MULTIPLE SCLEROSIS

Neurophysiological and olfactory biomarkers for multiple sclerosis

slowing of neuronal activity, as measured by resting-state MEG, correlated with cognitive impairment

Magnetoencephalography (MEG) measurements and olfactory biomarkers can provide insights into brain function and disease activity in multiple sclerosis (MS), according to two new papers published in *Multiple Sclerosis Journal*. In the first study, Deborah Schoonhoven and colleagues showed that slowing of neuronal activity, as measured by resting-state MEG, correlated with cognitive impairment in patients with MS. In the second study, Gabriel Bsteh and co-workers found that inflammation and neurodegeneration in MS were associated with specific impairments in olfactory function.

“Cognitive disturbances are present in an estimated 43–70% of patients with MS, but are often poorly understood,” comments Schoonhoven. “We believe that the search for objective measures of cognitive impairment in MS is important, since a wide variety of factors, including fatigue, mood disorders, anxiety and cognitive impairment, can lead to cognitive complaints.”

The study by Schoonhoven et al. included 83 patients with MS and 34 healthy controls. The participants underwent resting-state MEG, as well

as a battery of neuropsychological tests that enabled the patients with MS to be differentiated into three subgroups: cognitively preserved, mildly cognitively impaired and cognitively impaired (CI).

Compared with the other MS subgroups and the healthy controls, the CI group showed slowing of neuronal activity in parietotemporal cortical regions and the thalamus. “We provided strong evidence that global oscillatory slowing in CI patients takes place not only at a cortical level, but also in deeper structures such as the thalamus,” says Schoonhoven. MRI scans revealed that this slowing was associated with thalamic atrophy, which has previously been linked to cognitive decline in patients with MS.

For their study on olfactory biomarkers, Bsteh and colleagues recruited 260 patients with MS. Inflammatory activity was determined by the number of relapses in the preceding year, and measures of neurodegeneration included disability scores and peripapillary retinal nerve fibre layer (pRNFL) thickness. Using the Sniffin’ Sticks test, the researchers assessed three aspects of olfactory function: odour identification, odour discrimination and odour detection threshold.

“Previous studies from our group have shown that the detection threshold is impaired in early, active MS, whereas identification and discrimination are predominantly affected in progressive and more advanced MS,” explains Bsteh. “It was suggested that the detection threshold reflects inflammatory activity, while impairment of identification and discrimination

reflects neurodegeneration; however, the validity of this concept was questioned by the small sample sizes of the studies.”

Consistent with the earlier findings, Bsteh et al. found that the odour detection threshold correlated with the number of relapses, whereas reductions in the ability to identify and discriminate odours were associated with increased disability and pRNFL thinning. These observations reinforce the idea that different aspects of olfactory dysfunction reflect distinct disease processes in MS. “The next step in our research will be the evaluation of threshold, discrimination and identification capacity as biomarkers for quantifying or even predicting relapses and disability progression in MS,” says Bsteh.

Similarly, Schoonhoven and colleagues plan to explore the predictive value of resting-state MEG measurements in patients with MS. “We hope that in the future, we are able to use this simple, noninvasive method as a diagnostic and prognostic tool to improve the evaluation of the cognitive problems that many patients with MS experience on a daily basis,” Schoonhoven concludes.

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ORIGINAL ARTICLE Schoonhoven, D. N. et al. Resting-state MEG measurement of functional activation as a biomarker for cognitive decline in MS. *Mult. Scler.* <https://doi.org/10.1177/1352458518810260> (2018) | Bsteh, G. et al. Smelling multiple sclerosis: different qualities of olfactory function reflect either inflammatory activity or neurodegeneration. *Mult. Scler.* <https://doi.org/10.1177/1352458518814113> (2018)

FURTHER READING Bsteh, G. et al. Change of olfactory function as a marker of inflammatory activity and disability progression in MS. *Mult. Scler.* <https://doi.org/10.1177/1352458517745724> (2017)