

Neurotransmitters

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Neurotransmitters are the chemicals which allow the transmission of signals from one neuron to the next across synapses. They are also found at the axon endings of motor neurons, where they stimulate the muscle fibers. And they and their close relatives are produced by some glands such as the pituitary and the adrenal glands. In this chapter, we will review some of the most significant neurotransmitters.

Acetylcholine

Acetylcholine was the first neurotransmitter to be discovered. It was isolated in 1921 by a German biologist named Otto Loewi, who would later win the Nobel Prize for his work. Acetylcholine has many functions: It is responsible for much of the stimulation of muscles, including the muscles of the gastrointestinal system. It is also found in sensory neurons and in the autonomic nervous system, and has a part in scheduling REM (dream) sleep.

The plant poisons curare and hemlock cause paralysis by blocking the acetylcholine receptor sites of muscle cells. The well-known poison botulin works by preventing the vesicles in the axon ending from releasing acetylcholine, causing paralysis. The botulin derivative botox is used by many people to temporarily eliminate wrinkles - a sad commentary on our times, I would say. On a more serious note, there is a link between acetylcholine and Alzheimer's disease: There is something on the order of a 90% loss of acetylcholine in the brains of people suffering from Alzheimer's, which is a major cause of senility.

Norepinephrine

In 1946, a Swedish biologist by the name of Ulf von Euler discovered norepinephrine (formerly called noradrenalin). He also won a Nobel Prize. Norepinephrine is strongly associated with bringing our nervous systems into "high alert." It is prevalent in the sympathetic nervous system, and it increases our heart rate and our blood pressure. Our adrenal glands release it into the blood stream, along with its close relative epinephrine (aka adrenalin). It is also important for forming memories.

Stress tends to deplete our store of adrenalin, while exercise tends to increase it. Amphetamines ("speed") work by causing the release of norepinephrine, as well as other neurotransmitters called dopamine and serotonin.

Dopamine

Another relative of norepinephrine and epinephrine is dopamine, discovered to be a neurotransmitter in the 1950s by another Swede, Arvid Carlsson. It is an **inhibitory** neurotransmitter, meaning that when it finds its way to its receptor sites, it blocks the tendency of that neuron to fire. Dopamine is strongly associated with reward mechanisms in the brain. Drugs like cocaine, opium, heroin, and alcohol increase the levels of dopamine, as does nicotine. If it feels good, dopamine neurons are probably involved!

The severe mental illness schizophrenia has been shown to involve excessive amounts of dopamine in the frontal lobes, and drugs that block dopamine are used to help schizophrenics. On the other hand, too little dopamine in the motor areas of the brain are responsible for Parkinson's disease, which involves uncontrollable muscle tremors. It was the same Arvid Carlsson mentioned above who figured out that the precursor to dopamine (called L-dopa) could alleviate some of the symptoms of Parkinson's. He was awarded the Nobel Prize in 2000.

Recently, it has been noted that low dopamine may be related not only to the unsociability of schizophrenics, but also to social anxiety. On the other hand, dopamine has been found to have relatively little to do with the pleasures of eating. That seems to involve chemicals such as endorphin (see below).

GABA

In 1950, Eugene Roberts and J. Awapara discovered GABA (gamma aminobutyric acid), which is also usually an inhibitory neurotransmitter. GABA acts like a brake to the excitatory neurotransmitters that lead to anxiety. People with too little GABA tend to suffer from anxiety disorders, and drugs like Valium work by enhancing the effects of GABA. Lots of other drugs influence GABA receptors, including alcohol and barbituates. If GABA is lacking in certain parts of the brain, epilepsy results.

Glutamate

Glutamate is an excitatory relative of GABA. It is the most common neurotransmitter in the central nervous system - as much as half of all neurons in the brain - and is especially important in regards to memory. Curiously, glutamate is actually toxic to neurons, and an excess will kill them. Sometimes brain damage or a stroke will lead to an excess and end with many more brain cells dying than from the original trauma. ALS, more commonly known as Lou Gehrig's disease, results from excessive glutamate production. Many believe it may also be responsible for quite a variety of diseases of the nervous system, and are looking for ways to minimize its effects

Glutamate was discovered by Kikunae Ikeda of Tokay Imperial Univ. in 1907, while looking for the flavor common to things like cheese, meat, and mushrooms. He was able to extract an acid from seaweed - glutamate. He went on to invent the well known seasoning MSG - monosodium glutamate. It took decades for Peter Usherwood to identify glutamate as a neurotransmitter (in locusts) in 1994.

Serotonin

Serotonin is an inhibitory neurotransmitter that has been found to be intimately involved in emotion and mood. Too little serotonin has been shown to lead to depression, problems with anger control, obsessive-compulsive disorder, and suicide. Too little also leads to an increased appetite for carbohydrates (starchy foods) and trouble sleeping, which are also associated with depression and other emotional disorders. It has also been tied to migraines, irritable bowel syndrome, and fibromyalgia.

Vittorio Erspamer first discovered what we now call serotonin in the 1930s. It was found in blood serum in 1948 by Irvine Page, who named it serotonin (from "serum-tonic"). Another researcher in Page's lab - Maurice Rapport - proved that it was an amine (a group of chemicals that include the neurotransmitters). John Welsh found that it was a neurotransmitter in molluscs in 1954, and Betty Twarog (also at Page's lab) found it in vertebrates in 1952. All this gives you a sense of the cooperative nature of most of scientific discovery!

Prozac and other recent drugs help people with depression by preventing the neurons from "vacuuming" up excess serotonin, so that there is more left floating around in the synapses. It is interesting that a little warm milk before bedtime also increases the levels of serotonin. As mom may have told you, it helps you to sleep. Serotonin is a derivative of tryptophan, which is found in milk. The "warm" part is just for comfort!

On the other hand, serotonin also plays a role in perception. Hallucinogens such as LSD, mescaline, psilocybin, and ecstasy work by attaching to serotonin receptor sites and thereby blocking transmissions in perceptual pathways.

Endorphin

In 1973, Solomon Snyder and Candace Pert of Johns Hopkins discovered endorphin. Endorphin is short for "endogenous morphine." It is structurally very similar to the opioids (opium, morphine, heroin, etc.) and has similar functions: Inhibitory, it is involved in pain reduction and pleasure, and the opioid drugs work by attaching to endorphin's receptor sites. It is also the neurotransmitter that allows bears and other animals to hibernate. Consider: Heroin slows heart-rate, respiration, and metabolism in general - exactly what you would need to hibernate. Of course, sometimes heroin slows it all down to nothing: Permanent hibernation.