



**National
Multiple Sclerosis
Society**

VA



U.S. Department of Veterans Affairs
Veterans Health Administration
Multiple Sclerosis Centers of Excellence

Current Topics in MS

**Cognition in MS—
What You Can Do**

Presenters



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Neuropsychological Symptoms in Multiple Sclerosis (MS): Patient- ▶ Centered Approaches

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National MS Society Provider Call

03/29/21

VA



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Disclosures

▶ None

Outline

- ▶ Introductions
- ▶ Neuropsychological symptoms in MS
- ▶ Comorbidities
- ▶ Assessment & Treatment Approaches
- ▶ Resources

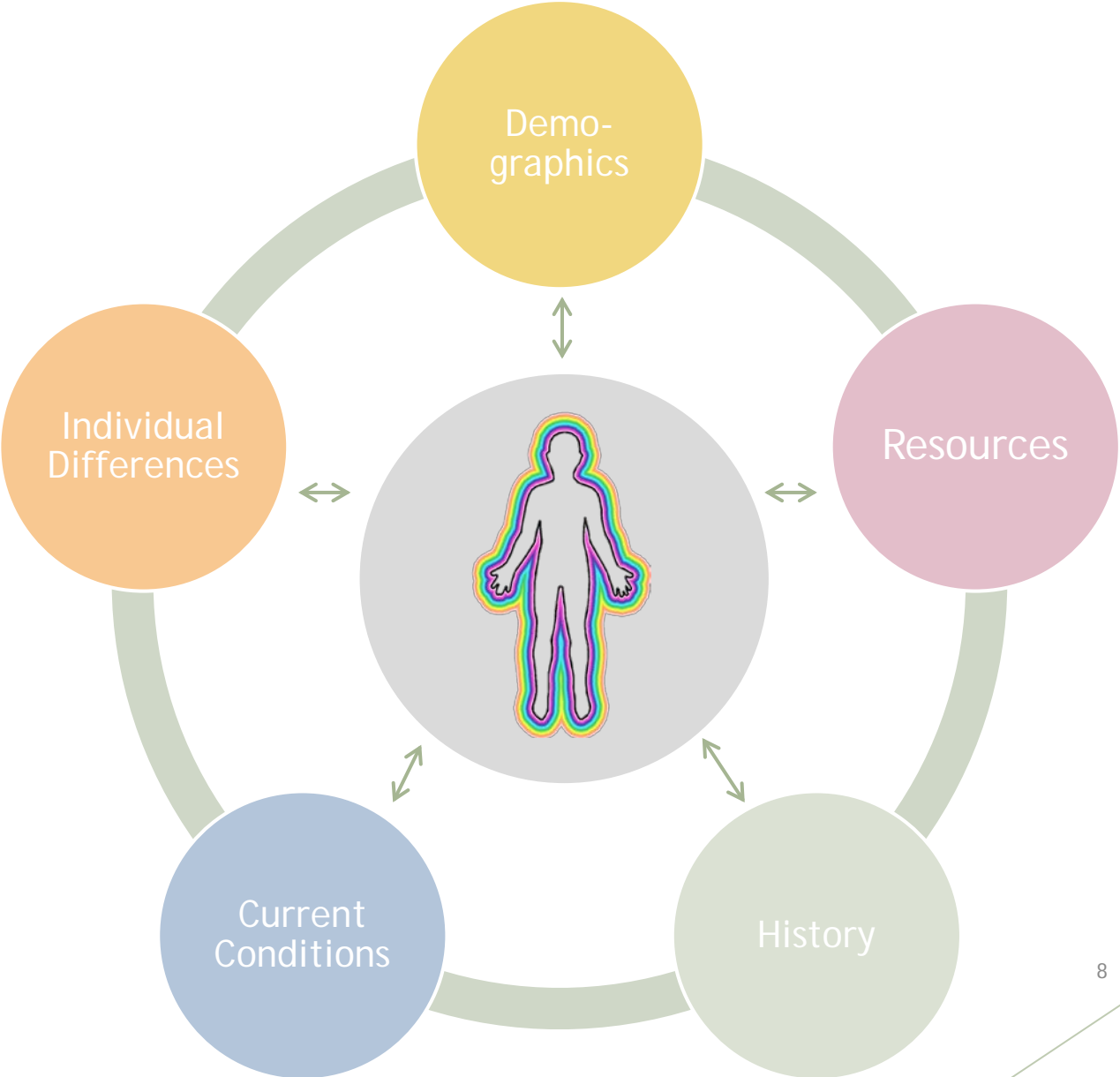
Introductions



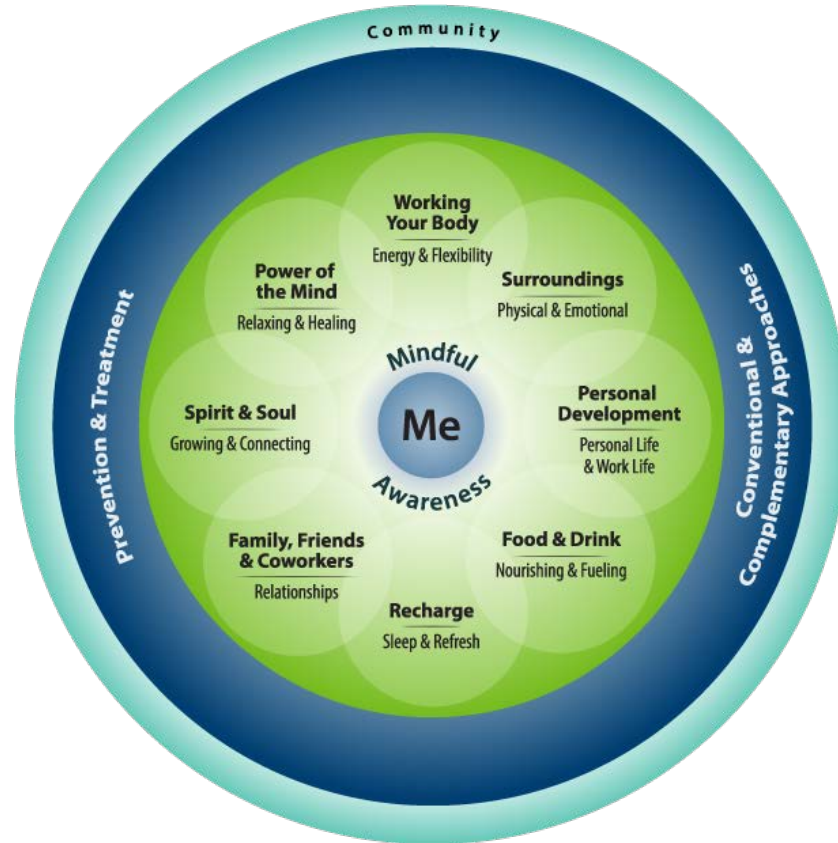
Take Home Point: Take a Tailored Approach



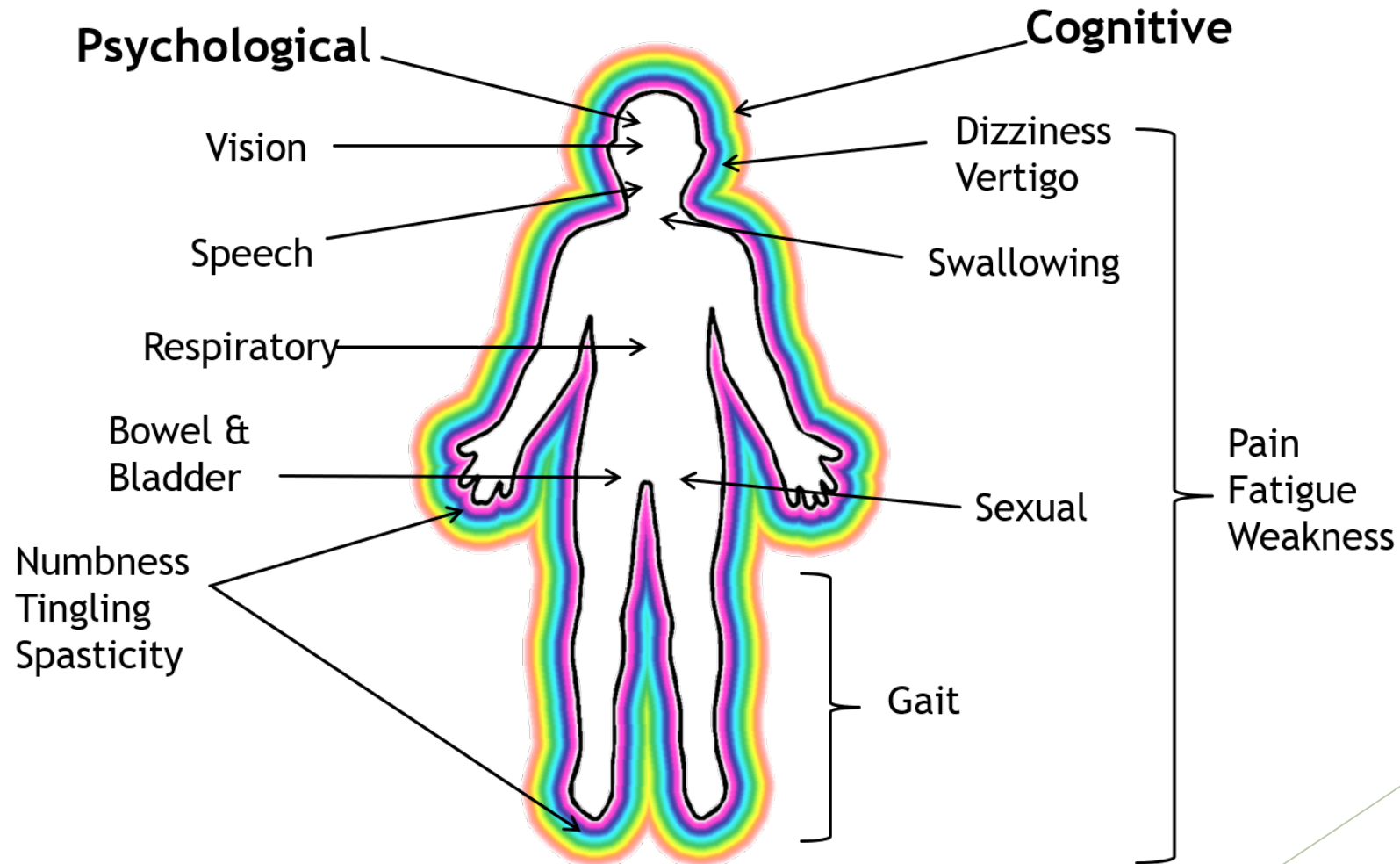
Patient-Centered Care



Whole Health Framework



What is Multiple Sclerosis?



When were Cognitive and Psychological Symptoms First Recognized as Part of MS?

- ▶ Dr. Friedrich von Frerichs (1849)—first to note cognitive symptoms in MS, approximately 25 years after initial clinical description
- ▶ Jean-Martin Charcot (1868): “a marked enfeeblement of the memory; conceptions are formed slowly...” He also described psychiatric symptoms such as pathological laughing and crying, euphoria, mania, hallucinations, and depression.
 - ▶ His patient, Mademoiselle V was characterized as having a fit of lypemania (severe depression), as well as hallucinations and paranoia.
- ▶ Late 19th and early 20th century: cognitive dysfunction not consistently recognized as a symptom of MS



What's the Historical Significance of Cognitive and Psychological Symptoms in MS?

- ▶ 1946: The National MS Society was founded by Sylvia Lawry
 - ▶ The MS Society remains a powerful force today and has extensive educational information and resources related to cognitive and psychological symptoms of MS.
- ▶ 1950s: Empirical research on the frequency of depression in individuals with MS commenced
- ▶ 1960s: Medical students typically taught that cognition not affected in MS
- ▶ 1970s: Medical students taught that cognition may be affected in a small proportion of individuals with MS (e.g., <5%)
- ▶ 1980s & 1990s: Increased awareness and empirical research related to cognitive and psychological symptoms associated with MS; introduction of MRI



Why Focus on Cognitive & Psychological Symptoms in MS?

- ▶ Historically, physical and sensory symptoms have garnered more attention and intervention from providers
- ▶ Cognitive and psychological symptoms have been under-recognized, inadequately assessed, and under-treated
 - ▶ Symptoms are “invisible” and may be associated with stigma
- ▶ Cognitive and psychological symptoms often emerge **early**, are **common** across different types of MS, can **persist** across the course of the disorder, and negatively impact a range of factors (e.g., occupation, quality of life)



▶ These symptoms *can* be addressed.

What are Less Common Psychological Symptoms in MS?

- ▶ **Euphoria:** Persistent happiness that is disproportionate to circumstances and can distort one's view of reality.
 - ▶ Early conceptualizations greatly overestimated this symptom (e.g., Charcot noted that "stupid indifference" affected "most" of his patients)
 - ▶ Current research suggests that approximately 5% of patients with MS demonstrate euphoria
 - ▶ More common in the later stages of the disease and in those with more advanced cognitive impairment
- ▶ **Pseudobulbar Affect:** Uncontrollable bouts of laughing and/or crying (mood incongruent). Affects approximately 10% of people with MS.

How Common is Suicidal Ideation & Death by Suicide in Individuals with MS?

- ▶ Lifetime prevalence of suicidal ideation is approximately 30% in people with MS. Research has demonstrated that individuals with MS are more than twice as likely to attempt suicide as the general population and about twice as likely to complete suicide. Factors associated with increased risk include:
 - ▶ Being male
 - ▶ Living alone
 - ▶ Severe depression
 - ▶ Overuse of alcohol



What Leads to Psychological Symptoms in Individuals with MS?



- ▶ MS-specific
 - ▶ Lesions in the brain (as opposed to spinal cord)
 - ▶ Association between lesions in the left frontal and temporal lobes and depressive symptoms
 - ▶ Some medications for MS can increase risk for psychological symptoms
- ▶ Other
 - ▶ Comorbidities (direct and indirect effects)
 - ▶ Reactions to stressors including adjustment to chronic illness
- ▶ Overall, a complex interplay between biological processes and psychosocial factors

How are Psychological Symptoms Assessed?



- ▶ Psychological assessment **should** be part of comprehensive care in MS
 - ▶ Multiple studies document relatively low treatment rates, likely due to undiagnosed psychological disorders
- ▶ Several studies have documented the utility of a range of brief assessment measures:
 - ▶ Generalized Anxiety Disorder-7 & 2-Item Scales (GAD-7/GAD-2)
 - ▶ Comparable sensitivity and specificity
 - ▶ Hospital Anxiety and Depression Scale (HADS)
 - ▶ Beck Depression Inventory-2nd Edition (BDI-2)
 - ▶ Patient Hospital Questionnaire-9 (PHQ-9)

How are Psychological Symptoms Treated?



Are Cognitive Symptoms Part of MS?

Approximately 40-70% of individuals with MS exhibit cognitive symptoms

What are the Most Common Cognitive Symptoms in MS?

Information Processing Speed

Learning & Memory

Executive Functioning

What's the Usual Onset, Course, and Severity of Cognitive Symptoms?

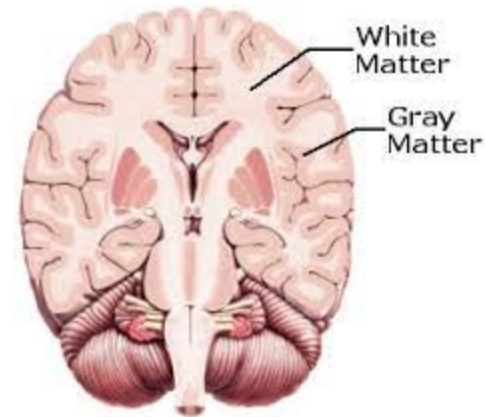
- ▶ Cognitive symptoms tend to emerge gradually, *early* in the disease course
 - ▶ In fact...cognitive impairment appears to predate the appearance of structural abnormalities on magnetic resonance imaging (MRI) and may serve as an early marker of disease activity (Cortese, et al., 2016)
- ▶ A majority of individuals with MS experience *mild* cognitive symptoms
- ▶ Cognitive symptoms are not ameliorated with disease-modifying treatments (DMTs)
- ▶ Some evidence that cognitive symptoms **increase** during MS relapses and cognitive function does not return to pre-relapse levels (e.g., Morrow et al., 2011)
- ▶ Cognitive symptoms are more frequent and often more severe in the progressive variants of the disease and in patients with comorbidities (e.g., cerebrovascular disease)

Why do Cognitive & Psychological Symptoms Matter?



What Factors Contribute to Cognitive Symptoms in Individuals with MS?

- ▶ White and gray matter demyelination in the brain
 - ▶ Approximately 15% of the neocortex is demyelinated & upwards of 30% demyelination in deep gray matter nuclei apparent
- ▶ Early in disease: deep gray matter demyelination > neocortex; opposite in later stages of disease
 - ▶ About a 20% reduction in neuronal density
- ▶ Gray matter may matter more for cognition
 - ▶ Cortical gray matter lesions associated with worse cognition



What Role Can Comorbidities Play?

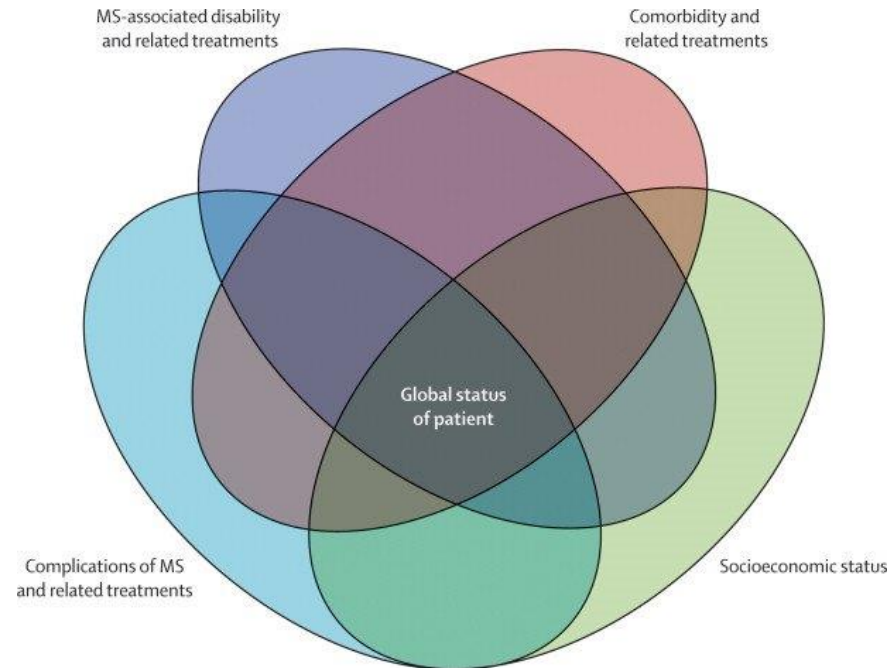


- ▶ Comorbidity typically refers to the total burden of illness other than the specific disease of interest and is distinct from complications of the disease
- ▶ That definition should also include comorbid health behaviors and lifestyle factors
 - ▶ Smoking
 - ▶ Obesity
 - ▶ Alcohol use
 - ▶ Physical activity



Mechanisms for Comorbidities?

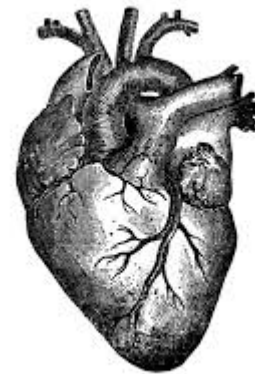
- ▶ Two disorders may co-occur by chance
- ▶ Pts with one chronic disease may be at increased chance to be dx'd b/c of increased utilization of health care services
- ▶ One disorder or its treatment can lead to another
- ▶ Common risk factors can lead to increased co-occurrence of a disease
- ▶ Independent factors (e.g., age, obesity) can lead to increased co-occurrence of a disease



What *Other* Factors Contribute to Cognitive Symptoms in Individuals with MS?

▶ Medical Comorbidities

- ▶ Vascular Disease
- ▶ Metabolic Disease
- ▶ Sleep Disorders
- ▶ Autoimmune Disorders
 - ▶ Inflammatory bowel disease
 - ▶ Lupus
 - ▶ Thyroid disease



COVID-19 Considerations?

- ▶ Data emerging on potential acute and long-term CNS effects of COVID-19
- ▶ COVID-19 may...
 - ▶ Directly impact CNS function
 - ▶ Exacerbate pre-existing CNS dysfunction
 - ▶ Increase vulnerability to future CNS dysfunction
- ▶ To date, primary mechanisms of CNS impact appear to be via cerebrovascular dysfunction and systemic neuroinflammation

What *Other* Factors Contribute to Cognitive Symptoms in Individuals with MS?

- ▶ Mental Health/Psychiatric Comorbidities
 - ▶ Depression
 - ▶ Anxiety
 - ▶ Serious Mental Illness
 - ▶ Substance Use



What *Other* Factors Contribute to Cognitive Symptoms in Individuals with MS?



▶ Adverse Health Behaviors & Lifestyle Factors

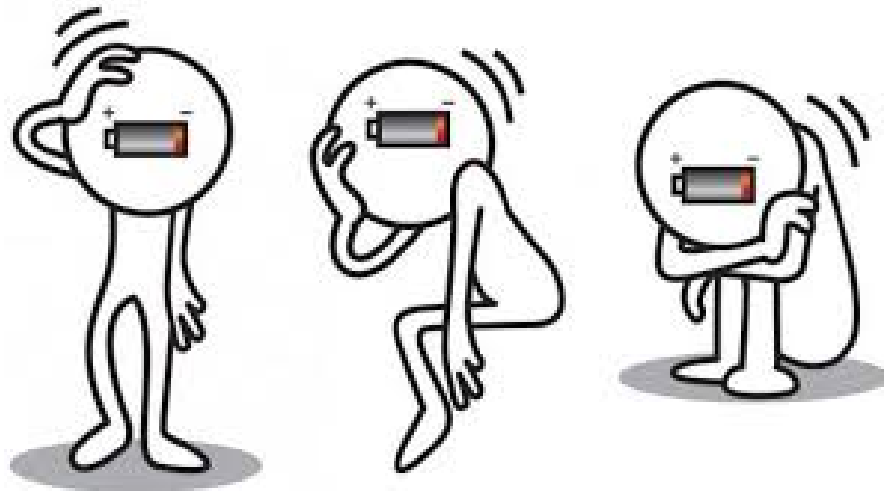
- ▶ Smoking
- ▶ Obesity
- ▶ Sedentary lifestyle
- ▶ Substance Use



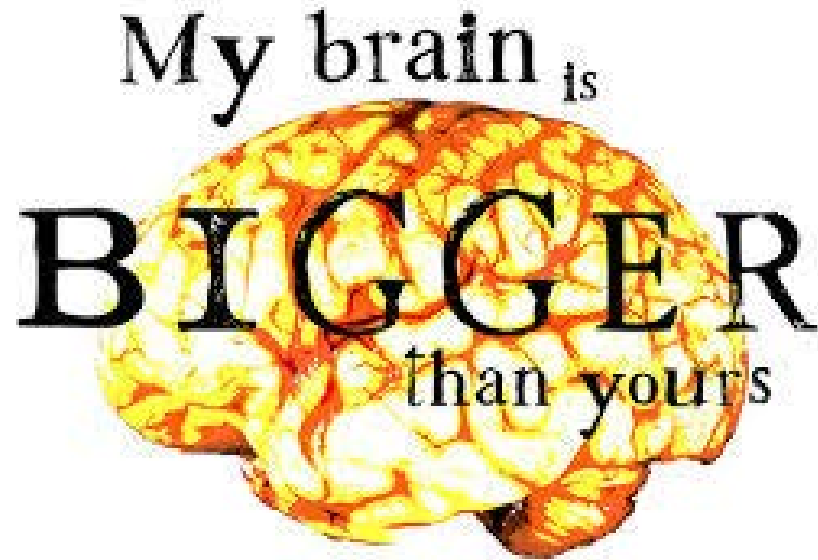
What *Other* Factors Contribute to Cognitive Symptoms in Individuals with MS?

- ▶ Exacerbating Factors

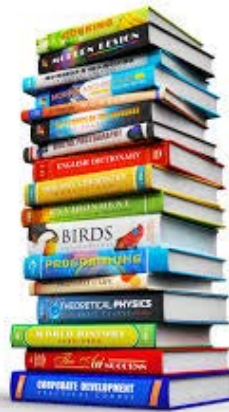
- ▶ Pain
- ▶ Fatigue
- ▶ Disrupted sleep



What may Protect Against Cognitive Decline?



Brain Reserve



Cognitive Reserve

Approaches to Cognitive Assessment?



Screening

Brief Evaluations

Comprehensive
Evaluations

Why is Objective Cognitive Assessment Important?

- ▶ *Per AAN, clinicians typically unable to detect cognitive impairment based on routine neurologic evaluation and interview
- ▶ Disability in MS is typically captured with the Expanded Disability Status Scale (EDSS) which relies primarily on clinician's perception of cognition (or report of an informant)
 - ▶ Studies have shown that when objective measures are used to assess cognition to inform EDSS score, the total score changes
- ▶ The National MS Society and AAN recommend *at least* annual cognitive evaluation
 - ▶ NMSS Guidelines (also endorsed by Consortium of Multiple Sclerosis Clinical Centers and the International Multiple Sclerosis Cognition Society): <https://pubmed.ncbi.nlm.nih.gov/30303036/>



NMSS Recommendations

- ▶ Increased professional and patient awareness/education about the prevalence, impact, and appropriate management of cognitive symptoms.
- ▶ *For adults and children (8+ years of age) with clinical or magnetic resonance imaging (MRI) evidence of neurologic damage consistent with MS:*
 - ▶ *As a minimum, early baseline screening with the Symbol Digit Modalities Test (SDMT) or similarly validated test, when the patient is clinically stable;*
 - ▶ Annual re-assessment *with the same instrument*, or more often as needed to (1) detect acute disease activity; (2) assess for treatment effects (e.g., starting/changing a disease-modifying therapy) or for relapse recovery; (3) evaluate progression of cognitive impairment; and/or (4) screen for new-onset cognitive problems.
- ▶ *For adults (18+ years):* more comprehensive assessment for anyone who tests positive on initial cognitive screening or demonstrates significant cognitive decline, especially if there are concerns about **comorbidities** or the individual is applying for disability due to cognitive impairment.
- ▶ Remedial interventions/accommodations for adults and children to improve functioning at home, work, or school.

Screening & Monitoring



- ▶ When & how to Screen?
- ▶ Screening tools validated in MS populations
 - ▶ The **Symbol Digit Modalities Test (SDMT; Smith, 1982)** has repeatedly been found to be reliable and sensitive, and correlated most robustly with other outcomes, such as brain MRI metrics and employment. As a result, the SDMT has figured prominently in brief, widely used international monitoring tools
 - ▶ **Processing Speed Test (PST; 5min)** - correlated with SDMT, software free, randomly generated key
 - ▶ **Computerized Speed Cognitive Test (CSCT, 5 min)** - similar to SDMT
 - ▶ **Multiple Sclerosis Neuropsychological Screening Questionnaire (MSNQ; 5 min)** - self report

Brief Assessment Batteries

- ▶ **Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS)**
 - ▶ 15 minutes
 - ▶ Adults and children
 - ▶ SDMT, CVLT-II, BVMT
 - ▶ strongly correlated with deep GM atrophy
 - ▶ A self-administered, computerized version of the test has recently been adapted to the iPad platform
- ▶ **Brief Repeatable Neuropsychological Battery (BRNB)**
 - ▶ 45 minutes (no longer available)
 - ▶ PASAT, SDMT, Selective Reminding Test, 10/36 Spatial Recall Test, COWAT

MACFIMS

Validity of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS)

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(RECEIVED January 23, 2006; FINAL REVISION March 23, 2006; ACCEPTED March 23, 2006)

- Measures: Paced Auditory Serial Addition Test, Single Digit Modalities Test, California Verbal Learning Test-2nd ed., Brief Visuospatial Memory Test-Revised, Controlled Oral Word Association Test, Judgment of Line Orientation Test, and Delis-Kaplan Executive Function System Sorting Test.

When to Refer to Neuropsychology?



- ▶ Complete comprehensive neuropsychological evaluation as early as possible following disease onset to establish a baseline
- ▶ Follow up annually with a screening battery (e.g., aMACFIMS, BICAMS, or other combinations)
- ▶ Administer more comprehensive evaluations at follow-up if:
 - ▶ Screening battery suggests progression of cognitive decline
 - ▶ Patient exhibits a new area of impairment upon screening
 - ▶ Decline in daily function related to cognition
 - ▶ Patient has need for accommodations (e.g., work, school)
 - ▶ A specific element of capacity is questioned (e.g., medical decision-making, financial)

What Happens in a Neuropsychological Evaluation?

- ▶ Clinical interview
 - ▶ Patient & collateral (if possible)
- ▶ Review of relevant records
 - ▶ Imaging
 - ▶ Labs
 - ▶ Medications
 - ▶ Reports/notes
- ▶ Neuropsychological battery
- ▶ Behavioral observations
- ▶ Comprehensive report
- ▶ Feedback session

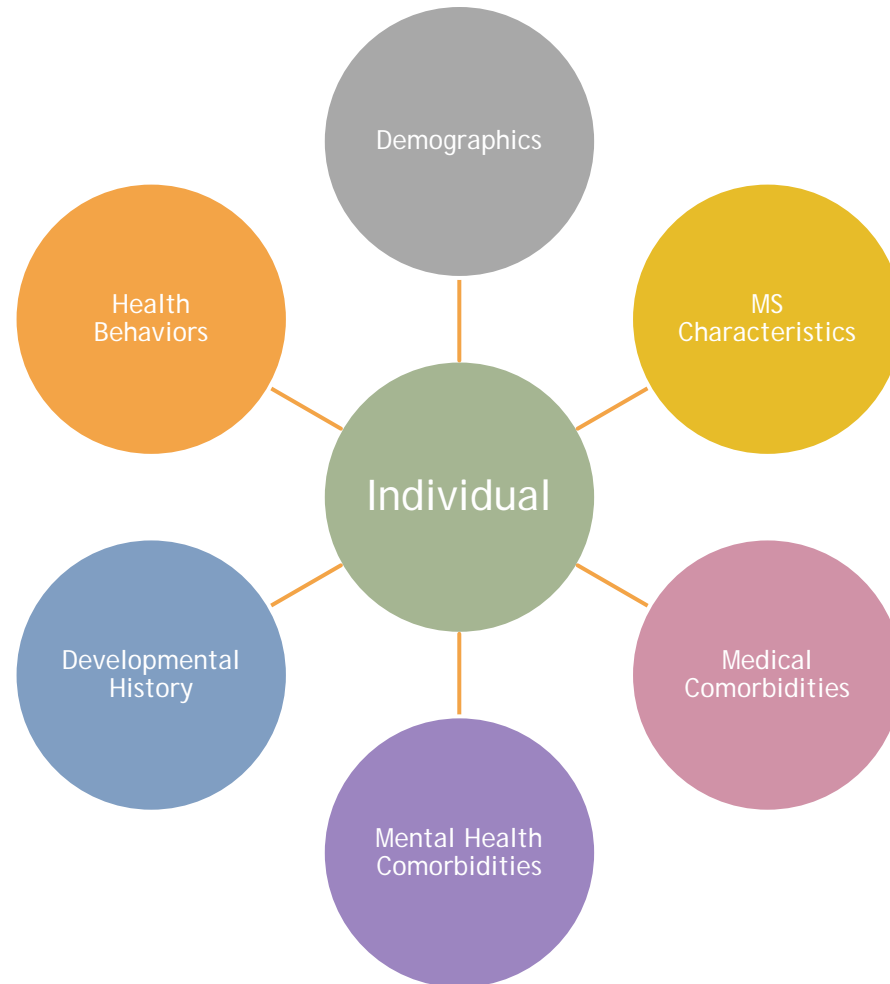


What Diagnostic Framework Do We Use?

- ▶ Demographics
- ▶ Symptom Type
 - ▶ Physical, cognitive, psychological/behavioral
- ▶ Onset
 - ▶ Gradual vs. abrupt
 - ▶ Precipitating event?
- ▶ Course
 - ▶ Stable, variable, progressive
- ▶ Functional status
- ▶ History
 - ▶ Developmental
 - ▶ Medical
 - ▶ Psychiatric
 - ▶ Social/Occupational



Interpretation of Neuropsychological Testing?

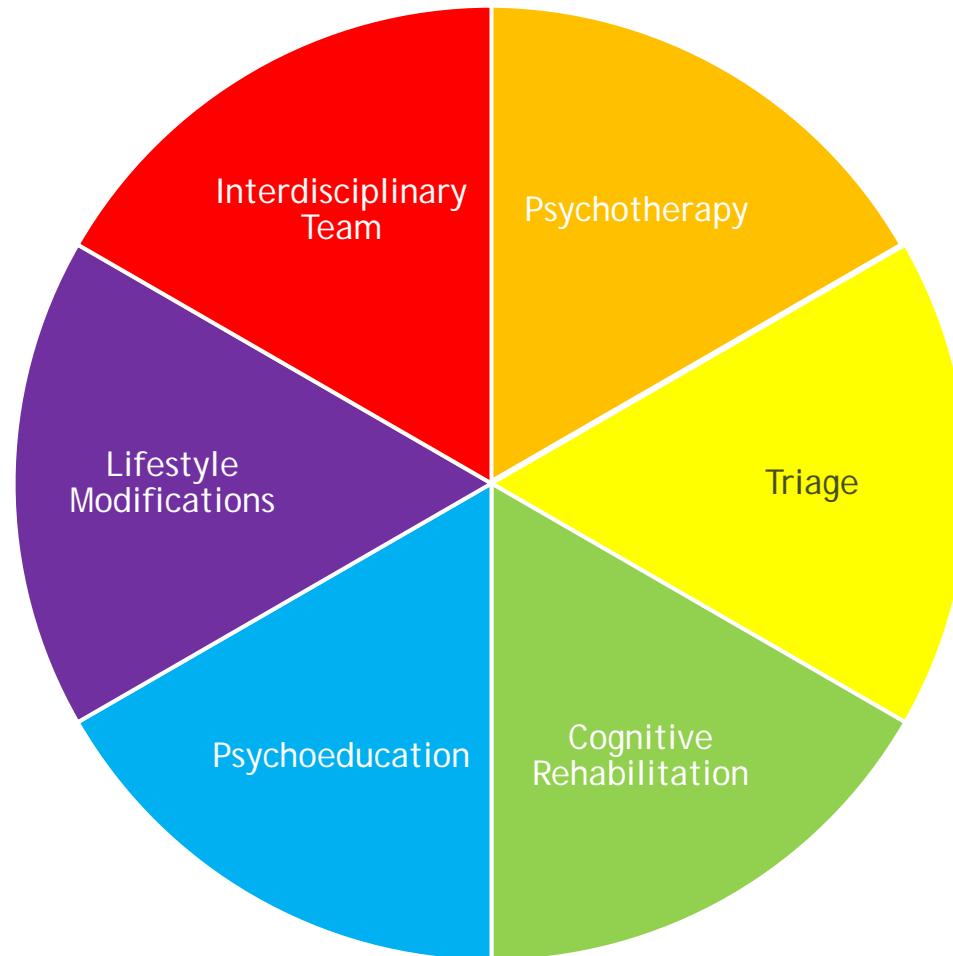


What Happens After Testing?



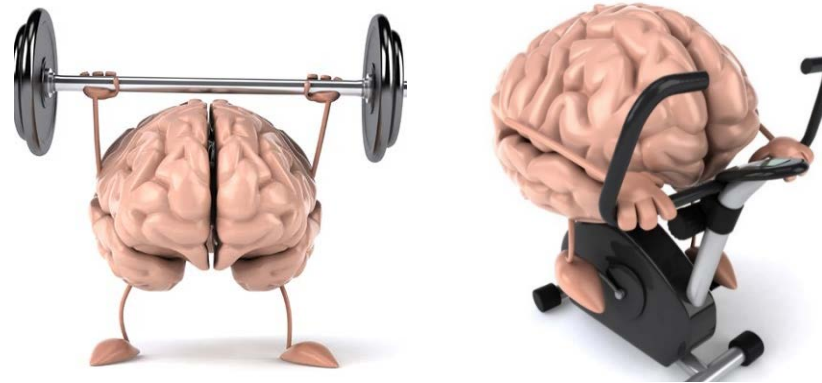
- ▶ **FEEDBACK:** A follow-up session for each patient (and family if desired)
 - ▶ Review results and impressions
 - ▶ Provide personalized & tailored recommendations

Recommendations



Mental Health Treatment

- ▶ Detection of cognitive & psychological changes may lead to earlier, more targeted treatment interventions
- ▶ Cognitive rehabilitation
 - ▶ The latest Cochrane review (das Nair, Martin, & Lincoln, 2016) indicates that there is significant support for memory rehabilitation for immediate and long-term follow-up, which significantly improves quality of life.
- ▶ Psychotherapy
 - ▶ Extensive empirical support for CBT-oriented tx

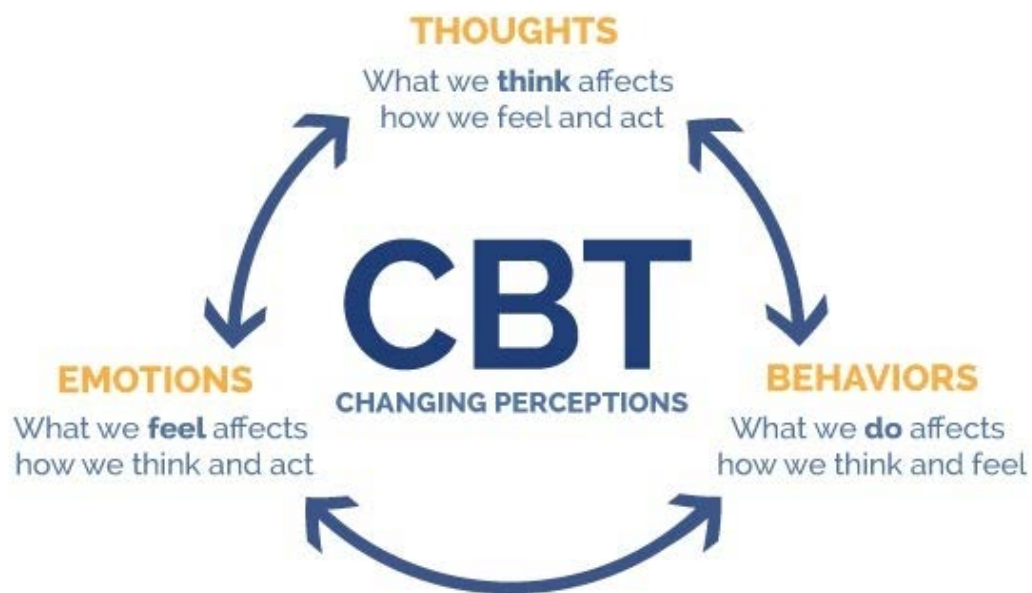
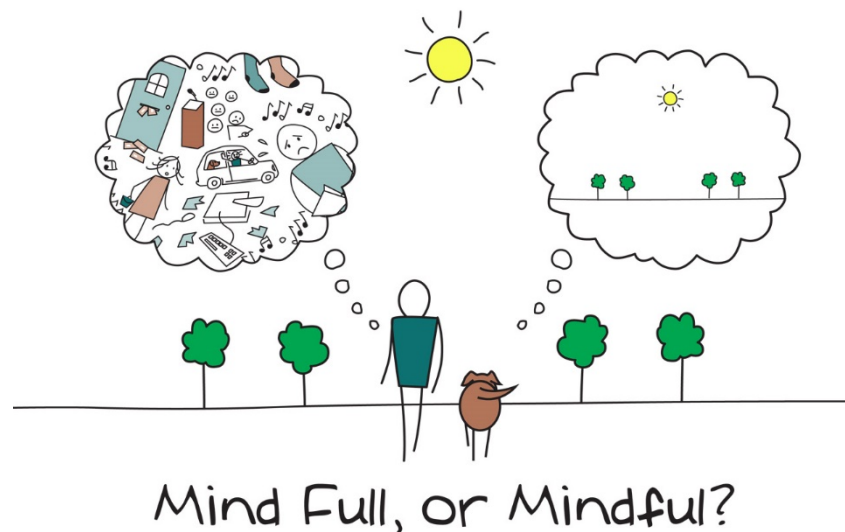


Cognitive Rehabilitation: Key Components

- ▶ **Orientation to the problem and setting goals**
 - ▶ Help the patient recognize specific problem(s)
 - ▶ Collaborate in establishing meaningful goals
- ▶ **Compensation**
 - ▶ Develop new ways of doing things
 - ▶ E.g., learning to use a memory notebook and a planner even though underlying impairment remains
- ▶ **Internalization**
 - ▶ Gradually increasing the automaticity of practiced strategies
 - ▶ Move from needing external reminders to check the calendar to making it a routine
- ▶ **Generalization**
 - ▶ Apply skills learned with one task to other similar tasks

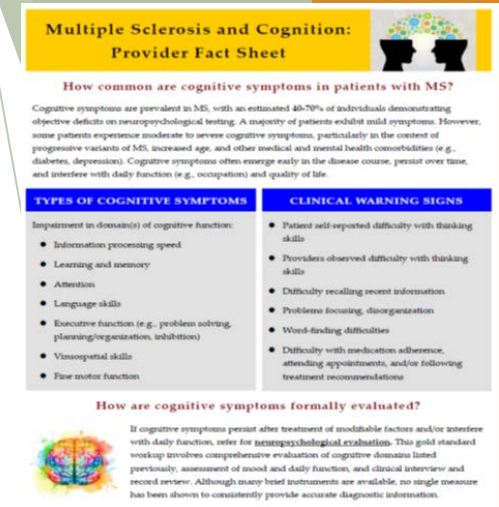


What Types of Therapy are Empirically Supported for MS?



Psychoeducation

- ▶ Providers: don't make assumptions about health literacy
- ▶ MS Resources For Patients & Providers
 - ▶ <https://www.va.gov/MS/veterans/resources/index.asp>
 - ▶ https://www.va.gov/MS/veterans/symptoms_of_MS/index.asp
 - ▶ https://www.va.gov/MS/Professionals/Resources/Patient_info_MS_and_cognition.pdf
 - ▶ <https://www.va.gov/MS/Professionals/Resources/index.asp>
 - ▶ https://www.va.gov/MS/Professionals/Resources/Provider_info_MS_and_cognition.pdf
- ▶ National MS Society Resources for Patients and Providers
 - ▶ www.nationalMSSociety.org/brochures
 - ▶ www.nationalMSSociety.org/PRC



Multiple Sclerosis and Cognition: Provider Fact Sheet

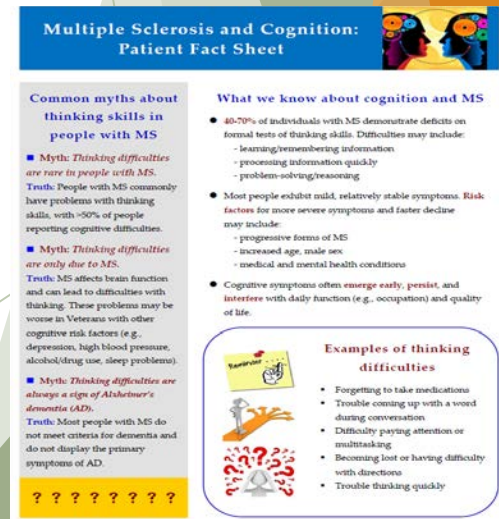
How common are cognitive symptoms in patients with MS?

Cognitive symptoms are prevalent in MS, with an estimated 40-70% of individuals demonstrating objective deficits on neuropsychological testing. A majority of patients exhibit mild symptoms. However, some patients experience moderate to severe cognitive symptoms, particularly in the context of progressive variants of MS, increased age, and other medical and mental health comorbidities (e.g., diabetes, depression). Cognitive symptoms often emerge early in the disease course, persist over time, and interfere with daily function (e.g., occupation) and quality of life.

TYPES OF COGNITIVE SYMPTOMS	CLINICAL WARNING SIGNS
Impairment in domain(s) of cognitive function: <ul style="list-style-type: none">• Information processing speed• Learning and memory• Attention• Language skills• Executive function (e.g., problem solving, planning/organization, inhibition)• Visuospatial skills• Fine motor function	<ul style="list-style-type: none">• Patient self-reported difficulty with thinking skills• Providers observed difficulty with thinking skills• Difficulty recalling recent information• Problems focusing, disorganization• Word-finding difficulties• Difficulty with medication adherence, attending appointments, and/or following treatment recommendations

How are cognitive symptoms formally evaluated?

If cognitive symptoms persist after treatment of modifiable factors and/or interfere with daily function, refer for neuropsychological evaluation. This gold standard workup involves comprehensive evaluation of cognitive domains listed previously, assessment of mood and daily function, and clinical interview and record review. Although many brief instruments are available, no single measure has been shown to consistently provide accurate diagnostic information.



Multiple Sclerosis and Cognition: Patient Fact Sheet

Common myths about thinking skills in people with MS

- **Myth: Thinking difficulties are rare in people with MS.**
Truth: People with MS commonly have problems with thinking skills, with ~50% of people reporting cognitive difficulties.
- **Myth: Thinking difficulties are only due to MS.**
Truth: MS affects brain function and can lead to difficulties with thinking. These problems may be worse in Veterans with other cognitive risk factors (e.g., depression, high blood pressure, alcohol/drug use, sleep problems).
- **Myth: Thinking difficulties are always a sign of Alzheimer's dementia (AD).**
Truth: Most people with MS do not meet criteria for dementia and do not display the primary symptoms of AD.

What we know about cognition and MS

- 40-70% of individuals with MS demonstrate deficits on formal tests of thinking skills. Difficulties may include:
 - learning/remembering information
 - processing information quickly
 - problem-solving/reasoning
- Most people exhibit mild, relatively stable symptoms. Risk factors for more severe symptoms and faster decline may include:
 - progressive forms of MS
 - increased age, male sex
 - medical and mental health conditions
- Cognitive symptoms often emerge early, persist, and interfere with daily function (e.g., occupation) and quality of life.

Examples of thinking difficulties

- Forgetting to take medications
- Trouble coming up with a word during conversation
- Difficulty paying attention or multitasking
- Becoming lost or having difficulty with directions
- Trouble thinking quickly

Behavior Modifications



Services Offered at the VA Maryland Health Care System



- ▶ Screening
- ▶ Brief and comprehensive inpatient & outpatient neuropsychological evaluation
- ▶ Multidisciplinary MS Clinics
- ▶ Capacity evaluations
- ▶ Teleneuropsychological evaluations
- ▶ Individual/group cognitive rehabilitation & psychotherapy
- ▶ **Group cognitive wellness**
- ▶ Computerized cognitive rehabilitation (research)
- ▶ MS Professional Outreach



Cognitive Wellness Examples at VAMHCS

- ▶ MS Intervention and Development of Skills (MINDS) Groups
 - ▶ MINDS 1.0, Master MINDS, Mr. MINDS, Ms. MINDS
 - ▶ Workshops
 - ▶ Caring MINDS & Open MINDS
 - ▶ Cognifitness (MS Society Program)



Local & National Resources

VA



U.S. Department of Veterans Affairs

Veterans Health Administration
Multiple Sclerosis Centers of Excellence

- ▶ MScCoE
 - ▶ Fact Sheets
 - ▶ You Tube Video Series for Veterans

https://www.youtube.com/playlist?list=PLgx1HLxE1T_rNKburBGq8A1rxEyeHeN4v

- ▶ National MS Society
 - ▶ MS Navigators
 - ▶ Healthcare Provider Councils
 - ▶ Educational and Connection Programs
- ▶ Paralyzed Veterans of America
 - ▶ Advocacy
 - ▶ Annual Summit
- ▶ Consortium of MS Centers



**Paralyzed Veterans
of America**

Reminder!



THINK
OUTSIDE
THE

BOX

QUESTIONS