Screening for Depression in MS

May 28, 2014
CMSC Conference
CE Workshop # 15

Dallas, Texas

Presenters

Peter Arnett, Ph.D.
Professor of Psychology & Director of Clinical Training
Penn State University

Ralph HB Benedict, Ph.D.
Professor of Neurology
University at Buffalo, State University of New York

Anthony Feinstein, M.D., Ph.D.
Professor of Psychiatry
University of Toronto
Different Ways of Screening for Depression Clinically

Peter Arnett, Ph.D.
Penn State University

Key Contributors

- Chris Higginson, PhD
- Bill Voss, PhD
- Bruce Wright, MD
- William Bender, MD
- Jared Bruce, PhD
- Dawn Polen, PhD
- Fiona Barwick, MS
- Brian Ahlstrom, MD
- Gray Vargas, MS
- Margaret Cadden, BS
- Jon Tippin, MD
- John Randolph, PhD
- Pamela Freske, PhD
- Lauren Strober, PhD
- Megan Smith, PhD
- Chris Bailey, PhD
- Alicia Grandey, PhD
- Amanda Rabinowitz, PhD
- Joe Beeney, PhD
- Dede Ukueberuwa, MS
Outline

• **Depression Assessment Problem in MS**: MS Disease & Neurovegetative Depression Symptom Overlap.

• **Ways of Addressing Assessment Problem**: Remove Neurovegetative Symptoms from Consideration.

• **Ways of Addressing Assessment Problem**: Use Trunk & Branch Approach.

• **Clinical Recommendations & Caveats**.
Assessment Problem:

Many MS Disease Symptoms Overlap With Depression Symptoms

- Fatigue
- Psychomotor retardation
- Decreased concentration
- Insomnia or hypersomnia

All of the above are neurovegetative symptoms of depression

How can this issue be addressed when assessing depression in MS?
Use measures that do not include neurovegetative symptoms

Overview

• Depression Assessment Problem in MS: MS Disease & Neurovegetative Depression Symptom Overlap.

• Ways of Addressing Assessment Problem: Remove Neurovegetative Symptoms from Consideration.

• Ways of Addressing Assessment Problem: Use Trunk & Branch Approach.

• Clinical Recommendations & Caveats.
Chicago Multiscale Depression Inventory (CMDI)

• Nyenhuis, et al. (1995)¹

CMDI: 3 Subscales of 14 Items Each

• Mood: Sad, glum, low
• Evaluative: Inferior, worthless, a failure
• Vegetative: Fitful sleep, exhausted, uninterested in sex, poor appetite

Mood & evaluative scales shown to be reliable and valid for use in MS

BDI – Fast Screen (BDI – FS)\(^1\)

- 7 items (rated 0-3)
- Mood and negative evaluative symptoms only
- Takes only a few minutes to complete
- Shown to be valid in MS\(^2\)


- Explored validity of BDI – FS in MS
- 54 patients with MS
- 48 informants interviewed


- BDI–FS significantly correlated with other self-report measures of depression ($P<0.001$)
- BDI–FS significantly correlated with informant reported depression ($P<0.001$)
- BDI–FS scores discriminated patients with MS undergoing treatment for depressive disorder from untreated patients with MS ($P=0.01$)
How else can the MS disease/depression symptom overlap be addressed?

Distinguish between “trunk” and “branch” symptoms.

Overview

- **Depression Assessment Problem in MS**: MS Disease & Neurovegetative Depression Symptom Overlap.

- **Ways of Addressing Assessment Problem**: Remove Neurovegetative Symptoms from Consideration.

- **Ways of Addressing Assessment Problem**: Use Trunk & Branch Approach.

- **Clinical Recommendations & Caveats**.

---

CE ASSESSMENT OF DEPRESSION IN MULTIPLE SCLEROSIS: DEVELOPMENT OF A “TRUNK AND BRANCH” MODEL

L. B. Strober\(^1\) and P. A. Arnett\(^2\)
\(^1\)Kessler Foundation Research Center, West Orange, NJ and
\(^2\)Department of Psychology, The Pennsylvania State University,
University Park, PA, USA

The objective of the present investigation was to improve the detection of depression in multiple sclerosis (MS). It has been hypothesized that the overlap of MS symptomatology and neurovegetative depression symptoms may lead to an over-diagnosis of depression in MS. Discerning what is depression and what is more attributable to the disease renders a complicated picture when assessing depression in medically ill people. Given this, “trunk and branch” models have been proposed. In such models “trunk” symptoms are purported to be the symptoms common to the medical condition and less likely reflective of depression. “Branch” items are those symptoms that are independent of the medical condition and likely reflect depression. In the present investigation we compared depressed individuals with MS, non-depressed individuals with MS, and non-depressed controls, to devise a “trunk and branch” model for use with individuals with MS. By identifying which symptoms are typical in MS, which exceed what is typical in MS, and which symptoms are independent of MS, but more often present in depressed individuals with MS, we hoped to present a better understanding of the nature of depression in MS.
Strober & Arnett (2010)¹

• **Trunk symptoms**: Common to the medical condition and less likely to reflect depression.

• **Branch symptoms**: Independent of the medical condition and likely to reflect depression.


---

**Proposed Trunk & Branch Model for MS**
Strober & Arnett (2010): Identification of Depressed Patients

- Depression group if 2 of 3 of the following:
  - Dx of MDD
  - 1.5 SD above mean of controls on CMDI – Mood scale, as rated by patients’ S.O.’s.
  - Above the median on the DPRS.

Strober & Arnett (2010): Groups

- 67 non-depressed patients with MS (56F/11M)
- 17 depressed patients with MS (14F/3M)
- 22 healthy controls (18F/4M)
Key Measure

• **Beck Depression Inventory (Beck & Steer, 1987).**

Results

• No significant differences between the three groups on age, education, or estimated IQ.

• No significant differences between the depressed and non-depressed MS groups on symptom duration and diagnosis duration, but depressed had slightly higher EDSS scores.
Trunk Symptoms
Trunk Symptoms: Endorsed more often by MS vs. Controls:

- Fatigue
- Work difficulty
- Indecision
- Irritability
- Loss of libido
- Loss of interest
- Crying
- Dissatisfaction
- Self-criticism


Branch Symptoms
Branch Symptoms: Endorsed More Often by Depressed vs. Nondepressed MS

- Sense of failure
- Appetite changes
- Pessimism
- Loss of interest
- Sadness
- Crying
- Feelings of guilt
- Dissatisfaction
- Disappointment
- Irritability
- Weight loss
- Self-criticism
Some common MS symptoms may still reflect depression

- Which symptoms, though common to depressed and nondepressed MS, were more severe in the depressed group?

![Graph showing differences in severity of depressive symptoms between depressed and non-depressed MS patients.](image)

**Figure 3** Differences in severity of depressive symptoms between depressed and non-depressed multiple sclerosis patients. 

*Note: *\( \dagger p < .05, \, \ddagger p < .01, \, \dagger p < .001 *\)
Symptoms Common to MS but More Severe in Depressed MS*

- Loss of interest
- Dissatisfaction
- Crying
- Irritability
- Self-Criticism

*But not already accounted for as core branch symptoms


Modified “Trunk and Branch” Model for MS
Trunk Items

• Symptoms Endorsed More by MS vs. Controls.

Branch Items

• Symptoms Endorsed More by Depressed MS vs. Nondepressed MS.

• But... *Not* Endorsed More by MS vs. Controls.

Additional Branch Items

• Symptoms Common to MS but More Severe in Depressed than Nondepressed MS.

Clinical Implications

• **Branch Items**: Most weight.

• **Trunk Items**: Next most weight if they exceed what is typical in MS.

• **Item Cutoffs**: More research necessary to determine these.

Strober & Arnett (2014)

• **Goal**: Develop a measure based on items derived from “Trunk & Branch” study.

• **MS-BDI**: Includes 7 “Branch” items and 5 “Excessive” items.

• Evaluate sensitivity & specificity of MS-BDI relative to some existing measures.
Strober & Arnett (2014): Identification of Depressed Patients

- Depression group if 2 of 3 of the following:
  - Dx of MDD
  - 1.5 SD above mean of controls on CMDI – Mood scale, as rated by patients’ S.O.’s.
  - Above the median on the DPRS.

Strober & Arnett (2014): Groups

- 67 non-depressed patients with MS (56F/11M)
- 17 depressed patients with MS (14F/3M)
- 22 healthy controls (18F/4M)
Strober & Arnett (2014): Methods

• All administered the following measures:
  – Beck Depression Inventory-II (BDI-II)
  – Chicago Multiscale Depression Inventory (CMDI)
  – Beck Depression Inventory- Fast Screen (BDI–FS)
  – MS-BDI


Strober & Arnett (2014): Analyses

• ROC curves

• Sensitivity & Specificity

• Positive Likelihood Ratios (PLRs)
What is PLR?

• Measure of diagnostic accuracy.

• Measure of the odds that an individual has the disease when obtaining a positive test result.

• Measure of the increase in the likelihood an individual has a condition (i.e., depression) if they score above a cutoff.

PLR Interpretive Guidelines

• 1-2: Unlikely chance that the individual has the condition (is depressed).

• 2-5: Small chance.

• 5-10: Moderate chance.

• Above 10: Almost conclusive.
BDI–FS

- Cutoff of 4:
  - AUC = 0.96
  - Sensitivity = 94%
  - Specificity = 82%
  - PLR = 5.26

CMDI Mood

- Cutoff of 23:
  - AUC = 0.91
  - Sensitivity = 94%
  - Specificity = 84%
  - PLR = 5.73

CMDI Evaluative

- **Cutoff of 21:**
  - AUC = 0.89
  - Sensitivity = 71%
  - Specificity = 91%
  - PLR = 7.88

MS-BDI

- **Cutoff of 7:**
  - AUC = 0.91
  - Sensitivity = 77%
  - Specificity = 95%
  - PLR = 12.81

Strober & Arnett (2014): Screening

- BDI-FS and CMDI Mood scales have best sensitivity.

- BDI-FS suggested for use in screening given its ease of administration.

- Cutoff of 4 on BDI-FS is optimal (also c/w Benedict et al., 2003, & BDI-FS manual).


Strober & Arnett (2014): Diagnosis

- CMDI Evaluative-21 & MS-BDI scales have best specificity.

- BDI-MS could be used in diagnosis given its ease of administration and higher PLR.

- Cutoff of 7 is optimal.

Strober & Arnett (2014): Best Screening & Diagnostic Measures

Guidelines for assessing depression in MS

<table>
<thead>
<tr>
<th>Measure</th>
<th>Suggested Cutoff</th>
<th>Screening</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI-II</td>
<td>13</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>BDI-FS</td>
<td>4</td>
<td>X (superior)</td>
<td></td>
</tr>
<tr>
<td>CMDI Total</td>
<td>81</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CMDI Mood</td>
<td>27</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CMDI Evaluative</td>
<td>24</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21</td>
<td></td>
<td>X (superior)</td>
</tr>
<tr>
<td>MS-BDI</td>
<td>7</td>
<td>X (superior)</td>
<td></td>
</tr>
</tbody>
</table>


Another check on the validity of these measures:

Point Prevalence Rates

Depression Point Prevalence With Different Measures in MS

Point Prevalence Rates

- **Gold Standard (2 out of 3): 20%**
- **BDI-II: 35%**
- **BDI-FS: 33%**
- **CMDI-Evaluative-21: 13%**
- **CMDI-Mood-23: 21%**
- **CMDI-Vegetative: 44%**
- **MS-BDI: 20%**
Outline

- **Depression Assessment Problem in MS**: MS Disease & Neurovegetative Depression Symptom Overlap.

- **Ways of Addressing Assessment Problem**: Remove Neurovegetative Symptoms from Consideration.

- **Ways of Addressing Assessment Problem**: Use Trunk & Branch Approach.

- **Clinical Recommendations & Caveats**.

Clinical Recommendations for **Screening** Depression in MS: BDI-FS

- Use a cutoff of 4

- Validated in at least two MS studies and consistent with BDI-FS manual recs.
Clinical Recommendations for Diagnosing Depression in MS: BDI-MS

- Best specificity.
- Highest PLR.
- Theoretically driven.
- Incorporates some neurovegetative symptoms.
- Prevalence rate c/w gold standard.

But......
Strober & Arnett (2014): Limitations

• Small MS depressed sample.

• Small healthy control sample.

Strober & Arnett (2014): Follow-up

• Cross-validate findings on another (larger) sample.

• Include a non-MS depressed group.

• Above needed before clinical application of BDI-MS.