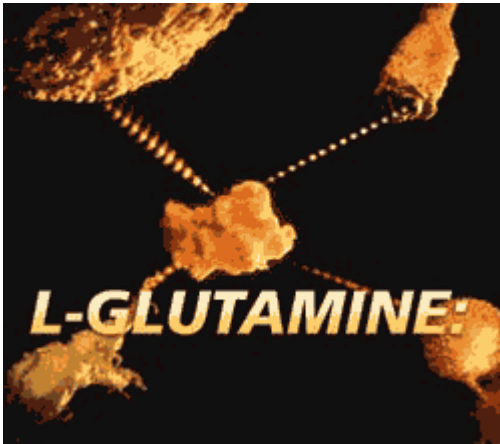


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## REPORT

Glutamine:  
The Essential "Non-  
Essential" Amino Acid

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Rapidly dividing cells, including certain immune cells, utilize glutamine as a source of energy.

Glutamine is classified as a "non-essential amino acid." This label may mislead some people into believing that we don't need it. But, in essence, "non-essential" means only that the body can synthesize this amino acid. It does not mean "unimportant."

In fact, glutamine is of crucial importance; we are lucky that we do not have to depend totally on dietary sources. It seems that every cell in the body uses glutamine. Some tissue types, however, depend on glutamine much more than others.

Specifically, glutamine is utilized as a source of energy and for nucleotide synthesis by all rapidly dividing cells, such as the cells of the intestinal lining and certain immune cells (thymocytes, lymphocytes and macrophages). Without sufficient glutamine, the intestines atrophy and the immune function breaks down.

Hair follicles, the fetus, and unfortunately also many types of tumors also greatly depend on glutamine for energy production and DNA and RNA synthesis. In addition, glutamine serves as a nitrogen donor and a carbon donor, and is thus an important muscle-building amino acid; it also helps replenish muscle glycogen after exercise. Without sufficient glutamine, muscles begin to atrophy. Thus glutamine is in fact essential for intestinal, immune and muscle functions, to mention just the most obvious.

And this is not the end of the story. The synthesis of glutamine protects the body, and the brain in particular, from ammonia toxicity. In fact, the synthesis of glutamine from glutamate is the key pathway for detoxifying ammonia. Excess ammonia is a crucial factor in the development of neurodegenerative diseases, since ammonia interferes with the oxidative metabolism of neurons and thus reduces the production of ATP, our "energy molecule." In addition, ammonia gives rise to very harmful nitrogen-based free radicals.

In the brain, glutamine is a substrate for the production of both excitatory and inhibitory neurotransmitters (glutamate and gamma-aminobutyric acid, popularly known as GABA). Glutamine is also an important source of energy for the nervous system. If the brain is not receiving enough glucose, it compensates by increasing glutamine metabolism for energy-hence the popular perception of glutamine as "brain food" and its use as a pick-me-up. Glutamine users often report more energy, less fatigue and better mood.

Glutamine also plays a part in maintaining proper blood glucose levels and the right pH range. The body has an exquisite mechanism for maintaining pH homeostasis. If the pH of the blood is too acidic, more glutamine is directed to the kidneys, where a certain type of glutamine results in the release of bicarbonate ions to correct acidosis. If the pH is too alkaline, more glutamine is sent to the liver, where a different kind of metabolism releases hydrogen ions to correct alkalosis.

And there is still more. Due to its dependence on sodium transport, glutamine is one of the amino acids that control the volume of water in the cells, and the osmotic pressure (osmoregulation) in various tissues. Glutamine also plays a vital part in the control of blood sugar. It helps prevent hypoglycemia, since it is easily converted to glucose when blood sugar is low. In addition, glutamine

regulates the expression of certain genes, including those that govern certain protective enzymes, and helps regulate the biosynthesis of DNA and RNA. Recently it has been discovered that glutamine is important for the cardiovascular system as well.

Thus, to say that glutamine is important for our health is an understatement. In view of its multiple functions, it is no surprise that glutamine is the most abundant free amino acid in the serum, muscle and cerebrospinal fluid. It constitutes 50% of all amino acids in the serum, and more than 60% of free amino acids within the body.

Glutamine is plentiful in both animal and plant protein. The typical American diet provides between 3.5 g and 7 g of glutamine; more is synthesized according to need. Even so, heavy stress, such as strenuous exercise, infectious disease, surgery, burn injury or other acute trauma leads to glutamine depletion with consequent immune dysfunction, intestinal problems and muscle wasting. Consequently, it has been proposed that glutamine should be classified as a "conditionally essential amino acid." During exceptionally severe stress, supplementing with glutamine (in the hospital setting, doses as high as 20-40 g may be used) can be a matter of life or death.

### **Benefits for the liver and the intestines**

People who use glutamine virtually ensure superior health of their intestinal lining. They need not worry about the "leaky gut syndrome" and all its troublesome consequences, including allergies, the "leaking out" of pathogens and possible arthritis. In fact, when it was first discovered, glutamine used to be called "intestinal permeability factor." It is by far the most important nutrient for intestinal health.

The importance of glutamine for the intestines is enormous-glutamine is the chief source of energy for the cells of the intestinal lining. Most glutamine in the diet (and also most dietary glutamate and aspartate) is metabolized by the intestines, both to serve as intestinal fuel and also to produce glutathione, nitric oxide, polyamines, nucleotides and the amino acids alanine, citrulline and proline, making these available to the rest of the body. Glutamine also maintains the structural integrity of the intestinal lining, supporting its quick turnover.

Those who use NSAIDs (non-steroidal anti-inflammatories) such as ibuprofen and indomethacin may have a special need for supplemental glutamine. Fortunately, sufficient glutamine can undo the damage caused by NSAIDs, maintaining permeability at a healthy level. For heavy NSAID users, supplementing with glutamine can spell the difference between healthy gastrointestinal tract versus ulcers and the "leaky gut syndrome."

Besides treating the "leaky gut syndrome" and ulcers, glutamine can also be used to treat colitis, Crohn's disease and diarrhea, in doses of up to 20 g/day. The soothing intestinal effect of glutamine taken as powder dissolved in water makes itself known quite soon after ingestion (by the way, the taste is quite pleasant, slightly sweet, so there is no need to mask it with juice). Even a small dose, such as 2-3 g, can quickly calm that "queasy" feeling. In high doses, glutamine also alleviates the devastating damage to the gastrointestinal tract that results from chemotherapy.

Likewise, glutamine protects the liver from the ravages of chemotherapy toxicity. But even under normal conditions, glutamine is beneficial for the liver, since it cleanses the liver of the waste products of fat metabolism, and helps prevent fatty buildup. It can aid in the treatment of early-stage cirrhosis. Once liver damage is advanced, however, glutamine cannot help since the liver can no longer metabolize it properly. People who take glutamine tend to have a healthier liver and healthier intestines, and thus better digestion and absorption of nutrients. That alone should be reason enough to add this super amino to your supplement regimen. But this is just the beginning of its benefits.

### **Strengthens the immune system**

Glutamine is the primary source of energy for the various cells of the immune system, including T cells and macrophages. Strenuous exercise, viral and bacterial infections, and stress and trauma in general cause glutamine depletion that starves the immune cells. They decline in number and/or show diminished activity. Up to 40 g of glutamine a day can be used to sustain the immune system of AIDS patients or cancer patients undergoing bone marrow transplantation. More typical doses, such as 2-5 mg/day, should be sufficient for healthy people. Athletes may want to increase their dosage on an as-needed basis if they tend to succumb to infections after heavy exercise such as marathon running.

In addition, glutamine is a substrate for glutathione, a tripeptide amino acid that acts as one of our master antioxidants, and also helps enhance the immune function. Though large doses of glutamine stimulate the immune response even under heavy stress, it is important to reduce stress as much as possible. Stress hormones may interfere with glutamine metabolism in the immune cells. This is where relaxation and DHEA supplementation might prove to be very helpful in addition to glutamine.

## **Maintains muscle mass**

Glutamine is one of the favorite supplements of body builders and others who exercise a lot. In its role as a carbon donor, glutamine is "muscle food," helping to replenish glycogen. But actually the function of glutamine as a nitrogen-donor might be even more important. Strenuous exercise such as weight lifting causes micro-injuries to the muscle tissue. By donating nitrogen, glutamine helps build proteins and repair the muscle, as well as help build up more muscle. Part of its muscle-building action may be due to its ability to induce the release of growth hormone. Serious fitness fans take glutamine both before and after workout. Taking 2-3 g after workout is particularly recommended. Long-term users of anti-inflammatory steroids tend to suffer from muscle atrophy. The concomitant use of glutamine has been shown to prevent most of this muscle loss.

But muscle isn't the only tissue where protein is being synthesized. Glutamine serves the anabolic (tissue-building) needs of the whole body. Since it can very easily donate nitrogen, it functions as a "nitrogen shuttle," delivering nitrogen wherever it is needed.

Very ill patients suffer both a decrease in glutamine levels and muscle loss. One way to counteract this is to add glutamine to their diet, or, if they can no longer consume food, to the iv drip that delivers parenteral nutrition. The use of glutamine has been documented to aid the survival of severely ill surgical and burn patients. It also speeds up wound and burn healing, and improves recovery in general.

## **Helps the heart**

It has recently been discovered that glutamine is an important source of fuel for the heart muscle. It is converted to glutamate, which then enters the Krebs cycle to produce ATP, our energy molecule. This is yet another reason why glutamine is so important during exercise, increasing endurance. In heart patients, glutamate infusions can be used during heart surgery to ensure a better outcome.

The action of the heart is under considerable control of the nervous system, and the pathways involved in the neural control of cardiovascular function happen to rely on glutamate and GABA. If the brain has a faulty glutamine / glutamate / GABA metabolism, we can expect the development of cardiovascular dysfunction as well. In addition, glutamine serves as a substrate for the synthesis of a special type of beta-endorphin, glycyl-l-glutamine. This dipeptide appears to be important for the regulation of blood pressure and prevention of cardiorespiratory depression. Glycyl-l-glutamine is also important for the immune response, since it enhances the activity of the natural killer (NK) cells.

## **Combats hypoglycemia by raising serum glucose**

Glutamine can enter the Krebs cycle and serve as a non-carbohydrate source of energy. In fact, this is the main way it usually contributes to the production of energy. However, if the blood sugar is low (hypoglycemia), glutamine is readily catabolized (broken down) in the liver to provide more glucose. Together with alanine, glycine, serine and threonine, glutamine is an important "gluconeogenic" amino acid, in fact the primary one. This production of glucose from glutamine takes place mainly in the liver. Recently, however, it has been discovered that the kidneys can contribute as much as 25% to whole-body glucose production, a phenomenon that occurs only during hypoglycemia. Actually this is not surprising, since the kidneys are especially equipped to process glutamine due to its importance in the detoxification of ammonia.

Providing abundant glutamine through diet and supplementation means that less muscle tissue (if any) will be broken down to provide glucose. This is of great importance to people on calorie-restricted diets, whose great problem is losing muscle mass more so than fatty tissue. Since it is the metabolically active muscle mass that helps keep us slender (not to mention strong and fit), extra glutamine can help dieters lose girth around the waist while preserving muscle mass.

Considering the effectiveness of glutamine in combating hypoglycemia, it is no wonder that alternative medicine recommends it for the purpose of eliminating sugar cravings, and alcohol cravings in the fight against alcoholism (many alcoholics appear to suffer from hypoglycemia).

Diabetics, however, need to exercise caution, since they have an abnormal glutamine metabolism. A much higher percentage of their glutamine is broken down for the production of glucose by the liver and the kidneys, a process called glutamine gluconeogenesis. This increased production of glucose from glutamine (and also from alanine, an amino acid in the same family) is probably related to the diabetes-related excess levels of the serum glucose-raising pancreatic hormone called glucagon. True, this excessive breakdown of glutamine into glucose in diabetes occurs without any supplementation, since the muscle and the fatty tissue release so much glutamine in response to the endocrine pathology.

Diabetics also show other enzymatic abnormalities in relation to glutamine, including poor function of the retinal glia (glia are cells that have various supportive functions in the nervous system, including detoxifying ammonia through the production of glutamine).

Thus the diabetic retina is prone to damage through glutamate excitotoxicity, since the glia are not converting enough glutamate to glutamine. While a plausible argument could be made for the benefits of glutamine even for diabetics-sparing of muscle mass, improved intestinal function, enhanced immune response-caution must be urged. A diabetic considering taking any amino acids should discuss the matter with his/her physician. The use of high doses of antioxidants, including vitamin E and various polyphenols, should be beneficial, as well as supplementation with taurine. Taurine is the one amino acid that seems to be very helpful to diabetics.

### **Effects on cancer, including breast cancer**

We have already said that glutamine is heavily used by all rapidly dividing cells. This includes many types of tumors. Thus it would seem plausible to argue that this is certainly the amino acid that cancer patients should avoid.

In reality, however, glutamine is frequently used as an adjuvant treatment of advanced cancer. It has been shown to prolong survival by slowing down catabolic wasting. In addition, since low immune function is a hallmark of cancer, glutamine is considered beneficial for the depleted immune system. It helps preserve intestinal function as well. Both clinical practice and animal studies suggest that glutamine can be given to cancer patients without stimulating tumor growth or metastasis. Nevertheless, the use of any amino acids in cancer remains controversial, and patients are urged to consult with their physicians first.

The most fascinating findings regarding glutamine and cancer, however, suggest that glutamine may be another weapon against breast cancer. In one animal study, rats implanted with breast cancer were given glutamine at the dose of 1g/kg/day. Their tumor growth was 40% less than in the control group. The natural killer cells in glutamine-supplemented rats showed 2.5 times greater activity. In addition, there was a 25% rise in glutathione levels and a decrease in inflammatory prostaglandins. Inflammatory prostaglandins (PGE2) have been found to fuel tumor growth. Glutamine can also be used as adjuvant therapy with chemotherapy such as methotrexate. Glutamine lowers the toxicity of methotrexate, augmenting its effectiveness against inflammatory breast cancer. In the words of the authors, "No toxicity of oral glutamine was detected. No patient showed any sign of chemotherapy-related toxicity." This is an extraordinary statement since the biggest problem with chemotherapy is its toxicity. The glutamine dose used in conjunction with methotrexate was .5g/kg/day.

One interesting clinical application of high doses of glutamine (30 g/day) is as adjuvant therapy for sickle cell anemia. In alternative medicine, glutamine is also used as part of the treatment for AIDS.

### **Is there a danger to the brain?**

First, let us try to clear up possible confusion by defining some terms. "Glutamate" as it functions within the body does not mean monosodium glutamate, a flavor enhancer discovered by East Asians, and originally manufactured from seaweed, its most abundant natural source. Monosodium glutamate is the sodium salt of glutamic acid-just as sodium ascorbate and calcium ascorbate are salts of ascorbic acid. MSG does, however, raise glutamate levels. In fact, when the use of glutamate is called for in clinical settings, MSG infusions are used.

"Glutamate" is the term used interchangeably with "glutamic acid," though strictly speaking glutamate is an anionic amino acid, or the anionic form (meaning it's a negative ion) of glutamic acid. ("Folate" and "pyruvate" are likewise increasingly used instead of folic acid and pyruvic acid.)

Glutamine differs from glutamate in that it has been formed from glutamate and ammonia, and thus has an extra nitrogen it can easily donate whenever nitrogen might be needed. The enzyme that catalyzes the addition of ammonia to glutamate is called glutamine synthase. An abundant supply of glutamine synthase is essential for our health, since the biosynthesis of glutamine is the process through which the body eliminates excess ammonia. As we will see later, glutamine synthase is of incredible importance in brain function. One could say that our very survival depends on this enzyme, and on the glial cells that secrete it.

Thus, MSG is the sodium salt of glutamic acid, while "glutamate," as the term is used most often these days, is the ionic form of glutamic acid. True, the body can use MSG as a source of glutamate, but there is also all that sodium coming in, perhaps causing sodium/potassium imbalance, dehydration, and disturbances in the constriction and dilation of blood vessels. Dehydration alone is enough to cause the kind of dull headache that some Western patrons of Chinese restaurants have complained about. I suspect that some (most?) Westerners eat much larger portions than Asians, and thus perhaps consume more MSG in one meal than is typical of Asians.

Nevertheless, those prone to migraines should avoid MSG and aspartame, and all of us should avoid these compounds in large doses. There is no question that very high doses of MSG can overwhelm brain defenses and cause neural damage. It is interesting that it is young children with immature nervous systems who are most susceptible to MSG damage, and not the elderly.

Stress has been shown to increase the permeability of the blood-brain barrier to exogenous glutamate. If you expect a business lunch to be stressful, it might be best to stay away from Chinese cuisine. The good news is that more and more Chinese restaurants advertise that they do not use MSG, or else MSG can be omitted by request.

Actually only a small percentage of people are truly sensitive to the small doses of MSG used as a seasoning. Billions of Asians consume it daily; the Japanese also consume seaweed, the richest natural source of monosodium glutamate. This chronic long-term consumption does not seem to cause any problems. In regard to Alzheimer's disease in particular, the Asian rates (including Japan) are a fraction of what they are in the West. It is also of interest that infusions of MSG are used in mainstream clinical practice to reduce high ammonia levels in the blood (hyperammonemia) by stimulating the conversion of glutamate to glutamine. Thus both glutamate (as MSG) and glutamine are used by conventional medicine for treating several very serious conditions.

The consumption of either glutamine, even in large doses, or glutamate in small doses by healthy people is unlikely to cause any problems, neural or otherwise. The reason for this is that, except in cases of severe pathology such as stroke, the metabolism of glutamine/glutamate is strictly regulated. Even though glutamine supplementation is indeed likely to raise glutamate levels in the brain, this does not mean that excess glutamate will therefore accumulate at the synapses and damage the neurons. On the contrary: clinical experience shows that better neural energy production and better neurotransmitter balance are a typical result, with improved mental performance and a sense of well-being, so opposite of the irritability and distractibility, along with cognitive dysfunction, characteristic of states where neurotransmitters are low.

In addition, we need to remember that most of the glutamate is used for energy production rather than as a neurotransmitter. As for the possibility of insomnia, it seems that some people take glutamine at bedtime as a growth hormone releaser, yet complaints of insomnia are not prevalent in the literature. And remember that in clinical settings, as much as 40 g of glutamine may be administered, and yet the literature makes no mention of any side effects. On the contrary, the non-toxicity of glutamine is emphasized as an important advantage. With some important exceptions that will be summarized at the end of this article, it seems that even the severely ill have no trouble metabolizing glutamine.

Glutamic acid has become very hard to find. Glutamine, on the other hand, is in all health food stores, being popular with body builders. One of the ironies is that glutamine is used mainly by the very fit and the very sick.

The apparent lack of side effects of glutamine supplementation is not surprising, considering the abundance of glutamine in the human body. Serum levels of glutamine are in the range of 390-650 mg/dl for adults, compared to 18-98 range for glutamate. Children have higher upper values for both glutamate and glutamine (140 and 730 mg/dl).

The glutamine cycle in the brain is simple and elegant. Glutamine readily crosses the blood-brain barrier. Neurons take up glutamine and convert it to glutamate or GABA (through the additional step of decarboxylating the glutamate). Some glutamate is used for energy, some for synthesis of glutathione and niacin, some as neurotransmitter. After either glutamate or GABA are released into the synaptic junction, the supportive cells called glia, with their high supply of glutamine synthase, take up the glutamate or GABA and resynthesize glutamine, detoxifying ammonia in the process. The glutamate that is not converted to glutamine is used by the glia as a source of energy, and also to produce energy nutrients alanine and alpha-ketoglutarate, which are then released to the neurons.

If excess glutamine accumulates through the action of the glia, the brain donates it to the body. Normally, however, very little glutamine is released by the brain, in contrast to muscle and adipose tissue, which donate a lot. In the brain, it's pretty much an internal affair. What we see is the glutamine glutamate GABA glutamine cycle.

If the glia are dysfunctional due to reduced aerobic metabolism, or the release and/or activity of the glial glutamine synthase is inhibited in any way (free-radical damage, toxins, certain drugs), not only glutamate, but GABA as well might accumulate in excess, possibly causing lethargy and cognitive dysfunction. It has been suggested that this too is one of the phenomena we see in the aging brain. On the one hand, glutamate excitotoxicity damages or destroys some neurons, leading to deficiencies in memory and learning; on the other hand, excess of GABA can lead to lethargy. At the same time, excess ammonia, not detoxified through sufficient glutamine synthesis by the glia, leads to further neural damage.

An interesting development related to glutamate is the increasing use of ampakines, a new class of drugs for Alzheimer's disease. Apparently an important factor in the pathogenesis of Alzheimer's disease is stroke or a series of undiagnosed mini-strokes. During stroke, the dying neurons release glutamate, which then unfortunately can cause more neuron death. Furthermore, ischemic episodes damage the glutamate receptors, so that later the glutamate can't work as a neurotransmitter. Without glutamate, there is no memory and no learning. Ampakines amplify the glutamate signal through a yet unknown mechanism, possibly by rebuilding glutamate receptors. In healthy people and in animals, ampakines have been shown to enhance cognitive performance, and can thus be classified as "smart drugs."

One current hypothesis is that glutamate is also deficient in schizophrenia, though probably many neurotransmitters are out of balance in neurological disorders.



At normal physiological levels, glutamate is beneficial and safe. It is an indispensable neurotransmitter that the brain produces according to need. When the central nervous system is aroused, surprisingly enough we do not see higher glucose consumption. Instead, some of the glucose is converted to glutamate. The other source of glutamate is, of course, glutamine. An abundant supply of glutamine makes it easier for the brain to maintain neurotransmitter balance, by increasing the production of glutamate when

required for alertness, learning and memory, and the production of GABA when its inhibitory properties are needed. In fact, some people report feeling more centered and calm after they start taking glutamine. Others report a lifting of depression.

Glutamate is our chief excitatory neurotransmitter. It is essential for learning and both short-term and long-term memory. Problems arise only if the normal process of glutamate removal and conversion to glutamine malfunctions and an excess of this excitatory neurotransmitter builds up in the synaptic junctions. Excess glutamate causes excessive influx of calcium ions into the neurons, causing excitotoxicity and ultimately even death of the neurons. It also destroys glutathione, a crucial brain-protective antioxidant. Low levels of brain glutathione are associated with neurodegenerative disorders. Glutathione depletion further leads to neuronal death.

Under what conditions do we see excess levels of glutamate at the synapses? Not surprisingly, we see evidence of damage associated with excess glutamate in Alzheimer's disease patients, AIDS patients (the AIDS virus inhibits glutamate uptake by the glia), cancer patients (according to one hypothesis, cancer basically starts with brain dysfunction), and in those who have suffered a severe brain injury. Very high fever or artificially induced hyperthermia can also result in excess glutamate release, leading to seizures.

However, the use of glutamine as a free amino acid has never been associated with any form of brain damage. Glutamine is in fact abundantly produced in the brain as a vital defense against ammonia and also against excess glutamate. The main defense against glutamate excitotoxicity is the synthesis of glutamine by cells called the glia, or, more specifically, astroglia or astrocytes, the most abundant type of cell in the central nervous system, exhibiting high amounts of glutamine synthase. The healthy brain is very well equipped to deal with glutamate. But when the brain is damaged, due to stroke or injury or the accumulation of various neurotoxins including certain drugs, the stage is set for glial dysfunction and hence for glutamate excitotoxicity.

Proinflammatory cytokines interleukin-1beta and tumor necrosis factor-alpha inhibit the induction of glutamine synthase. These proinflammatory cytokines are released after a brain injury and in neurodegenerative disorders. Thus, neuronal death may occur because the inflammatory process interferes with the conversion of glutamate into glutamine.

It thus appears plausible that reducing inflammation can prevent glutamate excitotoxicity by protecting the glia. This may be a partial explanation for the role of anti-inflammatories in the prevention of Alzheimer's disease. In addition, it has been shown that normal levels of anti-inflammatory hormones called glucocorticoids induce glutamine synthase. (Excess cortisol, however, can inhibit the uptake of glutamate by the glia.) Flavonoids, such as the catechins in green tea or proanthocyanidins in grape seed extract, can help protect against the excitotoxic injury due to glutamate buildup. So can uric acid, one of our endogenous antioxidants, and the amino acid taurine. It seems that the brain can produce its own taurine. Nevertheless, if high doses of glutamine are taken, or if foods seasoned with MSG are regularly consumed, it might be an extra precaution to take supplemental taurine.

Certain B vitamins, including methylcobalamine (one of the active forms of vitamin B12), are likewise protective. The real star here, however, seems to be Ginkgo biloba. A Chinese study found that a ginkgo extract, as well as one of its constituents, ginkgolide B, protects against glutamate excitotoxicity by reducing the rise in calcium ions. Thus it is an excellent idea to include ginkgo in your supplement regimen. You may also consider drinking green tea or taking green tea extract, as well as eating berries or taking bilberry extract, in order to obtain a good dose of flavonoids for general neural protection and prevention of neurodegenerative diseases.

Retinal damage in diabetes is also partly due to excitotoxic glutamate buildup. In this case we again see insufficient conversion of glutamate to glutamine, probably due to the malfunction of glial cells (both insufficient or excessive glucose levels can lead to cell dysfunction; diabetics also show higher levels of free radicals).

Finally, alcohol also inhibits glutamine synthase, which explains at least in part the neurotoxicity of alcohol. Certain drugs, including many anti-epileptic drugs, likewise inhibit glutamine synthase, and this may be partly responsible for their toxic side effects. One anti-epileptic drug, however, a fairly new medication called vigabatrin, has been shown to raise both GABA and glutamine while decreasing glutamate. This drug is considered both safe and effective.

There is also a suspicion that toxic residues from the compounds formerly used for bleaching white flour may have contributed to the increase in neurodegenerative diseases, again by inhibiting glutamine synthase. A big challenge in neuro protection is avoiding neurotoxins that might impair the quick conversion of glutamate to glutamine, and seeking to enhance the production of glutamine synthase, one of our most critical enzymes.

Malnutrition can likewise lead to glial malfunction, and thus to the inability of glia to remove excitatory neurotransmitters (glutamate and aspartate) from the synaptic junctions. In summary, glutamate excitotoxicity arises only under certain pathological conditions such as stroke, extremely high fever, certain viral infections, the presence of neurotoxins or severe inflammation. It can be due to excess release of glutamate by the neurons (stroke) and/or to glial malfunction, where the glia are incapable of secreting enough glutamine synthase in order to convert glutamate to glutamine. Glutamine as such cannot harm the brain. On the contrary, it is very beneficial to the brain. Any excess glutamine simply leaves the brain, being donated to the body.

### **Summary of benefits**

There are many reasons for taking glutamine: healthier intestines, a stronger immune system, bigger muscles, better blood sugar control and a more agile brain. For therapeutic uses, glutamine is especially recommended for people who suffer from intestinal problems, frequent NSAID users who need to protect their gastrointestinal tract, those with immune dysfunction, and anyone under heavy stress (including strenuous exercise) or recovering from injury or other trauma. It may also be helpful as adjunct therapy in the treatment of addictions such as alcoholism.

Glutamine is especially popular with body builders, and with those who wish to perk up their physical and mental energy. And-it tastes good!

**Precautions:** Even though glutamine is nontoxic, it is recommended that you consult a health practitioner before using high doses. Diabetics, cancer patients, patients with advanced liver disease, and those with neurological diseases including stroke and epilepsy should use glutamine only with the permission of their doctor.

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