The reversal of depression with the MAO inhibitor, iproniazid, provided the first important link between depression and the catecholamines. These are neurotransmitters that are involved with the reward pathways in the brain. We have already noted that stress reduces the levels of these neurotransmitters.

Neurotransmitters transmit messages from one neuron to another. Two of these neurotransmitters, norepinephrine and serotonin, are found in reduced quantities in a depressed person's brain.

Because of this too few messages get transmitted between neurons and the symptoms of depression occur. In clinical depression the chemicals in the brain are out-of-balance.

Imaging techniques such as f-MRI (functional magnetic resonance imaging) and PET scan (positron emission tomography) create images of how active different parts of the brain are and allow researchers to take pictures of the brain showing activity levels in different areas.

Some studies with these kinds of techniques have suggested that the patterns of activation in the brains of depressed people differ from those of healthy people.

This research is fairly new, so is not yet used to diagnose clinical depression, but these tests can help doctors and researchers learn more about depression and other mental illnesses.

A retired neuroscientist, E. Van Winkle, has suggested in

"The toxic mind: the biology of mental illness and violence"; ([1])
that the continual suppression of emotions during fight or flight reactions results in atrophy in some neurons and accumulation of toxins in regions of the brain.

During periodic ‘detoxification crises’ excess norepinephrine and other metabolites flood synapses, causing symptoms ranging from mild anxiety to violent behaviour.

Other neurotransmitters such as dopamine, epinephrine (adrenaline), serotonin, gamma-aminobutyric acid (GABA), peptides, amino acids, and various metabolic waste products, also alter neurotransmission.

There is a recognised association between anxiety and depression, and they share pathophysiology.

The neurotransmitters noradrenaline (norepinephrine), dopamine, and serotonin interact in a complex fashion to affect mood, emotion, and cognitive functioning.

Abnormalities in noradrenaline and serotonin, the amygdala (the brain region believed to regulate various aspects of emotional processing) and the neuropeptide corticotrophin-releasing factor, which is typically secreted in response to stress, are common among both patients with anxiety and those with depression.

Drug treatment of depression is based upon altering the levels of noradrenaline (norepinephrine) and serotonin. As a drug enters the brain, it immediately binds to and inhibits the transporters for serotonin and/or norepinephrine, thereby increasing the availability of these neurotransmitters at certain synapses (junctions between neurons).

For instance, MAO inhibitors facilitate the activity of the catecholamine systems by slowing the metabolism of these compounds. The tricyclic drugs interfere with the reuptake of catecholamines, thus raising the level.
Essentially, dopamine and norepinephrine are alerting chemicals, whereas serotonin is calming and relaxing.

Even the food we eat can influence our levels of brain chemicals. Foods containing tyrosine (protein foods especially fish, shellfish and poultry) are providing the building block for dopamine and norepinephrine.

Food containing tryptophan (meats of all types) provides the building block for serotonin.

The enzyme monoamine oxidase (MAO), initiates the metabolic breakdown of various chemicals including serotonin, norepinephrine, and dopamine, into forms that can be assimilated or eliminated by the body.

Thus MAO can decrease levels of dopamine. Often MAO inhibitors are used to block the actions of MAO, which could generate higher levels of dopamine.

MAO also breaks down tyramine, which is a chemical occurring in especially high concentration in aged cheese, nutmeg; possibly some smoked fish and aged wine. It is also a metabolite (end product) of PEA.

PEA is a molecule bearing close structural similarities with the following compounds; "amphetamine, the neurotransmitters norepinephrine and dopamine; phenylalanine, tyrosine, and L-dopa"; (2)

There are two types of MAO enzymes: MAO-A and MAO-B. MAO-B is responsible for the breakdown of dopamine and works primarily in the brain.

MAO-A works primarily in the digestive system, and can be stimulated by tyramine, thus breaking down epinephrine and norepinephrine.
This may lead to less conservation of dopamine. Eating aged cheese, which can produce tyramine, and other chemicals such as those that resemble PEA, can stimulate the production of MAO enzymes, which in turn causes conservation of dopamine.

Tyramine can displace stimulatory catecholamine neurotransmitters (dopamine, epinephrine and norepinephrine) from storage granules where they are stored in a dormant state.

They are then released from the neurons into the synapses- where they perform their function. Morgenthaler and Joy describe this catecholamine-releasing action “as a process similar to passengers entering and exiting a crowded elevator. As a load of passengers (tyramine molecules) enters the elevator (a catecholamine storage site inside a brain cell), old passengers (catecholamines) must flood out into the hallway (the synapse), in order to make room for the new passengers.

In the cheese effect, too much tyramine triggers excessive catecholamine release. (Better Sex Through Chemistry)

In turn, this may cause depleted dopamine levels.
