Neurobiology of Addiction and Recovery

Drugs and the Brain

In understanding the biological effects of the substances of abuse, it may be helpful to remember that all mental and emotional states are, at least in part, manifestations of our brain's chemical and electrical activity. Slight changes in the levels and activity of certain brain chemicals (called neurotransmitters) can make for noticeable, and sometimes dramatic, changes in our moods, emotions and thinking.

This is because the human brain is a collection of about two hundred billion cells called neurons, long, thin electrically-charged chemical-filled wire-like cells with electrochemical contacts on each end. Unlike other areas of our body where cells physically connect to one another, no two neurons actually touch. Neurons can act collectively, only if they are able to communicate with and affect the action of other neurons. Neurons communicate by exchanging chemical signals across the gaps that lie between them (called synapses). This process is called neurotransmission. Psychoactive drugs exert their effects by mimicking, amplifying, blocking or otherwise altering the process of neurotransmission (Perrino, 1996).

Science has so far identified about 80 chemicals (called neurotransmitters) in the human brain. Each of us has the same 80-odd neurotransmitters. These brain chemicals tend to function in a fairly task-specific way – accounting for a limited number of actions and effects depending in which part of the brain the neurochemical activity is taking place.

Of these 80-some neurotransmitters, several – including dopamine, norepinephrine and serotonin, and gamma-aminobutyric acid (GABA) have a strong influence on our moods. Individually, each of these chemicals affects our mood in a different way. Dopamine facilitates a feeling of pleasure or reward. An activity that leaves us feeling happy and pleased (like spending time with a loved one or enjoying a concert or ball game) is an activity that somehow stimulates our brain to activate dopamine. Unless dopamine is activated a person does not feel pleasure or reward. When dopamine is well regulated, a person gets a full measure of pleasure out of life and tends to be more outgoing and confident.

Norepinephrine, the fight or flight neurotransmitter, also helps us to be alert, interested and focused. People who have brains in which norepinephrine is well regulated usually have good capacity to focus despite distractions. People born with brains that have poor regulation of norepinephrine often feel distracted, disconnected and scattered. Serotonin helps with sleep and to moderate our moods and is responsible for a sense of satiety when we have eaten enough. Disregulation of serotonin can result in
mood variability, irritability and impulsivity (Aasved, 1996). Also, low levels of
serotonin and its metabolites have been associated with aggression and other aspects of
anti-social behavior in alcoholics – and even in children of alcoholics who have yet to be
exposed to alcohol (Perrino, 1996). GABA can block the release of dopamine and
produces feelings of distress (Aasved, 2003). When we take any mood-altering chemical
– whether that chemical is alcohol or cocaine or heroin – our brain chemistry is affected.

**Cocaine and Methamphetamine**

*Cocaine,* a powerful stimulant drug, works mainly by blocking the reuptake of
dopamine from the synapse, concentrating synaptic dopamine levels (most significantly
in the area of the brain known as the *nucleus accumbens*) to 400 times their normal level.
*Methamphetamine,* also a powerful stimulant, acts by triggering a huge release of
dopamine, and has an even more powerful effect on dopamine than cocaine – raising
intersynaptic levels of dopamine to over 1500 time normal levels. The euphorogenic
properties of both of these drugs are attributable to their powerful effects of the
dopaminergic system. Both drugs also dramatically increase the activation of
norepinephrine throughout the brain. Activating the neurotransmitters that facilitate
feelings of interest and reward, cocaine and methamphetamine result in a “high” that is,
at once, riveting and intensely pleasurable.

**Opiates**

*Opiates* are a category of drugs that includes all of those drugs that are derived
from opium. This class of drugs has been expanded to also include *opioids,* synthetic
drugs that are either molecularly similar or similar in pharmacological effect to the drugs
refined from opium. Some examples of opiates are *heroin,* *morphine* and *codeine.*
Opiates are effective in relieving pain, suppressing the cough response and paralyzing the
digestive tract.

Opiates work by mimicking or stimulating the production of endogenous opioid
peptides called *endorphins* and *enkephalins.* Endorphins are produced in the neural
system of all mammals, and are the body’s own pain relievers. In fact, when injected
directly into the brain, the pharmacological activities of endorphins are surprisingly
similar to those of morphine and synthetic opioids – drugs like methadone and fentanyl.
Endorphins are released during times of pain. Women undergoing childbirth experience
a substantial release of endorphins. Enkephalins are released in response to
psychological stress (Hughes, 1976). Endorphins and enkephalins work by binding to
opioid-specific receptor sites (the same receptor sites used by drugs like heroin and
morphine) activating a calming and/or pain-relieving response on neurons in various
parts of the brain.

Chronic use of opiates can affect the brain’s regulation of these neurotransmitters.
When a person uses opiates, the nervous system notices the presence of the opiate, and
mistakes the opiate for an *excess* of endorphins and enkephalins. In an effort to
normalize functioning, the brain will cease production of these natural pain and anxiety-
relieving neurotransmitters, and eventually – if the person continues to use exogenous opiates - reduce, or **downregulate** the number of opioid receptor sites in the user’s brain. The opiate user may notice the cessation of endorphin and enkephalin production and downregulation of opiate receptor sites, and will usually adjust to these changes by using larger doses of the drug. As the user’s brain continues to downregulate opioid receptor sites, a tolerance develops to the effects of opiates and the user needs increasingly larger doses of opiates to achieve the desired high.

**Alcohol**

*Alcohol*, the oldest known mood-altering drug, can cause changes in the chemistry, cell structure and electrical functioning within the brain. A small molecule, soluble in both lipid and aqueous matter, alcohol easily crosses the blood-brain barrier – which is mainly lipid in nature. Once in the brain, alcohol is thought to interact with the gamma-aminobutyric acid (GABA) inhibitory neurotransmitter system. Alcohol, however, can interact with *all* the synapse, and affect *all* the neurotransmitter-receptor interactions – alcohol can also dis regulate the brain’s electrical potential.

Some researchers also believe that alcoholism may be related to a pre-existing deficiency in certain neurotransmitters, principally dopamine, endorphins and enkephalins, and, possibly, a dearth of dopamine and opioid receptor sites (Aasvad, 1996). Also, alcohol not only seems to stimulate the production and release of endorphins and enkephalins but, in some people, actually converts other neurotransmitters into opiate-like neurotransmitters, the Tetrahydroisoquinolines (TIQs), which activates the same opioid receptor sites as heroin and morphine (Aasvad, 1996).

**Cannabis**

Usually referred to as *marijuana* or *hashish*, cannabis is a form of the flowering tops of *cannabis sativa* or *cannabis indica*, the common hemp plant. In the 1980s, researchers found that delta-9-tetrahydrocannabinol (THC) – the main active ingredient in cannabis, binds to a specific G protein-coupled receptor in the human brain. Several endogenous chemicals appear to interact with the cannabinoid receptor. In 1992, scientists found an endogenous agonist of this receptor and called it anandamide (arachidonylethanolamine) from the Sanskrit word for bliss (Devane, et al., 1992). When anandamide was administered to mice, it produced a cannabimemetic activity (Mechoulam, 1973). Some neuroscientists believe that a possible role of anandamide is to keep a person from becoming overwhelmed by too much stimulation. This idea may also suggest that the brain, sensing to presence of THC and mistaking the THC for excess anandamide, may adjust (like it does with users of opiates) by downregulating the number of anandamide receptor sites. A downregulation of anandamide receptor sites may leave the newly abstinent marijuana user poorly able to manage a highly stimulating environment.
Acute and Post-Acute Withdrawal

When a person takes mood-altering chemicals over a period of time, neurotransmitters can become disregulated or depleted. Users can experience this disregulation or depletion as a sour or dysphoric mood.

After the use of mood-altering chemicals is stopped, and the conditions for healing are in place, the brain begins a period of physiological and biological readjustment. This readjustment process is essentially a healing of neurochemical disregulation produced by the drug and/or alcohol use. While this process is underway — and until it is complete — the recovering person will likely experience their neurochemical deficits as unpleasant moods and/or difficulties in thinking or focusing.

The withdrawal syndrome (a syndrome is a group of symptoms that usually occur together) from any substance of abuse has two stages — Acute Withdrawal and Post-Acute Withdrawal. Though the acute phase of withdrawal is usually over relatively quickly - the post-acute phase, depending on the drug or drugs abused, and the severity and length of the abuse, can last up to eighteen months.

Acute Withdrawal

During the first few days after substance use has stopped, the user can feel distressing and uncomfortable withdrawal symptoms. With some substances (like barbiturates and benzodiazepines — and, in extreme cases, alcohol) withdrawal actually can be life threatening. Withdrawal symptoms can vary according to the amount, frequency, length of use and type of substance that was used.

For cocaine and methamphetamine users, the first three to ten days after their last use can be accompanied by depression, physical fatigue, low energy, sleep marathons and difficulty in concentrating. Because repeated use of cocaine or methamphetamine disregulates the activity of the neurotransmitters dopamine and norepinephrine – two brain chemicals that are involved in elevating and stabilizing our mood – the newly recovering cocaine/methamphetamine user is often suffering from a chemically induced clinical depression. Though these symptoms typically last only three to five days, they can, in rare cases, last up to several weeks.

When used over a period of time, alcohol can also affect the brain’s electrical potential (a healthy brain produces about enough electrical current to light a 20-watt light bulb). When a person stops drinking, the brain’s production of electrical current — which might have been inhibited by the alcohol — can suddenly spike. This increase in electrical potential is often experienced by the detoxifying person as tremors, mental agitation/confusion and sleeplessness. In severe cases the sharp increase in the brain’s electrical current can result in life-threatening convulsive seizures. Anyone who is considering detoxifying from alcohol should consult a physician to ensure a safe and effective detox. Some people must be hospitalized to come off alcohol safely.

The pattern of using increasingly larger doses of opiates often continues until the user either chooses or is forced to stop using opiate drugs. It is only then that they experience the deficit in endorphin and enkephalin levels and the dearth of opioid
receptor sites as the classic opiate withdrawal syndrome. Symptoms include nervousness, insomnia, restlessness, depression, muscle cramps and diarrhea. Other opiate withdrawal symptoms are teary eyes, runny nose, yawning and gooseflesh. Symptoms usually last 7-8 days for most opiates. Methadone and buprinophine, synthetic opioids are the exception; possibly due to their long half-life in the body, withdrawal symptomology for these drugs can last a month or longer.

Historically, most clinicians believed that there was no withdrawal syndrome associated with marijuana use, but some have changed that opinion in recent years. Due to the fact that today's marijuana is many times more potent than that smoked in the 60s and 70s, a marijuana withdrawal syndrome is now being recognized in some patients. Reported symptoms include insomnia, restlessness and irritability – though there seems to be substantial variability in symptoms from person to person. The period of acute withdrawal can last up to two weeks – longer than most substances of abuse – possibly because marijuana, being lipid soluble, rather than water soluble, tends to dwell in fatty tissue and stay in body longer. Lingering effects of marijuana use can include poor motivation, memory problems and a difficulty in distinguishing between trivial and pertinent information.

Post-Acute Withdrawal

After the acute phase of withdrawal is over, the more-lengthy post-acute phase of withdrawal begins. At the conclusion of the acute phase, levels of neurotransmitters affected by substance use have rebounded to about 80% of their pre-use levels. And, though the newly recovering person is feeling more comfortable and thinking more clearly, a lingering sub-clinical dysphoria reminds them that the healing process is not yet complete.

For cocaine and methamphetamine users, post-acute withdrawal can be experienced as feelings of emotional flatness, difficulty in experiencing pleasure, trouble in concentrating and mood swings. These symptoms result from the fact that dopamine, norepinephrine and serotonin activity in the ex-user's brain have still not returned to pre-use levels – a process that can take up to eighteen months. Until the healing process is complete, and - even though each day is generally better than the last - the recovering person can experience a vague sense of the symptoms described above. They might have good days and bad days, and may need to connect with their sober support system a little more closely during this time.

Post-acute withdrawal can also be a difficult time for ex-users of alcohol. In recovering alcoholics, this phase also can last up to a year and a half. It may take months for sleep patterns to return to a fully normal state, and thinking may also be a bit fuzzy at times. Because GABA may be a bit disregulated and the electrical functioning of the brain may not have returned to a normal level, the recovering alcoholic can feel a slightly heightened level of anxiety. As noted before, this is probably a good time for the newly sober person to build and use a sober-support system.

For opiate users, the post-acute period is characterized by gradual normalization of sleep patterns and a lessening of anxiety. A slow, steady improvement in symptoms can be expected for about a year or so. In cases of heavy and chronic opiate addictions,
however, it may take several months for normal sleep patterns to be re-established. Also, in the post-acute withdrawal phase, the newly recovering opiate user will probably experience a slightly elevated pain response and some heightened restlessness.

People who have been heavy users of *marijuana* can develop a strong psychological dependence on the drug and are prone to experience a strong trigger/cue response. This means that certain sights, sounds and smells can trigger cravings to use. Also, habitual use of marijuana impairs memory, comprehension, motivation and decision-making ability – though these deficits almost always resolve in time. The entire process of post-acute withdrawal from marijuana can also take over a year.

### Speeding-Up the Process

Anyone experiencing post-acute withdrawal from any substance of abuse would be well advised to cultivate and practice patience, acceptance and perseverance. As long as the recovering person maintains the conditions of healing (*total abstinence from all mood-altering chemicals – except those prescribed by an informed physician*) the process is inexorable – it will go forward on its own.

However, if person wants to speed the process a bit, this is possible. The keys to doing this are diet and exercise. To ensure that our bodies have the building-blocks necessary to rebuild depleted neurotransmitters, it is important to eat foods that are rich in the amino acids that are the chemical precursors of neurotransmitters such as dopamine, norepinephrine, serotonin and endorphins.

The amino acids most helpful in the process of rebuilding depleted neurotransmitters are *tryptophan* and *tyrosine*. Foods like turkey, other lean meats, green leafy vegetables and dairy products are rich in these amino acids. The more often one make the choice to eat healthy, fresh foods, the more quickly brain chemistry will attain pre-use levels – and the recovering person will feel better and think more clearly.

Moderate, regular exercise speeds the process even more. Now the major job is guarding and maintaining the recovery process by continuing to access sober support and not entertaining the attitudes and behavior that can eventually lead to relapse. Maintaining good physical and emotional health allows a person to develop a lifestyle conducive to supporting continued recovery. Although the most difficult “start-up” period is now over, continued hard work is needed to maintain and further improve the quality of life.
FOODS THAT STABILIZE MOOD

The following are the foods that contain the necessary vitamins, nutrients and minerals to produce the three primary brain chemicals (serotonin, norepinephrine, dopamine) that alleviate withdrawal, stabilize mood and enhance overall brain function (concentration, memory and emotional well being). Please understand that this is not a comprehensive list of what individuals need for health, but they are essential components in a diet that maintains emotional stability.

This information is derived from Mood and Food by Elizabeth Somer and Optimum Nutrition for the Mind by Patrick Holford.

1. **SEROTONIN** - a calming brain chemical that stabilizes mood, manages pain tolerance, enhances deep sleep and tempers the stress response

Serotonin is derived from carbohydrate-rich foods (2/3 of serotonin is produced in the stomach and intestinal tract):

Multi-grain or whole wheat cereals/breads/bagels/pasta/crackers/muffins/tortilla, sweet potatoes, wheat germ, oatmeal, quinoa, brown rice, millet, rye, lentils and foods high in complex carbohydrates

These foods contribute to the depletion of serotonin:

Caffeine (coffee, tea, cola), sugar, high-fat foods and alcohol (and smoking, too!)

2. **DOPAMINE** – an alerting brain chemical that is responsible for enhancing focus, concentration, attentiveness, curiosity and pleasure

3. **NOREPINEPHRINE** – another alerting brain chemical responsible for high alertness that is normally associated with the fight-or-flight response involving fear and stress

Both dopamine and norepinephrine are derived from protein-rich foods:

Brown rice, tuna (canned or fresh), cod, salmon, sardines, chicken, eggs, yogurt, cottage cheese, beans and rice

Other foods that provide a lesser amount of protein include maize, lentils, peas, chick peas (garbanzos), sunflower seeds, pumpkin seeds, cashews, almonds, broccoli and spinach
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ESSENTIAL FATS – these foods are needed for mood, memory and thinking abilities

Omega-3 sources: flax (liquid or ground), hemp, pumpkin seeds, walnut (oil or nut), salmon, mackerel, herring, sardines, anchovies, fresh tuna and eggs

Omega-6 sources: corn oil, safflower oil, sunflower oil, sesame oil and olive oil

SLEEP ENHANCING FOODS – these foods are high in calcium and magnesium, which are necessary for muscle relaxation and restful sleep

Magnesium-rich foods: seeds, nuts, green vegetables, whole grains and seafood

Calcium-rich foods: green vegetables, nuts, seafood and molasses

B VITAMIN SOURCES – these foods alleviate depression, memory loss, inability to cope with stress, anxiety, insomnia, appetite loss and lack of motivation

Whole grains, vegetables (especially green leafy ones), fresh fruit (especially apples, bananas, pears, citrus, melon and all berries), lean meat, fish, dairy products, eggs, nuts, seeds and tea

SUMMARY

Here are some guidelines that help insure the adequate production of the above brain chemicals, stabilize blood sugar and optimize proper brain function and overall mood.

1. Eat five or more servings of fruits and vegetables daily. Choose vegetables that are raw or lightly cooked such as dark green leafy and root vegetables, watercress, carrots, sweet potatoes, broccoli, brussels sprouts, spinach, green beans, red and yellow peppers.

2. Choose fresh fruits such as apples, pears, berries, melon, citrus and bananas (in moderation only). Eat dried fruits (preferably soaked in water) infrequently and in small quantities.

3. Eat four or more servings of whole grains, such as rice, millet, rye, oats, whole wheat, corn or quinoa, breads and pasta.

4. Eat whole foods – whole grains, lentils, beans, nuts, seeds, fresh fruit and vegetables and avoid refined, white and overcooked foods.

5. Combine protein foods with carbohydrate foods, such as cereals and fruits with nuts and seeds, and insure that you eat starch foods (potato, bread, pasta or rice) with fish, lentils, beans or tofu.

6. Avoid sugar, caffeine and high-fat foods.
References


