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Alternative Functions of Amino Acids and Their Effects on Human Physiology



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ABSTRACT

In recent years, the effects of specific amino acids beyond their nutritional benefits have garnered attention, and their consumption is considered beneficial in Japan. Amino acids are produced by the hydrolysis of proteins, one of the five major nutrients that we consume. Amino acids are used in the production of nitrogen-containing physiologically active substances and high-energy compounds, such as ATP. In this paper, we discuss the basic functions of amino acids as nutrients, introduce their additional functions and effects on human physiology reported in recent years, and state our conclusions regarding the same.



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INTRODUCTION

Proteins are one of the five major nutrient groups that we consume. The molecular weight of proteins reduces through catabolism (decomposition), and they break down into amino acids (Table 1). An amino acid is an amphoteric electrolyte with a carboxyl group and an amino group. Based on the substituent group attached, an amino acid can be acidic, neutral, or alkaline¹. More than 300 types of amino acids can be found in nature. Human proteins consist of about 20 amino acids, namely glycine, alanine, valine, leucine, isoleucine, asparagine, glutamine, serine, threonine, methionine, cysteine, tyrosine, phenylalanine, tryptophan, proline, aspartic acid, glutamic acid, lysine, histidine, and arginine¹. Amino acids are classified as essential and non-essential. There are nine essential amino acids, namely valine, leucine, isoleucine, threonine, methionine, phenylalanine, tryptophan, lysine, and histidine. These cannot be synthesized by the human body and must be ingested as part of our diet. Nutrients in our diet may include some components of proteins, peptides (with a small number of amino acids), or amino acids directly found in various foods. Proteins in ingested food account for about 50% of essential amino acids¹. The other amino acids are non-essential, but it is difficult to state which one of them is important². Essential amino acids differ depending on the species, and in humans, the synthetic pathways for the nine amino acids are believed to have disappeared in the process of evolution. Essential amino acids control our perception of food taste. If different types of specific amino acids are present, it is easier to taste acidity, sweetness, and bitterness; these tastes are determined by the ratio in which specific amino acids mix.

In recent years, the effects of specific amino acids beyond their nutritional benefits have garnered attention, and their consumption is considered beneficial in Japan. In this paper, we discuss the basic functions of amino acids as nutrients, introduce their additional functions and effects on human physiology reported in recent years, and state our conclusions regarding the same.

Basic functions of amino acids

On ingesting proteins and peptides contained in food, they pass through the digestive tract and undergo digestion. Their molecular weight is reduced, and they break down into amino acids, which are absorbed by the body³. These absorbed amino acids enter the bloodstream and are transported to cells. Then, they get metabolized within each cell. Upon metabolism,

amino acids perform one of the following basic functions: 1) they become a component of muscles; 2) they become a physiologically active substance, such as hormones containing nitrogen and neurotransmitters; 3) they get utilized to produce high-energy compounds, such as ATP, and the generated energy is used for life-sustaining activities; 4) they are used for the synthesis of non-essential amino acids through intermediate metabolic reactions³.

Alternative functions of amino acids

1. Muscle building effect of branched-chain amino acids (BCAAs)

Valine, leucine, and isoleucine are branched-chain amino acids (BCAAs) with carbon chains that branch into side chains. These side chains constitute the hydrophobic part of proteins in the skeletal muscles. All BCAAs are essential amino acids. BCAAs are primarily metabolized in peripheral tissues (especially muscle), except the liver tissue. BCAA content in muscle protein is as high as about 35%. For these reasons, BCAAs are attracting attention as a specific component of ingestible proteins that strengthen muscles and are often used in food supplements⁴. They can be obtained through high-protein food; however, to ensure efficient uptake of these amino acids by muscles, alternative sources of supply are being studied.

2. Improvement in quality of sleep with glycine

Sleep is an indispensable bodily function, and its quantity and quality are important for humans. Recent research by food companies in Japan has revealed that glycine plays an important role in getting good sleep. Volunteers, who were dissatisfied with their sleep, were asked to eat glycine or a control diet containing no glycine before going to bed, and their fatigue level was investigated the next morning. Volunteers who consumed glycine woke up refreshed and had reduced fatigue⁵. Brain waves revealed glycine not only helps reach deep sleep (slow-wave sleep) faster but also improves sleep quality by increasing sleep time (by stabilizing sleep). Glycine intake before bedtime raises the surface body temperature of the feet, increases heat dissipation, and lowers the core body temperature, leading to good sleep⁵.

3. Increased immunity with cystine, theanine, arginine, and glutamine

Cystine is produced by condensing two cysteine molecules to form a disulfide bond (SS). It is produced by the metabolism of sulfur-containing amino acids, cysteine and methionine, in the

human body. It is considered to be involved in maintaining the higher-order structure (shape and thickness) of proteins. Theanine, an amino acid abundant in tea leaves, is not found in humans.

Immunity or immune response is the self-defense mechanism of the body that works to eliminate pathogens when they invade the body. The immune response of a person gradually declines with aging. The immune response also decreases during vigorous exercise and extreme stress conditions. A study of the effects of cystine and theanine in preventing common cold during winter in 176 adult males found that fewer people in the group consuming these amino acids caught a cold and complained of chills and fever compared to those in the group not consuming them⁶. These amino acids enhance immunity and prevent common cold and suppress its symptoms. Arginine and glutamine increase the activities of macrophages and killer T cells, respectively⁷.

4. Improved efficiency of alcohol decomposition in the liver with alanine and glutamine

Excessive alcohol consumption results in symptoms, such as hangovers, due to the effects of acetaldehyde produced by the decomposition of alcohol in the liver. If acetaldehyde is further decomposed, the unhealthy symptoms subside; however, if the metabolism is stagnant, symptoms will persist. Alanine and glutamine are glycogenic amino acids³. They consume NADH (a type of coenzyme) produced in the process of alcohol decomposition and help the reaction proceed smoothly⁸. Therefore, consuming these amino acids increases the efficiency of alcohol decomposition in the liver and helps recover from a hangover. Alanine and glutamine are reported to promote liver regeneration.

5. Use of glycine, alanine, serine, cysteine, proline, and arginine in cosmetic products

Amino acids are an ingredient in several skin-moisturizing products. Amino acid supplements are beneficial for the beauty and health of the skin. Aging, atopic dermatitis, sudden temperature changes indoors and outdoors due to air conditioning, and ultraviolet rays reduce the amino acid and water content of keratin in the skin, resulting in poor skin health. Serine, alanine, and glycine are natural moisturizing agents. When a solution of these amino acids is applied to the skin, it penetrates deep into the keratin layer and increases the moisture content of the skin⁹. Skin application of a cream containing 22 types of amino acids, including serine, proline, and arginine, retained moisture in keratin and provided a barrier against dryness.

Amino acids regulate the moisture content in keratin and normalize skin metabolism, resulting in healthy skin.

Proline and arginine are used as raw materials in collagen production and help reduce wrinkles and sagging of the face. Cysteine suppresses excessive melanin production and helps prevent age spots⁷.

DISCUSSION

The functions of amino acids discussed in this paper are typically known and reported uses of amino acids. When examined from a different perspective, they are not necessarily new functions but are the same as the original physiological effects. The fact that BCAAs form the skeletal muscles of the body (due to their hydrophobic nature) is a known physiochemical property. This shows that the types of proteins that constitute the human body vary based on the organs and tissues they are present in. This information regarding specific properties of BCAAs can be applied to the manufacturing of supplements and pharmaceutical products, which can be used by athletes to strengthen their muscles and elderly people to maintain muscle function (walking ability). Nutrients ingested and absorbed are dispersed throughout the body and do not accumulate in any one part of the body. Maintained skeletal muscles are necessary for a healthy body. Food sources of BCAAs include brown rice, buckwheat, and soybeans¹, but a high intake of these foods should be avoided to prevent gaining other nutrients (for example, sugars) in excess.

The mechanism of the drug-like effect of glycine on sleep is still unclear. Glycine is the smallest amino acid and cannot exert such a strong effect alone. Various amino acids involved in the production of bioactive amines may affect physiological functions, such as sleep. Alternatively, a physiologically active substance produced by the metabolism of glycine may have a direct effect on sleep regulation. Glycine-rich foods include beans, nuts, meat, and fish¹; however, the total intake of these foods should be regulated to prevent fat and sugar excess.

Theanine does not naturally occur in humans. It prevents symptoms of common cold. Alanine and glutamine are used in the body for energy production during metabolism. Metabolism usually proceeds even in the absence of NADH formed during alcohol metabolism. In minors and people who abstain from alcohol consumption, alcohol metabolism is not a necessary process for energy production; however, for those consuming a lot of alcohol, it may have the

same effect as consuming drinks containing turmeric. Instead of affecting metabolism they might just help with ingestion and have a placebo effect. Glycogenic amino acids include 18 amino acids, excluding leucine and lysine³. Therefore, energy production is not limited to a few amino acids. However, since glycogenic amino acids were first considered as a supplement to prevent hangovers, adding another amino acid as a supplement could be a means of accelerating sales of such products.

Amino acids protect the skin from harmful external factors in addition to beautifying it. When externally applied to the skin as a cosmetic, amino acids penetrate the skin and moisturize it. It is important to consider the effects of other ingredients present in cosmetics, such as the base materials of cream, on the skin. Further, it is necessary to determine whether the moisturizing effect is due to amino acids or not. Supplementing cosmetics with oil appears to improve skin moisture, but it gives a sticky sensation and persists as a layer on the skin. Since cosmetics are applied externally and not through ingestion, the effects of amino acids on moisturization are supposed to be medicinal. However, it is necessary to consider whether the effects of temporarily absorbed and retained substances can be treated as medicinal or therapeutic.

CONCLUSION

Nutrients are substances ingested in the form of food. They help carry out physiochemical functions in a healthy manner and reduce the chances of falling sick. The role of amino acids in energy production and cell renewal is a conventionally known fact; however, the immunity-enhancing effect of theanine and improvement of sleep quality by glycine are some additional but less known functions of amino acids. The other effects of amino acids discussed in this study focus on known physiological effects. The tolerable upper limit of amino acid consumption is not set in Japan. High amino acid intake may lead to kidney dysfunction, such as the formation of kidney stones, owing to the presence of nitrogen. High amino acid intake may also result in obesity due to excess calories and disturbance of the intestinal environment¹⁰). Therefore, it is not advisable to consume excessive amounts for them to be effective. Nutrients are components of foods. It is necessary to consider the quantitative balance between proteins and the number of amino acids present in them during intake. It is recommended to consume food products with good quality proteins, such as eggs, milk, meat, and fish. A good quality protein contains a high percentage of essential amino acids. If essential amino acids are missing or deficient in food proteins, proteins constituting

components in the human body will not be synthesized, and growth and sustenance of life will not be possible. Therefore, a protein lacking even certain essential amino acids must be classified as a nutritionally defective protein¹⁾. However, if the effects of certain amino acids are to be enhanced, one must focus on ingesting large amounts of those specific amino acids and refrain from ingesting others. While this contradicts the previous argument of how excessive intake of proteins may result in poor health, we recommend consuming specific amino acids in the form of supplements and not as a diet. For example, the amount of BCAAs required to obtain a visible effect is 2 g. Because obtaining this amount through diet is difficult, there is no choice but to rely on supplements⁴.

Amino acid deficiency is generally considered from the nutritive perspective only by athletes, people who have unbalanced diets, and the elderly. Adequate nutrition, proper exercise, and maintenance of a healthy mind are necessary to lead a healthy life. Therefore, amino acid intake and balance may be regarded as supplementary⁷. Certain amino acids might have additional functions and effects on human physiology as discussed in this article. However, achieving these effects could be burdensome to the body. It can be harmful to health and may reduce performance. Hence, it is necessary to either obtain these amino acids through sustained intake of a range of nutrients or to use them as medicines for a very short period and cease if one begins to feel unwell.

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Table 1 Types of amino acids

Type	Aqueous pH	Essential	Taste	BCAA	Application in cosmetics	
Aspartic acid	Acid	×	Umami /	×		
Glutamic acid			sour			
Glycine	Neutral		Sweetness	○	○	
Alanine						
Valine		○	Bitter	○		
Leucine		×		Sweetness	×	×
Isoleucine						
Asparagine		○		Bitter	×	○
Glutamine						
Serine		×		Sweetness	×	×
Threonine						
Methionine		○		Bitter	×	○
Cysteine						
Tyrosine		×		Sweetness	×	×
Phenylalanine						
Tryptophan		○		Bitter	×	○
Proline						
Lysine	Basic	○	Bitter		○	
Histidine						
Arginine						×

BCAA: branched-chain amino acid; the cosmetological ingredients in this table are those contained in the amino acid composition of collagen. This table is based on the data in references^{1,9}.