

Neurochemistry of Addiction

Addiction is a complex disease of drug chemistry, brain chemistry, thought processes and social interactions. Research has shown that addiction involves the reward centers in the brain belonging to the limbic system, which is emotionally driven and recently shown involvement of the frontal cortex; our rational, conscious brain area.

Much focus on addiction centers on the brain chemical dopamine. Dopamine has shown to increase in concentration in the limbic (middle) brain regions when abusive drugs are consumed. As the magnitude of drug-induced dopamine increases, the reports of reinforcing properties (the "high"), appear to decrease. Thus, the addict must use larger amounts of the drug over time, to achieve their original "high" state.

This reaction implies that dopamine involvement in drug addiction is likely mediated by functional and structural changes in the neural circuits. Some of the structural changes observed recently are decreases in volume of the frontal lobe with certain drug use.

Research has demonstrated frontal lobe volume losses in abusers of cocaine, heroin and alcohol. With the frontal cortex being involved in rational, conscious thought, reduced function impairs these top-down processes causing a loss of self-directed, willed behavior. Thus the addicted loses their inhibitory controls and defaults to stimulus-driven behaviors, facilitated by the drugs.

The cycle of addiction can be broken down into 4 main areas; drug intoxication, drug craving, drug bingeing, and drug withdrawal.

As stated previously, drug intoxication involves higher extra cellular dopamine concentrations in the limbic as well as frontal regions of the brain.

Drug craving is a learned response involving social and environmental cues. Memory for the drug experience is housed in the amygdala and hippocampal regions, and involves activation of the thalamo-orbitofrontal and anterior cingulated areas to manifest the craving experience. Blood sugar metabolism has been shown to be intimately linked in the craving stage. Compulsive drug administration (bingeing) involves a loss of inhibitory processes and has been shown to involve dopamine, serotonin and glutamine circuitry in the thalamo-orbitofrontal and anterior cingulate gyrus areas.

Drug withdrawal results in disruption of behavioral circuits, culminating in dysphoria, dysthymia and irritability. These changes have been shown to involve frontal cortical circuitry, and the neurochemicals dopamine, serotonin and corticotrophin-releasing factor. It has also been noted that the dopamine receptor (D2) availability decreases with increased drug exposure. The D2 receptor pathway involves reward circuits in the brain, and thus with decreased receptor availability, a potential for increased risk of addictive behavior ensues.

It has been shown that the mesolimbic dopamine circuit which includes the nucleus accumbens, amygdala, and hippocampus, is associated with the acute reinforcing effects of the drug and also with the memories and conditioned responses linked to cravings. The mesocortical dopamine circuits, which include the prefrontal



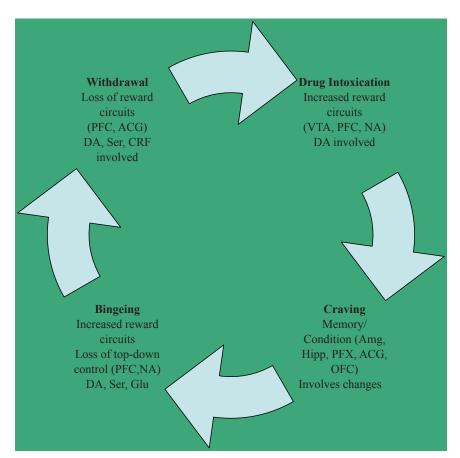
cortex, orbitofrontal cortex and anterior cingulate gyrus, are likely involved in the conscious experience of drug intoxication.

(See diagram at end outlining the cycle of addiction.)

At Agora, the NRR intravenous treatments utilize a select formulation of amino acids, vitamins and minerals. The amino acids selected are the building blocks for the creation of healthy neurochemicals and the vitamins and minerals are the cofactors in that process. Specifically tyrosine for dopamine, tryptophan for serotonin, glutamine for GABA and phosphatidyl choline for acetylcholine, in addition to others.

Thus, the addict's system has their chemical needs met in a positive way as these amino acids aid in reestablishing a healthy balance of neurochemistry. This reduces withdrawal symptoms as there is not a chemical void in the system but rather the replacement with a healthy alternative.

Over the course of treatment, neurochemistry stabilizes, cellular structures repair, and the addictive storm subsides, creating the potential for positive change.



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Cycle of Addiction

Key:

DA – dopamine VTA – ventral tegmental area PFC – prefrontal cortex NA – nucleus accumbens Amg – amygdale Hipp – hippocampus ACG – anterior cingulated gyrus OFC – orbitofrontal cortex Ser – serotonin Glu – glutamate CRR – corticotrophin-releasing factor

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