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Alterations in gut microbiome are associated with the onset of multiple sclerosis: an Italian pivotal study

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Background: The gut microbiome consists of a highly diverse ecologic community of microorganisms and plays an important role in immune functions: commensal bacteria are indeed necessary for the development and maintenance of a healthy immune system. Imbalance in the gut microbiota composition has been suggested as a risk factor for Multiple Sclerosis (MS): animal studies demonstrated that alteration of the gut microbiota could effectively modulate the immune-mediated demyelination through the generation of encephalitogenic T-helper (Th)17 cells or protective T-regulatory (Treg) cells in the gut followed by their transmigration in the periphery and in the central nervous system.

Aims: we investigated whether alteration in the composition of the gut microbiota, in terms of species richness, distribution and functional potential, could be associated with the onset of MS, namely the first episode of demyelination, and its immune system alteration in a small Italian cohort.

Methods: Stool and blood samples were collected from 18 newly diagnosed MS patients and 18 Healthy Volunteers (HV) highly matched for age, sex, diet and lifestyle. DNA isolated from stools were subjected to shotgun metagenomic sequencing strategy in order to discover the microbiota composition as well as the microbial function and to correlate it with fecal metabolites, analyzed with Gas chromatography-mass spectrometry, and with Th17 and Treg cells, analyzed by FACS, in the peripheral blood (PB).

Results: At the onset of MS, gut microbiome structure of patients is clearly different from that of HV and displayed a lower species richness and lower number of taxa. It was characterized by a reduction in abundance of genera belonging to Butyrate-producing bacteria that correlated with a lower butyrate amount in the feces and with the decrease of Treg cells producing IL-10 in the PB of MS patients compared to HV.

Conclusions: our data indicate that gut microbial dysbiosis exist at the onset of MS and could be associated with the autoimmune response in the periphery, highlighting the importance of gut microbiome in the etiology of MS.

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