current trials mainly focus on the peripheral immune response and studies with imaging outcomes are awaited. The question of whether correcting dysbiosis could promote remyelination in MS has not been studied directly, but this seems far-fetched in the context of the evidence to date.

As the literature linking the microbiota to host physiology has expanded in recent years, 'correcting gut dysbiosis' is sometimes touted as a panacea among academics and the public alike. However, as with any biological system, there will be limits to what the microbiota can achieve. While the idea is enticing, the promotion of remyelination for patients with MS most likely lies beyond these limits.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Multiple Sclerosis Journal
2021, Vol. 27(8) 1164–1165
DOI: 10.1177/13524585211018990

Correcting gut dysbiosis can ameliorate inflammation and promote remyelination in multiple sclerosis – Commentary

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Basic research has uncovered surprising connections between the gut microbiota and essential functions of the body. These exciting findings offer fascinating perspectives for the treatment of human diseases. Clinical application, however, lags behind the progress made in basic understanding of the microbiota. This sobering fact provides the background for the current controversy.

Laura Calvo-Barreiro and colleagues argue that therapeutic modulation of the microbiota can not only regulate peripheral immune responses but also induce

remyelination and neuroprotection.[1] This optimistic view is supported by proponents' studies in animal models.[2,3] By contrast, Christopher McMurran points out that remedying dysbiosis can improve inflammation but not demyelination in animal models.[4] His more sceptical view is based on his observation that modulation of the microbiota had only minimal impact on remyelination in toxic-induced (lysolecithin or cuprizone) mouse models.[5]

Taken together, there is convincing evidence that modulation of the microbiota can ameliorate (experimental) autoimmune responses. There is also firm evidence that the microbiota regulates neurobiological and microglial functions via the 'gut–brain axis'.[6] It is less clear, however, whether the microbiota has a direct influence on myelination.

What are the most urgent challenges for *human* microbiota research to push the field towards clinical translation? First, the number of studied subjects needs to be drastically increased. Many published studies indicate that in multiple sclerosis (MS) there is indeed a 'dysbiosis' of the commensal microbiota.[7] However, most of these studies were based on relatively small cohorts lacking rigorous controls. In this regard, the international MS Microbiome Study (iMSMS) takes a big step forward by aiming to collect a very large number of samples from people with MS. Household members serve as controls.[8] This large study should help to characterize the currently somewhat vaguely described state of 'dysbiosis'. Second, in order to identify disease-relevant microbes, it is essential that candidate bacteria are tested for their *functional* disease-promoting capacity. This can be achieved, for example, with gnotobiotic mouse models: colonization of genetically engineered autoimmune-prone, germ-free mice with human-derived microbiota helps to distinguish between disease-promoting and protective bacteria.[9,10] Identification of an MS-relevant microbial signature should open new doors for rational therapy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

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