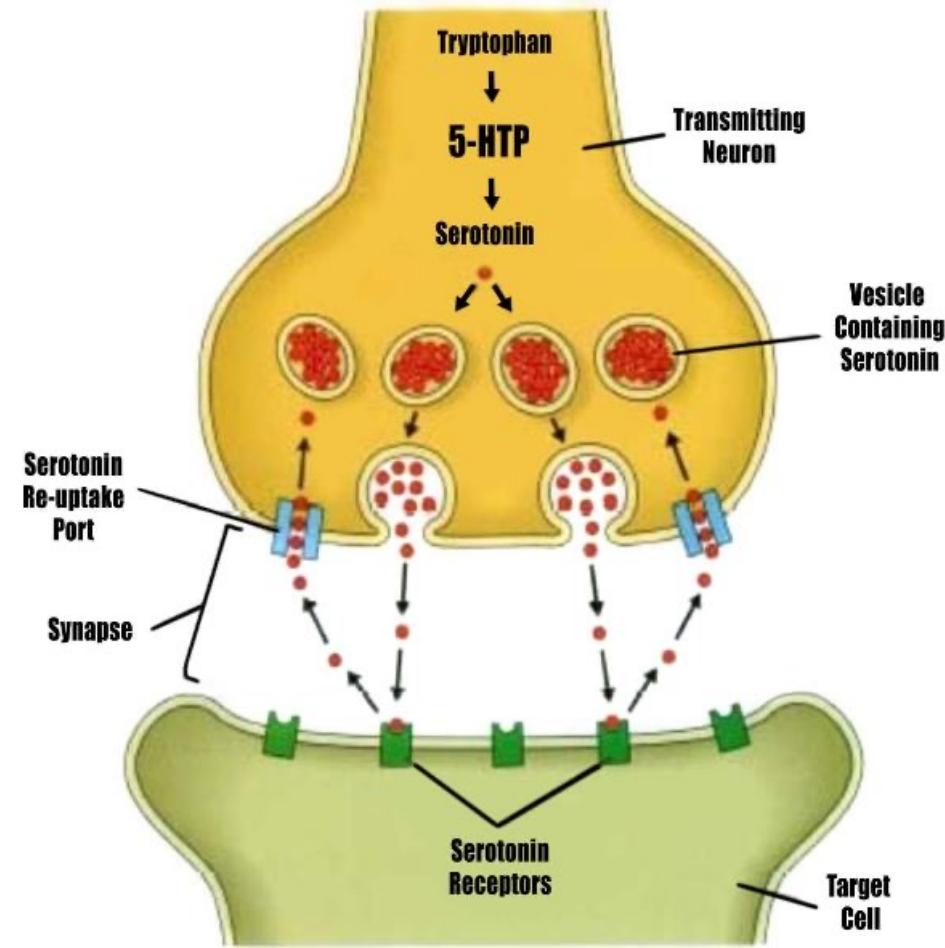
purple orange red blue

green red blue purple

Types of neurotransmitters

Selective Serotonin Reuptake Inhibitors

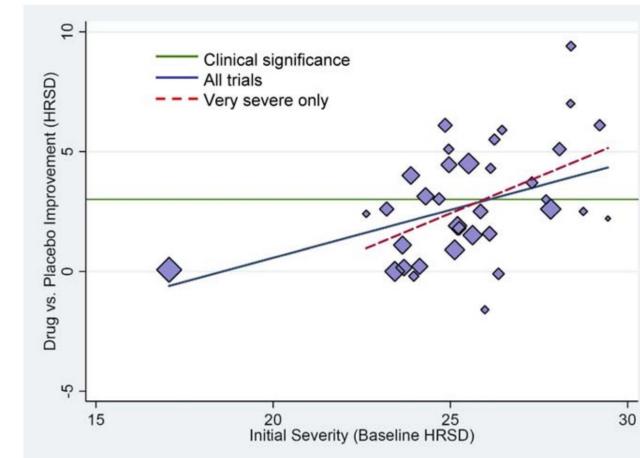
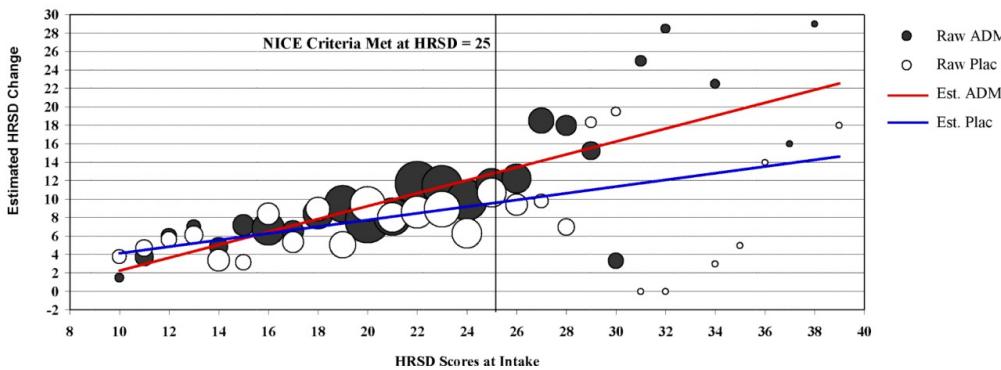
- aka SSRIs, e.g. Prozac (fluoxetine)
- For depression
- Block serotonin from being removed from the synapse
- Effects of SSRIs quick, improvements slow



Types of neurotransmitters

SSRI efficacy

- Meta-analyses: SSRIs no better than placebo for mild to moderate depression
- May help with major depression (BUT...)



Conclusions

Drug-placebo differences in antidepressant efficacy increase as a function of baseline severity, but are relatively small even for severely depressed patients. The relationship between initial severity and antidepressant efficacy is attributable to decreased responsiveness to placebo among very severely depressed patients, rather than to increased responsiveness to medication.

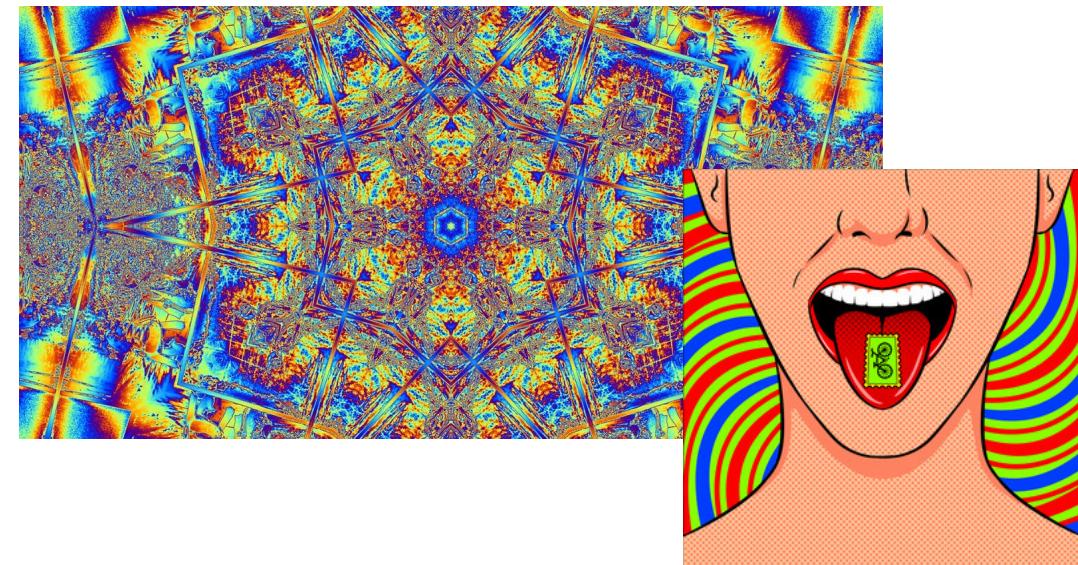
Types of neurotransmitters

Hallucinogens

Psychedelic drugs like LSD, DMT, psilocybin etc. are serotonin receptor agonists!

Radical changes to our conscious perception and thoughts, minimal effects on mood (implication?)

Recent reexamination of psychedelics' therapeutic value: end of life care, PTSD, addiction, and more

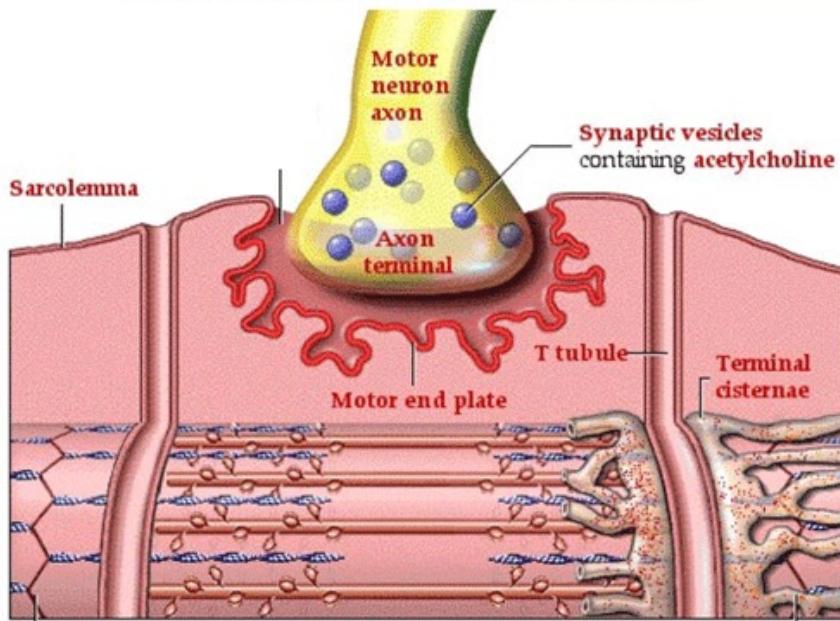


Types of neurotransmitters

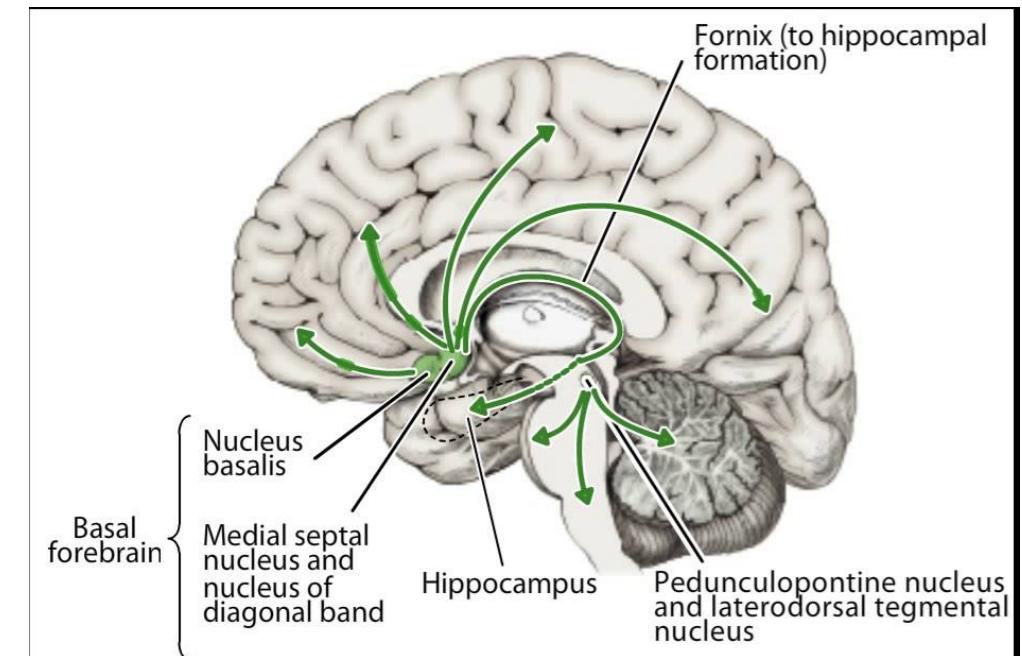
Acetylcholine

- The neuromuscular junction
- Also basal forebrain
 - Wakefulness, attention, etc.
- Nicotine

Neuromuscular Junction



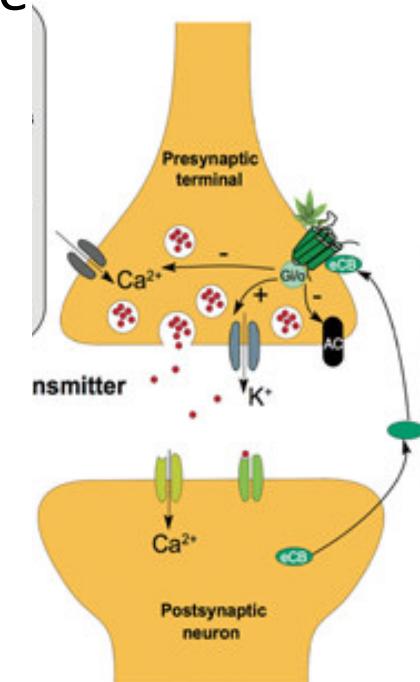
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Types of neurotransmitters

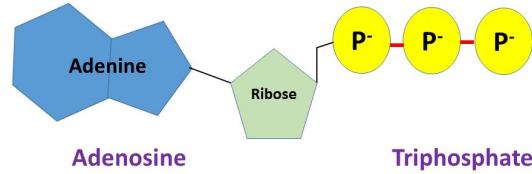
Endocannabinoids

- Two NTs, two receptors (GPCRs)
- Travel from dendrite to axon, i.e. retrograde transmission
- Weaken connection between two cells at a synapse
- Cannabis is a cannabinoid receptor agonist

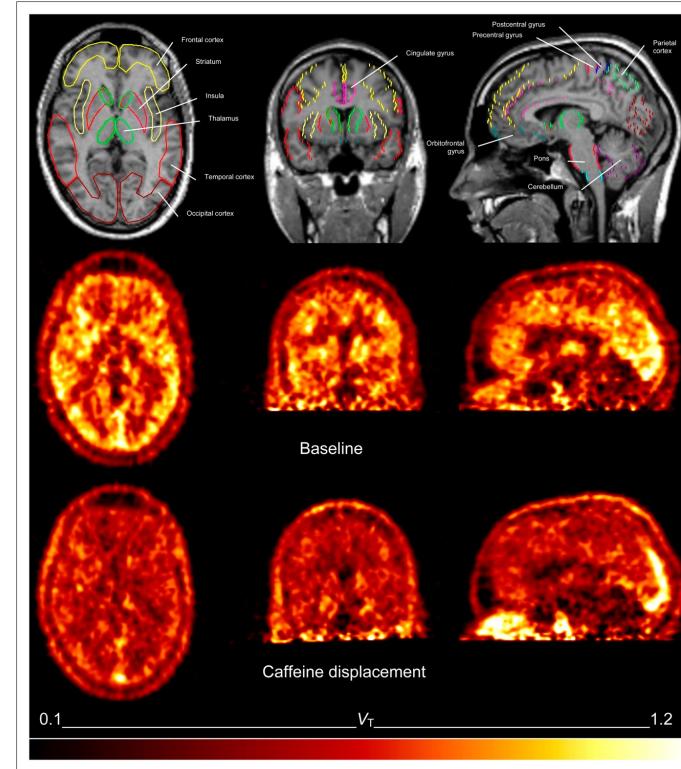


Types of neurotransmitters

Adenosine



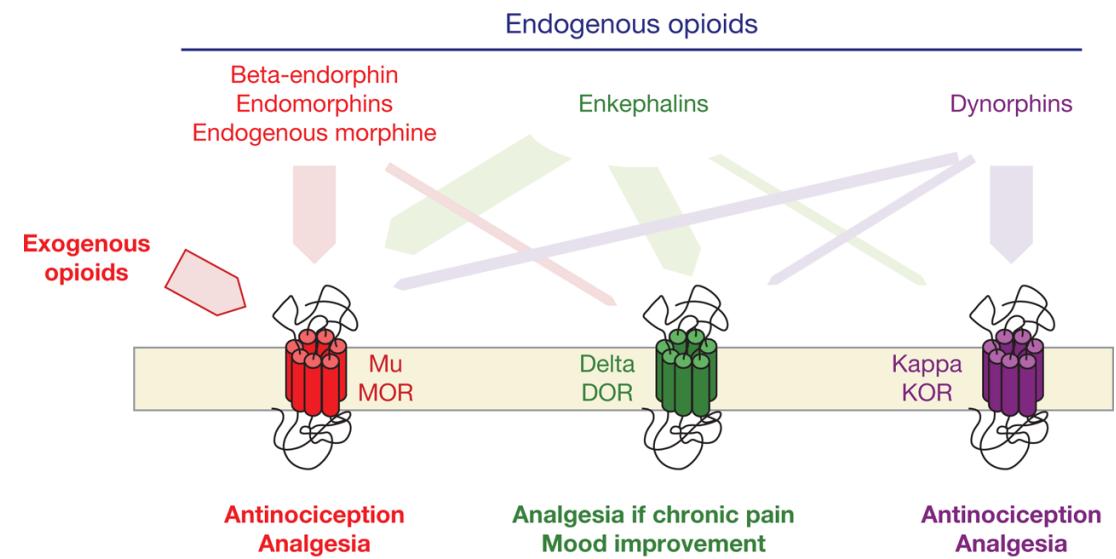
- Remember: ATP is cellular energy
- Adenosine is ATP byproduct
- Adenosine receptors
- Caffeine/theophylline



Types of neurotransmitters

Endogenous opioids

- aka Endorphins
- Giant peptide neurotransmitters
- The neurotransmitter system that exogenous opioids (e.g. heroin) mimic
- Fentanyl and naloxone
- Receptors are all GPCRs
- Receptors found in spinal cord, periacqueductal grey (PAG), nucleus accumbens, more



Types of neurotransmitters