Evidence lacking for drug treatment of multiple sclerosis-related cognitive impairment

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Dr, Genova is assistant director of the Center for Neuropsychology and Neuroscience Research at Kessler Foundation. She specializes in the study of social cognition in populations with neurological conditions, including multiple sclerosis, brain injury, and autism. Credit: Kessler Foundation

Researchers at Kessler Foundation conducted a comprehensive review of pharmacologic agents used in the treatment of multiple sclerosis, seeking evidence for efficacy for the cognitive dysfunction experienced by more than half of affected individuals. The article, "Cognitive efficacy of pharmacologic treatments in multiple sclerosis: A systematic review," was published open access in *CNS Drugs* 2020 May 02. The authors are Michelle H. Chen, Ph.D., Helen Genova, Ph.D., and John DeLuca, Ph.D., of Kessler Foundation. Yael Goverover, Ph.D., of New York University, is a visiting scientist at Kessler Foundation.

Researchers identified 87 articles, using the PubMed and PsycINFO databases and the 2017 American Academy of Neurology (AAN) criteria for therapeutic trials. Standardized effect sizes were calculated for comparison across trials.

Agents from the following therapeutic categories were represented: Disease-modifying therapies (DMTs) (interferon B-1a, B1b, glatiramer acetate, natalizumab, fingolimod); Symptomatic therapies (dalfampridine; cognition enhancers: rivastigmine, Gingko biloba, donepezil; Stimulants: modafinil, armodafinil, methylphenidate, amphetamine sulfate, amantadine); and 'Other' therapies that were neither DMTs nor stimulants (eg, estrogen, methylprednisolone, simvastatin, human erythropoietin).

Review of the studies of DMTs failed to support effectiveness for treating cognitive deficits, with a majority of class III and IV evidence. "We found no class I evidence, and class II evidence was minimal to none," said Dr. Chen, postdoctoral fellow in the Center for Neuropsychology and Neuroscience Research at Kessler Foundation.

Although most of the studies of symptomatic therapies were randomized controlled trials with primary cognitive outcomes (i.e., higher quality evidence), there were contradictory findings, resulting in inconclusive

evidence for the cognitive efficacy of symptomatic therapies. For studies involving 'other' agents, there was again insufficient evidence to support their use to treat cognitive problems.

In summary, there was insufficient evidence for cognitive efficacy across the spectrum of pharmacologic agents used in the treatment of multiple sclerosis. "Given the impact of cognitive dysfunction on individuals with MS, it is prudent to explore the potential for cognitive efficacy of available pharmaceuticals," explained Dr. Genova, director of the Center for Neuropsychology and Neuroscience Research. The design of future studies, especially of DMTs, must focus on cognitive outcomes and follow standardized criteria such as the AAN's," she said in conclusion. "Randomized, controlled studies with cognition as the primary outcomes will provide clinicians with the information they need to choose optimal treatments for patients."

More information: Michelle H. Chen et al. Cognitive Efficacy of Pharmacologic Treatments in Multiple Sclerosis: A Systematic Review, *CNS Drugs* (2020). DOI: 10.1007/s40263-020-00734-4

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