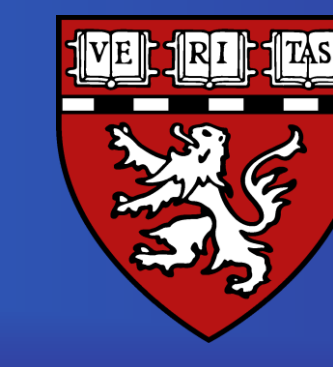


# Is it Depression? Clinical Presentation of Mood Disorders in Multiple Sclerosis



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## Background

The clinical presentation of mood disorders in the setting of neurological illnesses may differ from the classic presentation in primary psychiatric disorders. Patients with Multiple Sclerosis (MS) may present a high prevalence of symptoms such as irritability, affect and mood lability, apathy, fatigue and cognitive disturbances, with or without a concomitant major depressive syndrome (1,2,3).

In addition, non-depressed patients with MS frequently present symptoms of fatigue, cognitive, and sleep disturbances that may mimic depression (4).

A previous study validated the use of the PHQ-9 for the screening of depression in patients with MS (5).

Others cautioned that this scale may overestimate the presence and severity of depression due to the overlap of depression and MS symptoms (4).

These factors may misguide clinicians and cause patients to receive inadequate diagnosis and treatment.

## Objectives

- To examine the frequency of fatigue, sleep disturbances, cognitive dysfunction, irritability, and affect disturbances in 50 patients with MS referred to psychiatric treatment, and their relationship with these patients' psychiatric diagnoses.
- To assess the relationship between clinical psychiatric diagnoses and scores above cutoffs in selected scales.
- To evaluate the usefulness of standardized scales (PHQ-9, GAD-7, CNS-LS, MDQ, MFIS) in:
  - the screening and diagnosis of psychiatric disorders in patients with MS
  - the identification of comorbid symptoms

## Methods

Fifty (50) patients with MS referred to outpatient psychiatric treatment by their neurology provider were 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).

Patients were also evaluated clinically, in initial psychiatric visits lasting 75 minutes and follow up visits lasting 45-60 minutes. Findings from both, clinical evaluation and instruments were analyzed.

## Results

Table 1. Demographic characteristics

	Total Group (N=50)
Age	
≤ 40	22%
41-50	22%
51-60	38%
≥ 61	18%
Median age	53 y/o
Gender F:M	39:11

Table 2. Most Common DSM Diagnoses & frequency

Diagnosis	N= 50	% of sample with Dx.
Mood D/o 2dary MS	19	28%
Major Depressive Disorder	19	28%
Mood Disorder NOS (inc. Bipolar traits)	09	18%
Other Mood D/o	10	20%
Anxiety Disorders	30	60%
Cognitive Disorders	31	62%

Note: 94 % of patients had ≥2 diagnoses

Table 3. Clinically significant symptoms at index appointment

Clinical Syndrome	Percent of sample affected		
	Total	Mild sx	Syndrome
Depression/ depressive sx	62%	34%	28%
Anxiety/ anxiety sx	76%	46%	30%
Bipolar spectrum sx/ irritability	30%	28%	2%
Pseudobulbar Affect spectrum	8%	N/A	N/A
Cognitive Complaints	88%	N/A	N/A
Fatigue	88%	N/A	N/A
Sleep problems	24%	N/A	N/A

Table 4. Percent of sample population meeting score cutoffs

Measure (cutoff score)	Percent
PHQ-9 (5-9) (Mild depression)	40%
PHQ-9 (≥ 10) (Moderate+ depression)	40%
GAD-7 (5-9) (Mild Anxiety)	58%
GAD-7 (≥ 10) (Moderate+ anxiety)	22%
CNS-LS (≥ 13)	18%
MFIS (≥ 38)	70%

## Results

PHQ-9 sub-items Ratio	Percent of sample affected
PMR/SAD ratio (>1)	66%
PMR/SAD ratio (=1)	14%
PMR/SAD ratio (<1)	20%

### Relationship PHQ-9 & clinical depression:

•11 subjects had PHQ-9 Score ≥5 but not depression. 9 of them had PMR/ SAD ratio >1.

•8 subjects had PHQ-9 ≥10 but mild depression. 7 of them had PMR/ SAD ratio >1.

•There was a positive correlation between PHQ-9 scores and clinical depression:

-11% of the PHQ-9 <5 group had depression & 73% of the PHQ-9 ≥ 5 group had depression. (p-value for the difference: 0.0005)

-40% of the PHQ-9 <10 group had depression & 95% of the PHQ-9 ≥ 10 group had depression. (p- 0.0001)

-57% of the PHQ-9<15 group had depression & 100% of the PHQ-9≥15 group had depression. (p- 0.041)

**PHQ-9 PMR sub-scale & clinical depression:** The mean PMR score was 3.63 in the no depression group and 6.03 in the depression group (p=0.0011).

**PHQ-9 SAD sub-scale and clinical depression:** The mean SAD score was 1.00 in the no depression group and 4.32 in the depression group (p<0.0001)

**MFIS and Depression:** Strong correlation between MFIS scores (total, and sub-scales) and PHQ-9 scores. Correlation MFIS total score and PHQ-9: r=0.575, p<0.0001  
Correlation MFIS cognitive subscale scores and PHQ-9 summary score: r=0.677, p<0.0001

**MFIS and Anxiety:** Mild correlation between MFIS cognitive subscale scores and GAD-7 scores, but statistically significant (r=0.294, p=0.039).

### MDQ and Bipolar Disorder:

62% of individuals endorsed 1-3 items on the MDQ. This included relevant mood symptoms but also many non-relevant responses (eg, distractibility due to cognitive dysfunction).

6 individuals endorsed 4 – 6 MDQ items. Of these, 4 were assessed as presenting Bipolar spectrum symptoms. 4 individuals endorsed ≥7 items on the MDQ. Of these, 2 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.

## Discussion

Our data provides empirical support to previous findings (1,2,3) that mood and affect symptoms in patients with MS may be heterogeneous and mixed. This may include the presence of sub-syndromal bipolar and PBA symptoms that may still be clinically bothersome.

Screening tools may be an efficient way to identify relevant symptoms systematically, but clinical correlation is needed to reach an accurate diagnosis and to select adequate treatment. While the PHQ-9 can be helpful to identify depression, high scores in the items of sleep, concentration problems, fatigue, and psychomotor retardation may suggest depression in patients without this clinical problem, or may suggest more severe level of depression than clinically present. This may have treatment consequences: Some of these patients may benefit from measures to manage their fatigue, sleep, and cognitive problems but may not need antidepressants. This sample presents a high prevalence of psychiatric symptoms and disorders, as well as non-psychiatric symptoms such as fatigue, as previously reported in the MS literature. Since this sample contains individuals referred to psychiatric treatment, the prevalence of psychiatric symptoms is likely over-represented. The small sample size is also a limitation. On the other hand, this study provides the opportunity for detailed correlation between individuals' responses in self-report instruments and their clinical evaluation.

## Conclusions

Highly prevalent mood and affect symptoms in patients with MS may include a continuum of sub-syndromal depression, anxiety, bipolar, and PBA symptoms, as well as the full-fledged disorders. Patients may frequently present mixed presentations. Screening tools may help identify relevant symptoms efficiently, but clinical correlation is needed to reach an accurate diagnosis and select appropriate treatment. In particular, due to the high prevalence of fatigue, sleep, and cognitive problems in MS, clinical correlation is important when using the PHQ-9 as a screening tool for depression.

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