AMINO ACIDS

Amino acids are the basic structural building units of protein and other biomolecules; they are also utilized as an energy source. Daily intake of dietary protein is necessary to present tissue protein breakdown to supply the continuous, critical amino acid needs. The suppression of stomach acid can strongly inhibit digestion of dietary protein in the stomach. Impaired digestion and assimilation account for some of the individual variability of protein requirements. Utilization of amino acids is highly tissue and time dependent. Plasma from blood drawn at any given moment will reflect the state of the dynamic flux of amino acids leaving sites such as skeletal muscle and flowing into sites of utilization in the liver, brain and other tissues. During sleep, many tissues are more actively removing amino acids from the blood for tissue repair, neuronal plasticity and detoxification. In the morning, cortisol rises and amino acids are broken down from skeletal muscle and oxidized for energy.

Either a fasting plasma or whole blood amino acid profile will identify low amino acids and may be used to evaluate whether a patient is in need of essential or conditionally essential amino acids. The finding of low levels in fasting plasma or whole blood demonstrates that the patient is unable to sustain normal fasting (overnight) concentrations. Fasting blood plasma avoids recent dietary influences and has been the predominant specimen in published studies. The data can provide a high level of reliability for showing changes in individual amino acid demands due to chronic stresses. To detect metabolic disorders due to genetic polymorphisms, micronutrient deficiencies or toxicant abnormalities, urinary amino acid testing is the preferred test because levels can rise to very high values as separate amino acids spill from blood into urine.

A good way to organize amino acids is to consider them by function. The following is a list of functional groupings of amino acids:

ANABOLIC/CATABOLIC RESPONSES AND TISSUE PH REGULATION

- Glutamic Acid
- Glutamine

Glutamine is the dominant free amino acid in fasting plasma and it is in rapid, dynamic equilibrium with glutamate. Glutamine is produced from glutamate by the direct incorporation of ammonia, which is a nitrogen fixing reaction. Glutamate and glutamine are critical in human physiology for the following reasons: tissue pH buffering; carbon supply for gluconeogenesis; hepatic ammonia removal; genesis of glutathione; and neurotransmitter function. In the central nervous system, glutamate is the major excitatory neurotransmitter and source of the neurotransmitter gaba-aminobutyric acid (GABA), an inhibitory neurotransmitter. Glutamine functions include protein synthesis and as both a precursor and inhibitor of nitric oxide production. A large percentage of ingested glutamine may be used for energy production by enterocytes, never reaching systemic circulation.

THE UREA CYCLE AND NITROGEN MANAGEMENT

- Arginine
- Citrulline
- Ornithine
- Aspartic Acid
- Asparagine

The detoxification of ammonia is a critical metabolic process that requires the functioning of the urea cycle. Arginine, citrulline and ornithine are primary markers of urea cycle function. Aspartic acid, asparagines, glutamic acid, and glutamine are also important in collecting and eliminating nitrogen. Ammonia toxicity problems can deplete á-ketoglutarate and vitamin B6. Supplementation

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with these nutrients combined with a low protein, high-complex carbohydrate diet and branched chain amino acids can reduce ammonia loads and help to normalize urea cycle function.

ESSENTIAL AMINO ACIDS FOR PROTEINS AND ENERGY

- Isoleucine
- Leucine
- Valine
- Threonine
- Histidine
- Lysine
- Alpha-Aminoadipic Acid

The branched-chain amino acids valine, leucine and isoleucine are used for peptide and protein synthesis. They are important in promoting muscle growth and repair, particularly after strenuous training. Threonine, along with methionine and lysine, is typically a rare limiting amino acid in vegetarian diets. Histamine (derived from histidine) is critical for brain arousal and plays a suppressive role in seizure development and sleep disorders. By two separate pathways, lysine may be converted into alpha-aminoadipic acid. Thus elevated alpha-aminoadipic acid correlates with dietary lysine.

NEUROTRANSMITTERS AND PRECURSORS

- Phenylalanine
- Tyrosine
- Tryptophan
- Alpha-Amino-N-Butyric Acid
- Gamma-Aminobutyric Acid

Phenylalanine and tyrosine are converted to the catecholamines dopamine, DOPA, norepinephrine and epinephrine. Tryptophan is the precursor to serotonin and niacin. Plasma levels of these amino acids influence the concentration of the neurotransmitters, from which breakdown products can be seen in the Organix profile. Elevated plasma alpha-amino-N-butyric acid indicates a need for vitamin B6. Gamma-aminobutyric acid is an inhibitory neurotransmitter in the central nervous system.

SULFUR CONTAINING AMINO ACIDS FOR METHYLATION AND GLUTATHIONE

- Methionine
- Cystine
- Homocysteine
- Cystathionine
- Taurine

Methylation denotes the attachment or substitution of a methyl group. Methylation is a functionally important feature of DNA. Methionine is a major methyl donor in the body and is required for the synthesis of acetylcholine, choline, creatinine and epinephrine. Cystine is a double molecule of cysteine, a product of methionine and a component of glutathione. Glutathione is the body's natural antioxidant that allows the body to recycle its store of antioxidants. Taurine also serves antioxidant functions, especially in red blood cells. Dietary sulfur amino acid content is a major determinant of glutathione. Sulfur amino acid needs are largely met by intake of cysteine, methionine, and taurine

PRECURSORS TO HEME, NUCLEOTIDES AND CELL MEMBRANES

- Glycine
- Serine
- Sarcosine
- Alanine
- Ethanolamine
- Phospethanolamine
- Phosphoserine

Glycine is needed for heme biosynthesis, collagen formation, glycocholic acid formation for digestion, glycine conjugation in detoxification and direct neurotransmitter action in brain function. Glycine can be converted to serine. In times of excess supply, methyl groups may be transferred from SAM (S-adenosylmethionine) to glycine, forming sarcosine. Alternatively, glycine can directly contribute to methyl group and other single carbon pools as demand goes up. Thus, sarcosine and glycine serve to buffer the methyl group or single carbon supply system. Alanine is the major carrier of amino acid nitrogen from muscle to the liver. Ethanolamine, phospethanolamine and phosphoserine are closely related structurally and share principal roles in phospholipid metabolism.

BONE COLLAGEN SPECIFIC AMINO ACIDS

- Proline
- Hydroxyproline
- Hydroxylysine

Collagen, the protein of bone, tendons, and ligaments, is the most abundant protein in the human body. Its unique structural properties are due to proline and glycine residues and its great strength and stability are due to cross-linking afforded by lysine side chains. Cells that are dedicated to collagen synthesis make large demands on proline and glycine supply. Some of the proline and lysine residues are modified to hydroxyproline and hydroxylysine, which provide markers for bone loss due to the turnover of collagen during bone resorption. Hydroxylysine and hydroxyproline are also indicators of liver disease.

BETA-AMINO ACIDS

- Beta-alanine
- Beta-aminoisobutyric acid
- Anserine
- Carnosine

Beta-amino acids are so named because their amino groups are attached to the beta carbon. These compounds serve physiological functions ranging from bile acid precursor and antioxidant to neurotransmitter and metabolic control. They can be acquired from the diet or synthesized denovo.

METHYLHISTIDINES

- 1-methylhistidine
- 3-methylhistidine

High urinary excretion of 3-methylhistidine indicates active catabolism of muscle and is a marker for skeletal muscle breakdown. Urinary excretion of 1-methylhistidine has been used as a marker to distinguish meat-eating individuals from vegetarians.

RECENT AMINO ACID RESEARCH

Mizuno K, Tanaka M, Nozaki S, et al. Mental fatigue-induced decrease in levels of several plasma amino acids. *J Neural Transm*. 2007;114(5):555-561.

In an investigation of the relation between plasma amino acid levels and mental fatigue, the concentration of 20 amino acids was measured before and after an 8 hour fatigue-inducing mental task session. As a control, an 8-hour relaxation session was performed in the same subjects at an interval of 4 weeks. Immediately after the fatigue session, the plasma levels of branched-chain amino acids (BCAA), tyrosine, cysteine, methionine, lysine, and arginine were below those after a relaxation session. The values for other blood parameters including total protein, albumin, glucose, and total cholesterol did not show any differences between the 2 sessions. It is known that blood BCAA and free tryptophan compete for being transported into the brain through the blood-brain barrier, since they are carried by the same transport system. Thus, an increase in the ratio of plasma free tryptophan to BCAA accelerates the transport of free tryptophan into the brain; and because tryptophan is a precursor of 5-HT, an increase in the 5-HT content in the brain may be expected. Therefore, plasma BCAA and free tryptophan levels are considered to be associated with physical fatigue.

Ataka S, Tanaka M, Nozaki S, et al. Effects of oral administration of caffeine and D-ribose on mental fatigue. *Nutrition.* Mar 2008;24(3):233-238

The effect of caffeine and D-ribose on mental fatigue was examined. Plasma branched-chain amino acid (BCAA) levels were decreased by mental fatigue. The study found that caffeine could improve task performance, but it also decreased the level of BCAAs and thus is thought to lead to a deeper fatigue once the stimulant effect is gone.