

## Depression and Dementia

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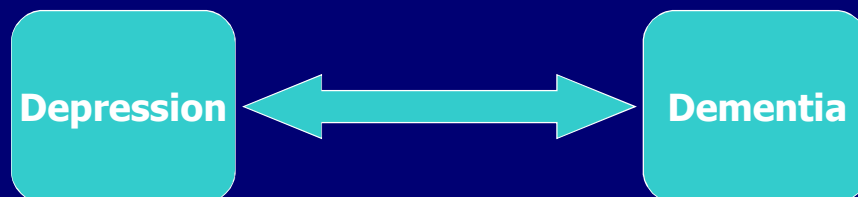
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### Objectives

- Discuss the prevalence and impact of depression in dementia
- Discuss identification and assessment of depression in dementia
- Discuss management strategies for depression in dementia

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## Causal Relationship Between Depression and Dementia



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

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## "Emotional Symptoms" in amnestic Mild Cognitive Impairment (MCI)

In amnestic MCI using Neuropsychiatric Inventory (NPI):

- Dysphoria (39%), apathy (39%), irritability (29%), anxiety (25%)<sup>1</sup>

<sup>1</sup> Hwang et al 2004

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## 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%

<sup>1</sup>Lyketsos et al 1997 , <sup>2</sup>Migliorelli et al 1995, <sup>3</sup>Bungemer et al 1996

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## Prevalence of Depression in other Dementias

- VaD: higher than AD (about 1/3)<sup>1</sup>
- DLB and Parkinson dementia: high rate of depression and similarity in presentation<sup>2</sup>
- Huntington's disease: may present with psychiatric symptoms including mood<sup>3</sup>
- PSP: apathy, sleep and depression<sup>4</sup>
- FTD: early symptoms may appear affective<sup>5</sup>

<sup>1</sup>Sultzer et al 1993, <sup>2</sup>Cummings 1992, <sup>3</sup>Dewhurst et al 1969, <sup>4</sup>Aldrich et al 1989, <sup>5</sup>Cummings & Duchon 1991

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## Impact of Depression on Dementia

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

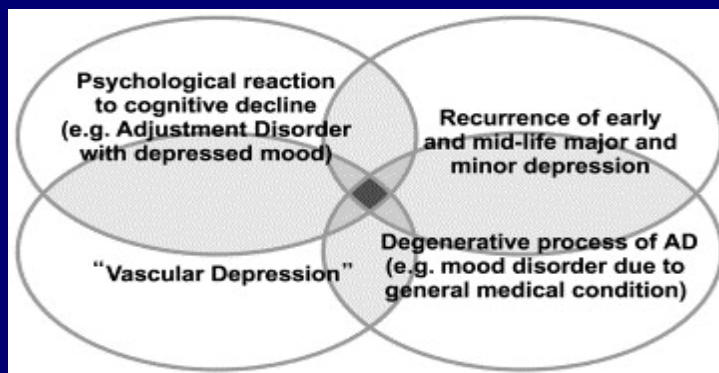
Lyketsos et al 1997, Boustani and Watson 2004

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## Basic Mechanism of Depression in Dementia

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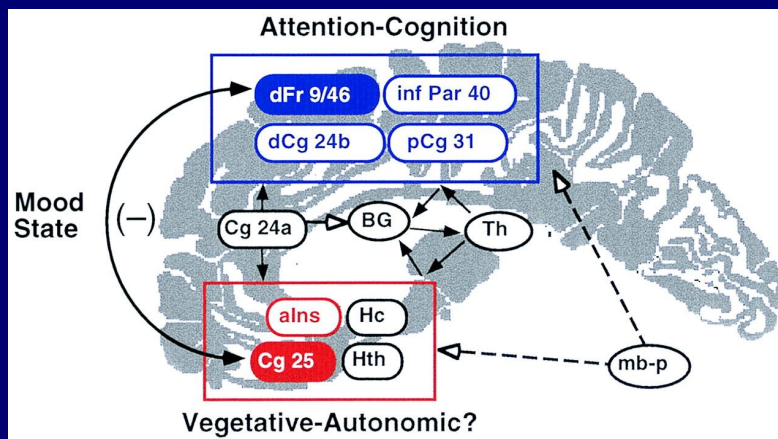
## Heterogeneity of causality of depression in dementia



Lee HB & Lyketsos CG 2003

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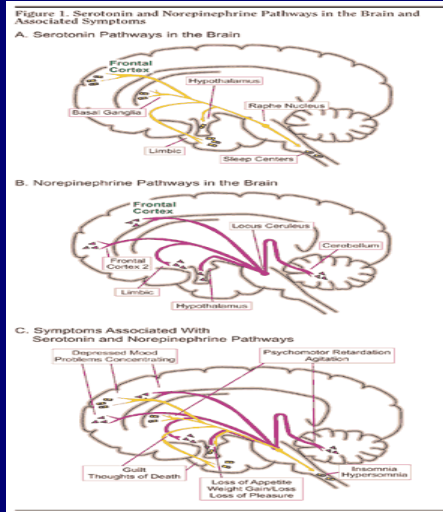
## General Depression Pattern of Brain Activity



Seminowicz et al Neuroimage 2004

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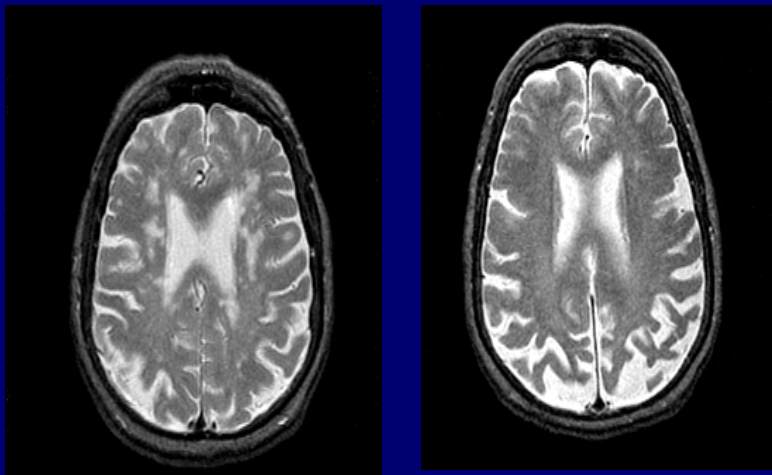
# Monoamine Modulators



Stephen M. Stahl

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# White Matter Changes



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## In Dementia

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

Levy-Cooperman, Burhan et al 2008, Forstl et al 1994, O'Brien et al 1996

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## Assessment of Depression in Dementia

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## 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

APA (2000), Diagnostic Statistical Manual-Forth edition Text Revision (DSM IV TR)

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## 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



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## 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.

Olin et al. Am J Geriatr Psychiatry 2002; 10:125-128.

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## 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

Olin et al. Am J Geriatr Psychiatry 2002; 10:125-128.

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## 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).

Olin et al. Am J Geriatr Psychiatry 2002; 10:125-128.

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## 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 interrater reliability ( $k_w = 0.67$ ), internal consistency (coefficient alpha: 0.84), and sensitivity
- Total scores correlates with depressive syndromes (0.83)
- Cut-off scores:  $\square 8$  for significant symptoms,  $\square 12$  for depressive syndrome (severity)

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

| Cornell Scale for Depression in Dementia                                                                                                                                     |                       |                          |            |   |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|--------------------------|------------|---|
| Name _____                                                                                                                                                                   | Age _____             | Sex _____                | Date _____ |   |
| Inpatient                                                                                                                                                                    | Nursing Home Resident | Outpatient               |            |   |
| <b>Scoring System</b>                                                                                                                                                        |                       |                          |            |   |
| 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. |                       |                          |            |   |
| <b>A. Mood-Related Signs</b>                                                                                                                                                 |                       |                          |            |   |
| 1. Anxiety: anxious expression, ruminations, worrying                                                                                                                        | a                     | 0                        | 1          | 2 |
| 2. Sadness: sad expression, sad voice, tearfulness                                                                                                                           | a                     | 0                        | 1          | 2 |
| 3. Lack of reactivity to pleasant events                                                                                                                                     | a                     | 0                        | 1          | 2 |
| 4. Irritability: easily annoyed, short-tempered                                                                                                                              | a                     | 0                        | 1          | 2 |
| <b>B. Behavioral Disturbance</b>                                                                                                                                             |                       |                          |            |   |
| 5. Agitation: restlessness, handwringing, hairpulling                                                                                                                        | a                     | 0                        | 1          | 2 |
| 6. Retardation: slow movement, slow speech, slow reactions                                                                                                                   | a                     | 0                        | 1          | 2 |
| 7. Multiple physical complaints (score 0 if GI symptoms only)                                                                                                                | a                     | 0                        | 1          | 2 |
| 8. Loss of interest: less involved in usual activities<br>(score only if change occurred acutely, i.e. in less than 1 month)                                                 | a                     | 0                        | 1          | 2 |
| <b>C. Physical Signs</b>                                                                                                                                                     |                       |                          |            |   |
| 9. Appetite loss: eating less than usual                                                                                                                                     | a                     | 0                        | 1          | 2 |
| 10. Weight loss (score 2 if greater than 5 lb. in 1 month)                                                                                                                   | a                     | 0                        | 1          | 2 |
| 11. Lack of energy: fatigues easily, unable to sustain activities<br>(score only if change occurred acutely, i.e., in less than 1 month)                                     | a                     | 0                        | 1          | 2 |
| <b>D. Cyclic Functions</b>                                                                                                                                                   |                       |                          |            |   |
| 12. Diurnal variation of mood: symptoms worse in the morning                                                                                                                 | a                     | 0                        | 1          | 2 |
| 13. Difficulty falling asleep: later than usual for this individual                                                                                                          | a                     | 0                        | 1          | 2 |
| 14. Multiple awakenings during sleep                                                                                                                                         | a                     | 0                        | 1          | 2 |
| 15. Early morning awakening: earlier than usual for this individual                                                                                                          | a                     | 0                        | 1          | 2 |
| <b>E. Ideational Disturbance</b>                                                                                                                                             |                       |                          |            |   |
| 16. Suicide: feels life is not worth living, has suicidal wishes, or makes suicide attempt                                                                                   | a                     | 0                        | 1          | 2 |
| 17. Poor self esteem: self-blame, self-depreciation, feelings of failure                                                                                                     | a                     | 0                        | 1          | 2 |
| 18. Pessimism: anticipation of the worst                                                                                                                                     | a                     | 0                        | 1          | 2 |
| 19. Mood congruent delusions: delusions of poverty, illness, or loss                                                                                                         | a                     | 0                        | 1          | 2 |

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## How to Distinguish Depression from Apathy?

- Greek *a-pathos*= lack of feelings
- Lack of interest, concern and feelings
- Common in CVA and in dementia<sup>1</sup>
- Associated with both cognitive<sup>2</sup> and functional impairment<sup>3</sup>
- Can be distinguished from depression on clinical grounds<sup>4</sup>

<sup>1</sup>Mega et al 1996, <sup>2</sup>Kusiz et al 1999, <sup>3</sup>Devanand et al 1992, <sup>4</sup>Marin et al 1993

Holthoff et al 2005



# Apathy Scale: Starsk

APPENDIX 1  
Original version of the Apathy Scale<sup>12</sup>

|                                                       |                |              |          |           |
|-------------------------------------------------------|----------------|--------------|----------|-----------|
| 1. Are you interested in learning new things?         | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 2. Does anything interest you?                        | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 3. Are you concerned about your condition?            | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 4. Do you put much effort into things?                | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 5. Are you always looking for something to do?        | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 6. Do you have plans and goals for the future?        | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 7. Do you have motivation?                            | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 8. Do you have the energy for daily activities?       | not at all (3) | slightly (2) | some (1) | a lot (0) |
| 9. Does someone have to tell you what to do each day? | not at all (0) | slightly (1) | some (2) | a lot (3) |
| 10. Are you indifferent to things?                    | not at all (0) | slightly (1) | some (2) | a lot (3) |
| 11. Are you unconcerned with many things?             | not at all (0) | slightly (1) | some (2) | a lot (3) |
| 12. Do you need a push to get started on things?      | not at all (0) | slightly (1) | some (2) | a lot (3) |
| 13. Are you neither happy nor sad, just in between?   | not at all (0) | slightly (1) | some (2) | a lot (3) |
| 14. Would you consider yourself apathetic?            | not at all (0) | slightly (1) | some (2) | a lot (3) |
| Total (0-42)                                          |                |              |          |           |

Marin et al 1991, Starkstein et al 2011

## • 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!

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## 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

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## 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

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## 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

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## Modalities of Treatment for Depression

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

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## 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

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## 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



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## Still for Severe Cases We Need to Treat

- “start low, go slow, but go all the way!”
- Chose antidepressants with less anticholinergic and less drug-drug interaction
- SSRI Sertaline, Citalopram/Cipralelex (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)

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## 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

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## 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, anticholinergic, 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

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## 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 than 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

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# Questions/discussion

