

Accelerated Cure Project for MS

March 2019



MS and Your Mind

When people think about MS, they may not associate it with cognitive difficulties, even though up to 65 percent of people with MS struggle with their thought processes at some point in the course of the disease. Some notice problems with their memory, particularly finding words or remembering events from the past. Others find they have trouble doing more than one thing at a time (multitasking), or they take longer to process information. Some people find they have problems learning new tasks, while others may struggle with organization, planning or prioritizing. For many, the cognitive effects of the MS represent its greatest challenges.



The medical term used to describe this loss of mental function is [cognitive impairment](#). While cognitive changes are more common later in the course of the disease, they can occur at any time (even as the first symptom of MS) and can vary considerably from person to person. Like the physical symptoms of MS, cognitive changes are likely to progress over time. They may worsen during an exacerbation and then improve afterwards. However, once changes in mental function occur, they rarely disappear completely. Overt [dementia](#) in MS is rare. Often a few specific abilities are affected while others are spared. Interestingly, cognitive functions that are generally preserved in MS include general intellect, long-term memory, conversational skills, and reading comprehension. The severity and frequency of cognitive symptoms may fluctuate, ranging from intermittent episodes to more pervasive changes, which can significantly impact a person's daily life. The degree of cognitive dysfunction does not appear to be related to the amount of physical disability a person with MS may have. Individuals with little

or no physical impairment can experience significant cognitive changes while those with severe physical disability may have very little or no cognitive impairment.



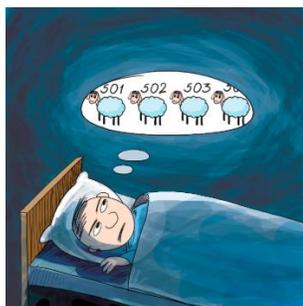
Cognitive dysfunction substantially impacts the lives of those with MS and their families, in some cases enough to interfere with work. [Studies](#) show half to three-quarters of people with MS are unemployed within 10 years of diagnosis and cognitive impairment is one of the leading causes of unemployment. Those with impaired cognition tend to participate in social activities less frequently and isolation is not uncommon. Cognitive dysfunction may also place significant additional strain on an individual's caregiver, who must help their loved one deal with its ramifications. In very rare instances, cognitive dysfunction may become so severe that the person with MS can no longer function independently.

Cognitive dysfunction in MS is primarily the result of changes in the brain due to progressive damage to the protective coating of nerve cells (called the myelin sheath) and the formation of lesions throughout parts of the central nervous system. Research is ongoing to identify the specific areas of the brain that may play a role in cognitive impairment with MS. The hope is that through such studies, treatments may eventually be designed to target these areas and minimize or prevent any effects that MS may have on mental function. In addition, the disease can cause atrophy, or shrinkage, in certain parts of the brain and spinal cord. [Some studies](#) suggest brain atrophy contributes to cognitive impairment. Because MS can affect any part of the brain, almost any cognitive function can be impaired.



Cognitive changes in MS are measured in a variety of ways. A full [neuropsychological evaluation](#), which involves multiple tests to measure memory, attention and many other parts of cognition, provides the most comprehensive information about the kinds of problems with thinking that may exist and whether they may be due to MS or some other complicating factor. Neuroimaging (MRI scanning) is frequently used to determine what specific areas of the brain may be affected and causing cognitive problems. In general, cognitive function correlates with the number of lesions on MRI, as well as the degree of brain atrophy. Research studies often use a test called the [Paced Auditory Serial Addition Test](#) (PASAT) to assess cognitive function, specifically auditory information processing speed and flexibility, as well as calculation ability. Single numbers are presented via an audio recording every two or three seconds and the person must add each new digit to the one immediately prior to it. The score for the PASAT is the total number correct out of 60 possible answers. Another commonly used assessment in research is the [Symbol Digit Modalities Test](#) (SDMT). Participants in this test are given a reference key that they must use to help them associate numbers to a series of geometric shapes. The SDMT is scored based on the number of correct substitutions within a 90 second period. For both tests, higher scores indicate less cognitive dysfunction.

Although there is no way to predict whether or not an individual will develop MS-related cognitive impairment, there are a number of risk factors involved. [Research](#) shows that people with progressive forms of MS experience more cognitive decline than those with relapsing remitting MS (RRMS). Earlier onset of MS increases one's chance of developing MS-related cognitive decline. Race also plays a role in the impact of MS on cognition. African-American patients with MS develop cognitive deficits earlier in the disease course compared to Caucasian patients. However, African Americans also tend to have a more aggressive disease course and the cognitive findings may be a result of that. [Studies](#) show gender is another risk factor for cognitive impairment in MS, with the incidence and severity of cognitive deficits being higher in men than women. Intelligence and education also play a role in the likelihood of cognitive decline not only in people with MS, but in the general population. According to the [cognitive reserve theory](#), the more you use your brain, the greater your chances of avoiding symptoms of cognitive impairment. A [study](#) following patients with MS over a five-year period showed that those with a high cognitive reserve at baseline experienced no loss of cognitive function, while those who started with a low cognitive reserve suffered significant cognitive decline.



There are many factors that can interfere with thinking and, as a result, may further impair mental processes. In cases like this, cognitive function may improve with treatment of the underlying exacerbating factor. In general, those who drink alcohol excessively or who use drugs may have altered thinking. People with sleep disorders may experience cognitive problems related to sleep deprivation. Individuals with some medical conditions, such as low thyroid, may also have problems with memory. A [recent study](#) reported heavy smokers with MS have increased cognitive impairment when compared to nonsmokers. [Research](#) has also

revealed a significant association between depression in MS and cognitive dysfunction. In addition, many medications used to treat MS and its symptoms can cause problems with thinking, such as steroids, muscle relaxants and some antidepressants (to name a few). It's important to discuss your medications with your healthcare team to see if one or more of them could be causing cognitive problems and, if so, to see if they can be reduced or stopped, or if there are alternative treatments that can be used.

Researchers are working to identify treatments that may stabilize, or improve, cognitive dysfunction in MS. A number of commonly used MS disease modifying medications are thought to be of benefit. A [2012 study](#) showed that early treatment with Betaseron provides sustained benefit with regards to mental function in MS. A [2014 study](#) showed Avonex and Rebif are also helpful in this regard. A [study](#) published in 2018 showed individuals treated with Tysabri (natalizumab) demonstrated significant improvement in mental function over 2 years of treatment. [Italian researchers](#) reported the same benefit from Tysabri treatment over a 3-year period. Other agents have also been evaluated for their ability to treat cognitive impairment in MS. [One study](#) recently evaluated four drugs (ginkgo biloba, donepezil, rivastigmine, and memantine) in people with MS in large-scale, double blind, placebo-controlled clinical studies. Unfortunately, none of these compounds demonstrated beneficial, reproducible improvements in mental function.



[Cognitive rehabilitation therapy](#) is the process of relearning cognitive skills that have been lost or altered as a result of damage to the brain. This type of treatment centers on the concept that practicing a specific cognitive task strengthens the communication between neurons required for that task. If skills cannot be relearned, then new ones have to be taught to enable the person to compensate for their lost cognitive function.

Results from trials focusing on cognitive rehabilitation in MS are mixed. A [recent study](#) showed that, while cognitive rehabilitation therapy may not be of direct benefit, it does help alleviate fatigue in people with MS and this may, in turn, help improve cognitive function.

There is evidence that physical activity may improve cognitive function in people with MS. A [2010 study](#) shows yoga may reduce fatigue and improve attention in people with MS. [Data](#) presented at the 2016 [ACTRIMS Forum](#) suggest that treadmill walking has beneficial effects on inhibitory control (the ability to focus on relevant stimuli and ignore irrelevant ones) in people with MS who can walk.



Other [research](#) indicates physical activity may improve cognitive processing speed, but not learning and memory. While definite conclusions cannot be drawn from these studies, the positive association between physical activity and cognitive function suggests that exercise might be an effective non-drug treatment for cognitive impairment in MS.

While cognitive difficulties may be challenging at times, there are many strategies that may help. However, it's important to note that those struggling with cognitive difficulties should first consult with their physician. Mental or emotional changes may be symptoms of depression, which is not only common in people with MS, but may be easily treated. A [2010 study](#) found that people with MS are unlikely to use coping strategies. Instead, many avoid situations in which their cognitive impairment might be evident or obvious to others. It's important to have a [support system](#) in place, rather than coping alone. Sharing these concerns with others may offer reassurance to those living with MS that they are not alone in their experiences. There are also a number of preventive measures that may be helpful. The brain benefits from mental exercise in the same way the body benefits from physical exercise. The more individuals challenge their brain with things like mental math, memory games or puzzles, the more likely they are to retain [certain mental functions](#). Getting enough sleep is also crucial to optimize mental functioning. Avoiding mental stimulation before bedtime and maintaining the same sleep schedule every day may be helpful. Some people with MS find that planning their day so the most challenging tasks are at a time of day when they feel sharpest to be of benefit. Those having difficulty concentrating may also find it helpful to take a break and refresh before continuing in their task.



One of the best methods for improving memory is to take notes wherever and whenever information needs to be recalled. Keeping notes organized in a central place, along with other important things like bills and other mail, keys, purses/wallets or shopping lists may be helpful. Using things like calendars, checklists and alarms for reminders about things like taking medications or appointments may also be of benefit.

Many find repeating what they hear and verifying it is correct, or repeating the information at intervals spread out over time will improve their ability to remember it. Others build associations to help their memory.

Combining different modes of learning to reinforce the same information may also help with information retrieval. In other words, an individual may be more likely to remember something if they “see it, say it, hear it, write it, and do it.”

An important strategy for improving attention is to reduce or eliminate distractions. Sometimes people have thoughts that interfere with attention to the matter at hand. With this type of distraction, a good plan is to write down any ideas that might be monopolizing one’s thoughts and try to set them aside to focus on at a later time. Many find doing one thing at a time is helpful in keeping their attention on the task at hand. Avoid switching back and forth from one topic or task to another.



MS is a complex disease with many psychological aspects. It is important for people living with MS to understand and address these changes along with the physical ones. Cognitive changes can have a significant impact on a person’s ability to work and fulfill family responsibilities. Family members may not realize that MS can cause cognitive problems and this misunderstanding can result in stress and hard feelings. Research is ongoing to understand the underlying mechanisms and causes of cognitive decline in MS in hopes of discovering new therapeutic targets. In the meantime, employing a number of strategies to increase attention and memory can help people with MS and their families minimize its effect in their day-to-day lives.