Depression and Dementia

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Objectives

• Discuss the prevalence and impact of depression in dementia
• Discuss identification and assessment of depression in dementia
• Discuss management strategies for depression in dementia
Causal Relationship Between Depression and Dementia

Green et al 2003 (MIRAG study), Panza et al 2010

“Emotional Symptoms” in amnestic Mild Cognitive Impairment (MCI)
In amnestic MCI using Neuropsychiatric Inventory (NPI):

- Dysphoria (39%), apathy (39%), irritability (29%), anxiety (25%)\(^1\)

\(^1\) Hwang et al 2004
How Prevalent Depression in Alzheimer’s Disease?

• Depressive symptoms: more than 50 %
• Major Depressive Disorder (MDD) up to 20% in hospital and nursing home setting
• Dysthymia or “Minor” depression: 8-26%


Prevalence of Depression in other Dementias

• VaD: higher than AD (about 1/3)1
• DLB and Parkinson dementia: high rate of depression and similarity in presentation2
• Huntington’s disease: may present with psychiatric symptoms including mood3
• PSP: apathy, sleep and depression4
• FTD: early symptoms may appear affective5

Impact of Depression on Dementia

- Added subjective suffering
- Further functional decline
- Increased caregiver burden
- Greater health care utilization
- Lower overall quality of life

Lyketsos et al 1997, Boustani and Watson 2004

Basic Mechanism of Depression in Dementia
Heterogeneity of causality of depression in dementia

Lee HB & Lyketsos CG 2003

General Depression Pattern of Brain Activity

Seminowicz et al Neuroimage 2004
Monoamine Modulators

White Matter Changes
In Dementia

- There is evidence for frontal hypoperfusion in depressed Alzheimer’s patients
- Disproportional loss of monoamine and Ach neurons
- Increased white matter hyper-intensities


Assessment of Depression in Dementia
Types of Depression Disorders in Dementia

- Major depressive disorder (MDD): at least 5 symptoms for at least 2 weeks
- Minor depression: less than 5 symptoms or less than 2 weeks
- Dysthymia: 1-2 symptoms for up to 2 years with no 2 months of remission


Depression in Dementia: overlap of Symptoms

- Decrease food intake and weight change
- Sleep change
- Reduced interest
- Mood fluctuation
- Psychomotor changes (agitation or retardation)
- Cognitive symptoms
Provisional Diagnostic Criteria for Depression in Alzheimer’s Disease

A. Three or more of the following symptoms over the same 2-week period, representing a change from previous baseline:
At least one of:
1. Depressed mood (sad, hopeless, discouraged, tearful)
2. Decreased positive affect or pleasure in response to social contacts and activities.


other symptoms...

3. Social isolation or withdrawal
4. Disruption in appetite
5. Disruption in sleep
6. Psychomotor agitation or retardation
7. Irritability
8. Fatigue or loss of energy
9. Worthlessness, hopelessness or excessive guilt
10. Recurrent thoughts of death or suicidal ideation

Other criteria...

B. All criteria are met for dementia of the Alzheimer’s type
C. Symptoms cause distress or disruption in functioning
D. Symptoms do not occur exclusively during delirium
E. Symptoms are not due to substances (medications or drugs of abuse).


In summary...

• A sub-acute (within few weeks) change from baseline mood and functioning
• Evidence of at least 3 mood symptoms, must include low mood and/or reduced positive affect or pleasure
• In a person diagnosed with Alzheimer’s
• And NOT in the course of delirium or due to substances
Cornell Scale for Depression in Dementia (CSDD)

- Designed for this patient population
- Info obtained from patients and caregivers
- Reasonable intrarater reliability (kw = 0.67), internal consistency (coefficient alpha: 0.84), and sensitivity
- Total scores correlates with depressive syndromes (0.83)
- Cut-off scores: ≥8 for significant symptoms, ≥12 for depressive syndrome (severity)

Alexopoulos et al 1988, Lam et al 2004 (Chinese), Amuk et al 2003 (Turkey)

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<table>
<thead>
<tr>
<th>Cornell Scale for Depression in Dementia</th>
<th>Name</th>
<th>Age</th>
<th>Sex</th>
<th>Date</th>
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</table>

**Scoring System**

- A = unable to evaluate
- 0 = absent
- 1 = mild or intermittent
- 2 = severe

Ratings should be based on symptoms and signs occurring during the week prior to interview. No score should be given in symptoms result from physical disability or illness.

A. Mood-Related Signs

1. Anxiety: various expression, rumination, worrying
   - 0
   - 1
   - 2

2. Sadness: sad expression, sad voice, tearfulness
   - 0
   - 1
   - 2

3. Lack of reactivity to pleasant events
   - 0
   - 1
   - 2

4. Irritability: easily annoyed, short-tempered
   - 0
   - 1
   - 2

B. Behavioral Disturbance

5. Agitation: restlessness, pacing, shouting
   - 0
   - 1
   - 2

6. Retardation: slow movement, slow speech, slow reactions
   - 0
   - 1
   - 2

7. Multiple physical complaints (score 0 if all symptoms only)
   - 0
   - 1
   - 2

8. Loss of interest: less involved in usual activities
   - 0
   - 1
   - 2

9. Appetite loss: eating less than usual
   - 0
   - 1
   - 2

10. Weight loss (score 2 if greater than 5 lbs in 1 month)
    - 0
    - 1
    - 2

11. Lack of energy: fatigued easily, unable to maintain activities
    - 0
    - 1
    - 2

D. Cyclic Functions

12. Diurnal variation of mood: symptoms worse in the morning
    - 0
    - 1
    - 2

13. Difficulty falling asleep later than usual for this individual
    - 0
    - 1
    - 2

14. Multiple awakenings during sleep
    - 0
    - 1
    - 2

15. Early morning awakening: earlier than usual for this individual
    - 0
    - 1
    - 2

E. Ideational Disturbance

16. Suicide feels life is not worth living, has suicidal wishes, or makes suicide attempt
    - 0
    - 1
    - 2

17. Poor self-esteem: self-blame, self-depreciation, feelings of failure
    - 0
    - 1
    - 2

18. Preoccupations: anticipations of the worst
    - 0
    - 1
    - 2

19. Mood congruent delusions: delusions of poverty, illness, or less
    - 0
    - 1
    - 2
How to Distinguish Depression from Apathy?

- Greek *a-pathos* = lack of feelings
- Lack of interest, concern and feelings
- Common in CVA and in dementia
- Associated with both cognitive and functional impairment
- Can be distinguished from depression on clinical grounds

# Apathy Scale: Starls

**APPENDIX I**

Original version of the Apathy Scale

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all (0)</th>
<th>Slightly (1)</th>
<th>Some (2)</th>
<th>A lot (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are you interested in learning new things?</td>
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<tr>
<td>2. Does your condition bother you?</td>
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<tr>
<td>3. Are you interested in your condition?</td>
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<tr>
<td>4. Do you prefer to do this thing?</td>
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<td>5. Are you always looking for something to do?</td>
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<td>6. Do you have plans and goals for the future?</td>
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<td>7. Do you have motivation?</td>
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<tr>
<td>8. Do you have the energy for daily activities?</td>
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<tr>
<td>9. Does someone have to tell you what to do each day?</td>
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<tr>
<td>10. Are you the sort of person who is motivated?</td>
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<tr>
<td>11. Are you uninterested in many things?</td>
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<tr>
<td>12. Do you need a push to get started on things?</td>
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<tr>
<td>13. Are you neither happy nor sad, just in between?</td>
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<tr>
<td>14. Would you consider yourself apathetic?</td>
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</tbody>
</table>

| Total (0-42)                                                            |                |              |          |           |

_Muran et al 1991, Starkstein et al 2011_

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### Depression

- I feel miserable
- I'm suffering, I can't do anything

### Apathy

- I don't care
- I'm fine, I don't want to do anything

So Leave Me Alone!

_Amer M Burhan, MBChB, FRCP(C)_: 13
Detection of Depression in Dementia: Practical Tips

- Is this a recurrent depression
- Is this a sub-acute change from baseline
- Is there a precipitant(s): Loss (all spheres)
- Are there statements indicating depression
- Do others see any indicators of depression
- Is there diurnal variation: morning worse?
- Use appropriate screening tools

Treatment Approach: Depression

- Rule out medical causes and correct
- Address unmet needs (isolation, hygiene) and environmental factors
- If no response, decide on treatment options based on risk-benefit analysis and patient/caregiver preference
- Identify target symptoms and follow them
Course of Treatment

- **Acute phase:**
  - Goal is remission of episode
  - Can take as long as 3 months in seniors
- **Continuation phase:**
  - Period of rehabilitation
  - Continue same treatment for 6 months, close follow-up
- **Maintenance Phase: Keeping well**

Modalities of Treatment for Depression

- **Psychological**
  - IPT and CBT for mild cognitive impairment,
    Problem Solving and supportive therapy,
    behavioral activation etc.
- **Pharmacotherapy: Antidepressants**
- **ECT**
Evidence for Antidepressants In Dementia

- After several small open label and double blind placebo controlled trials of several antidepressants (TCAs, SSRIs) a meta-analysis concluded that Antidepressants are safe and efficacious

Thompson S et al 2007

But...

- A recent UK, multi-centre, community-based, placebo controlled Sertaline or Mirtazepine trial showed no efficacy and added side effects!

Banerjee S et al 2011
Still for Severe Cases We Need to Treat

• “start low, go slow, but go all the way!”
• Chose antidepressants with less anticholenergic and less drug-drug interaction
• SSRI Sertaline, Citalopram/Cipralex (keeping in mind cardiac risk x dose)
• Switch to an SNRI if no response
• If no response combination therapy might be necessary (you may want to consult geriatric psych at that time)

Antidepressants In Dementia

• Citalopram 10-20 mg, S-citalopram 5-10 mg
  – Well tolerated, general SSRI side effects, dose in AM with food, if sedating move to supper, new cardiac warning at high doses
• Sertaline 25-150 mg (up to 200 mg): well tolerated, common SSRI side effects, dose AM with food unless sedating then move to supper
• Venlafaxine 37.5-150 mg (up to 375mg), activating, GI side effects, jitteriness, insomnia, high BP, dose in AM with food
Antidepressants In Dementia

- Duloxetine 30-60 mg (up to 90 mg), dose in am with food unless sedating then move to supper/HS, same general SE
- Mirtazepine 7.5-45 mg, sedating, anticholenergic, dose at HS but can activate with vivid dreams
- Trazodone 12.5-300 mg, use for anxiety and insomnia, minority of patients get agitated on it especially with iron deficiency
- Bupropion 75-300 (different preparations): activating, use in AM, can combine with SSRIs

Electroconvulsive Therapy (ECT)

- Psychotic depression, catatonia, limited oral intake, acute suicidality, severe agitated mood
- Safe and effective treatment in the elderly depressed including those with dementia
- Practiced very differently these days but still faces stigma
- Cognitive side effects more common in dementia but mainly episodic memory rather then global cognition, which improves!

Oudman E 2012
Conclusions...1

• Depression is common in patients with dementia and result in several added negative consequences
• There is significant overlap in symptoms between depression and dementia for example Apathy
• Depression can be identified using diagnostic tools focusing on identifying negative affect

Conclusions...2

• When depression is diagnosed, an individualized approach need to be developed identifying and addressing medical and psychosocial issues contributing to it.
• Psychological/behavioral strategies are good starting point in treating depression in dementia
• Anti-depressant and ECT could be used depending on the severity, after careful risk/benefit assessment and with appropriate consenting process
Questions/discussion