

<b>Amino Acid</b>	<b>Restored brain chemical</b>	<b>Addictive substance</b>	<b>Amino acid deficiency symptoms</b>	<b>Expected behaviour change</b>
D or L-Phenylalanine	Enkephalins and endorphins	Heroin, alcohol, marijuana, sweets, starches, chocolate & tobacco	Reward Deficiency syndrome (RDS) - conditions sensitive to physical/emotional pain. Crave comfort & pleasure/Desire certain foods/drugs	Reward stimulation. Anti-craving. Mild anti-depression, improved energy/focus. D-P promotes pain relief, increases pleasure
L-Phenylalanine or L-Tyrosine	Norepinephrine Dopamine	Caffeine, speed, cocaine, marijuana, aspartame, chocolate, alcohol, tobacco, sweets, starches	RDS conditions - depression, low energy, lack of focus/ concentration, ADHD	Reward stimulation. Anti-craving. Anti-depression, increase energy, improved mental focus

<b>Amino Acid</b>	<b>Restored brain chemical</b>	<b>Addictive substance</b>	<b>Amino acid deficiency symptoms</b>	<b>Expected behaviour change</b>
L-Tryptophan or 5-hydroxytryptophan (5HTP)	Serotonin	Sweets, alcohol, starch, ecstasy, marijuana, chocolate, tobacco	Low self-esteem, OCD, irritability/rage, sleep problems, afternoon/eve cravings, negativity, heat intolerance, fibromyalgia, SAD	Anti-craving, anti-depression, anti-insomnia, improved appetite control, enhanced mood and other serotonin deficiency symptoms
GABA (Gamma-amino butyric acid)	GABA	Valium, alcohol, marijuana, tobacco, sweets, starches	Feeling of being stressed out, nervous, tense muscles, trouble relaxing	Promotes calmness and relaxation
L-Glutamine	GABA (mild enhancement, fuel source for entire brain)	Sweets, starches, alcohol	Stress, mood swings, hypoglycaemia	Anti-craving, anti-stress, regulates blood sugar levels and mood; GABA (mild enhancement), fuel source for entire brain

**Note:** *to assist in amino-acid nutritional therapy, the use of a multi-vitamin/mineral formula is recommended. Many vitamins and minerals serve as co-factors in neurotransmitter synthesis. They also serve to restore general balance, vitality and well-being to the RDS patient, who typically is in a state of poor nutritional health.*

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## Nutritional Gene Therapy: Natural Healing in Recovery

Feature Articles - Alternative

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We believe that the core of impulsive, addictive and compulsive behaviors is biological in nature, although it is influenced by psychological and spiritual factors. Over the last three decades we have learned a lot about the brain and the physiology of personality. We have learned that at least one-third of Americans are hard wired to become addicted. The “addictive brain” is the result of a simple molecular genetic rearrangement of DNA. In simple terms, the part of the brain that brings about feelings of well-being and provides comfort and stress reduction is compromised in some individuals. In fact, addiction begins and ends in the brain.

Each nerve cell in the brain is separated from its neighboring cell by a synapse. A nerve may release chemical messengers, called neurotransmitters, into this synapse 1,000 times a second, and each chemical must be trapped by the site on the opposite nerve cell to receive its message. For us to feel good, the brain must function with incredible precision. There are at least four major neurotransmitter pathways involved in this functioning: serotonergic, enkephalinergic, gabaergic and catecholaminergic (dopamine and norepinephrine).

It is our belief that a major reason for addiction treatment failure and high relapse rates is

due to untreated neurotransmitter depletion. In this article we will discuss how genetics and certain drugs of abuse deplete important key neurotransmitters and how we can repair these deficiencies by what we have termed “Nutritional Gene Therapy.”

## **Understanding the Addictive Brain**

### **The normal brain**

A person’s sense of well-being is due to the action of key neurotransmitters working in a cascade fashion in the brain. The final site of action of these neurotransmitters is in the limbic system located near the center of the brain. The most important transmitters are serotonin (our natural antidepressant), enkephalins (along with endorphins, our natural pain killers), GABA (our natural sedative) and dopamine (along with norepinephrine, our natural stimulant) working in concert to bring about a feeling of well-being and stress reduction. Certainly, as addiction professionals, we know the importance of increasing well-being and reducing stress in preventing relapse.

The nucleus accumbens, the “reward site,” in the brain is the master of simple but powerful drives. When all of the neurotransmitters, working in harmony and in conjunction with one another, stimulate the production, transportation, and reception of dopamine at the “reward site,” a person is calm, at ease and satisfied. This process of the neurotransmitters working in harmony and in conjunction with one another has been termed by Kenneth Blum (KB) the “Brain Reward Cascade.” In the hypothalamus, serotonin stimulates the enkephalins, which in turn inhibits GABA in the substantia nigra, which in turn fine tunes dopamine in the ventral tegmental area causing the release of dopamine at the nucleus accumbens.

## **The deficit brain: craving behavior**

If, however, the brain reward cascade is impaired so that there is insufficient production of dopamine, or the dopamine is not transported to the appropriate site, or specific dopamine receptors are impaired or deficient, the results are a sense of incompleteness, unease or anxiety which leads to seeking a substance or behavior for relief. This condition has been termed by KB the “Reward Deficiency Syndrome” (RDS).

When there is a lack of dopaminergic function via a breakdown of the reward cascade (usually genetic), then “craving behavior” will occur. It has been well established in rats that alcohol, cocaine, heroin, marijuana, glucose, and nicotine all cause the preferential release of dopamine. This is the same driving force that provides the biochemical motivation in humans to use and abuse psychoactive substances.

Many genes may be involved, genes that control the synthesis, storage, release and reception of any one of the four neurotransmitters described above. The RDS manifests as a variety of impulsive, compulsive, and addictive disorders from attention deficit/hyperactivity disorder to conduct disorder, from post-traumatic stress syndrome to pathological gambling, from caffeine addiction to heroin addiction.(See Table 1 Below)

## **Genetic antecedents**

Reward Deficiency Syndrome can be caused by certain genetic variants (types). In searching for a gene(s) for alcoholism over ten years ago, KB’s laboratory in conjunction with Ernest P. Noble, former director of NIAAA, found a genetic variant in the dopamine D2 receptor gene that significantly associated with a severe form of alcoholism. This same gene type, the dopamine D2 A1 variant, has been found over the last decade to also associate with other impulsive, addictive and compulsive disorders and has been found to

be present in 33 percent of the U.S. population.

Later work showed that carriers of the dopamine D2 A1 variant had significantly lower D2 receptors in the brain and had a 74 percent chance to become addicted to alcohol, cocaine, opiates, smoking, glucose, etc. Having low D2 receptors causes a lack of dopamine activity. Since dopamine is considered to be the “pleasure molecule” as well as the “anti-stress molecule” (in fact, dopamine is released into the synapse 100 times more during a stressful event), its function is essential if we are to maintain “normal” drives and successfully cope with stress.

### **Drug use as self-medication for RDS: The Paradox**

Alcohol and other drugs work to reduce anxiety and depression and to satisfy the feelings of incompleteness that accompany RDS because they temporarily enhance neurotransmitter function. Some people with RDS find out for the first time what it is like to feel good when they begin to use alcohol or other drugs. This leads the user to believe that the sub-stance is actually beneficial. And in many ways it is. Once people with RDS discover a way to feel good, it is to be expected that they will continue to use the substance that produces those good feelings. (See *Overload: Attention Deficit Disorder and the Addictive Brain* by Miller and Blum.)

However, excessive use of these substances causes nutrient depletion and tissue damage that only increases the problems associated with RDS. For example, excessive caffeine can damage brain neurotransmitters; alcohol damages the liver and kidneys and can cause high blood pressure; nicotine raises blood pressure and the risk of cancer and cataracts; and too much sugar can lead to insulin resistance and diabetes.

Because low D2 receptors lead to craving and ultimately substance seeking, a major

question for all of us in the recovery field is: If there is indeed a genetic variant in the dopaminergic system, how can we identify it in an individual and then repair it? We can now carry out DNA non-invasive tests. We can extract the DNA from cheek cells and immediately tell an individual which gene form they may have with regard not only to dopaminergic genes but to many others including serotonin, opioids, GABA and acetylcholine. But, even though this can be accomplished, what can we do with the information? At this juncture we cannot manipulate the gene by gene therapy. However, there is an alternate approach that has demonstrated real effectiveness.

### **Nutritional Pathways**

As we have said, craving for abusable substances is a result of malfunctions of the reward centers of the brain involving the neurotransmitters, the enzymes that control them, and neurotransmitter imbalances. We now know how to manipulate the brain chemistry in a natural way that over time will increase proliferation of D2 receptors in people that have the dopamine D2 A1 gene variant. We call this “Nutritional Gene Therapy.”

We know as a result of a number of double-blind, open-trial studies in humans that we can significantly lower drug hunger, reduce stress, reduce “building-up to drink” score, reduce AMA rates, prevent relapse and DUI recidivism, reduce or eliminate the need for benzodiazepine medication during withdrawal, reduce or eliminate withdrawal tremors, reduce cocaine-induced dreams, increase libido, reduce physiological stress, improve behavior, reduce depression as measured by standard instrumentation, increase focus, reduce weight, prevent weight gain, reduce bingeing of carbohydrates, reduce fat, increase fat mobilization, reduce smoking behavior, stabilize blood pressure, increase glucose receptor sensitivity, and restore neurotransmitters such as serotonin, dopamine, enkephalins, GABA and acetylcholine.

All this has been accomplished by using specific nutritional therapies. In fact the nutritional manipulation of the “molecules of emotion” in the brain is the missing link in successful addiction treatment and long-term recovery. In the early '70s, KB realized that the brain required very specific “brain foods,” amino acids that are the precursors (direct building blocks) to key neurotransmitters: L-tryptophan, L-5-hydroxytryptophan chromium salts for serotonin; L-Glutamine for GABA (the use of GABA has not been shown in any double-blind study to unequivocally reduce craving but clinical experience indicates positive results); L-phenylalanine, L-tyrosine for dopamine. In addition, research on genetically bred alcohol-preferring mice showed that a d-amino acid called D-phenylalanine reduced alcohol consumption and increased the levels of brain endorphins/enkephelins. As a result of these discoveries, KB developed amino acid compounds for neurotransmitter restoration.

Another substance has now been identified which has improved Blum's original formulation: *Rhodiola rosea*. This is a Chinese herb, studied in Russia and shown to inhibit the breakdown of another very important enzyme called catecholamine-o-methyltransferase (COMT). In the presence of this herbal, both serotonin and dopamine levels increase in the synapse naturally.

Another interesting herbal known as huperzine A was found in a number of double-blind studies to inhibit the action of acetylcholinesterase, thereby naturally increasing brain levels of acetylcholine. This could be quite important when enhanced focus is required, especially in children with attention deficit/hyperactivity disorder (AD/HD). Without detailing all the studies involved, we can tell you that it is now known that the same dopamine D2 A1 gene variant found to associate with substance-use disorders is also found in children diagnosed with AD/HD. (See *Overload: Attention Deficit Disorder and the Addictive Brain*, David Miller & Kenneth Blum.) In fact, untreated AD/HD children have a 500-to-one chance compared to non-AD/HD children to abuse drugs in later life. The

amino acids described have been found to enhance focus and memory and reduce hyperactivity in AD/HD (see Table 1 below). We are now studying its effectiveness against Ritalin in a placebo-controlled study.

### **Nutritional Gene Therapy**

Amino acids are critical for stopping cravings because they are essential building blocks of the neurotransmitters that tell the brain whether or not we are satisfied. The key therapeutic amino acids are all readily available as individual supplements in health stores, pharmacies and markets. (See *The Healing Nutrients Within* by Eric Braverman, Keats, 1997 for more information on the use of individual amino acids.)

Blended amino-acid formulations based on Blum's pioneering neuronutrient therapy work are also available. They combine all of the amino acids needed to restore the neurotransmitters and the reward cascade in a single supplement for easier use and less guesswork. Blum's most recent formulation is called REWARD (distributed by Nutrigenomics in Pittsburg, California.)

It is known that if someone carries the dopamine D2 A1 gene variant (and possibly other gene variants) with low D2 receptors and thus RDS behavior, this individual will have this genetic trait all of his/her life. This raises the question as to how long "nutritional therapy" in the addicted person in recovery should be used. There will always be a need for nutritional therapy of some kind.

Collectively we have treated thousands of addicts and other RDS sufferers since 1982 with amino-acid therapy. We believe that many will need to use the aminos long term, probably for life. There are others who seem to correct the neurochemical deficiencies in six months to two years. They no longer require regular use of amino-acid supplements if

they have a healthy diet emphasizing adequate protein — the dietary source of all amino acids — and avoid all addictive substances including nicotine and caffeine.

The nutritional approach mimics the “reward cascade” of the brain, reducing symptoms of RDS such as depression, anxiety and craving. Amazingly enough, nutrient therapy brings about dopamine release and the creation of more dopamine receptors, even against genetics. Nutrition plays a critical role in healing addictions, not only because key nutrients can help to normalize or restore pre-existing neurotransmitter deficiencies that spur cravings, but also because they heal the body of the many harmful physiological effects of addictive substances.

### **Amino-acid Therapy: Safety**

Amino acids are critical for stopping cravings because they are important building blocks of the neurotransmitters that tell the brain whether or not you are satisfied. Since the inception of amino-acid therapy in the mid-'80s, thousands of people have benefited with few side effects. In fact, a recent search of FDA complaints found almost no complaints with regard to amino-acid use.

The notable exception in the past 15 years was the amino acid L-tryptophan, used primarily for insomnia in addiction treatment programs until 1990. The problem that occurred with L-tryptophan has been conclusively linked to a single contaminated batch produced in 1989 by a company in Japan that no longer manufactures the product. L-tryptophan has been available from compounding pharmacies by prescription for some years and is just becoming available again without prescription through a distributor in Phoenix called Lidtke Technologies with full disclosure to the FDA.

It should be pointed out, however, that there are several physical conditions and

prescription medications with which use of amino-acid supplements might be contraindicated. (See note following Table 1.) We recommend medical consultation when there is any question of safety.

### **Amino Acid Nutritional Therapy — Table 1**

Use this table to determine who can benefit from using these amino acids. The minimum effective starting dosage is 500 mg per day, and can be increased gradually to 3,000 mg per day (except for 5HTP which ranges in dosage from 50 to 300 mg per day) until the desired benefits are observed. Most people should respond to daily dosages of 500 mg to 1,500 mg in divided dosages 2 to 3 times per day. Amino acids are most effective taken on an empty stomach with water. Discontinue use if any adverse side effects are observed. Individuals on medication should only use these amino acids under medical supervision and should not use them if taking MAO-inhibitors or any drugs affecting the particular brain chemicals listed in this table.

### **But What About Diet?**

It is our contention that once good nutrition and nutritional supplements have freed the mind from cravings, people are ready to do the hardest work, through self-help programs and counseling. To most effectively enhance neurotransmitter function, it is essential to increase dietary protein (since protein is composed of amino acids, the building blocks of neurotransmitters) and eliminate sweets and refined starches. This dietary approach has been used successfully in residential and court-mandated programs (See *Under the Influence* by James Milam; *Potatoes Not Prozac* by Kathleen Des Maisons; *Eating Right to Live Sober* by Ann Mueller and Katherine Ketchum; *Beyond the Influence* by Katherine

Ketchum; “*The Role of Nutritional Therapy*” in *Journal of Biosocial Research* by Ruth Guenther).

But in voluntary outpatient programs these dietary improvements can be impossible to achieve because of overwhelming cravings for drug-like carbohydrates that provide some neurotransmitter enhancement in the absence of alcohol and drugs (See *The Diet Cure* by Julia Ross, and *Seven Weeks to Sobriety* by Joan Matthews-Larson, Fawcett, 1997). This is where amino-acid therapy can offer vital support by eliminating cravings for drug-like foods as well as other addictive substances and behaviors.

### **Closing The Gap**

We believe that it is time to close the gap between what is now known about the nature of addiction and what we do to treat it. What we have learned about recovery in recent years is that it requires neurotransmitter repair and restoration. We have long said that addiction is a physical disease; yet treatment has primarily consisted of interventions that address the mind, emotions and spirit but little that addresses the body. This is because there has been so little known about the physical nature of addictive disease. There is now enough information about addiction and the brain to add treatment components that address the physiology and the genetic antecedents of the disease.

This does not mean we should throw out what has helped so many in the past. What it does mean is that we must add new therapies that enhance brain chemistry such as nutritional therapy. We must remember that in order to maintain recovery, people need and deserve to feel good. This can occur only through a marriage of new physiological/neurological therapies with the spiritual, psychological, and cognitive interventions that have been used in the past.

When more recovering people are able to enhance their sense of well-being, reduce their cravings, and increase their ability to enjoy life, we will see less relapse and more comfortable, meaningful recovery. Only a combination of all of these approaches will make that possible.

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**Daniel Gastelu**, MS, MFS, is director of U.S. Healthcare of Goldshield Pharmaceuticals Limited, director of Nutritional Sciences of the International Sports Sciences Association and founder of Supplementfacts International. He developed and co-authored the ISSA's Performance Nutrition certification program, which is used to certify doctors, therapists, fitness trainers, strength coaches and nutritionists world-wide. Gastelu is a pioneer in the health products industry and has delivered several hundred healthcare products in the past 14 years.

**Julia Ross**, MA, author of "The Diet Cure", (Penguin, USA, reissue May 2000) founded and directed six outpatient addiction and eating disorder treatment programs in San

Francisco since 1980. She is executive director of Recovery Systems, Mill Valley, Calif.

**Carolyn Reuben, LAc**, is founder and president of Community Acupuncture Recovery Association, a nonprofit organization dedicated to the use of Chinese medicine, including nutrition, herbs and massage to treat substance abuse and addiction. She administers the nutrition education and acupuncture components of the Sacramento County Drug Court. She is author of several books including, "Cleansing the Body, Mind and Spirit" (Berkeley, 1998).

Sources of amino acids: Organic chia seeds/SON Formula/Spirulina/chlorella

Phosphatidyl se B complex and folic acid

Because our intake of EFA's it's important to convert into DHA for the brain food for the brain

Whole blood brain barrier, nutrition's hard to absorb

Fulvic acid - diabetes and arthritis – source: Beckey - Optimally Organic - that is organic source

Very restorative – loads of minerals, converts into?

<http://www.optimallyorganic.com/>