Current Topics in MS

Cognition in MS—What You Can Do
Presenters

Terry Lee-Wilk, PhD

Moira Dux, PhD
Neuropsychological Symptoms in Multiple Sclerosis (MS): Patient-Centered Approaches

Terry Lee-Wilk, Ph.D. & Moira Dux, Ph.D.
National MS Society Provider Call
03/29/21
Disclosures

- None
Outline

- Introductions
- Neuropsychological symptoms in MS
- Comorbidities
- Assessment & Treatment Approaches
- Resources
Introductions
Take Home Point:
Take a Tailored Approach
Patient-Centered Care

Demographics

Individual Differences

Current Conditions

History

Resources
Whole Health Framework
What is Multiple Sclerosis?

Psychological
- Vision
- Speech
- Respiratory
- Bowel & Bladder
- Numbness
  - Tingling
  - Spasticity

Cognitive
- Dizziness
- Vertigo
- Swallowing
- Pain
- Fatigue
- Weakness

Gait

Sexual
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.
How Common are Psychological Symptoms in MS?

- Estimates vary between studies but approximately 30-50% of individuals with MS experience some form of psychological distress (e.g., depression, anxiety).

- Rates of psychological distress are higher than the general population & higher compared to other chronic illnesses.
  - Empirical evidence suggests that psychological symptoms, to an extent, may be direct manifestations of the disease.
  - Chronic daily stressors can tax the immune system and some recent studies suggest a correlation between stressful life events and MS relapses.
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 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
Validity of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS)

RALPH H.B. BENEDICT, DIANE COOKFAIR, REBECCA GAVETT, MARK GUNTHER, FREDERICK MUNSCHAUER, NEETA GARG, AND BIANCA WEINSTOCK-GUTTMAN

1State University of New York (SUNY) at Buffalo School of Medicine, Department of Neurology, Division of Departmental and Behavioral Neurosciences, Buffalo, New York, USA
2Jacobs Neurological Institute, Buffalo General Hospital, Buffalo, New York, USA

(Received January 23, 2006; Final Revision March 23, 2006; Accepted March 23, 2006)

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

- Psychotherapy
- Triage
- Cognitive Rehabilitation
- Psychoeducation
- Lifestyle Modifications
- Interdisciplinary Team
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/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
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

MSCoE
- 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
Reminder!