

## Cognitive Function in MS



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## INFOCORNER



### What is NARCOMS?

NARCOMS is a registry for people who have multiple sclerosis (MS). Registry participants complete two surveys each year to provide information about themselves and their experience of having MS. Data from these surveys are used in research studies and to help further our understanding of MS. Participation in the registry is voluntary, and responders' identity and privacy are carefully secured.



### What is the Goal of NARCOMS?

The NARCOMS Global MS Patient Registry helps to facilitate research about multiple sclerosis in North America and around the world. Collaboration between MS centers of excellence throughout the world helps to increase knowledge, improve clinical care, and enhance the quality of life for persons with MS.



### How Private Is My Information?

We will keep the information that you provide us private and confidential by storing your data in a secure database. All information will be used for research purposes only. We do not share any personally identifying information with any person or research institution. We follow all Federal (HIPAA) laws regarding confidentiality.



### Not Yet a NARCOMS Participant?

Please contact us at [www.NARCOMS.org](http://www.NARCOMS.org) to enroll online, or call toll free at 1-800-253-7884.



### Tell Us Your Thoughts!

**Have an idea? We would love to hear from you!**  
Send us your questions, comments, and suggestions.

**Call:** 1-800-253-7884 (toll-free U.S.)

**Email:** [MSRegistry@narcoms.org](mailto:MSRegistry@narcoms.org)

**Online:** [www.narcoms.org/contact-us](http://www.narcoms.org/contact-us)

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For more information on the CMSC visit [www.ms-care.org](http://www.ms-care.org).

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# DIRECTOR'S LETTER

Dear NARCOMS Now Readers:

Cognition refers to how we think, identify knowledge and understand it. People with MS often report problems with cognition. As with so many other things - the more you know about it, the easier it becomes to address it.

Let's get started.

Although the general public tends to associate forgetfulness and other cognitive issues with older age, it is important to realize that problems with cognitive functioning can occur at any age – whether you have MS or not. Overall health and well-being, properly managed medications and healthy lifestyle choices in terms of sleep, diet, physical activity and moderating alcohol consumption, can all play a role. With MS these potentially modifiable factors become all the more important.

In this issue of NARCOMS Now, Professor Anthony Feinstein discusses the typical symptoms of cognitive dysfunction in MS and provides insight into the latest approaches to cognitive rehabilitation. The MS News section provides recent findings from cognitive research studies and the Snapshot offers a brief summary of the responses from you and your fellow registry participants. Thank you very much for assisting in MS research by participating in the NARCOMS registry!



Robert Fox, MD

Sincerely,

A handwritten signature in black ink that reads 'Robert J. Fox'.

Robert Fox, MD

Managing Director, NARCOMS





## Cognitive Function in MS

**M**ultiple Sclerosis (MS) is the most common non-traumatic cause of neurological disability in young and middle-age adults. MS affects balance, vision, strength and coordination. These symptoms are often quite visible. However, some symptoms are invisible and may be even more disabling. Examples include pain, fatigue, depression and cognitive dysfunction.

### **Prevalence and nature of symptoms**

Cognition refers to how we think, identify knowledge and understand it. Cognitive difficulties affect between 40 and 70%



of people with MS. Individuals with progressive MS are more likely to have cognitive problems than individuals with relapsing-remitting MS. Problems with thinking and memory can start early in the disease. These problems may worsen over time interfering with day-to-day functioning.



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The typical cognitive abnormalities that occur in people with MS are a decrease in processing speed, impairments in working memory and learning and deficits in executive functions.

**Processing speed** refers to the time it takes to do a mental task. **Executive function** refers to a person's ability to plan and execute solutions to problems while remaining flexible in terms of the decision-making processes. Of all these cognitive challenges, it is the slowing of information processing speed that is considered the cardinal cognitive difficulty linked to MS.

### **Assessment**

Processing speed can be assessed in many ways. Researchers who study cognitive function in MS agree that the **Symbol Digit**

“Of all these cognitive challenges, it is the **slowing of information processing speed** that is considered the cardinal cognitive difficulty linked to MS.”

**Modalities Test (SDMT)** is the best method. The SDMT is a sensitive way of detecting problems. The test is short, can be done easily in individuals who are experiencing fatigue and it is not anxiety-provoking. Given the usefulness of this particular test, several versions of the original test are being used in MS research.

The original SDMT was conducted in-person and administered by a tester. Newer versions of the SDMT can be self-administered with an iPad or through voice recognition on a computer. Studies show that these self-administered versions of the SDMT work as well as the original tester-driven method for assessing information processing speed in people with MS. Indeed, some data suggest that people with MS prefer the computerized administration.

“One of the challenges of cognitive testing is to ensure that the data collected has **real world meaning**.”

One of the challenges of cognitive testing is to ensure that the data collected have real world meaning. Until now, neuropsychological



(cognitive) testing has taken place in an office with a sign outside the door asking passersby to be quiet. As such, an environment free of distraction is created for the cognitive assessment. There is now a movement underway to change this by making the testing environment more reflective of the situations confronted by people with MS in the real world. Introducing cognitive testing into a person’s home is one way to do this. It is one of the reasons why voice recognition, computer administered tests like the SDMT have been developed.

### **Managing cognitive symptoms**

Assessing cognition is the first step in determining whether an individual with MS has cognitive deficits. If the testing reveals the presence of deficits then attention turns to treatment. Treatment can take various forms. The most widely available approach is to introduce *cognitive compensatory strategies*. This refers to helping people with MS learn certain techniques that allow them to work around their cognitive problems to reduce their impact. For example, if a person



has memory difficulties then one of the compensatory strategies is to make lists or to use electronic reminders on a smart phone or tablet.

In addition to cognitive compensatory strategies there is now an emerging literature that speaks to the potential benefits of cognitive rehabilitation. Currently, this particular intervention is only available within clinics and rehabilitation centers. Here the aim is to see whether one can bring about an improvement in a person's cognitive difficulties. Much research still needs to be done to determine exactly how such an intervention works and the degree to which it can bring about clinically meaningful change. It has taken many years of research and

**“...there is now an emerging literature that speaks to the potential benefits of *cognitive rehabilitation*.”**

advocacy for the medical profession to understand the importance of cognitive difficulties in a disease like MS. Individuals with cognitive impairment have greater difficulty finding work, sustaining work, managing relationships, pursuing leisure activities and enjoying a good quality of life. Therefore it is imperative that researchers and clinicians work together to make testing for cognitive impairment readily accessible. Technology may help to achieve this goal, and could support evaluation of treatments in the future.

**WOULD YOU LIKE TO READ MORE ON THIS TOPIC?  
HERE'S A LIST OF ONLINE RESOURCES:**

<https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms/Cognitive-Changes>

[https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Managing-Cognitive-Problems\\_1.pdf](https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Managing-Cognitive-Problems_1.pdf)

<https://www.nationalmssociety.org/Living-Well-With-MS/Cognitive-Health>





# MS MESSENGER

WHAT TO EXPECT ON THE NEXT NARCOMS SURVEY

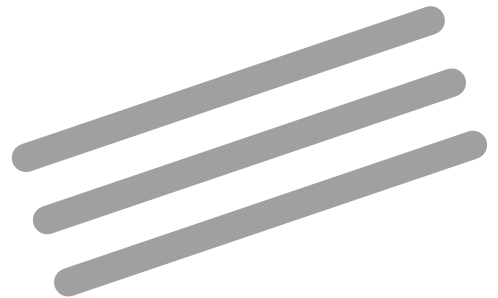
Cheerful summer greetings from all of us at NARCOMS! The spring update survey was closed in June and we are entering the remaining paper responses into the data base. We have a minor request. Please do not include your return address or a sticker on the outside envelope. We are required to remove all identifying information before discarding the envelope. Cutting out thousands of stickers slows down the processing quite a bit. Our own return address code is already embedded in the business reply envelopes we use, so there really is no need to add a sticker – although some of them are very pretty. :)

Special thanks to those of you who stopped by the NARCOMS booth at the CMSC annual meeting in Seattle or participated in the educational event afterwards. Michele really enjoyed chatting with you and we hope to meet many more participants at the Orlando meeting next year! More on that later in the year – please stay tuned.



We have many new projects coming up this summer and fall. One of them involves testing out a tool that measures cognition, the auto-SDMT (**S**ymbol **D**igit **M**odality **T**est) and takes about 10 minutes to complete. We plan to start with a small group trying out this on-line tool and will expand later to include more registry participants interested in helping out with the project.

Thank you for your continued participation in the NARCOMS registry and your enthusiasm in assisting MS research!





## **The Relationship Between Physical Activity and Symptoms of Fatigue, Mood, and Perceived Cognitive Impairment in Adults with Multiple Sclerosis**

Researchers in Canada looked for low-cost behavioral treatments that would be effective in reducing MS symptoms, such as fatigue, depression and perceived cognitive impairment. They focused on physical activity which has been proposed as a potential way to slow the neurodegenerative progression of MS. The research group analyzed responses from 86 people who returned a set of validated questionnaires.

They found that engaging in higher levels of leisure time physical activity was associated with less fatigue and depression. More physical activity was also associated with better memory, although not with the total cognitive score. The overall pattern was similar for RRMS and progressive subtypes of MS, although the effect was not as strong in the progressive MS group.

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Reference: J Clin Exp Neuropsychol. 2019 May 16;1-8. doi: 10.1080/13803395.2019.1614535. [Epub ahead of print]

## **Why Sex Matters: A Cognitive Study of People With Multiple Sclerosis**

Dr. Donaldson and colleagues reviewed the medical charts of 408 people with MS.

They aimed to find out whether sex affects the results of cognitive testing. Their review included only people who had been referred to neuropsychology testing. Specifically, they had to complete a group of tests referred to as the Minimal Assessment of Cognitive Functioning in MS. The research group used statistical methods to control for other factors that could affect the results, such as age, years of education, disease course, illness duration and disability, anxiety, and depression scores.

Men were more likely than women to have primary progressive MS. Men and women did not differ with respect to age, disability, depression or anxiety scores. Men were more impaired than women on tests of verbal learning and memory.

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Reference: Cogn Behav Neurol. 2019 Mar;32(1):39-45. doi: 10.1097/WNN.000000000000188.

## **Robust Regional Cerebral Blood Flow Perfusion Deficits in RRMS Patients with Executive Function Impairment**

A recent study in Greece involved 17 cognitively impaired people with RRMS. The participants completed a comprehensive battery of neuropsychological tests and underwent a radiopharmaceutical evaluation of blood flow in their brain. The authors were especially interested in seeing how the blood flow rate and pattern were associated with executive functioning of the brain (e.g. the



ability to generate strategies, think divergently, solve and estimate problems and reason in abstract terms).

When compared to demographically matched controls, study participants had less blood flow perfusion in several areas of the brain. However, blood flow was reduced especially in the frontal lobes and other related prefrontal areas that are associated with executive functions. Moreover, the reduction was more prominent in the left hemisphere of the brain. The authors also report that that the more severe the reduction in the perfusion in the left frontal lobes the worse executive function was.

**Reference:** Hell J Nucl Med. 2019 Jan-Apr;22 Suppl:147-159. PMID: 30877732

## Comorbid Anxiety, Depression, and Cognition on MS and Other Immune-Mediated Disorders

A group of Canadian researchers conducted a study to determine whether anxiety and depression are associated with cognition in MS. They were also interested in finding out whether those associations were similar in other immune-mediated inflammatory diseases (IMIDs).

Study participants included 255 people with MS, 244 people with inflammatory bowel disease, 154 people with rheumatoid arthritis and 308 anxious or depressed individuals who did not have an IMID. The participants completed a structured psychiatric interview, the Hospital Anxiety and Depression test and a set of cognitive tests (Symbol Digit Modalities Test, the California Verbal Learning Test and Letter Number Sequencing test). The scores



were converted to age, sex and education *adjusted z-scores* (this method evens out the effect of demographic differences between the groups and the general population and allows for a more accurate statistical comparison).

As compared to general population norms, members of each group in the study had lower processing speed, verbal learning, and delayed recall memory.

Higher levels of anxiety symptoms were associated with slower processing speed, lower verbal learning, and lower working memory performance. Higher levels of depression symptoms were associated with slower processing speed. These associations did not differ across the different groups studied.

The results demonstrated that anxiety and depression are associated with cognition not only in MS but also in other IMIDs as well as among those without an IMID.

These findings led the authors to emphasize the importance of managing symptoms of anxiety and of depression when addressing cognitive issues in MS and other IMIDs.

**Reference:** January 2019 Neurology 92(5):10.1212/WNL.0000000000006854  
DOI: 10.1212/WNL.0000000000006854

## Identifying the Unmet Needs of Adults with Multiple Sclerosis (MS) Experiencing Cognitive Difficulties and their Support Partners

Cognitive difficulties, such as memory lapses and word-finding trouble, are often overlooked in persons with MS. It is important to understand how these difficulties can impact the daily lives of people with MS and their support partners. 15 NARCOMS volunteers and their support partners participated in a MyHealios research study on this topic. Each individual was interviewed separately regarding their personal experience of cognitive difficulties associated with MS and how they coped with the resulting daily challenges.

The research group was particularly interested in ways in which couples described how they dealt with difficulties to improve their quality of life, such as how they approached communicating about these difficulties, or strategies they used to try and make things easier. The information gained was used in the development of an online resilience building program for people with MS and their support partner. A separate group of NARCOMS participants and their support persons were invited to participate in that phase of the study.

According to Dr. Halstead, the principal investigator, commonly recurring themes that emerged from the interviews include the following:

- Cognitive difficulties can be as difficult, sometimes more difficult, to cope with

than physical difficulties, especially because they are invisible and often not recognized by other people.

- It is hard to recognize the extent to which cognitive difficulties affect someone's life early on. Often, the full extent was not known until an individual had to leave a job, or until they faced a dangerous situation, such as getting lost while driving, due to cognitive problems.
- People with MS and support partners alike find it challenging to know how to cope with cognitive problems. Many participants reported trying different systems, such as note-taking or diaries, but the variable nature of symptoms made it hard to find consistent solutions.
- Support partners recognized the need to negotiate between providing help and preserving their loved one's independence. This got harder as cognitive difficulties grew more severe.
- Many participants said despite the challenges of coping with cognitive problems, by coping with humour, or focusing on the importance of their relationship, they could overcome these challenges. However, almost all participants said they would benefit from a program to teach them more about the impact of cognitive difficulties, and how to cope as a couple.

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**Reference:** Study findings were presented at the CMSC meeting in 2018 (poster FC02) and in 2019 (poster EPI05).



# SNAPSHOT

WHAT WE CAN LEARN FROM NARCOMS SURVEYS

## Cognitive Self-Assessment among NARCOMS participants

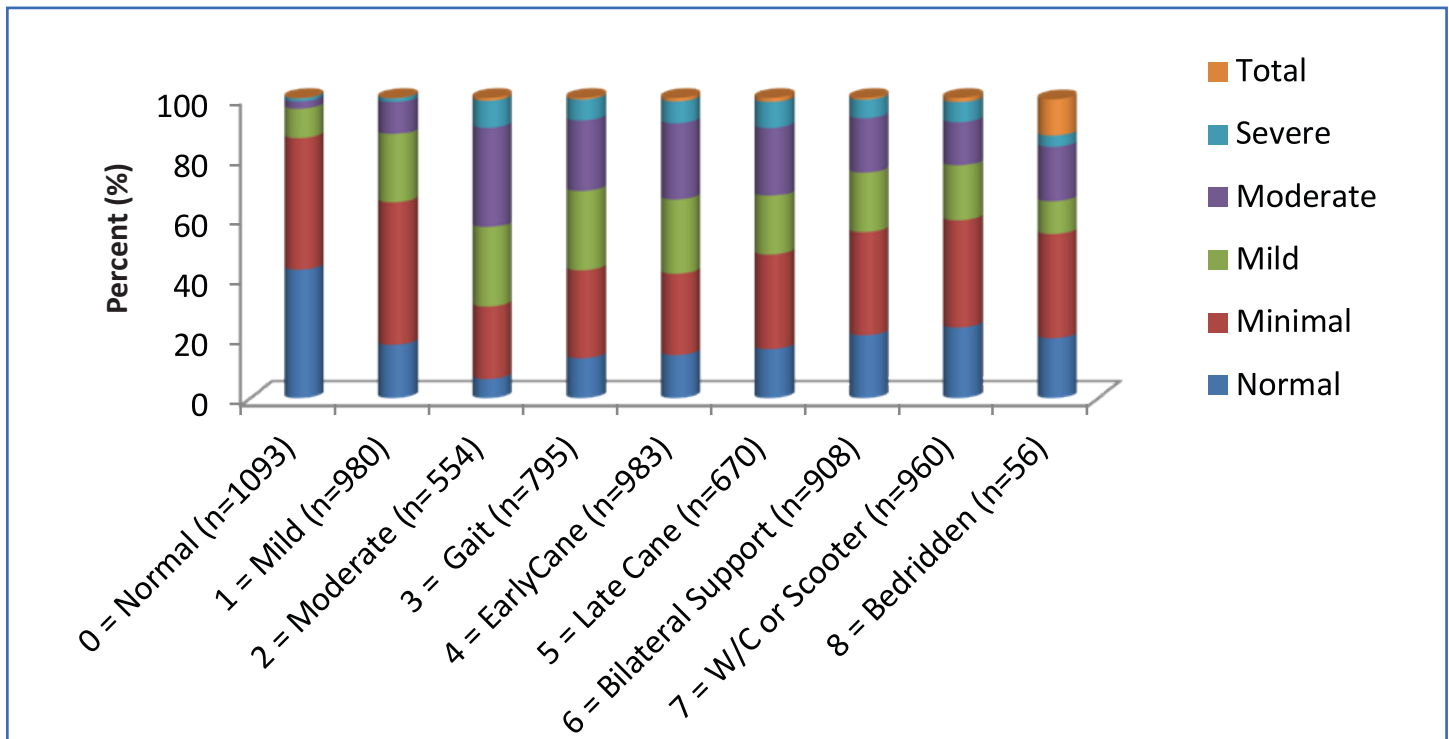
Each semi-annual update survey includes a set of questions about MS symptoms. One of the topics is *perceived* (self-assessed) cognitive function, including memory. This analysis is based on the responses submitted by about 7,000 NARCOMS registry participants in spring 2018.

For this analysis, we looked at 3 questions about cognitive function. We grouped people reporting the same Patient Determined Disease Step (PDDS) level together. Then, within each group we calculated the percentage of answers

given for each response option.

The cognitive performance subscale asks about general cognitive symptoms defined as *“Problems with remembering, thinking, difficulties with calculations, confusion, difficulty remembering what you read, word recall etc., compared to before you developed MS.”* The response options range from 0 (normal cognition) to 5 (total cognitive disability). Figure 1 shows the responses we received.

The Health Utilities Index (HUI) survey includes two questions about cognition. One of them



**Figure 1. Cognitive Performance Scale Scores by PDDS level (n=6998)**

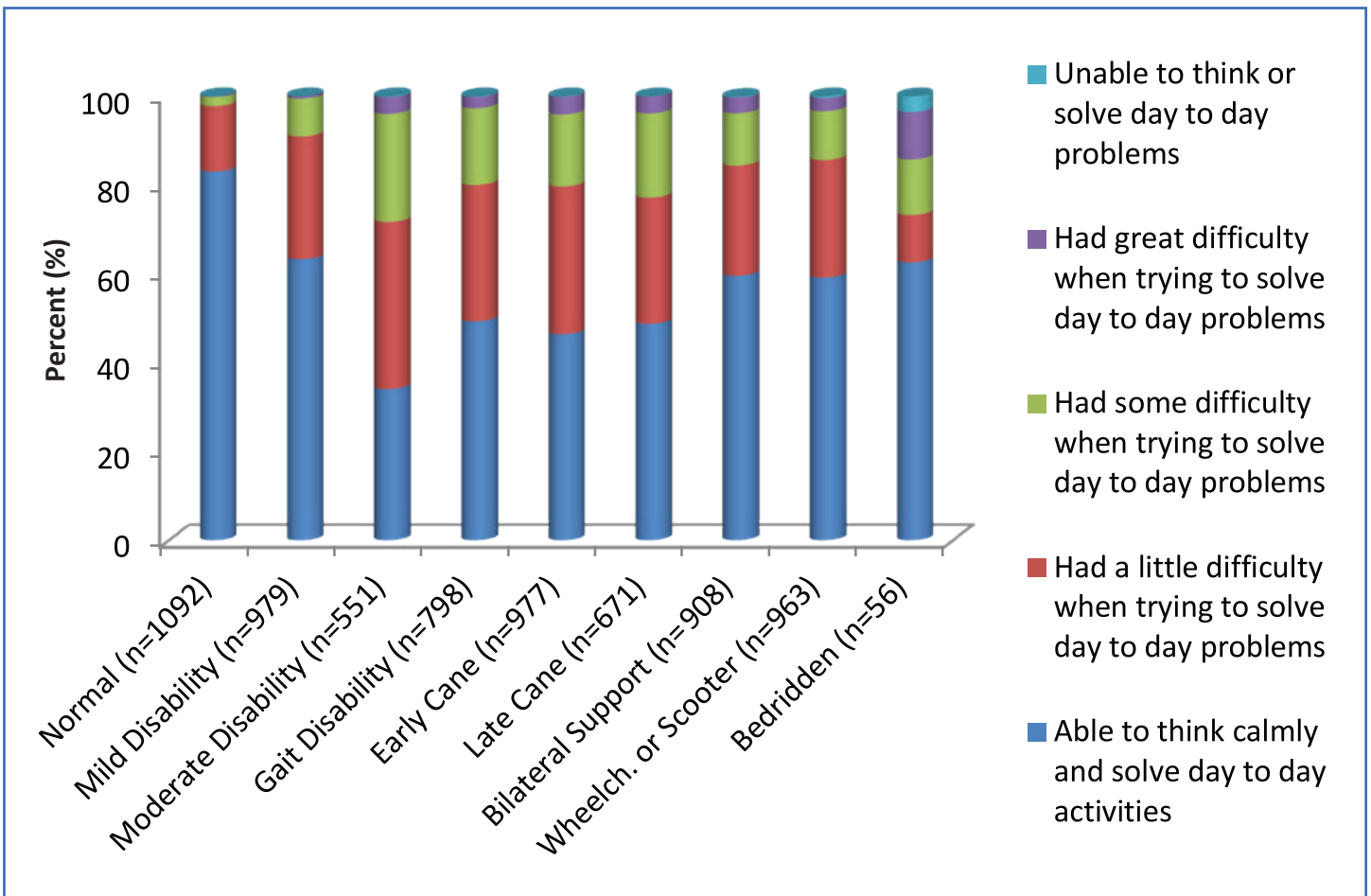
Performance Scales Copyright Registration Number/Date: TXu000743629/1996-04-04; assigned to DeltaQuestFoundation, Inc., effective October 1, 2005. U.S. Copyright law governs terms of use.



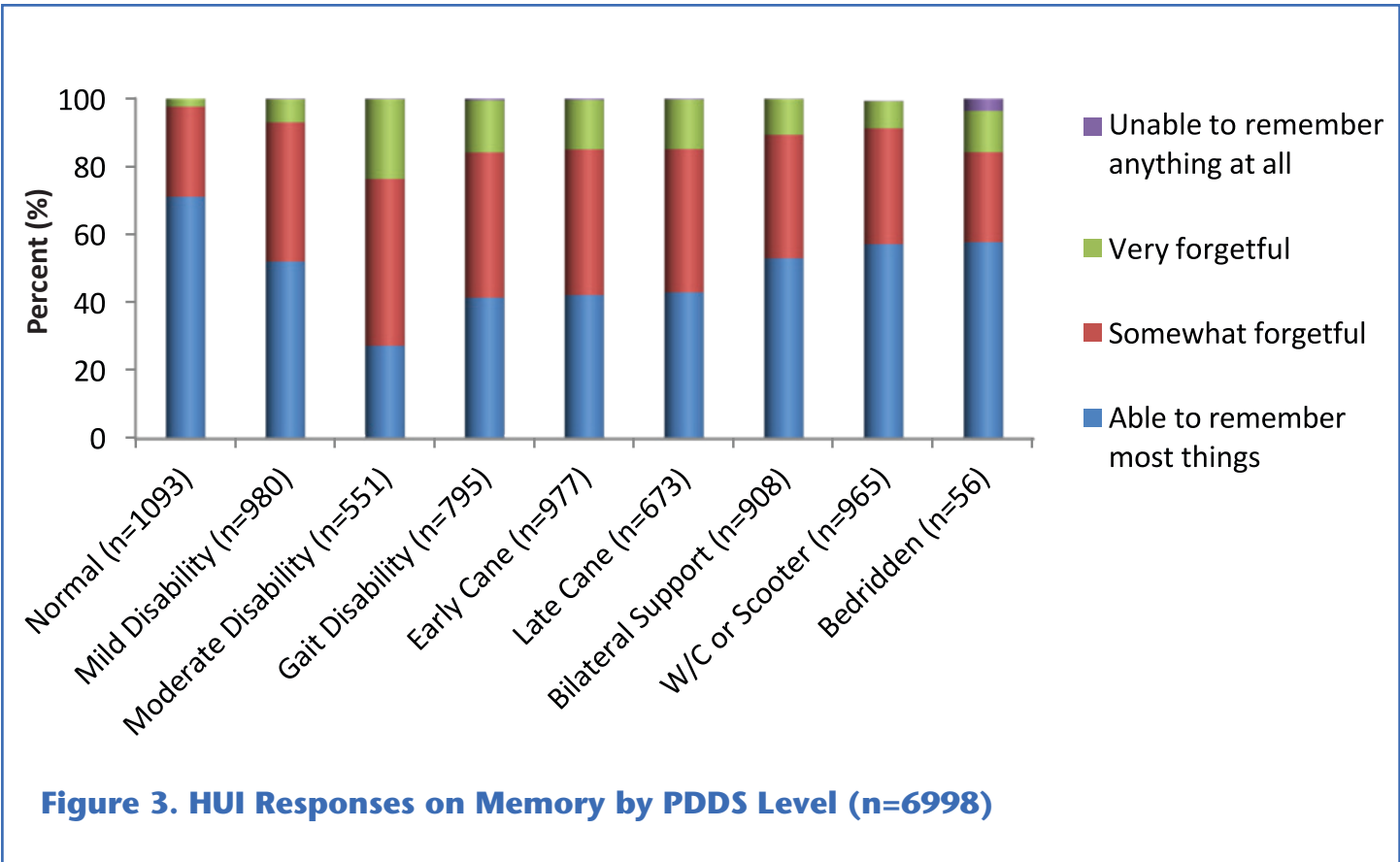
asks about thinking and being able to solve day to day problems. These cognitive tasks are examples of what is called executive function. The response options are provided along with the results in figure 2. The other question focuses solely on memory function; see figure 3 for the response options and breakdown of the responses.

The results demonstrate that cognitive problems are quite common among NARCOMS participants. However, for a majority of the responders they are relatively mild. Even at the most advanced disability levels as measured by the PDDS scale, less than 15% of the responders reported severe or

total overall cognitive disability, great difficulty or inability in solving day to day problems or being very forgetful or unable to remember. On the other hand, milder levels of cognitive dysfunction affected a fair number of people at every level, indicating the importance of addressing cognitive issues with healthcare providers early on. The noticeable dip in the perceived cognitive functioning at PDDS level 2 (moderate disability) in all three figures coincides with the time when such temporary changes are often seen in other aspects of life as well. Figuring out the best coping strategies and life hacks may be especially important at this point.



**Figure 2. HUI Responses on Thinking and Problem Solving by PDDS Level (n=6995)**



# Play WORDSEARCH

Find the following hidden words relating to cognitive function.

INSIGHT  
LEARN  
STORE  
REASON

BRAIN  
THINK  
THOUGHT  
COGNITION

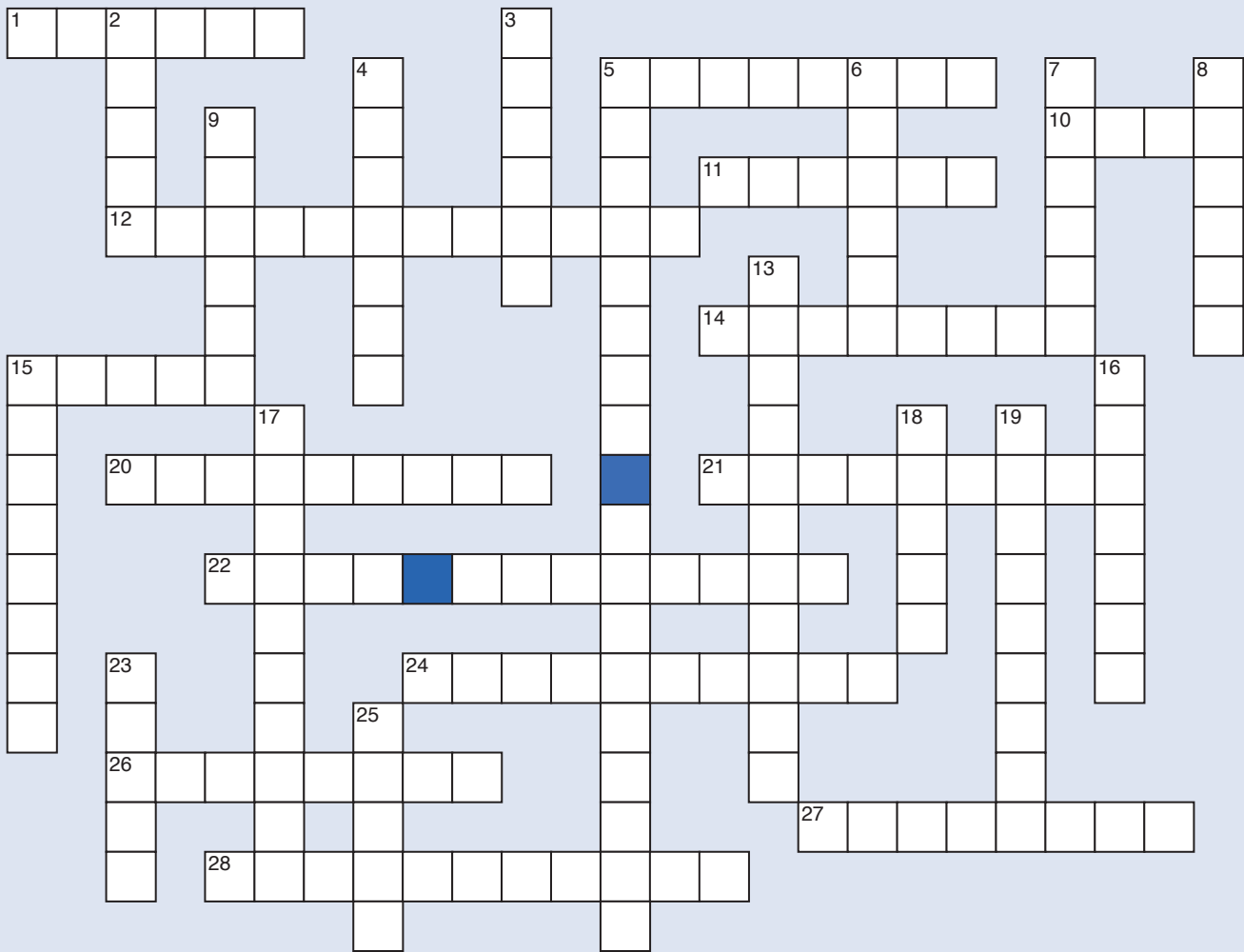
MEMORY  
REMEMBER  
ACCESS  
CEREBRAL

REMINDER  
IMPRESSION  
PERCEPTION  
LEARN

T D U Q R G J C P T O P J A V V H V P F  
T Z E I S C C X O E T R Y J N K G I K T  
U V C D X K C P T H R N R A E L L R H L  
M A Y S J S N R G M K C Y O V N E I E R  
Y T Y N O I T I N G O C E F M M N A E Q  
V K W R L H S O P P K U I P E K B D R I  
Q H D N O N L I R J D D U M T T N W V N  
A R Y U I R G G M E Z C B X C I G W M O  
F T G S K A V J G P Y E Y G M Q O P X G  
J H S U Q I R X V R R R X E K B W N U I  
T C X M D W A B A M Q E R E F J U D N K  
M S Q K N U X X B K R B S I M H B V Y G  
O Q J M E C M Z H P R R U S H A A I Z K  
X Q W J P Y J E N Q S A O X I L M E R P  
Y C Y R O M E M L Y S L N G K O Q V N V  
K P Y C N D V X T B E W W S Z K N F W J  
V R W U Y A U V I R C G S F H J E N Y H  
B Y V F P D R P P T C J Z N O S A E R Q  
J K Y K N P K A W S A K K I U C M J N Q  
K H F N D R T N C R Y O I F K M C V W J



# Play **CROSSWORD**



## Across

1. A consequence, effect, or outcome of something
5. A periodical publication containing articles and illustrations
10. Physical suffering or discomfort caused by illness or injury
11. An involuntary quivering movement
12. People who takes part in something
14. Systematic investigation into and study of materials and sources in order to establish facts and reach new conclusions
15. Allow one's mind to dwell on difficulty or troubles
20. A family member or paid helper who regularly looks after a child or a sick, elderly, or disabled person
21. The mental action or process of acquiring knowledge and understanding through thought, experience, and the senses
22. Practical use or purpose of the end part of a person's arm beyond the wrist, including the palm, fingers, and thumb (two words)
24. A mental condition characterized by feelings of severe despondency and dejection
26. The faculty of perceiving sounds
27. A place or office where registers or records are kept
28. Facts provided or learned about something or someone

## Down

2. A resting condition of body and mind that recurs for several hours every night
3. Relating to seeing or sight
4. North American Research Committee on Multiple Sclerosis
5. A chronic, typically progressive disease involving damage to the sheaths of nerve cells in the brain and spinal cord (two words)
6. Resistant to a particular infection or toxin
7. The expression of or the ability to express thoughts and feelings by articulate sounds
8. Officially register as a member
9. An investigation of the opinions or experience of a group of people, based on a series of questions
13. A specialist in the anatomy, functions, and organic disorders of nerves and the nervous system
15. The state or condition of lacking strength
16. Relating to sensation or the physical senses; transmitted or perceived by the senses
17. The state of being free from tension and anxiety
18. In need of sleep or rest; weary
19. A sensation of spinning around and losing one's balance
23. Organ of soft nervous tissue contained in the skull
25. Relating to muscular movement or the nerves activating it

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# NARCOMS NOW

## ***BE PART OF NARCOMS—HELP TO ADVANCE RESEARCH IN MS***

Whether you were recently diagnosed with multiple sclerosis (MS) or have lived with it for years, your personal history with the disease helps contribute to improving the lives of others with MS.

Participation in the NARCOMS registry allows you to be part of the process. The data provided by participants gives researchers a clearer picture of how a condition like MS impacts the lives of those affected.

Participation in NARCOMS is confidential—your information is kept secure and completely private. If you have MS and are not yet participating in NARCOMS, or have been out of touch for a while, we would love to hear from you! Contact us at 1-800-253-7884 (toll-free U.S.) or via email at [MSRegistry@narcoms.org](mailto:MSRegistry@narcoms.org).



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