Neurotransmitters

Conrad.Perry@Adelaide.edu.au

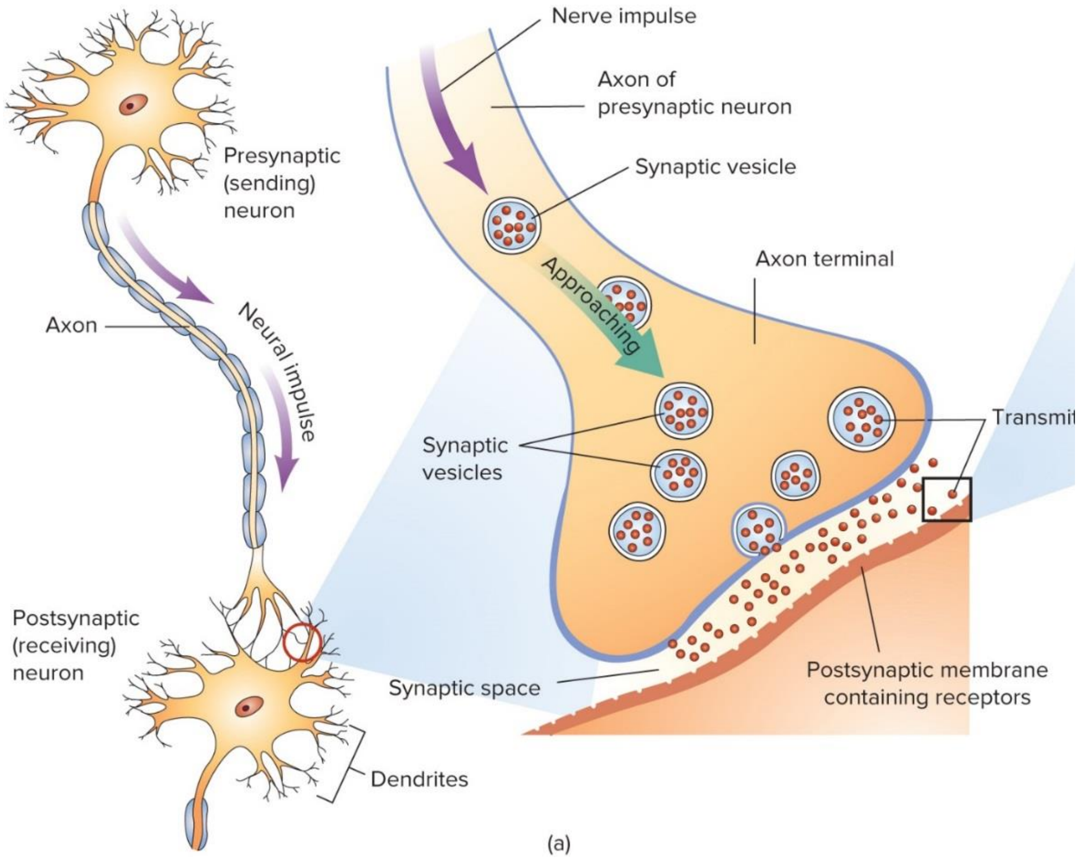
What are neurotransmitters?

Neurotransmitters are the messages used by neurons

The basic neurotransmitter system that we use evolved around 500-600 million years ago

- Almost all animals (including insects) use much the same system with much the same transmitters – serotonin, dopamine etc. .

In the last video..



There are a lot neurotransmitters with lots of different properties

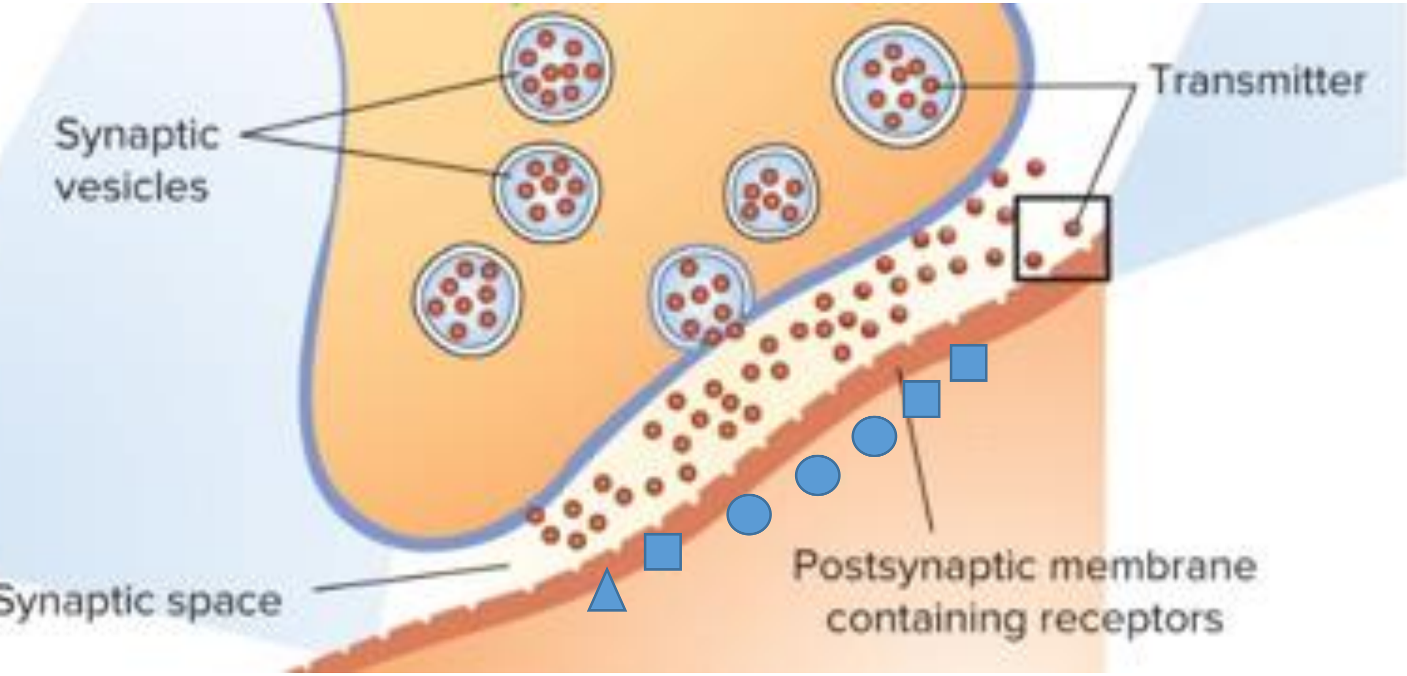
Table 4.1 **Some neurotransmitters and their effects**

Neurotransmitter	Major function	Disorders associated with malfunctioning	Additional discussion
Acetylcholine (ACh)	Excitatory at synapses involved in muscular movement and memory; involved in regulation of sleep	Memory loss in Alzheimer's disease (undersupply); paralysis (absence); violent muscle contractions and convulsions (oversupply)	Chapter 8
Noradrenalin	Excitatory and inhibitory functions at various sites; involved in neural circuits controlling learning, memory, wakefulness and eating	Depression (undersupply); stress and panic disorders (overactivity)	Chapters 6, 14
Serotonin	Inhibitory or excitatory; involved in mood, sleep, eating and arousal, and may be an important transmitter underlying pleasure and pain	Depression; sleeping and eating disorders (undersupply); obsessive–compulsive disorder (overactivity)	Chapters 6, 13, 15, 16
Dopamine	Excitatory; involved in voluntary movement, emotional arousal, learning, memory and experiencing pleasure or pain	Parkinson's disease and depression (undersupply); schizophrenia (overactivity)	Chapters 6, 15, 16
GABA (gamma-aminobutyric acid)	Inhibitory transmitter in motor system; reduces anxiety and stress	Destruction of GABA-producing neurons in Huntington's disease produces tremors and loss of motor control, as well as personality changes	Chapter 6
Glutamate	Excitatory; involved in all behaviours; important for memory and learning	Excess is associated with seizures and linked to dementia, too little can cause psychosis	Chapter 15
Endorphin	Inhibits transmission of pain impulses (a neuromodulator)	Insensitivity to pain (oversupply); pain hypersensitivity, immune problems (undersupply)	Chapters 5, 6, 14

Remember from last lecture:
Excitatory and inhibitory transmitters work by opening and stopping the opening of different types of ion channels.

Neurons are selectively affected by certain transmitters
How they are affected depends on the type of receptors they have

Presynaptic transmission



Different types of receptors only allow certain types of neurotransmitters to activate them -- this allows ion channels to be opened and thus affects whether a neuron has an action potential
The same type of receptor may be affected by more than one type of neurotransmitter
There is no simple one-to-one relationship between types of receptors and types of transmitters

The neuron which releases transmitters may take some back: This is known as **reuptake.**

“Too much, too little”

The amount of neurotransmitters and their effect across the whole distribution is important to know

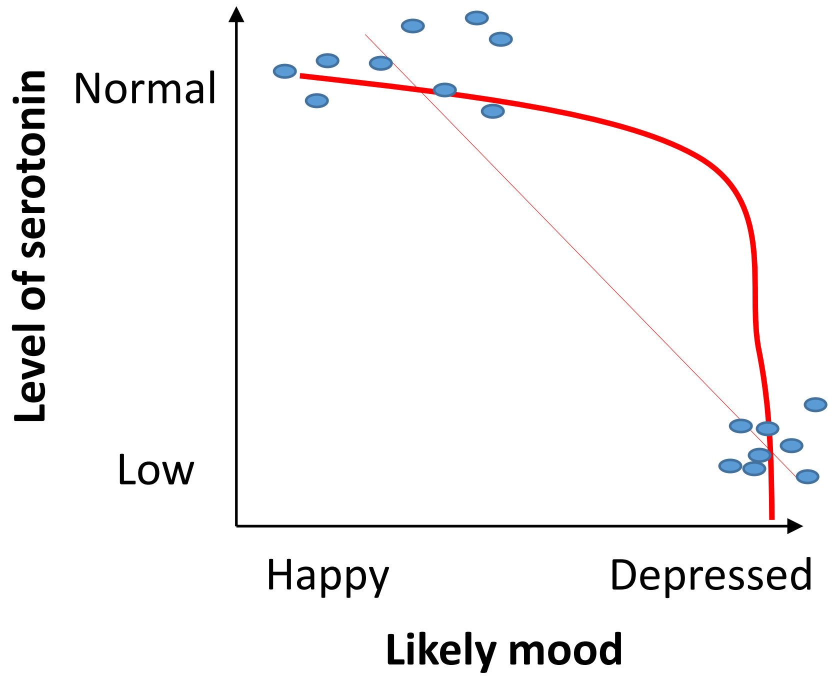
- C.f., “Not enough serotonin causes depression”

But we often don’t think about things this way

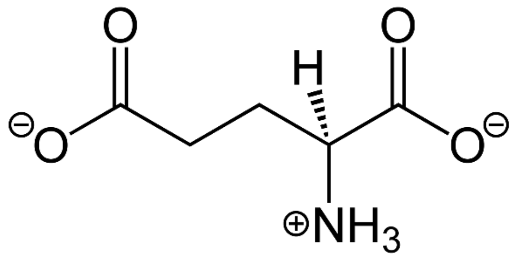
- A lot of data comes from extremes and animal studies

You should *not* infer that there is a simple linear relationships between “too much” and “too little”

If you looked around at any group of people without disorders, you would find a lot of variation in the levels of these transmitters, but, often, little predictive ability excluding the extremes



An example: Glutamate



Excitatory

The most common neurotransmitter

- Occurs in 90% of synaptic connections
- Involved in essentially everything
- Strong role in synaptic plasticity
  - The strengthening/weakening of the signal between neurons over time “Long-term potentiation”
  - Learning
  - Absolutely critical in the cortex and hippocampus

You need just the right amount

- Too little will cause exhaustion
- Too much is toxic

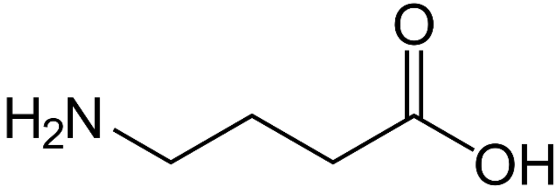
Brain injury or disease can cause glutamate excess glutamate to occur outside cells which can destroy certain types of receptors

- Associated with many nasty things: stroke, dementia, autism, and schizophrenia

Drugs that affect glutamate

- Ketamine: Increases levels in frontal cortex via inhibiting the effects of an inhibitor (GABA)

Another example: GABA



Gamma aminobutric acid

Most common inhibitory neurotransmitter

- Occurs in around 1/3 of synapses
- Concentrated in thalamus, hypothalamus, and occipital lobes

Effects

- Low levels associated
  - Increased anxiety
  - Seizure disorders
  - Parkinson’s disease
  - Mood disorders
- High levels associated
  - Calming effects (anxiety, stress, sleep)

Drugs that affect GABA

- Alcohol increases GABA
- Valium increases GABA
- Exercise increases GABA

Common drugs

What neurotransmitters/receptors do the drugs affect?

- Mainly one class (e.g., opioids – opioid receptors. Changes levels of endorphin and enkephalin)
- Many classes (e.g., cocaine – dopamine, norepinephrine)

Drugs of dependence

- Vastly increase dopamine signalling in the nucleus accumbens
- Leads to the euphoric experience

Work many different ways

Mimic neurotransmitters (opioids, THC)

- But stimulate very large numbers of receptors

Changing signalling dynamics

- Cocaine attaches to a dopamine transporter that stops reuptake
  - This increases the amount of dopamine for the receiving neuron
- Benzodiazapines enhance GABA receptors

Consequences

Short term

- “I feel terrible”. Many reasons, some obvious, like lack of sleep and dehydration. Things like LSD which get stuck inside serotonin receptors and last a long time may deplete neurons of some transmitters.

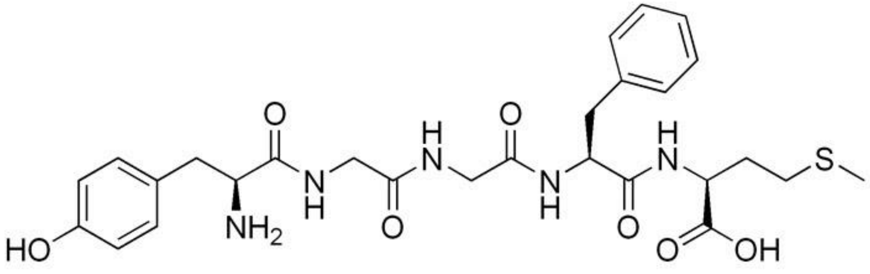
Long term

- Reduces the amount of functioning receptors (addiction)
  - Dopamine
  - Opioid receptors
- Cell damage
  - Ecstasy damages axons that release serotonin (memory problems)

Very long term

- Genetic transcription may be affected
  - Cocaine and possibly nicotine causes genes to express differently – and this may be passed on to the next generation (epigenetic effects).

Endorphins



Endogenous morphines

Produced and stored in the pituitary gland

Modulate post-synaptic activity of neurons

- Blocking GABA which causes increased production of dopamine

Change emotional responses and pain

- Released due to fear & trauma and decreases feelings of pain
- Released due to physical harm
- Increase positive feelings

Exercise “high”

Probably why some athletes can finish games after serious injury

Interesting stuff

Ctenophora use an entirely different neurotransmitter system than all other types of animals.

Once upon a time people thought they were jellyfish until they investigated their signalling system.

They give us some idea of how alternative pathways for evolution may have worked!