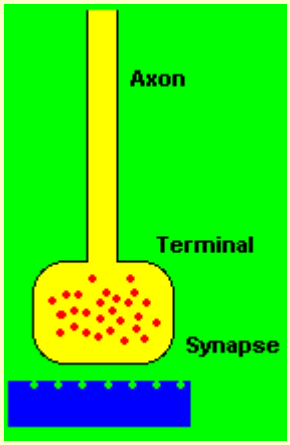
Neurotransmitters and Neuroactive Peptides

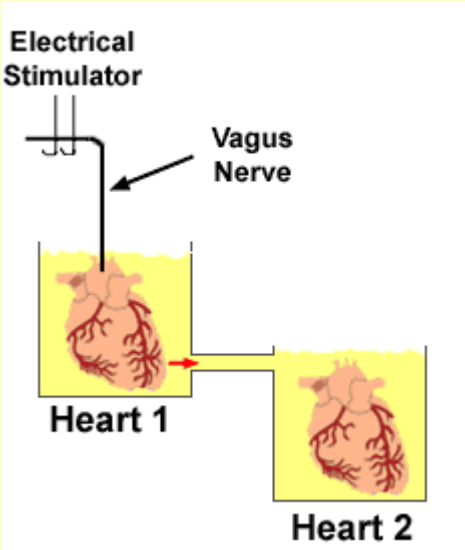


Communication of information between neurons is accomplished by movement of chemicals across a small gap called the synapse. Chemicals, called neurotransmitters, are released from one neuron at the presynaptic nerve terminal. Neurotransmitters then cross the synapse where they may be accepted by the next neuron at a specialized site called a receptor. The action that follows activation of a receptor site may be either depolarization (an excitatory postsynaptic potential) or hyperpolarization (an inhibitory postsynaptic potential). A depolarization makes it MORE likely that an action potential will fire; a hyperpolarization makes it LESS likely that an action potential will fire.

Discovery of Neurotransmitters

Back in 1921, an Austrian scientist named Otto Loewi discovered the first neurotransmitter. In his experiment (which came to him in a dream), he used two frog hearts. One heart (heart #1) was still connected to the vagus nerve. Heart #1 was placed in a chamber that was filled with saline. This chamber was connected to a second chamber that contained heart #2. So, fluid from chamber #1 was allowed to flow into chamber #2. Electrical stimulation of the vagus nerve (which was attached to heart #1) caused heart #1 to slow down. Loewi also observed that after a delay, heart #2 also slowed down. From this experiment, Loewi hypothesized that electrical stimulation of the vagus nerve released a chemical into the fluid of chamber #1 that flowed into chamber #2. He called this chemical "Vagusstoff". We now know this chemical as the neurotransmitter called acetylcholine.

Otto Loewi's Experiment



Neurotransmitter Criteria

Neuroscientists have set up a few guidelines or criteria to prove that a chemical is really a neurotransmitter. Not all of the neurotransmitters that you have heard about may actually meet every one of these criteria.

The chemical must be produced within a neuron. 	The chemical must be found within a neuron. 	When a neuron is stimulated (depolarized), a neuron must release the chemical. 
When a chemical is released, it must act on a post-synaptic receptor and cause a biological effect. 	After a chemical is released, it must be inactivated. Inactivation can be through a reuptake mechanism or by an enzyme that stops the action of the chemical. 	If the chemical is applied on the post-synaptic membrane, it should have the same effect as when it is released by a neuron. 

Neurotransmitter Types

There are many types of chemicals that act as neurotransmitter substances. Below is a list of some of them.

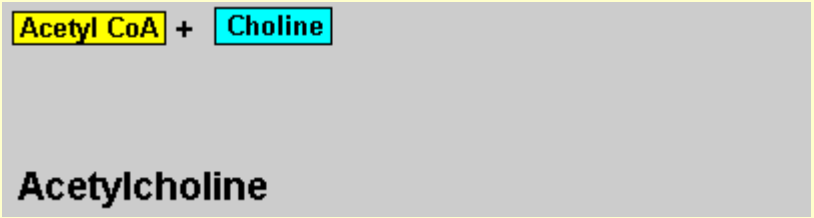
Small Molecule Neurotransmitter Substances		
Acetylcholine (ACh)	Dopamine (DA)	Norepinephrine (NE)
Serotonin (5-HT)	Histamine	Epinephrine

Amino Acids		
Gamma-aminobutyric acid (GABA)	Glycine	Glutamate
Aspartate		

Neuroactive Peptides - partial list!!</FONT< td>			
bradykinin	beta-endorphin	bombesin	calcitonin
cholecystokinin	enkephalin	dynorphin	insulin
gastrin	substance P	neurotensin	glucagon
secretin	somatostatin	motilin	vasopressin
oxytocin	prolactin	thyrotropin	angiotensin II
sleep peptides	galanin	neuropeptide Y	thyrotropin-releasing hormone
gonadotropnin-releasing hormone	growth hormone-releasing hormone	luteinizing hormone	vasoactive intestinal peptide

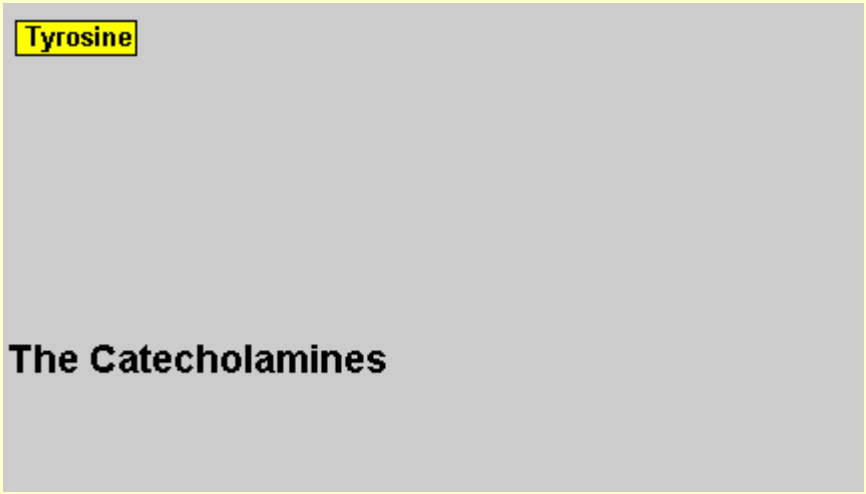
Soluble Gases	
Nitric Oxide (NO)	Carbon Monoxide

Synthesis of Neurotransmitters



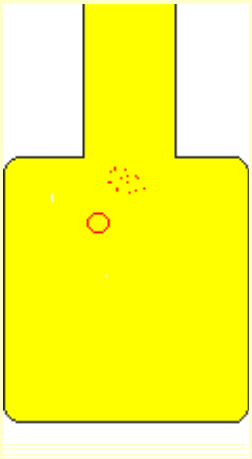
Acetylcholine is found in both the central and peripheral nervous systems. Choline is taken

up by the neuron. When the enzyme called "choline acetyltransferase" is present, choline combines with acetyl coenzyme A (CoA) to produce acetylcholine.



Dopamine, norepinephrine and epinephrine are a group of neurotransmitters called "catecholamines". Norepinephrine is also called "noradrenalin" and epinephrine is also called "adrenalin". Each of these neurotransmitters is produced in a step-by-step fashion by a different enzyme.

Transport and Release of Neurotransmitters



Neurotransmitters are made in the cell body of the neuron and then transported down the axon to the axon terminal. Molecules of neurotransmitters are stored in small "packages" called vesicles (see the picture on the right). Neurotransmitters are released from the axon terminal when their vesicles "fuse" with the membrane of the axon terminal, spilling the neurotransmitter into the synaptic cleft.

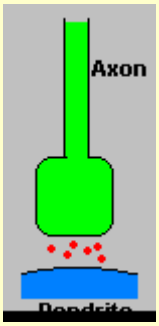
Unlike other neurotransmitters, nitric oxide (NO) is not stored in synaptic vesicles. Rather, NO is released soon after it is produced and diffuses out of the neuron. NO then enters another cell where it activates enzymes for the production of "second messengers."

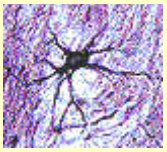
Receptor Binding

Neurotransmitters will bind only to specific receptors on the postsynaptic membrane that recognize them.

Inactivation of Neurotransmitters

The action of neurotransmitters can be stopped by four different mechanisms

1. Diffusion: the neurotransmitter drifts away, out of the synaptic cleft where it can no longer act on a receptor.	Diffusion 
2. Enzymatic degradation (deactivation): a specific enzyme changes the structure	Enzymatic degradation

of the neurotransmitter so it is not recognized by the receptor. For example, acetylcholinesterase is the enzyme that breaks acetylcholine into choline and acetate.	
3. Glial cells: astrocytes remove neurotransmitters from the synaptic cleft.	 Astrocyte Image courtesy of Biodidac
4. Reuptake: the whole neurotransmitter molecule is taken back into the axon terminal that released it. This is a common way the action of norepinephrine, dopamine and serotonin is stopped...these neurotransmitters are removed from the synaptic cleft so they cannot bind to receptors.	Reuptake