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Editorial

Progress in the Nutritional Importance of Tryptophan

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Tryptophan, a large neutral amino acid (LNAA), was discovered in 1900s when it was isolated from a milk protein called casein [1]. Soon thereafter its molecular structure determined and the existence of two isomeric forms of tryptophan vis; L-tryptophan and D-tryptophan was reported. It was found to be an essential amino acid which like other amino acids served as building block of many important peptides and proteins. Apart from its essential role in the synthesis of proteins, it was found to be the precursor of many important biologically active compounds such as serotonin, melatonin and kynurenine which played critical role in maintaining metabolic and physiologic homeostasis [2,3].

Protein based food and food products which we eat daily such as meat, dairy, fruits and seeds [4] are good sources of tryptophan. Daily dietary intake of tryptophan is required because very little of this amino acid is stored in the body and compared to other amino acids its plasma concentration is very low. Plasma levels of tryptophan largely depend upon on its dietary intake and its subsequent utilization for the synthesis of proteins [4]. According to an estimate daily intake of 250 - 425 mg of tryptophan is required for maintaining normal physiological functions. A dietary deficiency of tryptophan can limit synthesis of not only proteins but the synthesis of many bioactive metabolites of tryptophan involved in the maintenance of optimal physiological and mental functions is also reduced.

Accumulating research on the role of tryptophan and its metabolites in health and disease has revealed a key role of this amino acid in responses to stress, plasticity, aging, cognition and a number of mental illnesses (Figure 1). Following absorption from the gastrointestinal tract (GIT), tryptophan is largely metabolized via hepatic kynurenine pathway [5]. Not only a dietary insufficiency of tryptophan but also an increase in the hepatic utilization of tryptophan via kynurenine pathway can reduce availability of this amino acid for other metabolic routes. Enzymes of hepatic kynurenine pathway are highly regulated by glucocorticoid (GC)-induction. Thus stress-induced increases of plasma GCs or medicinal use of GCs increases hepatic utilization of tryptophan making it less available for the synthesis of other bioactive metabolites such as serotonin (5-hydroxytryptamine; 5-HT) and melatonin [4].

The synthesis of serotonin from tryptophan occurs in the central nervous system as well as in the periphery [4]. Promising role of central serotonin in mental disorders such as anxiety, depression, psychosis and eating disorders are well established [3]. In addition,

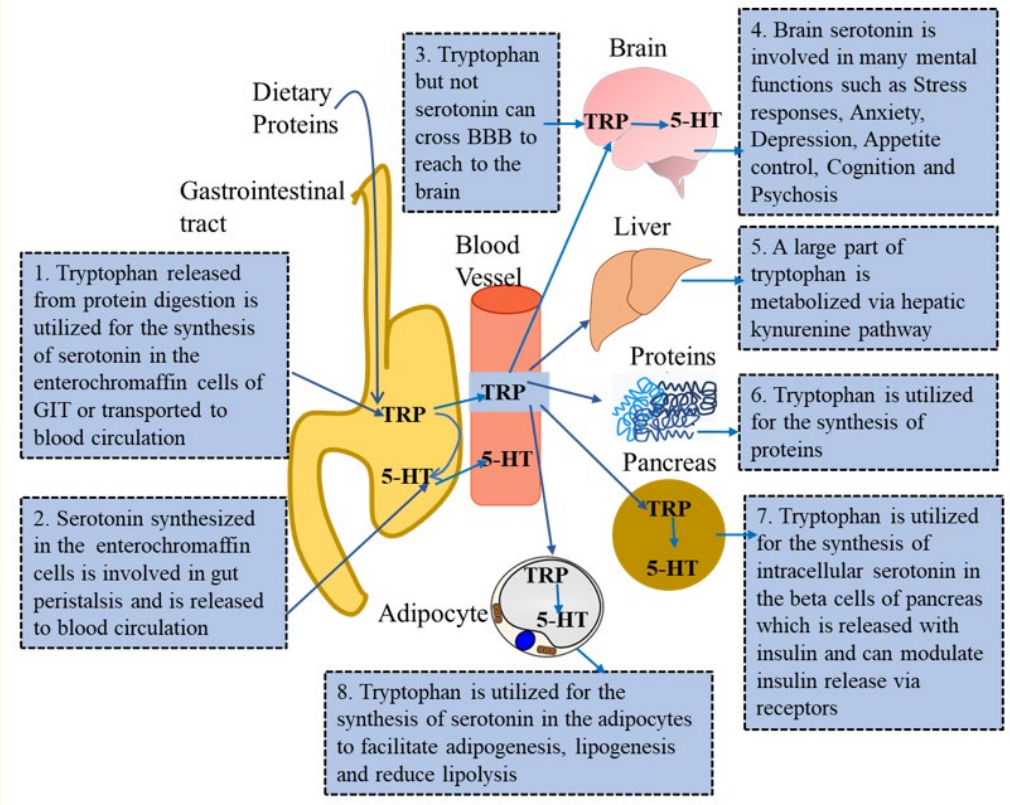

Figure 1: *Absorption, distribution and metabolism of tryptophan. It is utilized for the synthesis of serotonin largely in the periphery and also centrally. Functional responses of serotonin synthesized from the essential amino acid tryptophan suggest its role in mental, metabolic and other physiological disorders.*

emerging evidence support important role of peripheral serotonin in nutrient absorption, gut peristalsis, lipid metabolism and insulin release. A large amount of serotonin is synthesized in the enterochromaffin cells (EC) of GIT. Peripheral serotonin is therefore considered as a key biomarker of lipid absorption and storage [6]. That serotonin receptor type 3 antagonists improve obesity-associated fatty liver disease in mice has been also shown [7].

Tryptophan is also utilized for the synthesis of intracellular serotonin in the beta islets of pancreas where it plays an essential role in insulin release to combat diabetes [4]. On the other hand, adipocytes also express a functional system for serotonin synthesis, reuptake and receptor activation which facilitates lipogenesis and adipogenesis [8] and reduces lipolysis [9].

In view of important role of tryptophan in a number of metabolic and physiologic processes its effect in human health is complex. It is an essential amino acid, which is needed for the synthesis of proteins, central and peripheral serotonin, melatonin and kynurenine. These biologically active metabolites are implicated in many pathological states. It is important to note that not only adequate dietary intake of tryptophan is essential for health but very high levels, largely from pharmacological intervention, can produce adverse effects on health. The concentration of tryptophan in the serum of healthy donors is normally 73 ± 14.9 µmol/l [10,11]. Higher circulating levels are less likely to occur from natural dietary sources because this amino acid is not stored in the body, but pharmacological interventions

to modulate tryptophan metabolism should be carefully designed to target specific need. Future research on tryptophan metabolism in health and disease is highly needed to explore clinical significance of this essential amino acid and/or its metabolites as a biomarker or therapeutic agent.

Bibliography

1. Hopkins FG and Cole SW. "A contribution to the chemistry of proteids: Part II. The constitution of tryptophane and the action of bacteria upon it". *Journal of Physiology* 29.4-5 (1903): 451-466.
2. Correia AS and Vale N. "Tryptophan metabolism in depression: a narrative review with a focus on serotonin and kynurenine pathways". *International Journal of Molecular Sciences* 23.15 (2022): 8493.
3. Haleem DJ. "Improving therapeutics in anorexia nervosa with tryptophan". *Life Sciences* 178 (2017): 87-93.
4. Haleem DJ. "Nutritional importance of tryptophan for improving treatment in depression and diabetes". *Nutrition Reviews* 81.1 (2023): 133-149.
5. Xue C., *et al*. "Tryptophan metabolism in health and disease". *Cell Metabolism* 35.8 (2023): 1304-1326.
6. Iqbal J and Hussain MM. "Intestinal lipid absorption". *American Journal of Physiology-Endocrinology and Metabolism* 296.6 (2009): E1183-E1194.
7. Haub S., *et al*. "Serotonin receptor type 3 antagonists improve obesity-associated fatty liver disease in mice". *Journal of Pharmacology and Experimental Therapeutics* 339.3 (2011): 790-798.
8. Stunes AK., *et al*. "Adipocytes express a functional system for serotonin synthesis, reuptake and receptor activation". *Diabetes, Obesity and Metabolism* 13.6 (2011): 551-558.
9. Hansson B., *et al*. "Serotonin (5-HT) and 5-HT2A receptor agonists suppress lipolysis in primary rat adipose cells". *Biochemical and Biophysical Research Communications* 474.2 (2016): 357-363.
10. Widner B., *et al*. "Simultaneous measurement of serum tryptophan and kynurenine by HPLC". *Clinical Chemistry* 43.12 (1997): 2424-2426.
11. Hagen IV., *et al*. "Serum concentrations of amino acids and tryptophan metabolites are affected by consumption of a light breakfast: a clinical intervention study in adults with overweight or obesity". *BMC Nutrition* 9.1 (2023): 10.

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