

How to improve multiple sclerosis therapy

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Medications currently used to treat multiple sclerosis (MS) can merely reduce relapses during the initial relapsing-remitting phase. Many patients, however, develop progressive MS at a later stage, with disability becoming progressively worse. This type cannot be sufficiently treated at yet. Possible causes why an effective therapy for progressive MS is still lacking have been compiled by an international research team in a review article in the journal *Nature Reviews Drugs Discovery* from 9 August 2019.

For the purpose of the study, Bochum-based medical practitioners Professor Simon Faissner and Professor Ralf Gold from the Department of Neurology at St. Josef-Hospital, University Hospital at Ruhr-Universität Bochum, collaborated with Professor V. Wee Yong from the University of Calgary and Professor Jason Plemel from the University of Alberta in Edmonton. In their article, they discuss the mechanisms underlying progressive MS as well as data regarding potential therapy approaches collated in lab experiments and clinical trials. In the process, the authors link the discussion of therapy targets with results from pharmacological studies conducted with cell culture and animal models, as well as current clinical studies.

One disease, numerous mechanisms

"A bottom line of our analysis is that the reason why it is so difficult to treat progressive MS is the fact that progression is caused by various mechanisms," says Simon Faissner. "In order to provide more efficient treatment, we will probably need precise therapy approaches targeting



various pathomechanisms." According to the authors, another problem is the fact that the full range of underlying mechanisms is not represented in any of the existing animal models. "Therefore, identifying potential therapeutic agents for a clinical study poses a considerable challenge," says Faissner.

Moreover, clinical studies to date have frequently followed different objectives, which means that the definition of what constitutes therapeutic success varied from study to study. The authors state that consistent criteria should ideally be implemented in order to render the studies comparable and to verify reliable treatment effects.

There are also financial aspects that impede the development of new drugs. There is evidence that drugs approved for another indication may also prove effective against multiple sclerosis. "But as patents for such medication have expired, pharmaceutical companies can't further develop them," explains Simon Faissner. "The implementation of studies to test the efficacy of those drugs for MS often fails due to a lack of funds."

Nevertheless, the authors conclude that the treatment of patients suffering from progressive MS will improve, as researchers gain a better and more detailed understanding of the underlying disease mechanisms. "These findings will enable us to introduce a more targeted therapy that will prevent patients from suffering more severe impairments as the disease progresses," predicts Faissner.

About Multiple sclerosis

Multiple sclerosis is a chronic inflammatory disease of the central nervous system, which manifests as relapsing-remitting MS in approximately 85 percent of the patients. In the western world, it is the main cause of neurological disabilities in young people. The early stage



of the disease is characterised by relapses with neurological symptoms such as optic neuritis, impairment of the motor function, and sensitivity impairments; today, more than twelve approved drugs exist that can be used to treat this type fairly effectively.

Despite <u>effective therapy</u>, the so-called secondary-chronic progressive MS emerges in the majority of patients after approximately 15 to 20 years, characterised by a scarcity of relapses and by progressive accumulation of disability. 10 to 15 percent of the patients present with a primary progressive disease course at initial diagnosis. Today, new drugs for the progressive types of MS are available, such as Ocrelizumab and Siponimod. However, the therapy effects are as yet limited.

More information: Simon Faissner et al. Progressive multiple sclerosis: from pathophysiology to therapeutic strategies, *Nature Reviews Drug Discovery* (2019). DOI: 10.1038/s41573-019-0035-2

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