**Inhibitory Neurotransmitters** are the nervous system's "off switches", decreasing the likelihood that an excitatory signal is sent. Inhibitory transmitters regulate the activity of the excitatory neurotransmitters, much like the brakes on a car. Physiologically, the inhibitory transmitters act as the body's natural tranquilizers, generally serving to induce sleep, promote calmness, and decrease aggression.

**Excitatory Neurotransmitters** are the nervous system's "on switches", increasing the likelihood that an excitatory signal is sent. Excitatory transmitters can be likened to the accelerator of a car, regulating many of the body's most basic functions, including thought processes, higher thinking, and sympathetic activity. Physiologically, the excitatory transmitters act as the body's natural stimulants, generally serving to promote wakefulness, energy, and activity.

(Green)A number of chemicals within the body and nervous system serve as modulators or precursors to neurotransmitters and do not necessarily have excitatory or inhibitory properties.

## Neurotransmitters must meet the following criteria to be classified as such:

Must be present within a neuron Must be released in response to neuron depolarization Must have a post- synaptic receptor present

**Neuromodulators** are chemicals that meet the criteria of a neurotransmitter, however can serve both inhibitory and excitatory roles. Most neuromodulators tend to be either primarily excitatory or primarily inhibitory.

### 5-HIAA Serotonin Metabolite

5-Hydroxyindoleacetic acid (5-HIAA) is a major metabolite of serotonin, generated via a two step process, involving monoamine oxidase A (MAO-A) and aldehyde dehydrogenase. Measurement of 5-HIAA in combination with serotonin may offer insight into mechanisms underlying various clinical symptoms. The ratio of serotonin to 5-HIAA may be used to evaluate serotonin turnover and monoamine oxidase activity. Abnormal levels of 5-HIAA have been associated with depression, suicidal behaviors, aggression, chronic psychotropic medication use, and Parkinson's Disease.

#### **Agmatine -** Inhibitory neuromodulator

Agmatine is an inhibitory neurotransmitter that can block the action of glutamate on the NMDA receptor. This mechanism is important in preventing the harmful effects of excess glutamate. Research has shown that agmatine can act to help with swelling which can help protect from chronic neuropathic pain.

#### **Aspartic Acid** -Excitatory Neuromodulator

Aspartic Acid, also known as aspartate, is an excitatory neurotransmitter in the brainstem and spinal cord. Aspartic acid is the excitatory counterpart to glycine, an inhibitory neurotransmitter. Low levels have been linked to feelings of fatigue and low mood, whereas high levels have been linked to seizures and anxiousness.

# **DOPAC-** Dopamine Metabolite

After neuronal dopamine is released it is inactivated primarily via reuptake mechanisms that remove it from the synapse and the extraneuronal space and return it to the presynaptic dopaminergetic neuron or adjacent noradrenergic neurons. Some of the enzymes that degrade dopamine are only found in specific regions of the body. As such some dopamine metabolites are only produced in specific tissues. Understanding how and where these enzymes function can proved valuable insight about how dopamine is functioning in specific regions of the body. In order to understand these functions one must first realize Monoamine oxidase (MAO) is an enzyme present within the cytoplasm of neurons that breaks down dopamine to DOPAL. DOPAL in turn is very rapidly converted to DOPAC by a second cytoplasmic enzyme aldehydedehydrogenase (AD). Because both of these enzymes are primarily found inside neurons, DOPAC levels are dependent on the amount of cytoplasmic dopamine. Combined measurements of DOPAC and dopamine have been used to assess the activity of dopaminergic neurons. This combination provides additional information than either parameter alone because a large portion of DOPAC is formed from dopamine without ever being released to the synaptic cleft. This suggests that DOPAC may be more closely related to the presynaptic dopamine levels while dopamine and similarly HVA levels, another important metabolite in dopamine that is formed outside of the neuron via the actions of catechols-Omethyltransferase (COMT) are related to the rate of neuron signaling. Said another way, extracellular DOPAC is related to the amount of dopamine made and stored in the presynaptic neuron while extracellular dopamine levels are related to the rate of dopamine released via the depolarization of dopamine neurons.

#### **Dopamine-** Excitatory neuromodulator

Dopamine is an excitatory and inhibitory neurotransmitter, depending on the dopaminergic receptor it binds to. It is derived from the amino acid tyrosine. Dopamine is the precursor to norepinephrine and epinephrine, which are all catecholamines. The function of dopamine is diverse but plays a large role in the pleasure/reward pathway (addition and thrills), memory, and motor control. Dopamine, like norepinephrine and epinephrine, is stored in vesicles in the cenral nervous systems. The dopaminergic neurons have dendrites that extend into various regions of the brain, controlling different funtions through the stimulation of adrenergic and dopaminergic receptors (D1-D5). Common symptoms with low dopamine levels are loss of motor control, addictions, cravings, compulsions, and los of satisfaction. When dopamine levels are elevated symptoms may manifest in the form of anxiety or hyperactivity. Some therapies utilize L-DOPA for parkinsonian symptoms which can also cause elevations in dopamine.