All Kerala Govt. Ayurveda College Teacher's Association
KERALA JOURNAL OF AYURVEDA
An International Journal of Ayurveda Specialties

ISSN 2583-8555 (ONLINE)
Vol 3(4):06-09 (2024)
https://doi.org/10.55718/kja.324

REVIEW ARTICLE

The role of *Agni* in epilepsy - A Scoping Review

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ARTICLE HISTORY

Received: 23 November 2024
Accepted: 09 December 2024

Available online
Version 1.0 : 30 December 2024

Keywords

Epilepsy; *Agni*; Ketogenic diet; Metabolism; gut microbiota

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

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CITE THIS ARTICLE

Veena M, Anjali Sivaram, Pradeep K. The role of Agni in epilepsy - A Scoping Review. Kerala Journal of Ayurveda. 2024;3(4):06-09. https://doi.org/10.55718/kja.324

Abstract

Ayurveda is the knowledge-based science of life or a rational way of living. Ayurveda explains several parameters like *dosha, prakriti, agni, koshta, sara,* etc., that have a significant role in health and disease. *Agni* pertains to the principle concerned with generating heat and the several processes of breakdown in the body, namely digestion and metabolism. Epilepsy is a disorder of the brain characterized by repeated, episodic, paroxysmal and involuntary clinical episodes that are linked to aberrant neuronal electrical activity. It may correlate with *apasmara,* one of the *manasika roga* mentioned in the Ayurveda. Basic translational research has revealed that there are intricate, two-way interactions between brain metabolism and epileptic seizures. This creates a harmful cycle that worsens the negative effects on the brain. A ketogenic diet is a good option for controlling seizures in drug-resistant epilepsy, believed to work by altering the metabolism. The four functional states of *agni* may be comparable to different states of metabolism. While considering the metabolic basis of epilepsy and *agni* as an agent in metabolism, an assumption about the influence of *agni* in epilepsy can be derived. Recent studies suggest that there is variation in gut microbiota among people with epilepsy compared to healthy controls. Also, studies show that a healthy microbiome can boost the effectiveness of *agni* by enhancing nutrient absorption, regulating inflammation, and impacting metabolism; it also supports the influence of *agni* in epilepsy. This article is an attempt to review the role of *agni* in the disease epilepsy.

Introduction

Epilepsy is a condition of the brain that can be identified by a persistent propensity to generate seizures as well as by the cognitive, neurological psychological and communal manifestations of this condition.[1] The pathophysiology of epilepsy is not understood completely, even now. The diagnosis of epilepsy can't be done merely by a seizure. The term epilepsy refers to the peripheral incidents that arise from aberrant electrical discharges from the brain, showing up twice or more times.[2] The brain uses a lot of energy and needs to be flexible in how it gets that energy. This flexibility is crucial for maintaining a balance between the abnormal processes that can

lead to repeated seizures and normal brain function.[3] Ayurveda has explained epilepsy under the context of *apasmara*, a condition manifested by an anomaly in recollection (*smriti*), intellect (*buddhi*), thoughts and mental functioning resulting in intermittent loss of consciousness along with unusual actions and behavior.[4] *Manodosas, rajas* and *tamas* have a greater influence on the pathogenesis of *apasmara*.

Agni is a unique concept in Ayurveda that should be understood with respect to digestion and metabolism. *Agni* in Ayurveda is reflected in the concept of '*pitta*' which is one of the *tridosha*. After a careful scrutiny of *panchavidha pitta*, *agni* may correlate with *pachaka pitta,* which has *tyakta dravatva,* unlike other types of *pitta.*[5] *Acharya* Charaka has mentioned that after the stoppage of *agni*, the individual dies, and if the *agni* is *sama,* he will live for many years without any diseases.[6] As per Acharya Vagbhata, the root cause of all diseases is the diminution of *agni.*[7] *Newer studies reveal the difference in gut microbiota among people with drug-resistant epilepsy and healthy individuals.*[8] *Also the link 'gut-brain axis' fixed this connection. The action of the ketogenic diet in intractable epilepsy also supports the influence of agni in epilepsy.*[3]

Objectives

To review the concept of *agni in relation with epilepsy*

Materials and methods

Data were collected from Ayurveda *Samhitas, brhatrayees and laghutrayees, different modern textbooks and also from articles published in online databases like PubMed, Medline, Cochrane etc.*

Agni and metabolism

Agni is an inevitable factor behind digestion and metabolism. All the changes in the body are driven by agni.[9] Metabolism involves a series of chemical reactions within our cells that convert food into energy. This process breaks down carbohydrates, proteins and fats to generate energy and create new molecules to support various bodily functions.[9] A key player in these processes is *Agni,* which is categorized into three phases of digestion:

1. *Amavastha* (*Madhuraavastha) Paka* occurs in the stomach.
2. *Pachyamanavastha* (*Amlaavastha) Paka* happens in the *Grahani* (the small intestine).
3. *Pakavastha* (*Katuavastha) Paka* takes place in both the small and large intestines.[10]

These phases illustrate how the qualities of *rasa* (taste) change during digestion. By the end of this process, the digested food maintains the original *rasa* of what was consumed. Each type of *rasa* has a unique metabolic transformation (*Vipaka)*: *Madhura* and *Lavana Rasa* have *Madhura Vipaka*, *Amla Rasa* has *Amla Vipaka* and *Katu* and *Kashaya Rasa* exhibit *Katu Vipaka.*

Agni, or digestive fire, is crucial for effective digestion, metabolism, and waste elimination. *Jatharagni* is responsible for digestion, while *Bhootagni* and *Dhatvagni* are key to metabolism. *Bhootagni* metabolizes the five basic elements-earth, water, fire, air and ether-transforming them from food into energy. *Dhatvagni,* on the other hand, manages the metabolism of the seven *Dhatus* (tissues), including *Rasa, Rakta, Mamsa, Meda, Asthi, Majja* and *Shukra*, converting nutrients into the building blocks for these essential tissues. Alteration in *jataragni fairly affects bhootagni and dhatvagni, which corresponds to tissue-level metabolism and clearly explains how digestion affects the overall metabolism of the body.*[11]

Metabolic basis of epilepsy [3,12,13]

Metabolism can influence the disease both positively and negatively. In seizures that occur due to any etiology, for the generation and prevention of seizures, a great amount of energy is needed which substantiates the influence of metabolism in seizures. When considering the treatment option also, metabolism plays a crucial role. The ketogenic diet, which is high in fat and low in carbohydrates, is the well-established metabolic treatment for epilepsy. It works by shifting the metabolism, from glucose to fat metabolism. While using a ketogenic diet, the reduction in the consumption of brain glucose and the lower production of ATP through glycolysis can cause ATP-sensitive potassium channels to open. This results in the hyperpolarization of the neuronal membrane, which decreases the brain's electrical excitability and raises the threshold for seizures. Also it prevents excessive firing of neurons. It offers strong evidence that focusing on bioenergetics and metabolism can help to reduce seizure activity, especially in those with intractable epilepsy.

Agni and gut microbiome

The gut-brain axis refers to the two-way communication that occurs between the digestive system and the brain. This involves biochemical signals that influence both the gut and the central nervous system. Alteration in gut microbiome due to various environmental and lifestyle factors is known as dysbiosis.[14] *Agni* is a much broader concept than just the gut microbiome. It's fair to say that one of its many roles is to help maintain the balance of the gut and its microbiome. As *agni* is responsible for digestion,

metabolism and assimilation of nutrients, it can be considered as a factor behind dysbiosis.

Gut microbiota is unique for each individual, shaped by genetic factors, diet, host physiology and various environmental influences. Research shows that monozygotic twins, even when living apart, tend to have similar gut microbiota, whereas marital partners sharing the same environment and diet often have significant differences. This shows the influence of genetic factors in the gut microbiome.[15] The fetal gut is sterile while in the womb, becoming colonized within the first year of life, and by age four, it reaches a mature state. Once it develops into an adult-type gut microbiota, it generally remains stable until around the seventh decade of life, although it can be affected by medications like antibiotics.

Positive gut health is characterized by effective digestion and absorption of nutrients, regular bowel movements with normal stool consistency, and the absence of gastrointestinal issues. These factors reflect the functions of *Agni* at the gut level. *Jatharagni* can be seen as the functional components of the gut, including gut microbiota and the gastrointestinal barrier. Additionally, the genetic makeup of gut microbiota highlights its strong connection to aging, which is influenced by an individual's body constitution, or *Prakriti*.

In the case of *Mandagni*, the digestive enzymes are insufficient for the proper breakdown of food. As a result, microbes struggle to process undigested food, leading to the formation of *ama* which is a root cause of many diseases. On the other hand, *tikshnagni* can burn food completely, turning it into ash and leading to proper nutrition. A well-functioning microbiome can enhance *tikshnagni* by improving nutrient absorption, reducing inflammation, and supporting metabolism. With *vishamagni* (irregular digestive fire), undigested and partially digested food can create toxic compounds resulting in a pathological condition known as *vishtabdhajirna* which disrupts the balance of *apanavayu* and *samanavayu*. Gut microbes fail to interact properly with this mixture, leading to dysfunction in the digestive tract. [16]

Gut microbiome and epilepsy

Gut dysbiosis plays a major role in the development of epilepsy.[17] Studies have shown that individuals with epilepsy tend to have higher levels of the Proteobacteria phylum, while healthy controls have a lower abundance of this phylum. Additionally, the healthy control group shows higher levels of Bacteroides and lower levels of Firmicutes and Actinobacteria compared to those with epilepsy. Overall, there are significant differences in gut microbiota between people with epilepsy and healthy individuals.[18] Evidence suggests that the ketogenic diet in controlling epilepsy also works by altering the gut microbiota.[18] Zhang et al. reported that after 6 months on a ketogenic diet, 20 children with drug-resistant epilepsy showed a decrease in overall microbial diversity (α-diversity). They also observed a significant increase in Bacteroides, along with a decrease in Firmicutes and Actinobacteria.[19] Certain studies also reveal the difference in microbiota among people with drug -resistant and drug-responsive seizures.[20]

Discussion

While discussing the role of *agni in epilepsy, facts to be considered include the influence of metabolism in epilepsy and gut microbiome. Metabolic changes can affect both seizure genesis and remission. Agni, as an agent in metabolism could have a role in the pathogenesis of epilepsy. The action of the ketogenic diet in drug-resistant epilepsy substantiates this view.* The ketogenic diet works by altering the metabolism, switching carbohydrate to fat metabolism thereby mimics a fasting state. [12] Ketone bodies induce chemical messengers and alterations in neuronal metabolic activities to regulate neuroprotective mechanisms towards oxidative damage to decrease seizure rate. A ketogenic diet controls seizures by inducing a state of ketosis in people with epilepsy. On the other hand, recent studies revealing the alteration in gut microbiomes in people with intractable epilepsy compared to healthy controls also substantiate the influence of *agni* in epilepsy [21], as studies revealing *agni* as a factor behind gut dysbiosis are available.[16] While considering the four functional states of *agni* as four stages of metabolism, the stage with hypermetabolism and erratic metabolism, i.e *tikshnagni* and *vishamagni* may induce seizures.

Conclusion

Agni is a concept that has to be evaluated in connection with digestion and metabolism. *Agni* has a role in the pathology of almost all diseases. If the *agni* of a person is disturbed, the whole metabolism gets hampered. There seems to be a connection between *agni* and the pathogenesis of epilepsy. The antiseizure activity of the ketogenic diet by altering the metabolism substantiates this view. Alteration in gut microbiomes in people with drug-resistant epilepsy compared to healthy controls also supports this view. For a complete understanding of this, further research has to be conducted to check the influence of *agni* in epilepsy.

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