Inter-influence of brain and gut: osteopathic approach to communication with microbiome

Ayako Oshima (S220901)

Thesis for the D.O and D.N Program

MUMSS

7 May 2024

Introduction

The quote "All disease begins in the gut" is commonly attributed to the Ancient Greek physician Hippocrates, dating back almost 2500 years.

The brains passes the stress onto your organs and create an organ behavior relationship which means that the brain and stomach are co-mobility between mental problem and gastrointestinal problems. Many of us recognize the idea that the experiences of our guts related to how we mentally feel. We also see that depression and anxiety maybe the early stages of that the related to bloating. The saying "following gut instinct", it is not just a metaphorical expression describing the connection between gut and brain but as your brain can send butterflies to your stomach, your gut can relay its state of calm or alarm to the brain. The intimate and bidirectional connection between the gut and the brain is a highly researched and studied subject and there has been a lot of scientific interest in the gut microbiome in relation to health.

During the late 1800s, as Andrew Taylor Still was developing and sharing his ideas on osteopathy, there was limited understanding of the immune system, gut bacteria, and their impact on our general well-being. Still dedicated himself to the study of the human body "anatomy" and spent much of his time reviewing the elements of anatomy, physiology and chemistry. Believing that the human body contained with in it all the remedies it needed to maintain health. During the 200 years in the history of osteopathy, it has been developed and approach numerously. This is also the reflection of a world nowadays that is changing more rapidly and those changes require that we may look with new eyes for health new knowledge, in the context of the viscera in especially. The effects and benefits of osteopathic treatment of various gut structures would be far reaching than we might think. The close relationship between the brain and gut is crucial for treating gastrointestinal and psychiatric disorders, as the microbiome can have a significant impact on our emotions. This thesis will explore the maturation and functionality of the intestines, emphasizing their significance as a crucial component of the brain-gut axis. Additionally, it will delve into the role of microbiome colonization in digestive disorders and potential underlying factors. Lastly, the study will examine the potential applications of osteopathic treatment in diagnosing and addressing issues related to intestinal flora and bacterial colonization.

Contents

1. Development of the intestine and its function

This chapter addresses various of the development of the intestine and its function, the development of the intestine and its function.

1.1. Embryology of the GI Tract

The intestine is best known for its digestive function, orchestrating the breakdown of macronutrients, regulating absorption, and secreting waste. The intestinal tract is one of the most architecturally and functionally complex organs of the body. The human intestine is 8 meters in length and is subdivided into five functional domains along the proximal-to-distal axis: the duodenum, jejunum, and ileum are segments of the small intestine, while the cecum and colon constitute the large intestine.

From around the second week of pregnancy, when the fertilised egg (zygote) has not yet implanted in the endometrium, cell division begins to double, and organogenesis commences. Once the fertilised egg is implanted, the inner cell mass divides into the upper blastocoel (the undifferentiated cell population that will develop into all the body tissues in the future) and the lower blastocoel (also known as the yolk sac, which supplies nutrition for the baby until the placenta is fully developed). It decreases in size as the placenta grows and finishes its role around 13 weeks of gestation. In the upper blastocoel, some of the cells fold inwards, resembling a balloon with a smaller balloon inside it.

After the invagination movement, these cells push away the lower blastoderm to form the endoderm, or position themselves between the endoderm and upper blastoderm to form the mesoderm. The remaining cells in the upper blastoderm develop into the ectoderm, thus establishing the three germ layers as follows:

Endoderm - epithelium and associated glands.

Mesoderm (splanchnic) - mesentery of the gut, connective tissues, smooth muscle, and blood vessel

Ectoderm (neural crest) - Enteric Nervous System

The germ layers, which are created during gastrulation, are established by the end of the second week and consist of endoderm and mesoderm. In humans, germ tissues are the basis for all tissues and organs in the body. Both the endoderm and mesoderm will also make significant contributions to the development of associated organs. Viscera, in particular, develop from the endoderm and mesoderm of the embryo in a segmental fashion. Organs that grow out of the same embryological segment, such as the liver, gallbladder, and pancreas (all originating from T5-7), will share a common neurological supply connected to those spinal segments[1].

---

[1] Mullin, Gerard E., and others, 'An Osteopathic Approach to Functional Digestive Disorders', in Gerard E. Mullin, and others (eds), Integrative Gastroenterology, 2 edn, Weil Integrative Medicine Library (New York, 2019; online edn, Oxford Academic, 1 Mar. 2020) :195–C9.P86.

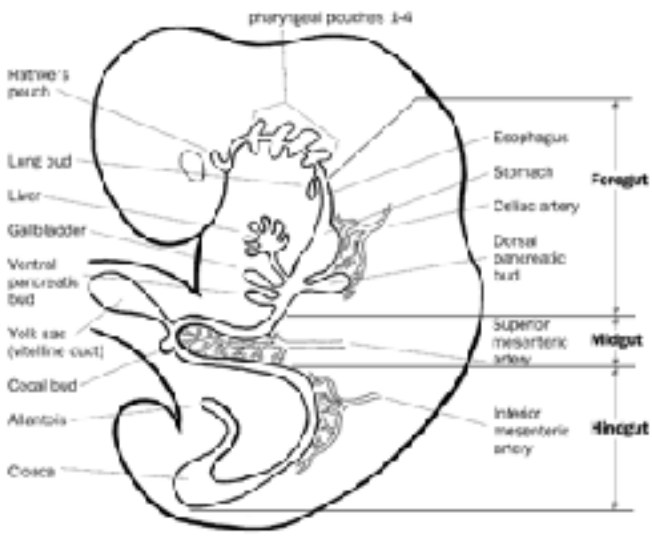
1.2. Gut tube divisions

The primitive gut tube develops during weeks 3-4 through the incorporation of the yolk sac during the craniocaudal and lateral folding of the embryo. The tube is divided into three distinct sections. These divisions are also later defined by the arterial supply to each of these divisions: foregut, midgut, and hindgut.

Foregut - celiac artery (Adult: pharynx, esophagus, stomach, upper duodenum, respiratory tract, liver, gallbladder, and pancreas)

Midgut - superior mesenteric artery (Adult: lower duodenum, jejunum, ileum, cecum, appendix, ascending colon, half transverse colon)

Hindgut - inferior mesenteric artery (Adult: half of the transverse colon, descending colon, rectum, and the superior part of the anal canal)



Primitive Digestive Tract
(https://www.med.umich.edu/lrc/coursepages/m1/embryology/embryo/10digestivesystem.htm)

The gut, originally in the very early embryological phase, is an inflexed tube that protrudes into the umbilical cord. The gut tube protrudes outside of the body because the body grows less rapidly than the gut tube. Hence, the gut tube grows outside the body.

The development of the midgut is characterized by the rapid elongation of the gut and its mesentery, resulting in the formation of the primary intestinal loop. If the midgut does not complete the rotation or if the loop rotates the wrong way, this can lead to anomalies such as malrotation. This shows that the proper development of the midgut is crucial to the overall function of the human digestive tract.

2. Human microbiota

This chapter addresses the structure and characteristics of human microbiota, particularly focusing on gut microbiota, which is considered the most significant one in maintaining our health and well-being.

2.1. Human Microbiota in Early Life Development

The human body is composed of approximately 37.2 trillion cells[2]. The 100 trillion bacteria, viruses, fungi, and other microbes dwell in organized communities inside and outside of the body. This vast amount of microorganisms inhabiting an environment is called a microbiome. They can be found in and on nearly every part of the body, including the oral cavity, lungs, vagina, and skin. Particularly, a vast number of microbes colonies our intestines, forming what is known as gut microbiota. Our gut harbors a complex community of over 100 trillion microbial cells that influence human physiology, metabolism, nutrition, and immune function. There is a notable scientific focus on the gut microbiome in relation to both physical health and psychological wellness, as evidenced by the publication of numerous popular science books on the subject.

We are born with a very simple microbiome that we inherit from our mothers. Although intestinal bacterial colonization begins when a fetus is in the lower uterus, an infant's gut microbiota is established after birth[3]. After the first several days of life, there is a shift towards a microbiota population focused on extracting nutrients to support the rapid development of the brain and body of the host.[4] As we progress through early life development, the diversity of bacteria in our gut continues to expand within the first three years of life. The variety of microorganisms in our bodies serves important functions at different stages of life. The initial colonization of microbes in early childhood is linked to overall health during that period. The makeup of the microbiome evolves significantly in the first years of life, shaped by factors like prenatal and postnatal environments, as well as delivery method and breastfeeding. Breast milk introduces and supports the growth of beneficial bacteria in the microbiome until it reaches full maturity.

2.2. Gut microbiota function

The gut microbiota assist in a variety of bodily functions, including the digestion of food, gut motility, gut immune regulation, drug metabolism, detoxification, and maintenance of gastrointestinal physiological homeostasis. The gut microbiota interacts with our immune

---

[2] The Medical University of South Carolina (MUSC) . [Internet] Digestive Health, Digestive Organs, Small Intestine. [MUSC Health]

[3] Masaru Tanaka, Jiro Nakayama. [Internet]. Allergology International; Elsevier : Allergology International 66 (2017) 515-522. Development of the gut microbiota in infancy and its impact on health in later life. [Elsevier]

[4] Koenig JE, Spor A, Scalfone N, et al. [Internet]. Succession of microbial consortia in the developing infant gut microbiome. Proc Natl Acad Sci U S A. 2011;108 Suppl:4578–4585. 10.1073/pnas.1000081107

system to prevent the colonization of pathogenic bacteria. Gut bacteria play a crucial role in regulating digestion throughout the gastrointestinal tract. Commensal bacteria play a crucial role in extracting, synthesizing, and absorbing various nutrients and metabolites, such as bile acids, lipids, amino acids, vitamins, and short-chain fatty acids (SCFAs). These components are essential for maintaining the health of the cells lining the gut, regulating the immune system, and reducing inflammation.[5]

2.3. Intestinal disorders and their possible link to gut microbiota

Even though we typically coexist peacefully in symbiosis with our gut microbiota, there is mounting evidence that our gut microbiota is implicated in various diseases. While there are beneficial bacteria in the gut, there are also harmful bacteria that can enter the gastrointestinal tract and cause infections, including food poisoning and other gastrointestinal diseases that result in diarrhea. Gut microbial imbalance, known as dysbiosis, can include an increase in the proportion of small bowel bacteria, alterations in the relative proportion of beneficial microbes to pathogenic ones, as well as the translocation of colonic bacteria. These gut microbiota variations have significant implications in intestinal and extra-intestinal disorders. Research suggests that bacterial populations in the gastrointestinal system play a role in developing gut conditions, including inflammatory bowel diseases (IBD) . The examples of several digestive diseases with alterations in gut microbiota composition are:

Irritable bowel syndrome (IBS)

Irritable bowel syndrome (IBS) is the most prevalent functional gastrointestinal disorder in Western countries. It is a complex condition influenced by various factors such as genetics, physiological and psychological reactions to stress, dietary habits, age, geographic location, infections, and antibiotic usage. Symptoms of IBS are connected to issues with the movement of the gastrointestinal tract, increased sensitivity, immune system activation, and alterations in the makeup and operation of gut bacteria (microbiota) and the gut lining[6]. Due to the complex nature of the disease, patients with IBS may experience changes in symptoms and may transition between different disease entities as the condition progresses[7].

The main contributors to the continuation of IBS symptoms are the interconnected functions and interactions between the microbiota and the autonomic nervous system. This communication pathway affecting each other is referred to as the Gut-Brain Axis, which will be discussed in more depth in the upcoming Chapter 3.

Inflammatory bowel disease (IBD)

---

[5] Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, Mele MC. [Internet]. What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. Microorganisms. 2019 Jan 10;7(1):14.

[6] Collins SM, Bercik P. [Internet]. The relationship between intestinal microbiota and the central nervous system in normal gastrointestinal function and disease. Gastroenterology 2009; 136:2003-14.

[7] Everhov AH, Sachs MC, Malmborg P, et al. [Internet]. Changes in inflammatory bowel disease subtype during follow-up and over time in 44,302 patients. Scand J Gastroenterol. 2019;54(1):55–63. doi: 10.1080/00365521.2018.1564361 [PubMed] [Google Scholar]

Inflammatory bowel disease (IBD) is a persistent condition of unknown origin characterized by inflammation in the gastrointestinal tract, typically categorized as ulcerative colitis (UC) and Crohn's disease (CRD). While the exact etiology of UC and CRD remains unclear, the microbial composition of the colon is recognized as a significant contributing factor to the pathogenesis of IBD.

Colorectal cancer

Colorectal cancer is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases. It is also the second leading cause of cancer-related deaths globally[8]. It predominantly affects older individuals, with the majority of cases occurring in people aged 50 and above. In recent years, the rise of CRC in individuals under 50 years of age, known as early-onset CRC (EOCRC), has become an increasing problem. The increased incidence of early-onset colorectal cancer (EOCRC) may be attributed to the generational shift towards higher body mass index and obesity. This shift is attributed to exposure to carcinogenic factors early in life, such as interactions of the gut microbiome and inflammation, along with other specific external factors[9]. The transition to a Western diet, characterized by low-quality, highly processed, and additive-laden food in traditional countries, is associated with an increased incidence of certain conditions. This shift is closely connected to a decrease in the number of microbes and a loss of microbial diversity. Obesity during early life, especially when associated with maternal obesity or obesity during infancy or childhood, may contribute to dysbiosis and inflammation, ultimately leading to EOCRC.[10]

[8] World Health Organization. [Internet]. Colorectal cancer 11 July 2023. https://www.who.int/news-room/fact-sheets/detail/colorectal-cancer

[9] Rebersek, Martina. [Internet]. Gut microbiome and its role in colorectal cancer. *BMC Cancer* **21**, 1325 (2021). https://doi.org/10.1186/s12885-021-09054-2

[10] Rebersek, Martina. [Internet]. Gut microbiome and its role in colorectal cancer. *BMC Cancer* **21**, 1325 (2021). https://doi.org/10.1186/s12885-021-09054-2

3. Gut-brain axis

The previous chapter highlighted the relationship between gut microbiota and gastrointestinal diseases and disorders, including IBS and IBD. One of the systems believed to be impacted by the interaction and communication pathway between the gut microbiota and signaling is known as the gut-brain axis.

This chapter addresses the definition of the gut-brain axis and the mechanisms of microbiota to gut-brain signaling, highlighting key players in this axis.

3.1. The gut-brain axis

The gut-brain axis is a bidirectional neurohumoral communication system that integrates brain and gastrointestinal functions, such as gut motility, appetite, weight regulation and the microbiota plays a critical role in these functions[11]. The bidirectional communication between the gut and the brain occurs through several pathways. The neural pathways consist of the central nervous system (CNS), the enteric nervous system (ENS), and the vagus nerve. Additionally, the gut and the creation of microbial byproducts like short-chain fatty acids (SCFAs), immune regulators, and hormonal signaling play crucial roles in the interaction between the microbiota, gut, and brain[12][13][14]. This is the reason why gastrointestinal and psychological issues frequently impact one another. For instance, mood disorders like anxiety or depression are commonly linked to individuals with Irritable bowel syndrome (IBS) despite the unknown exact cause of IBS[15].

3.2. A key mediator in the microbiota-gut-brain interaction

3.2.1. Vagus Nerve

The vagus nerve (CN X) which is the longest nerve in the human body, is known as the "wandering nerve". As it travels from the brainstem to lowest viscera of the intestines, the nervous system connects with the heart, lungs, and various vital organs. Lima-Ojeda et al.

---

[11] Grenham S, Clarke G, Cryan JF, Dinan TG. [Internet]. Brain-gut-microbe communication in health and disease. Front Physiol 2011; 2:94; PMID:22162969; http://dx.doi.org/ 10.3389/fphys.2011.00094 [PMC free article]

[12] Borkent J, Ioannou M, Laman JD, Haarman BCM, Sommer IEC. [Internet]. Role of the gut microbiome in three major psychiatric disorders. Psychological Medicine. 2022;52(7):1222-1242.

[13] Cryan, J. F., O'riordan, K. J., Cowan, C. S. M., Sandhu, K. V., Bastiaanssen, T. F. S., Boehme, M., ... Dinan, T. G. (2019). [Internet]. The microbiota–gut–brain axis. Physiological Reviews, 99(4), 1877–2013. https://journals.physiology.org/doi/epdf/10.1152/physrev.00018.2018

[14] Cryan JF, Dinan TG. [Internet]. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. Nat Rev Neurosci. 2012 Oct;13(10):701-12. doi: 10.1038/nrn3346. Epub 2012 Sep 12. PMID: 22968153. [PudMed]

[15] Margolis KG, Cryan JF, Mayer EA. [Internet]. The Microbiota-Gut-Brain Axis: From Motility to Mood. Gastroenterology. 2021 Apr;160(5):1486-1501. doi: 10.1053/j.gastro.2020.10.066. Epub 2021 Jan 22. PMID: 33493503; PMCID: PMC863475. [PMC free article]

describe the vagus nerve by highlighting that "A key feature of this system is its bidirectionality, which involves a neuro-endocrino-immunological connection. The gut-brain axis plays a crucial role in regulating gastric and intestinal function as well as energy homeostasis. The tenth cranial nerve, known as the vagus nerve, comprises both afferent and efferent fibers, serving as a crucial connection between the gastrointestinal tract and the brain[16]". The communication pathway from the gut to the brain is significantly more abundant than the pathway from the brain to the gut, with a ratio of approximately nine to one[17]. The vagal afferent pathways are specifically associated with the hypothalamic-pituitary-adrenal (HPA) axis, which is essential for the body's reaction to various types of psychophysical stress.

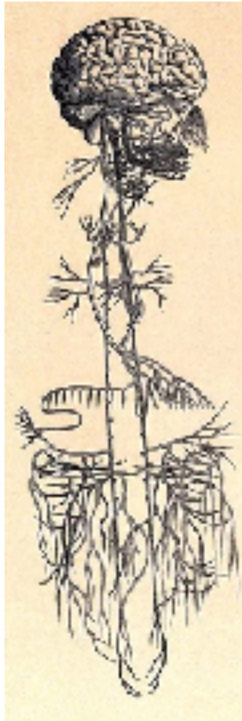


Image: Wellcome Library/ Public Domain

Certain microorganisms can stimulate the vagus nerve, which is quite fascinating. Additionally, it is proposed that this stimulation could boost oxytocin levels in the brain, resulting in beneficial alterations in behavioral aspects of brain function.

This highlights the impact of an imbalanced gut microbiota on our overall well-being, emphasizing the crucial role of the intestines in hosting the numerous microbes in the gut.

3.2.2. Enteric Nervous system (ENS)

The vagus nerve serves as a crucial neuronal pathway connecting the gut microbiota to the brain. However, it is important to note that the gastrointestinal tract possesses its own distinct nervous system known as the enteric nervous system (ENS). The ENS is situated exclusively within the gastrointestinal tract wall, constituting the largest and most intricate component of the peripheral nervous system (PNS).

The enteric nervous system (ENS) is essential for coordinating various functions in the small intestine, including controlling muscle activity for movement and secretion. It is made up of two main plexuses: the myenteric plexus, which regulates bowel motility between the muscle layers, and the submucous plexuses, which are responsible for mucus secretion beneath the gut lining. These plexuses also play a role in regulating blood flow and impacting the enteric immune system.

The enteric nervous system (ENS) has around 100 million neurons, a number that is almost the same as the neurons in the spinal cord. Additionally, the ENS is accountable for generating more than 30 neurotransmitters. For instance, serotonin acts as a neurotransmitter at synapses within the microcircuits of the ENS, with the gut providing around 95% of the body's serotonin. Interestingly, serotonin functions not only as a neurotransmitter but also as a signaling molecule that ultimately triggers peristaltic and secretory reflexes. Many other

---

[16] Lima-Ojeda JM, Rupprecht R, Baghai TC. [Internet]. "I Am I and My Bacterial Circumstances": Linking Gut Microbiome, Neurodevelopment, and Depression. Front Psychiatry. 2017 Aug 22;8:153. doi: 10.3389/fpsyt.2017.00153. PMID: 28878696; PMCID: PMC5572414.

[17] Breit S, Kupferberg A, Rogler G, Hasler G. [Internet].Vagus Nerve as Modulator of the Brain-Gut Axis in Psychiatric and Inflammatory Disorders. Front Psychiatry. 2018 Mar 13;9:44. doi: 10.3389/fpsyt.2018.00044. PMID: 29593576; PMCID: PMC5859128.

chemicals, such as serotonin, are produced in the gut and play a crucial role in the functioning of the nervous system. This is because of the the ENS communicates with the CNS, sympathetic, and parasympathetic nerves, allowing it to operate independently. That is why if we cut a part of the gut and disconnect it from the nerves that connect it to the brain and spinal cord, its peristaltic reflex will still continue for some time. This particular trait is exceptionally distinctive, with no other organ possessing such a sophisticated intrinsic neural system.

4. Possibilities of osteopathy treatment approach for the digestive tract, communication with the microbiome

Osteopathic Manipulative Treatment (OMT) primarily aim to restore balance to organs, muscles, joints, and tissues that are not functioning properly. Digestive issues are often caused by disruptions in blood and nerve flow, muscle tension, organ movement restrictions, and spinal problems. The sympathetic innervation of the gastrointestinal tract starts at T5-L2, with specific focus on segments like T5-7 which are crucial for organs like the liver, gallbladder, and pancreas. By addressing dysfunction in these spinal segments, sympathetic tone can be regulated, and restoring ligament tension is important for achieving autonomic balance in the digestive system.

In the previous chapter, it was discussed that the vagus nerve (CN X) is the cranial nerve responsible for providing innervation to the digestive tract. This nerve plays a crucial role in the brain-gut axis, where stress, emotional distress, depression, and anxiety can impact digestive issues by disrupting peristalsis, affecting gut wall permeability, and altering gut microbiota balance. Additionally, the vagus nerve also supplies the crural area of the diaphragm. Therefore, osteopathic techniques like indirect diaphragm release, rib raising, indirect myofascial release, and mobilization of the abdominal diaphragm can be beneficial in enhancing the mechanical functions of gastrointestinal oxygen supply and lymphatic fluid movement.

Visceral osteopathy is a technique that focuses on identifying and releasing tension in the organs and related tissues to improve overall body function. By addressing dysfunctional patterns that restrict movement and vitality, this method aims to stabilize organs and ligaments in their proper positions. Therefore, maintaining the gastrointestinal system's proper function through visceral osteopathy may contribute to keeping organs stable in their designated places as well as releasing the restrict pattern.

Among the various techniques in visceral osteopathy, I would like to highlight two specific techniques: treating the abdominal sphincters and the mesenteric lift. Given that these techniques are thought to have a substantial impact on both the gastrointestinal system and gut microbiota.

According to Katherine Heineman, DO, FAAO (2022), the objective of treating the abdominal sphincters is to regulate the smooth muscle tone of the sphincters located at transitional areas throughout the gastrointestinal tract. These areas include the ileocecal valve, the duodenojejunal junction, the sphincter of Oddi, the pylorus, and the gastroesophageal junction. The abdominal sphincters demonstrate a continuous clockwise/counterclockwise movement that can be felt in the coronal plane. The typical natural movement is in a clockwise direction. Hence, it is advised that if any sphincters are not functioning properly (turning counterclockwise), gentle pressure should be applied to engage the dysfunctional sphincter and guide it indirectly (counterclockwise) until it naturally reverts back to a clockwise motion[18]. The objective is to enhance the movement and functionality of these areas and the small bowel.

A study[19] has demonstrated that the application of the mesenteric lift technique can decrease abdominal congestion, improve lymphatic and venous drainage, and relieve lower back tension. Another study,[20] has demonstrated that the application of the mesenteric lift technique can enhance bowel movements and optimize the absorption of nutrients, medications, and fluids. This study specifically examines individuals with severe traumatic brain injury (TBI) who frequently encounter autonomic dysfunctions that interfere with normal gastrointestinal motility. The study suggests that Osteopathic Manipulative Treatment (OMT) may provide benefits to a broader population by enhancing gastrointestinal system functionality.

---

18 Heineman, Katherine. "An Osteopathic Manipulative Treatment (OMT) Evaluation and Treatment Protocol to Improve Gastrointestinal Function." The AAO Journal (2022): n. pag.

19 Collebrusco, Luca et al. "Osteopathy and Emergency: A Model of Osteopathic Treatment Aimed at Managing the Post-Traumatic Stress—Brief and Useful Guide—Part 2." Health 10 (2018): 1597-1608.

20 Berry JAD, Ogunlade J, Kashyap S, Berry DK, Wacker M, Miulli DE, Saini H. Clinical Efficacy of Mesenteric Lift to Relieve Constipation in Traumatic Brain Injury Patients. J Am Osteopath Assoc. 2020 Aug 4. doi: 10.7556/jaoa.2020.094. Epub ahead of print. PMID: 32750717

5. Conclusion

The health of the gut is essential for our overall body health. Any disruption in the equilibrium of the microbiome may result in the onset of gastrointestinal disorders. Maintaining gut health is of paramount importance. While the etiology and pathophysiology of intestinal disorders like IBS remain uncertain, it appears that IBS arises from the dysregulation of the "brain-gut axis." Therefore, a treatment plan based on evidence-based literature has been formulated, incorporating Osteopathic Manipulative Treatment (OMT) to alleviate symptoms of Irritable Bowel Syndrome (IBS). It is suggested that osteopathic manipulative treatment (OMT) could be considered a safe alternative treatment for patients with IBS and other gastrointestinal disorders.

The central nervous system communicates with the gut by mediating the sympathetic and parasympathetic branches of the autonomic nervous system. The stimulation of visceral afferents by OMT visceral techniques is crucial for activating and enhancing the function of the intestine. Furthermore, one of the key players in the gut-brain axis is the vagus nerve, which innervates the small intestine and colon up to the splenic flexure. It is important to consider when playing a role in modulating emotions. By stimulating visceral afferents, it may reduce intestinal symptoms and improve intestinal function.

Finally, as Hippocrates was the first to suggest, "He who does not know food, cannot understand the diseases of man". Many aspects of our modern lifestyles can disrupt our gut flora and lead to a state of dysbiosis. Modern diets may significantly contribute to dysfunction in our intestines. The diet is also an important aspect, with the underlying factor being our gut health, which is fundamental to our overall body health.

References

- Mullin, Gerard E., and others, 'An Osteopathic Approach to Functional Digestive Disorders', in Gerard E. Mullin, and others (eds), Integrative Gastroenterology, 2 edn, Weil Integrative Medicine Library (New York, 2019; online edn, Oxford Academic, 1 Mar. 2020) :195–C9.P86. [LINK] [Google Scholar]

- Jordan C. Malone; Tafline C. Arbor; Abdul Basit Shah. [Internet]. StatPearls Publishing; Treasure Island (FL): 2024 Jan. 2023 March 6. Embryology, Midgut. [PubMed]

- Christine Waasdorp Hurtado, MD, MSCS, FAAP. [Internet]. NASPGHAN: NASPGHAN Physiology Lecture Series. Embryology and Anatomy of the Gastrointestinal Tract. [LINK]

- Dr Mark Hill 2024, *UNSW Embryology* ISBN: 978 0 7334 2609 4 - UNSW CRICOS Provider Code No. 00098G. Gastrointestinal Tract - Intestine Development. [LINK] (2024, March 13)

- The Medical University of South Carolina (MUSC) . [Internet] Digestive Health, Digestive Organs, Small Intestine. [MUSC Health]

- InformedHealth.org. [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. How does the intestine work?, Large Intestine. [LINK]

- Standring, S. (2016) Gray's Anatomy: The Anatomical Basis of Clinical Practice. Gray's Anatomy Series 41st edn.: Elsevier Limited. [LINK]

- Elsevie. [Internet]. Complete Anatomy, Large Intestine. [Elsevier]

- Stakenborg N, Di Giovangiulio M, Boeckxstaens GE, Matteoli G. [Internet]. The versatile role of the vagus neve in the gastrointestinal tract. EMJ Gastroenterol. (2013) 1:106–14. [Google Scholar]

- Koenig JE, Spor A, Scalfone N, et al. [Internet]. Succession of microbial consortia in the developing infant gut microbiome. Proc Natl Acad Sci U S A. 2011;108 Suppl:4578–4585. 10.1073/pnas.1000081107 [PMC free article][CrossRef] [Google Scholar]

- Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, Mele MC. [Internet]. What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. Microorganisms. 2019 Jan 10;7(1):14. [Google Scholar] [PubMed] [PMC free article]

- Dinan TG, Cryan JF. [Internet]. The Microbiome-Gut-Brain Axis in Health and Disease. Gastroenterol Clin North Am. 2017 Mar;46(1):77-89. [PubMed]

- Collins SM, Bercik P. The relationship between intestinal microbiota and the central nervous system in normal gastrointestinal function and disease. Gastroenterology 2009; 136:2003-14. [PubMed][Google Scholar]

- Mohajeri MH, La Fata G, Steinert RE, Weber P. Relationship between the gut microbiome and brain function. Nutr Rev. 2018 Jul 1;76(7):481-496. doi: 10.1093/nutrit/nuy009. PMID: 29701810.
- Everhov AH, Sachs MC, Malmborg P, et al. Changes in inflammatory bowel disease subtype during follow-up and over time in 44,302 patients. Scand J Gastroenterol. 2019;54(1):55–63. doi: 10.1080/00365521.2018.1564361 [PubMed][Google Scholar]
- Rebersek, Martina. [Internet]. Gut microbiome and its role in colorectal cancer. *BMC Cancer* **21**, 1325 (2021). https://doi.org/10.1186/s12885-021-09054-2
- Breit S, Kupferberg A, Rogler G, Hasler G. Vagus Nerve as Modulator of the Brain-Gut Axis in Psychiatric and Inflammatory Disorders. Front Psychiatry. 2018 Mar 13;9:44. doi: 10.3389/fpsyt.2018.00044. PMID: 29593576; PMCID: PMC5859128.[PubMed]
- Ece Alim1,2,3 İD , I. Nadir Gülekon1 İD , Kerem Atalar4 İD , Meltem Bahçelio¤lu1,2,3 İD. [Internet]. Enteric nervous system, gut-brain connection and related neurodevelopmental disorders. Anatomy 2020;14(1):61–67 ©2020 Turkish Society of Anatomy and Clinical Anatomy (TSACA). doi:10.2399/ana.20.008. [LINK]
- Collebrusco, L. and Lombardini, R. (2013) Osteopathic Manipulative Treatment and Nutrition: An Alternative Approach to the Irritable Bowel Syndrome. Health, 5, 87-93. https://doi.org/10.4236/health.2013.56A2013
- Collebrusco, Luca et al. “Osteopathy and Emergency: A Model of Osteopathic Treatment Aimed at Managing the Post-Traumatic Stress—Brief and Useful Guide—Part 2.” Health 10 (2018): 1597-1608. https://www.scirp.org/journal/paperinformation?paperid=88772
- Bischoff SC. 'Gut health': a new objective in medicine? BMC Med. 2011 Mar 14;9:24. doi: 10.1186/1741-7015-9-24. PMID: 21401922; PMCID: PMC3065426. [LINK]
- Heineman, Katherine. “An Osteopathic Manipulative Treatment (OMT) Evaluation and Treatment Protocol to Improve Gastrointestinal Function.” The AAO Journal (2022): n. pag.
- Berry JAD, Ogunlade J, Kashyap S, Berry DK, Wacker M, Miulli DE, Saini H. Clinical Efficacy of Mesenteric Lift to Relieve Constipation in Traumatic Brain Injury Patients. J Am Osteopath Assoc. 2020 Aug 4. doi: 10.7556/jaoa.2020.094. Epub ahead of print. PMID: 32750717