Neuropsychiatric Disorders in Multiple Sclerosis: Assessment and Management

Laura Safar, MD
Brigham and Women’s Hospital
Neuropsychiatry Division
Center for Brain/Mind Medicine

Neuropsychiatric Disorders in MS

- Adjustment Disorder
- Mood / Affect Disorders:
  - Major Depression
  - Bipolar Disorder
  - Other Mood Syndromes
  - Pathological Laughing and Crying (PLC)
- Apathy; disinhibition
- Anxiety Disorders
- Cognitive Disorders
- Somatic Symptom Disorder
- Psychosis
- Substance-Related Disorders
- Comorbid syndromes & disorders:
  - Fatigue
  - Sleep Disorders
  - Pain

Neuropsychiatric disorders in MS
General Considerations

- Highly prevalent
- Impact on QOL, adherence to DMTs, prognosis
- They may be the initial clinical presentation
- They may signal a relapse

Psychiatric Disorders in MS: Pathophysiology

- Primary psychiatric illness
- Secondary to MS (inflammatory/ autoimmune, brain lesions)
- Secondary to medications
- Secondary to MS symptoms (fatigue, pain, sleep disorders)
- Psychosocial factors (stress/support, coping style)
- All of the above combined and interacting
Ms. B: Depression since 20s, +FH. Sx worsened since MS onset. Anxiety, Cognitive Dysfunction, Isolation, hypoactivity. Baclofen, tizanidine, BZD, steroids. MS physical sx: Pain, fatigue, Sleep Problems, Isolation, hypoactivity.

General Approach: Analyze complexity
- Screen, evaluate, & treat
- Screen/evaluate:
  - PHQ-9: Depression (BDI, HADS)
  - GAD-7: Anxiety
  - CNS-LS: PBA
  - MDQ: Bipolar Disorder
  - MFIS: Fatigue: Physical, cognitive, social
  - Audit-C: Alcohol, substances
  - MoCA: Cognitive performance
  - ADLs and IADLs
  - Risk: Meds, suicide, falls, abuse, driving, fire, financial.

...and also evaluate:
- Associated MS symptoms (fatigue, pain)
- Medical comorbidities (OSA, DM)
- DMTs: Therapeutic & side effects
- Symptomatic treatments including CAMs
- Coping style, values & priorities, motivations
- Support system, stressors, access to treatment, treatment team

DMTs- possible side effects

<table>
<thead>
<tr>
<th>DMT</th>
<th>Brand name</th>
<th>Psychiatric Side effects / other notes</th>
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<tbody>
<tr>
<td>Interferon beta 1a</td>
<td>IM, SC Avonex (IM), Rebin (SC)</td>
<td>Depression</td>
</tr>
<tr>
<td>Interferon beta 1b</td>
<td>SC Betaseron, Extavia</td>
<td>Depression</td>
</tr>
<tr>
<td>Glatiramer</td>
<td>SC Copaxone</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>IV Tysabri</td>
<td>Depression</td>
</tr>
<tr>
<td>Fingolimod</td>
<td>PO Gilenya</td>
<td>Neutral or ?Benefit for depression</td>
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<tr>
<td></td>
<td></td>
<td>(Montalban- Mult Scler 2011). Monitor QTc</td>
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Symptomatic treatments in MS

- Bowel and Bladder
  - Oxybutynin
  - Tolterodine
  - Darifenacin
  - Trospium
- Fatigue
  - Amantadine
  - Stimulants
  - Modafinil
- Spasticity
  - Baclofen
  - Diazepam
  - Dantrolene
  - Tizanidine
  - Intrathecal Baclofen
- Steroids (depression, agitation, euphoria, insomnia, psychosis)
- Pain Treatment
  - Phenytoin
  - Carbamazepine
  - Amitriptyline or Nortriptyline
  - Gabapentin
  - Pregabalin
  - Duloxetine
  - Opioids
  - Dalfampridine (Ampyra)
  - Psychotropics/ sleep agents
  - CAMs
  - Cannabinoids

Treatment: Bring it all back together

- Bio-psycho-social
- Individualized: Preferences & values
- Longitudinal: Needs vary: Educate, anticipate, accompany, assist with planning
- Support higher functioning, positive coping skills
- Interdisciplinary

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Mood Disorders in MS Study

- Fifty (50) patients with MS seen for treatment in outpatient neuropsychiatry clinic.
- Examined on the Patient Health Questionnaire-9 (PHQ-9), the Generalized Anxiety Disorder 7-item scale (GAD-7), the Center for Neurologic Study-Lability Scale (CNS-LS) for pseudobulbar affect (PBA), the Mood Disorder Questionnaire (MDQ), and the Modified Fatigue Impact Scale (MIFS).
- Also evaluated clinically, in initial psychiatric visits lasting 75 min and follow up visits lasting 45-60min.
- Findings from both, clinical evaluation and instruments were analyzed.
Results

- PHQ-9 analysis: 66% of our patients had a PMR/SAD ratio ≥ 1.
- PMR= Fatigue, sleep, concentration, psychomotor retardation items
- SAD = Decreased interest, sadness, negative self-thoughts, suicidal thoughts
- 11 subjects had PHQ-9 Score ≥5 but not depression.
- 8 subjects had PHQ-9 ≥10 but mild depression.
- Positive correlation between PHQ-9 scores and clinical depression

Conclusions

- Mood and affect symptoms in MS may include subsyndromal depression, anxiety, bipolar, and PBA symptoms, as well as the full-fledged disorders.
- Patients frequently present combined presentations.
- Screening tools may help identify relevant symptoms efficiently
- Clinical correlation is needed to reach an accurate diagnosis and select appropriate treatment.

Results

- MFIS and Depression: Strong correlation between MFIS scores (total, and sub-scales) and Depression
- MDQ and Bipolar Disorder:
  - 62% of individuals endorsed 1-3 items on the MDQ. This included “non-relevant” responses (e.g., distractibility due to cognitive dysfunction).
  - 10 patients endorsed 4 or more MDQ items. Of these, 6 were assessed as presenting bipolar spectrum symptoms.

CNS-LS Questionnaire and PBA:

- 9 individuals had scores ≥13 (suggestive of PBA; highly sensitive but less specific). 3 of those were considered to have mild PBA symptoms, in the context of clinical depression.

Depression

- Prevalence: 30-50% (Major Depression)
- Clinical Presentation: Similar to primary depression
- Comorbid MS symptoms: Fatigue, sleep disturbances, cognitive deficits, PMR
- Comorbid psychiatric symptoms:
  - Irritability, disinhibition, mood lability
  - PLC (Pseudobulbar affect)
  - Apathy: Syndrome of decreased motivation/ interest
  - Anxiety
### Depression: Treatment

- **Antidepressants:**
  - Small RCTs: Desipramine (marginal); Sertraline
  - Open-label trials: Duloxetine; Moclobemide; Fluoxetine; Sertraline; Imipramine; Tranylcypromine
- **ECT:** Severe, TRD
- **rTMS, tDCS:** Small trials- more research needed
- **Exercise:** Possible reduction in depressive symptoms
- **Psychotherapy:** CBT, MBT, ACT, Positive Psychology
- **Treat associated symptoms:** Fatigue, cognition, other mood symptoms
- **Treat MS (this may need to go to top)**
- **Treat MS symptoms, treat comorbidities**

### Bipolar Disorder

- **Prevalence:** Twice as common in MS as in the GP
- **Steroids, baclofen, stimulants, may contribute**
- **Treatment:** Mood stabilizers & atypical antipsychotics
- **Steroids- induced mania:** Prophylaxis with mood stabilizers or atypical antipsychotics
- **Sub-syndromal “bipolar” symptoms:** Irritability, emotional lability, agitation, disinhibition:

### Anxiety Disorders in MS

- **Prevalence 15-55 %**
- **Adjustment:** Post- diagnosis & relapses
- **Unpredictability- MS course, disability**
- **It increases suicide risk**
- **Increased use of benzodiazepines, other sedatives, alcohol, cannabis**
- **Clinical presentation:**
  - GAD
  - Somatic complaints; differential with MS physical symptoms
  - PD
  - OCD
- **Treatment:** Meds and psychotherapy as in primary anxiety disorders
- **Stress-management, ACT, mindfulness**

### Cognitive Disorder

- **40-70% of individuals with MS exhibit cognitive dysfunction**
- **Common complaints:** Difficulty multitasking; organizing; things take longer to do; increased effort for same tasks; less sharp
- **Abilities most commonly affected:**
  - Information Processing Speed
  - Memory: Encoding & retrieval
  - Attention
  - Executive function
  - Word retrieval
- **Deficits may occur early, before physical disability; profile broadens with MS progression; 10-25% of patients develop dementia**
- **Office screening:** MoCA = Dagenais Can J Neurol Sci 2013
- **Neuropsychological testing**
Cognitive Disorders: Treatment

- Treat depression, anxiety, insomnia, fatigue
- Treat MS: DMTs may improve cognition
- Reduce polypharmacy
- Amphetamine; methylphenidate: May improve attention; processing speed; learning & memory - Benedict 2008; Morrow 2013 & 2009
- Modafinil may improve attention - Lange J Neurol 2009
- AChEi: Donepezil: Possible benefit. Rivastigmine: Small studies; from none to marginal benefit
- Memantine: No benefit; possible neurological worsening (Lovera/Villoslada 2009)
- Amantadine/pemoline: Small trial; no significantly different from placebo
- Cognitive Rehabilitation

Thank you

Brigham and Women's Hospital
Neuropsychiatry Division
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Partners MS Center