Multiple Sclerosis: Thoughts about thinking

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Multiple Sclerosis: thoughts about thinking objectives

- Review MS epidemiology pathophysiology, & immunology, diagnosis & treatments and goals
- Review the symptoms of MS with a focus on cognition and depression
- Understanding of the role of nurses in Multiple Sclerosis
- Understand the complexity and uniqueness of the disease for each patient
What is Multiple Sclerosis?
Multiple Sclerosis: Epidemiology

- It is reported that there is approximately 400,000 cases in the United States\(^1\)
  - (estimates range from 250,000–500,000)
- Estimated 2.5 million cases worldwide\(^2\)
- Higher prevalence in those with northern European ancestry\(^3\)
- Highest incidence in Caucasians
- Higher incidence in women (≥3:1)\(^3\)
- 3/4 of cases present between ages of 15-45

Multiple Sclerosis: Pathophysiology

- The most common chronic disease affecting the central nervous system (CNS) in young adults
- Clinically characterized by relapses and remissions of neurological symptoms and progression of disability over time
- Pathologically, the hallmark is inflammation, demyelination and axonal loss in the CNS
- Immune-mediated, chronic, inflammatory disease, precipitated by unknown environmental factors in genetically susceptible individuals

Multiple Sclerosis: Immunology

- Unknown triggering actor
- MS is predominantly a T-cell mediated inflammatory disorder with overproduction of pro-inflammatory cytokines
- B-cells are also involved in the inflammatory process
- Disease is limited to the CNS
- T cells are activated against the CNS
- Lesions result from a highly selective, destructive process orchestrated by the immune system
  - These include dynamics at the level of the BBB:
    - the effects of the CNS responses on the biology of invading inflammatory cells
- New lesions are mixed with old lesions:
  - Old lesions: few immune cells, may have scars
  - New lesions: activated immune cells
In a demyelinated area, a remyelinating oligodendrocyte (arrow) extends its processes (arrowheads) to myelin internodes.
Pathophysiology: Axonal Loss

Arrowheads = areas of active demyelination.
Arrow = terminal axon ovoid.

Brain Atrophy in MS

- Brain atrophy can occur early in the disease and represents the cumulative effect of:
  - Demyelination and axonal loss
  - Diffuse, non-focal tissue damage
- Global brain atrophy: brain tissue decreases at an approximate mean rate of
  - 0.7%–2.0% per year in patients with MS
  - 0.1%–0.32% per year in normal controls

How do we diagnosis and treat MS?
How do we diagnose MS?

- History of “typical MS” presenting symptoms of more than 24 hrs duration
- Dissemination of CNS lesions in TIME & SPACE
- Objective neurological evidence on examination
- Supportive paraclinical tests: MRI or Evoke Potentials
- Laboratory: CSF- oligoclonal bands & ↑ IgG index
- Exclusion of all other causes
- Patient susceptibility
Typical presenting MS Symptoms

- Generalized weakness
- Visual changes
- Focal muscle weakness
- Fatigue
- Depression
- Bowel and bladder dysfunction
- Gait problems, spasticity
- Paresthesias
- Heat intolerance

- Dysarthria, scanning speech, dysphagia
- L’Hermitte’s sign*
- Neuritic pain
- Vertigo, ataxia
- Cognitive dysfunction
- Tremor, incoordination
- Sexual dysfunction
- Depression
- Pain

*Electric shock-like sensation down the spinal cord when flexing the neck
MS Diagnosis: McDonald MRI Criteria

- Gd-enhancing
- T2-hyperintense
- Infratentorial
- Juxtacortical
- Periventricular
- Spinal Cord

Courtesy of Kathleen Costello.
Why do we treat early in MS?

- Irreversible axonal injury occurs early
- Inflammation predominates early in the disease and is probably responsible for axonal injury
- Inflammatory changes diminish with time, so therapy directed at reducing inflammation is best started early
- Patients with greater amounts of early inflammatory events also experience earlier progression
## Treatments for RRMS: Disease Modifying Therapies (DMT’s)-

* CIS  **PPMS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Dosage &amp; Frequency</th>
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<tbody>
<tr>
<td>Alemtuzimab</td>
<td>IV</td>
<td>12 mg x 5 days 1\textsuperscript{st} yr., 12 mg x3 days 2\textsuperscript{nd} yr</td>
</tr>
<tr>
<td>Dimethyl fumarate</td>
<td>oral</td>
<td>120mg 2x /d x7 then 240mg -2x/d</td>
</tr>
<tr>
<td>Daclizumab</td>
<td>SQ</td>
<td>150 mg monthly</td>
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<tr>
<td>Fingolimod</td>
<td>oral</td>
<td>0.5mg daily</td>
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<tr>
<td>Glatiramer acetate</td>
<td>SQ</td>
<td>20mg daily * or 40mg 3x/wk</td>
</tr>
<tr>
<td>INF β- 1a</td>
<td>IM &amp; SQ</td>
<td>30mcg IM wk * or 44mcg SQ 3x/wk or 125 mg SQ q 14</td>
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<tr>
<td>INF β-1b</td>
<td>SQ</td>
<td>0.25 mg QOD *</td>
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<td>Natalizumab</td>
<td>IV</td>
<td>300 mg q month</td>
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<tr>
<td>Teriflunomide</td>
<td>oral</td>
<td>7 mg or 14mg daily</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>IV</td>
<td>600 mg q 6 months **</td>
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Brain Atrophy

Symptom presentation depends on lesion location

Neurologic Origins

Sensory symptoms
Lhermitte’s pain
Proprioception

Optic neuritis
Diplopia
Vertigo
Dysarthria

Tremor
Ataxia

Cognitive loss
Emotional disinhibition

Bladder dysfunction

Multiple Sclerosis: Cognitive Dysfunction & psychological effects
What Is Cognition?

- Thinking skills
- Understanding language and expressing yourself
- Concentrating, shifting attention, multitasking
- Learning and remembering new information
- Planning and performing complex tasks
- Solving problems
Cognitive Dysfunction in MS

- May affect 45%–70% of people with MS
- Not related to physical disability
- May occur early in the disease
- Is often under-recognized, underdiagnosed, and misdiagnosed
- In MS, self-reports of cognitive dysfunction are confounded by depression

Cognitive Dysfunction Often Correlates With MRI Findings

- Number of lesions
- Location of lesions
  - White matter
  - Gray matter
- Presence of atrophy

Brain Atrophy: MRI Findings
(Represents the cumulative effect of demyelination, axonal loss, and diffuse, nonfocal damage)

33-year-old man with RRMS for 2 years

47-year-old man with RRMS for 20 years

Courtesy of Dr. D. Mikol.
Cognitive Dysfunction Affects

- Activities of daily living
  - Household management
  - Personal care; family care
- Employment
- Recreational activities
- Relationships
- Social interactions
Areas Affected

- Speed of information processing
- Verbal and visual memory; information acquisition and retrieval
- Attention and concentration
- Word retrieval; verbal fluency
- Reasoning and problem solving
- Visual and spatial organization
- Executive functioning
Cognitive Functions Unaffected

- Overall intellect
- Long-term (remote) memory
- Recognition memory
- Conversational skill
- Reading comprehension
Signs of Cognitive Dysfunction

- Trouble remembering
- Difficulty finding the right words
- Inability to understand or slowness in understanding what is heard or written
- Forgetting a thought midsentence
- Difficulty following directions
- Trouble with decision making
- Emotional changes
Signs of Cognitive Dysfunction (cont)

- Poor performance reviews at work
- Taking more hours to accomplish a familiar task
- Difficulty starting a project
- Difficulty finishing a project
- Problems balancing a checkbook
- Problems following a recipe
- Car accidents
Memory

- 22%–31% of patients are affected
- Involves memory of events and conversations
- Involves both learning and recall
- Short-term memory is affected; may be related to poor concentration
- Long-term memory is spared

Information Processing and Attention

- 22%–25% of patients are affected

- Decreased processing speed; mental functioning slows

- Difficulty filtering out distractions

- Cannot focus on more than one task at a time (multitasking)

Verbal Fluency

- 22% of patients are affected
- Ability to retrieve words
- Ability to express thoughts in words

Executive Function

- 13%–19% of patients are affected
- Difficulties are more apparent to others than to the patient
- Difficulty understanding complex concepts
- Difficulty with organization
- Problems starting or completing projects
- Inability to solve problems or use good judgment in certain situations

Visual and Spatial Perception

- 12%–19% of patients are affected
- Affects activities of daily living
- Affects ability to drive
- Trouble operating machines
- Trouble assembling items

Language

- 8%-10% of patients are affected
- Patient engages in meaningless conversation
- Significant effect on relationships

Occurrence of Cognitive Deficits

- Patients with no problems: 24%–36%
- One area affected: 43%–56%
- Multiple areas affected: 20%–22%

Cognitive Dysfunction in MS: Other Causes

- Fatigue
  - Physical fatigue has less impact on cognition than once thought
  - Cognitive fatigue slows speed of information processing, accuracy, and reaction time

- Depression
  - Affects working memory

Medications That May Affect Cognition

- Anticholinergics and antimuscarinics
- Gabapentin, topiramate, phenytoin
- Amantadine, modafinil
- Diazepam, clonazepam
- Baclofen, tizanidine
- Morphine
- Tricyclic antidepressants
- Steroids
Diagnosis

- Neuropsychologist
- Speech–language pathologist
- Occupational therapist
Cognitive Evaluation

- Battery of tests designed to assess areas of reported difficulties, as well as pre-existing and current strengths
- Clinical neuropsychologist; occupational therapist; speech–language pathologist
- Full battery of tests: 6–8 hours over 2 days
- Expensive; often not covered by insurance
- Several screening tests are available
Cognitive Evaluation Is Appropriate When

- It is necessary to establish a baseline
- Changes in the patient’s abilities have been reported
- The patient’s condition is potentially treatable
- The patient is being started on a new treatment
- A patient’s application for Social Security Disability Insurance or vocational rehabilitation is being considered

Do Medications Help?

- Treatment with a disease-modifying therapy (DMT) early in the disease course may reduce the number of new lesions and ultimately play a role in preventing cognitive changes.

- Managing fatigue and treating depression may help with cognition.

- Donepezil may help some patients who have early cognitive impairment.
  - However, study results from AAN 2010 found no significant improvements in memory, attention, fluency, or visual or spatial processing in patients with MS.
  - Further study is needed.

Cognitive Rehabilitation

- Addresses affective and social issues
- Teaches compensatory measures
Depression
Depression

- Syndrome of signs and symptoms that are episodic or clustered and both psychological and physiological\(^1\)
- Occurs in 3%–5% of the general population\(^1\)
- May occur in approximately 60% of patients with MS\(^1\)
- “Profound sense of discomfort or withdrawal that lasts most of every day for at least 2 weeks”\(^2\)

What Do We Know?

- Depression differs from normal grieving
- People with MS are at increased risk for depression
- >50% of MS patients will experience a major depressive episode at some point over the course of the disease
- Suicide is 7.5 times more common in MS patients than in the general population

Characteristics of Depression

- Feelings of sadness or despair
- Loss of interest or enjoyment
- Fatigue and sleep disturbances
- Appetite changes
- Inability to concentrate
- Psychomotor slowing
- Irritability or anxiety
Depression and MS

- Increased incidence in patients with MS compared with patients who have other chronic disabling diseases
- Suggests a pathophysiological mechanism related to demyelination in the brain
- Seen less frequently in patients who have spinal cord disease only
- Increased in patients with brain atrophy
- May be related to interferon DMTs

Depression—Diagnosis and Treatment

- Symptoms of depression can be confused with other symptoms of MS such as fatigue and cognitive dysfunction; therefore, depression is difficult to diagnose.

- Best treatment for depression:
  
  Psychotherapy + Medication (+ Exercise)

- If the patient complains of depressed mood but doesn’t meet the criteria for major or minor depression, treatment may improve quality of life.

- Encourage the patient to seek strength in spiritual beliefs.
Depression—Implications

MS patients who are depressed:

- Carry an additional, painful burden
- Can’t participate actively in their own care
- Can’t plan or solve problems effectively
- Are difficult to live with
The incidence of depression is quite high among caregivers and family members of patients with MS.

Depression in caregivers increases as the patient’s disability increases.

Caregivers need to report signs of depression in themselves to their own physicians.

Emotional Lability

- Inability to control emotions
- Usually out of proportion to the degree of sadness or happiness
- May be a sign of emotional distress
- Usually responds well to antidepressants
Facts About MS and Depression

- Depression increases with:
  - Recent diagnosis
  - Changes in or loss of physical function
  - Lack of or decreased social support
  - Presence of comorbidities

- Younger patients are more likely to be depressed

- Men may be as likely as women to be depressed
Depression is one of the most treatable symptoms of MS
Management of Depression

- The patient should be asked about mood status at every appointment with any healthcare provider, both primary care physician and neurologist.
- Monitor depression carefully, especially if the patient is on an interferon or steroids.
- Refer the patient to appropriate mental health professionals as necessary.
- A dual approach of medications and psychotherapy is usually most beneficial.
- Exercise is a nonthreatening treatment.
MS Nursing Care Model

- Established Care
- Establishing Care
- Continuing Care
- Sustaining Care

- New or Probable MS
- Progressive MS
- Advanced MS
- Relapsing MS
Establishing Care

- Relationship building
- Open communication
- Building trust
- Sharing information
- Assessment
Continuing Care

- Patient and family education
  - Disease modifying therapies
  - Symptom management
  - Side effect management
- Encourage self-care strategies
- Assist with vocational issues
Sustaining Care

- Maintain patient well being
- Coordinate referrals
- Identify community resources
- Advocate for and help insure comprehensive MS care
Summary

- MS is a complex immune mediated disease that affects the central nervous system with inflammation, demyelination and axonal damage.
- Diagnosis is based upon history, clinical findings and paraclinical testing: MRI, spinal fluid, exclusionary lab findings, evoked potential testing
- While the majority of individuals will start with RRMS, most will develop progression of disability if untreated
- It is believed that early intervention with disease modifying therapy may stabilize the disease and/or delay progression of disability
Cognitive problems and depression are commonly seen in patients with MS.

There is considerable symptom crossover between MS and depression.

Providers need to be alert to the symptoms of depression and should attempt to diagnose depression and treat it appropriately.
Wish list

- Better ways to identify how patients are going to be affected by the disease
- Tools to measure if our medications have effect on brain volume and ultimately cognition
- Ability to predict how a patient will respond to a certain medication
- Regenerative therapies & remyelination
- Better medications to help manage the symptoms of MS
- Better lives for the patients and their families that live with this disease
Multiple Sclerosis: Complicated disease & each patient is unique
We must accept finite disappointment, but never lose infinite hope.

Martin Luther King, Jr.