

# Neuropsychiatric Disorders in Multiple Sclerosis: Assessment and Management

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## Neuropsychiatric Disorders in MS

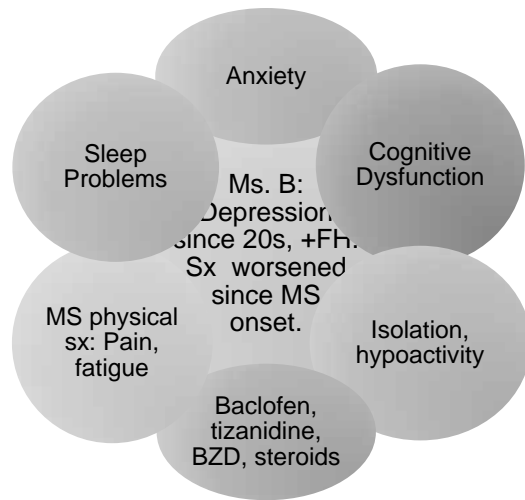
- **Adjustment Disorder**
- **Mood / Affect Disorders:**
- Major Depression
- Bipolar Disorder
- Other Mood Syndromes
- Pathological Laughing and Crying (PLC)
- **Apathy; disinhibition**
- **Anxiety Disorders**
- **Cognitive Disorders**
- **Somatic Symptom Disorder**
- **Psychosis**
- **Substance- Related 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



## 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

DMT		Brand name	Psychiatric Side effects / other notes
Interferon beta 1a	IM, SC	Avonex (IM), Rebif (SC)	Depression
Interferon beta 1b	SC	Betaseron, Extavia	Depression
Glatiramer	SC	Copaxone	Anxiety
Natalizumab	IV	Tysabri	Depression
Fingolimod	PO	Gilenya	Neutral or ?Benefit for depression (Montalban- Mult Scler 2011). Monitor QTc

## Symptomatic treatments in MS

- Bowel and Bladder
  - Oxybutynin
  - Tolterodine
  - Amitriptyline
  - 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
- Neurologist / neurological team
- Mental Health team (Psychiatrist, nurse practitioner, Social Worker/ psychotherapist, Neuropsychologist)
- Case manager
- OT, PT, CRT
- PCP, Pain specialist, sleep specialist, urologist, other.
- Patient and caregivers
- MS society, community resources, web
- Attorney (disability/ labor, estate planning)

## Neuropsychiatric Disorders in MS

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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  $\geq 1$ .
- PMR= Fatigue, sleep, concentration, psychomotor retardation items
- SAD= Decreased interest, sadness, negative self-thoughts, suicidal thoughts
- 11 subjects had PHQ-9 Score  $\geq 5$  but not depression.
- 8 subjects had PHQ-9  $\geq 10$  but mild depression.
- Positive correlation between PHQ-9 scores and clinical depression

## 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 (eg, 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  $\geq 13$  (suggestive of PBA; highly sensitive but less specific). 3 of those were considered to have mild PBA symptoms, in the context of clinical depression.

## Conclusions

- Mood and affect symptoms in MS may include sub-syndromal 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.

## 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)(Villostada 2009)
- Amantadine/pemoline: Small trial; no significantly different from placebo
- Cognitive Rehabilitation

# Thank you



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