ERAD, 2022, Volume 1, Issue (2), pages 1-3

Excellence in Rheumatic & Autoimmune Diseases
ERAD
THE OFFICIAL JOURNAL OF INSTITUTE OF RHEUMATIC AND AUTOIMMUNE DISEASES

Commentary

The role of lung microbiome on multiple sclerosis

Running title: Lung microbiome and multiple sclerosis

Vasileios Siokas

Department of Neurology, Laboratory of Neurogenetics, University Hospital of Larissa, Greece, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece

Corresponding Author's e-mail: bill_s1983@hotmail.com

Abstract

Microglia is involved in the pathophysiology of multiple sclerosis (MS) as it is considered the neuroinflammation primer in MS. Several environmental and genetic risk factors possibly contribute to MS. Among them are smoking, and lung infections. Moreover, while the gut microbiome has gained the main focus regarding the ongoing research on central nervous system (CNS) and autoimmunity, a recent study suggests that a connection between the local lung microbiome and the brain, also exists, in which the microglia plays a crucial role. In this commentary, we further discuss the important findings of this study considering the lung microbiome as a modifiable environmental factor, which could provide an alternative method for prevention, management and modification in the course of diseases with autoimmune mechanisms, such as MS.

(Submitted 11 February 2022; accepted 23 March 2022)

Keywords- lung microbiome; autoimmunity; multiple sclerosis; gut microbiome; environmental risk factors

I. INTRODUCTION

Multiple sclerosis (MS) is a common autoimmune disease of the central nervous system (CNS) [1]. The mechanisms that are responsible for the induction of the MS are not yet fully understood [2]. Inflammation, demyelination, ionic imbalance, astrocyte and microglia activation, glutamate excitotoxicity, axonal damage, neurodegeneration are among the pathophysiological processes that are implicated in MS development [3].

Interestingly, microglia is considered as the neuroinflammation primer in MS and constitutes more than one third of early MS lesion's mass [4]. Multiple sclerosis is considered to be a multifactorial disease, where both environmental and genetic risk factors confer susceptibility to its development [5]. Regarding genetics, MS is regarded as a polygenic disease, with a complex genetic pattern [6]. Among the several environmental risk factors that possible contribute to the development of MS are smoking, an Epstein-Barr Virus (EBV) infection, the degree of physical exercise, lifestyle conditions, lung infections, vitamin D deficiency and dietary habits [7, 8]. There is also a complex interplay between the environmental and the genetic factors leading possibly to autoimmunity [9].

The gut microbiome has attracted main scientific attention as a possible regulator of CNS regarding autoimmunity [10].The gastrointestinal tract and especially the intestine seems to have an effect on several human systems, including the immune and CNS systems-[11, 12]. The enteric nervous system has been considered as a second brain, while the gut–brain axis offers the bilateral manner of contact, by which the two organs communicate with each other [13]. As far as MS is concerned, the gut microbiota may be deemed as factors that have an effect on the intestinal milieu and their modification may alter the risk and course of MS [14].

While the gut microbiome has gained the main focus regarding the ongoing research on CNS and autoimmunity [9, 15, 16], a recent study suggests that a connection between the local lung microbiome and the brain, also exists [17]. The recipients of the messages from the lung microbiome are the microglia cells, that are regarded as the neuroinflammation primers in MS [4]. Therefore, according to the study by Hosang et al. (2022), the existence of a lung–brain axis has been reported, and thus, the pulmonary microbiome may have an effect on immunological processes conferring susceptibility to the development of autoimmune disorders, even in the CNS [17].

Given that continuous research into modifiable risk factors for several diseases attracts attention, this finding is of particular interest. More precisely, considering the lung microbiome as a modifiable environmental factor, this could provide an alternative method for the prevention, management and modification of the course of diseases with autoimmune mechanisms, such as MS (e.g. with the use the antibiotics, as in the example of the gut microbiota) [9, 14]. At this point, the differences that exist between the gut microbiota and the lung microbiome should be mentioned [17]. Firstly, lung microbiome is in more direct contact with the external environment and exposed to infectious factors. Secondly, the immune response occurs with small changes in the lung microbiota. Finally, the microbial substances require shorter distance to pass from the lungs to the blood without any flirtation, compared to the gut microbiota. These data may indicate a greater impact of the lung microbiome on autoimmunity, in comparison to the gut microbiota.

The lung microbiome is possible to have an effect on the development of diseases, both respiratory and systematic (e.g. rheumatoid arthritis) [18-21]. Nevertheless, the novel findings of this study by Hosang et al. (2022), are of great importance, in ~~a~~ relation to autoimmunity and development of diseases of the CNS with immunological pathophysiological processes, like MS. Modulation of the lung microbiome and of the multiple factors that affect it, even from early life (infections, use of antibiotics, feeding, mode of birth), or later (smoking) [22], may alter the immune reactivity of the brain [17].

II. CONCLUSION

More data and evidence are required from future studies which should be focused in the role of lung microbiome on CNS autoimmunity and MS. Firstly, it would be interesting if the lung microbiome serves as a modifiable environmental factor for MS. Consequently, the modification of the lung microbiome with a dietary, therapeutic or lifestyle approach (e.g. probiotics, antibiotics, change of crowding conditions, smoking) may be added to the prophylaxis and management of MS. In view of the latter, it should be examined when ~~a~~ microbiome-based intervention would be more effective. Should those be done during early life or later (e.g. after the disease development)? Also, the identification of specific microorganism, the modification of which has the major impact on CNS immune reactivity, would help to make more accurate and targeted studies regarding the role of lung microbiome and MS. Moreover, it would be worth if research could focus on how Disease-Modifying Treatment (DMT) may affect the lung microbiome and thus the possible immune CNS reactivity in MS. Finally, studies on MS preclinical state, although difficult to perform, would give robust data on whether immunological processes of the CNS could be preceded and also alter the lung microbiome.

REFERENCES

1. Ciccarelli O. Multiple sclerosis in 2018: new therapies and biomarkers. The Lancet Neurology. 2019;18(1):10-2. doi: 10.1016/S1474-4422(18)30455-1.
2. Lima M, Aloizou AM, Siokas V, Bakirtzis C, Liampas I, Tsouris Z, Bogdanos DP, Baloyannis SJ, Dardiotis E. Coronaviruses and their relationship with multiple sclerosis: is the prevalence of multiple sclerosis going to increase after the Covid-19 pandemia? Rev Neurosci. 2022. Epub 20220307. doi: 10.1515/revneuro-2021-0148. PubMed PMID: 35258237.
3. Thompson AJ, Baranzini SE, Geurts J, Hemmer B, Ciccarelli O. Multiple sclerosis. The Lancet. 2018;391(10130):1622-36. doi: 10.1016/S0140-6736(18)30481-1.
4. Guerrero BL, Sicotte NL. Microglia in Multiple Sclerosis: Friend or Foe? Front Immunol. 2020;11:374. Epub 20200320. doi: 10.3389/fimmu.2020.00374. PubMed PMID: 32265902; PubMed Central PMCID: PMCPMC7098953.
5. Siokas V, Tsouris Z, Aloizou AM, Bakirtzis C, Liampas I, Koutsis G, Anagnostouli M, Bogdanos DP, Grigoriadis N, Hadjigeorgiou GM, Dardiotis E. Multiple Sclerosis: Shall We Target CD33? Genes (Basel). 2020;11(11). Epub 20201112. doi: 10.3390/genes11111334. PubMed PMID: 33198164; PubMed Central PMCID: PMCPMC7696272.
6. Sawcer S, Franklin RJ, Ban M. Multiple sclerosis genetics. Lancet Neurol. 2014;13(7):700-9. Epub 20140519. doi: 10.1016/s1474-4422(14)70041-9. PubMed PMID: 24852507.
7. Siokas V, Katsiardanis K, Aloizou A-M, Bakirtzis C, Liampas I, Koutlas E, Rudolf J, Ntinoulis K, Kountouras J, Dardiotis E, Deretzi G. Impact of Body Mass Index on the Age of Relapsing-Remitting Multiple Sclerosis Onset: A Retrospective Study. Neurol Int. 2021;13(4):517-26. doi: 10.3390/neurolint13040051. PubMed PMID: 34698268.
8. Olsson T, Barcellos LF, Alfredsson L. Interactions between genetic, lifestyle and environmental risk factors for multiple sclerosis. Nat Rev Neurol. 2017;13(1):25-36. Epub 20161209. doi: 10.1038/nrneurol.2016.187. PubMed PMID: 27934854.
9. Boziki MK, Kesidou E, Theotokis P, Mentis A-FA, Karafoulidou E, Melnikov M, Sviridova A, Rogovski V, Boyko A, Grigoriadis N. Microbiome in Multiple Sclerosis; Where Are We, What We Know and Do Not Know. Brain Sci. 2020;10(4):234. doi: 10.3390/brainsci10040234. PubMed PMID: 32295236.
10. Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. Cell. 2014;157(1):121-41. doi: 10.1016/j.cell.2014.03.011. PubMed PMID: 24679531.
11. Browning KN, Travagli RA. Central nervous system control of gastrointestinal motility and secretion and modulation of gastrointestinal functions. Compr Physiol. 2014;4(4):1339-68. doi: 10.1002/cphy.c130055. PubMed PMID: 25428846; PubMed Central PMCID: PMCPMC4858318.

12. Zouali M. B lymphocytes, the gastrointestinal tract and autoimmunity. Autoimmun Rev. 2021;20(4):102777. Epub 20210217. doi: 10.1016/j.autrev.2021.102777. PubMed PMID: 33609796.
13. Rutsch A, Kantsjö JB, Ronchi F. The Gut-Brain Axis: How Microbiota and Host Inflammasome Influence Brain Physiology and Pathology. Front Immunol. 2020;11:604179. Epub 20201210. doi: 10.3389/fimmu.2020.604179. PubMed PMID: 33362788; PubMed Central PMCID: PMCPMC7758428.
14. Metz LM, Li DKB, Traboulsee AL, Duquette P, Eliasziw M, Cerchiaro G, Greenfield J, Riddehough A, Yeung M, Kremenchutzky M, Vorobeychik G, Freedman MS, Bhan V, Blevins G, Marriott JJ, Grand'Maison F, Lee L, Thibault M, Hill MD, Yong VW. Trial of Minocycline in a Clinically Isolated Syndrome of Multiple Sclerosis. N Engl J Med. 2017;376(22):2122-33. doi: 10.1056/NEJMoa1608889. PubMed PMID: 28564557.
15. Bogdanos DP, Sakkas LI. From microbiome to infectome in autoimmunity. Curr Opin Rheumatol. 2017;29(4):369-73. doi: 10.1097/bor.0000000000000394. PubMed PMID: 28394824.
16. Sakkas LI, Bogdanos DP. Multiple hit infection and autoimmunity: the dysbiotic microbiota-ACPA connection in rheumatoid arthritis. Curr Opin Rheumatol. 2018;30(4):403-9. doi: 10.1097/bor.0000000000000503. PubMed PMID: 29538012.
17. Hosang L, Canals RC, van der Flier FJ, Hollensteiner J, Daniel R, Flügel A, Odoardi F. The lung microbiome regulates brain autoimmunity. Nature. 2022;603(7899):138-44. doi: 10.1038/s41586-022-04427-4.
18. O'Dwyer DN, Dickson RP, Moore BB. The Lung Microbiome, Immunity, and the Pathogenesis of Chronic Lung Disease. J Immunol. 2016;196(12):4839-47. doi: 10.4049/jimmunol.1600279. PubMed PMID: 27260767.
19. Chioma OS, Hesse LE, Chapman A, Drake WP. Role of the Microbiome in Interstitial Lung Diseases. Front Med (Lausanne). 2021;8:595522-. doi: 10.3389/fmed.2021.595522. PubMed PMID: 33604346.
20. Scher JU, Joshua V, Artacho A, Abdollahi-Roodsaz S, Öckinger J, Kullberg S, Sköld M, Eklund A, Grunewald J, Clemente JC, Ubeda C, Segal LN, Catrina AI. The lung microbiota in early rheumatoid arthritis and autoimmunity. Microbiome. 2016;4(1):60-. doi: 10.1186/s40168-016-0206-x. PubMed PMID: 27855721.
21. Moffatt MF, Cookson WO. The lung microbiome in health and disease. Clin Med (Lond). 2017;17(6):525-9. doi: 10.7861/clinmedicine.17-6-525. PubMed PMID: 29196353.
22. Man WH, de Steenhuijsen Piters WAA, Bogaert D. The microbiota of the respiratory tract: gatekeeper to respiratory health. Nature Reviews Microbiology. 2017;15(5):259-70. doi: 10.1038/nrmicro.2017.14.

AUTHORS CONTRIBUTION

VS conceptualized and wrote the manuscript.

CONFLICT OF INTEREST

The author declares no conflict of interest.