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ORIGINAL PAPERS

# The Role of Intestinal Microbiote in Neuromuscular Diseases in Paralized Dogs

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**Abstract**

In order to be able to move, animals like man need the nervous and muscular system to function optimally. The brain, spine, nerves and muscles must work together. If there is a disturbance, the messages will not reach the destination and the animal will not be able to move. Depending on the location and extent of the neurological lesions, the dog may paralyze in whole or in part. Post-traumatic paralysis is a complex condition that requires proper treatment and thorough investigations to establish an accurate diagnosis. There are several conditions that can cause paralysis in the dog. The interaction between the health of the microbiome and that of the brain as well as the way it communicates immune and neuronal cells has been studied. Intestinal cells affect the cells of the central nervous system in the brain. The intestinal-brain axis may influence different neurological disorders and it is possible that dysbiosis in the intestinal tract may lead to disturbance of the transmission of nerve controls on the neuromuscular plate. By-products of microorganisms in the intestine, which appear as a result of tryptophan processing in the diet, can limit the level of inflammation in the brain by the influence they have on microglial cells. The current research focuses on the influence that the gut microbiota has on microglial cells and astrocytes that play an important role in the health of the central nervous system. To reach these observations, the authors examined how intestinal microbiota and diet influence amelioration of paralysis in dogs. In conclusion, the link between the health of the microbiome and the health of the brain, shows how the microorganisms in the intestine influence the evolution of paralysis.

**Keywords:** microbiome, intestinal dysbiosis, neuroimmunomodulation, paralysis, dog.

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The motivation of the communication was the study of the influence of the canine intestinal microbiota on the health and the appearance of the neurological diseases.

The research focuses on maintaining the balance of the normal intestinal microbiota and its interaction with those of two types of cells that play an important role in the health of the central nervous system: microglial cells and astrocytes.

In this presentation, we will discuss the biological interaction on the intestinal-brain axis and explore how this communication may be involved in neurological diseases. Moreover, we highlight new ideas in altering the composition of the gut microbiota, which may appear as a promising therapeutic approach to treat CNS disorders.

Recent specialist studies draw attention to the relationships between canine microbiome health and brain health, how the gut microbiota influences the appearance and evolution of neurological disorders. There are important factors in this interaction regarding the health of the gut and brain microbiota, as well as the maintenance of immune and neuronal cell communication. The new findings help us to understand more clearly how to care for intestinal epithelial cells that affect nerve cells.

The microglial cells are an integral part of the immune system and are responsible for normal functions in the body. On the other hand, microglia can secrete substances with the protective role of neurons.

Current studies refer to the modulation of the microbiota that influences microglial cells to prevent inflammation. Research into efforts for effective therapies may also apply to neurological diseases. There are several causes that can cause paralysis in dogs. Any process that disrupts the communication of the intestinal-brain axis can lead to loss of coordination and movement, inability to move. As in the human intestinal axis the brain can cause neurological disorders and in dogs it is possible that the dysbiosis of the intestinal microbiota may lead to the dysfunction of the transmission of nervous controls at the level of the neuromuscular plate. Paralysis in dogs can occur when the ability of nerve coordination of body movements is diminished or completely lost.

The human gut contains $10^{13}$-$10^{14}$ microorganisms, far more than the body's cells and 100 times more genes than the human genome. The weight of the microbiota is about 1 kg per adult. The vast majority of bacteria reside in the colon. The last decade has made remarkable progress in understanding the significant role that intestinal microbial metabolites play in modulating host health. Moreover, to fully utilize the potential of the gut microbiota for disease prevention, it is necessary to understand how dietary components and host genetics affect the production of different microbial metabolites (1).

However, little is known about how the gut microbiome influences the host's locomotion or the molecular and cellular mechanisms involved (2).

The literature has shown that bidirectional signaling between the brain and the gut microbiome involves multiple neurocrine and endocrine signaling mechanisms (3).

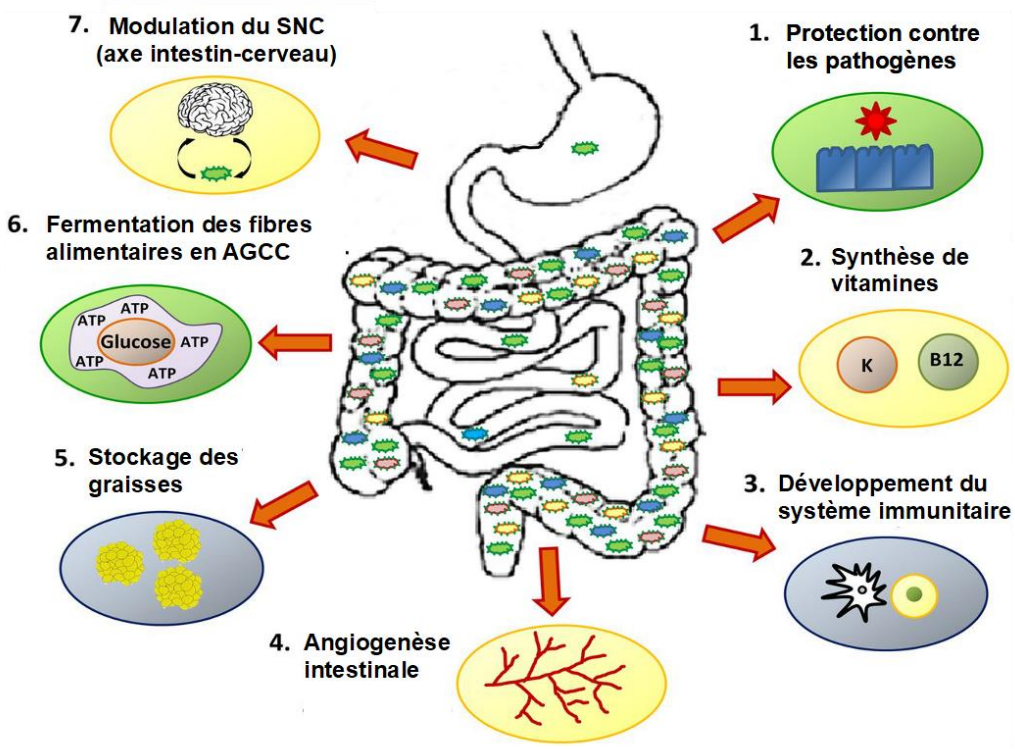


**Figure 1** The human microbiome plays an important role in control of vital homeostatic mechanisms in the body. These include enhanced metabolism, resistance to infection and inflammation, prevention against autoimmunity as well as an effect on the gut–brain axis. SCFA, short-chain fatty acid. (https://commons.wikimedia.org/wiki/File:Microbiota_roles.png)

A link between the gut microbiota and the brain has long been suggested, but in recent decades, studies have begun to report the causal effects of the gut microbiota on the brain and host behavior, and basic molecular mechanisms have begun to be elucidated (4).

Some animal studies have provided evidence that stress can disrupt the gut microbiota composition and affect host behavior. Indeed, much research has focused on serotonin as a key substance in gut-brain microbiota interactions. The gut microbiome-brain signal was at the center of countless researches (5).

Evidence from multiple sclerosis and stroke models has suggested that changes in the gut microbiota may indirectly influence the central nervous system through effects on immune homeostasis and immune responses (6).

In fact, subsequent research has begun to discover other means of intestinal-brain communication, in particular, products derived from microorganisms that can directly or indirectly signal the nervous system. The presence of the intestinal microbiota, of the short-chain fatty acids produced in the intestine causes neuro-inflammation, motor deficiencies and α-synuclein pathology. Metagenomic analyzes were performed which indicated that the potential of microorganisms to synthesize certain neuroactive metabolites may also be correlated with mental well-being (7).

The intestinal-brain axis provides the biochemical signaling that occurs between the gastrointestinal tract (GI tract) and the central nervous system (CNS). The term "gut-brain axis" is sometimes used to refer to the role of the gut microbiota in interaction, while the term "gut-microbiome-brain" axis explicitly includes the role of the gut microbiota in biochemical signaling events that occur between the GI tract and SNC (8).

Limited, the intestinal-brain axis includes the central nervous system, neuroendocrine and neuroimmune systems, the hypothalamus-pituitary-adrenal (HPA) axis, the sympathetic and parasympathetic branches of the autonomic nervous system, including the enteric nervous system (9).

The intestinal microbiota is the complex community of microorganisms that live in the digestive tract of humans and animals. The gut is a niche in which the human microbiota exists. In humans, the gut microbiota has the highest number of bacteria and the highest number of species compared to other areas of the body. The composition of the human gut microbiota changes over time, when the diet changes and, with the change of the general state of health. The intestinal-brain axis, a two-way neurobehavioral communication system is important for maintaining homeostasis and is regulated through the central and enteric nervous system and on the nerve, endocrine, immune and metabolic pathways, in particular through the HPA axis. This term has been extended to include the role of the gut microbiota as part of the "gut microbiome-brain" axis (10).

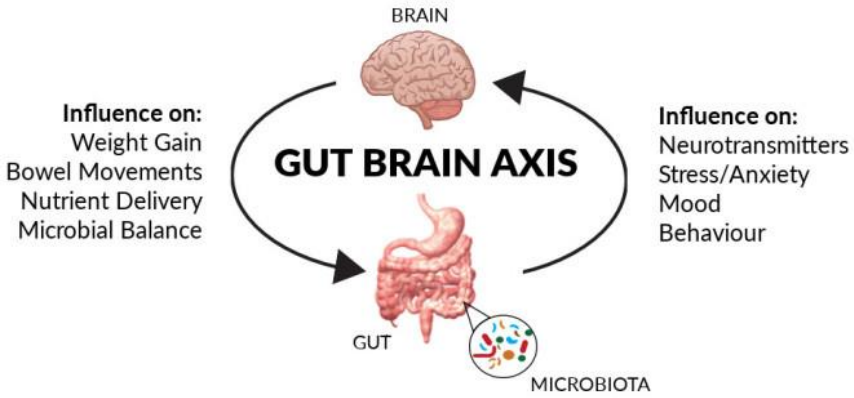


Figure 2 The gut-brain microbiome axis
https://www.laurenderrico.com/blog/2018/8/5/anxiety-and-the-gut-brain-axis

The intestinal microbiota produces a range of neuroactive molecules, such as acetylcholine, catecholamines, γ-aminobutyric acid, histamine, melatonin and serotonin, which are essential for the regulation of intestinal peristalsis. Changes in the composition of the intestinal microflora due to diet, drugs or diseases are correlated with changes in circulating cytokine levels, some of which may affect brain function. Research on the intestinal-brain axis has traditionally been focused on the psychological state that influences the function of the GI tract. These recent discoveries regarding the new role of the gut microbiota in the gut-brain axis imply that the gut microbiota may be associated with brain functions, as well as with neurological diseases through the gut-brain axis (11).

The aim of the study was to systematically review the effects of probiotics on the function of the central nervous system in animals and humans, to summarize the effective interventions (probiotic species, dose, duration). As many of the baseline studies have shown some efficacy of probiotics on CNS function, this context may guide and promote further preclinical and clinical studies (10).

Recent studies suggest that many of these metabolites that derive from microbial transformation of dietary components have significant effects on physiological processes, such as intestinal and immune homeostasis, energy metabolism, vascular function and neurological behavior. The impact of microbiota metabolites on health and disease is discussed in detail and current strategies for modulating the levels of these metabolites for promoting human health are analyzed (1).

This detailed understanding of diet-microbiota-host interactions suggests significant possibilities for creating new therapeutic approaches, including selectively modifying the microbial production of molecules to promote human health and prevent disease (12).

The microbiota, the intestine and the brain communicate through the microbiota-gut-brain axis in a bidirectional way that involves the autonomic nervous system (13).

A huge amount of data has highlighted a potential role of microbial dysbiosis in various chronic conditions (14).

The microbiota, intestine and brain communicate through the microbiota-intestinal-brain axis and a disturbance of this axis is involved in the pathophysiology of neurodegenerative disorders (15).

The brain and intestine communicate bidirectionally (13).

Most of these microorganisms, including bacteria, archaea, fungi and viruses are in the human gastrointestinal tract and are generically referred to as the gut microbiota (16). Evidence suggests that the microbiota is involved in the physiology and pathology of cellular organisms and therefore has implications for both health and disease (17).

It has been reported that microglia protect the brain against various pathological disorders, by implicating in the activation of the immune response, phagocytosis and cytokine production. In addition, microglia regulates synaptic transmission, synaptic disruption and neuronal circuit formation, which are involved in homeostasis. Recent studies have shown that the microbiome has an influence on the properties and function of microglia (18-20).

Research on the secondary mediators of the gut microbiota, which acts in the processes of transforming tryptophan assimilated by the body in the diet, may limit inflammation in the microglial cells. There is a need for consensus on how to examine the gut microbiota and diet that may influence the onset of multiple sclerosis.

The study showed that compounds resulting from tryptophan breakdown can cross the blood-brain barrier by activating the anti-inflammatory pathway that limits neurodegeneration. It is very likely that the mechanisms will be valid in the event of manifestation of other neurological diseases besides multiple sclerosis. All cases of canine paralysis are motivated for care and visit to the veterinarian.

Symptoms of canine paralysis may vary depending on the cause. The paralysis of the posterior train may have several causes and the complexity of care required, appropriate treatment and thorough investigations to establish an accurate diagnosis are possible. The possible cause that can be related to the paralysis of the posterior train is the degeneration of the spinal cord that exists especially in the older dogs.

The diagnosis is made in a veterinary clinic. It is possible to check how well you can stay on your feet, the reflex analysis test and the sensitivity to touch. A hemogram, biochemical blood tests, a drug test if it can cause a bacterial or viral infection, or a toxin are required. An X-ray of the spine is often needed, which may reveal an infection, or malformation, in the vertebrae or a disc that presses the spinal cord. Most have interrupted nerve pathways.

Treatment for paralyzing dogs depends on the causes of the condition. Depending on the cause of the paralysis, the treatment given during the recovery period may be shorter or longer. If the gut microbiota of the dog is not healthy, the dog cannot be healthy. Bacteria in the gut microbiota have key functions in the dog's body. For example, bacteria in the gut of the dog are responsible for the production of many vitamins that help absorb nutrients. Intestinal bacteria help the absorption of vitamins and other micronutrients that are essential to the health of the dog, regulate immunity. The microbiota is an important part of the immune system and can increase or decrease inflammation in the body. Bacteria in the gut microbiome can be beneficial. If the gut microbiota is balanced, everything will be fine for the dog, but it can be messy and then the dog's health will suffer. A delicate balance lies between the two types of beneficial and harmful bacteria. The microbiome is most commonly affected by antibiotics. The problem with antibiotics is possible because they are destroyed without being able to discriminate against bacteria. This can only disturb the balance, but it can destroy the entire microbial species, only germs remain resistant. Dysbiosis occurs, and the intestinal mucosa becomes inflamed, increasing the permeability of the intestinal epithelium as a consequence of the passage of bacterial neurotoxins called lipopolysaccharides. These are in circulation reaching the liver, kidneys, heart and other organs causing chronic inflammation. Dysbiosis of the microbiome can cause hypersensitivity reactions, neurological diseases. Prebiotics help intestinal bacteria produce fatty acids that protect cells in the intestinal epithelium.

40 years ago, being psoriasis patient, to cure myself, I discovered a combination of medicinal plants that proved to be the only way to act on the internal causes that trigger and maintain this disease. Some of the plants used grow them personally, others are of spontaneous flora. Watching how the bees visit the flowers of the plants, I thought to use in addition to honey and pollen, propolis and other bee-keeping products (cinnamon sticks, pods). With the pollen of these plants and other ingredients, we created the product Polenoplasmin under the license of the DENIPLANT brand owner Gheorghe Giurgiu, which acts as a modulator of the gut microbiome in animals.

After I healed my own dog that was paralyzed with the hind legs, I watched over 50 cases of paralyzed dogs, and the healing rate was over 80%.

Negative results were recorded in paralyzed dogs for a long time (4-6) months.

http://www.deniplant.ro/polenoplasmin_catel.htm

An interesting case of a puppy from Cyprus, who was hit by a car was broken in his spine and was paralyzed with his back legs.

http://www.deniplant.ro/catelusa.mp4

https://youtu.be/OcQ2NXgZnXs

For 4 months he was given Polenoplasmin, in addition to the physical recovery treatments and the dog was able to walk again.

This puppy lives and walks alone and today as can be seen in the following video:

Movie

https://youtu.be/lwzywDfKsnI

**Conclusions**

(1) Paralysis in dogs being not only an inflammatory condition but also one of the muscular and nervous system, which affects approximately 5% of the canine population, must be treated multidisciplinary and personalized, the microbiome of each dog being a unique entity that responds in particular for allopathic and natural treatment.

(2) The realization of functional foods (nutraceuticals) with a dual role of nutrition and health, is a desire of both food producers and those who care for the health of animals, as they can naturally modulate the activity of the canine microbiome, restore eubiosis, the processes of nerve cell recovery and healing of paralysis. Although it is known how and where prebiotics and probiotics work, it is necessary to find ways to personalize them according to the medical condition we want to solve, and their recommendation is not generally indicated.

(3) Since we have first observations that prove the relationship between the modulation of the intestinal microbiome and human diseases, future research will focus on modulating the human intestinal microbiome with the help of dietary restrictions.

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