

# The Multiple Intersections Between Depression and Dementia

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## Learning Objectives

- Understand that depression may occur prior to dementia symptoms, early in the course of dementia or late in the progression of dementia, and each has implications for treatment.
- Review the difference between depression as a risk factor for dementia and depression as a presenting symptom of dementia

# Raw facts

- Prevalence of major depression in elderly (ages 65-100) 2.7% (SE, 0.37) in men and 4.4% (SE, 0.40) in women (Cache County Study - *Arch Gen Psychiatry*. 2000;57(6):601-607. doi:10-1001)
- Prevalence of Alzheimer's disease in elderly (ages 65-100) is 6.5% and all-cause dementia is 9.6% (Cache County Study - *Int Rev Psychiatry*, 2013;25(6), 673–685. doi:10.3109/09540261.2013.849663)
- Prevalence of Alzheimer's disease and dementia rises with age. Dementia prevalence increases with age, from 5.0% of those aged 71–79 years to 37.4% of those aged 90 and older. *Neuroepidemiology*, 2007; 29(1-2), 125–132. doi: 10.1159/000109998

## Depression as a Risk Factor for Dementia

- Can depression be an early symptom of a progressive dementia?
- Does having depression or depressive symptoms lead to an increased risk of dementia?
- Does treatment for depression with antidepressants or electroconvulsive therapy lead to increased risk of dementia?
- An 8 year prospective study of people 75 and older with every 18 month observations did not show increased dementia in those with depression.

Luppa, M., Luck, T., Ritschel, F., Angermeyer, M. C., Villringer, A., & Riedel-Heller, S. G. (2013). Depression and incident dementia. An 8-year population-based prospective study. *PLoS ONE*, 8(3), e59246. <http://doi.org/10.1371/journal.pone.0059246>

## Depression as a Premonitory Symptom of Dementia

- Using the National Alzheimer's Coordinating Center Uniform Data Set from September 2005 to March 2013, 2,416 cognitively normal individuals aged 50 years or older were followed for seven years.
- Individuals developing dementia were twice as likely to demonstrate depression prior to reaching diagnostic criteria for dementia than those that did not develop dementia.

Masters, M. C., Morris, J. C., & Roe, C. M. (2015). "Noncognitive" symptoms of early Alzheimer disease: a longitudinal analysis. *Neurology*, 84(6), 617–622. <http://doi.org/10.1212/WNL.0000000000001238>

- Conclusion – the jury is out whether depression is a risk factor or just an early symptom of dementia

## Depression as a Potentially Treatable Cause of Dementia Symptoms (Pseudo-Dementia)

- Since some people who will develop dementia first present with symptoms of depression, AND depression may contribute to poor performance on memory screening tests, there may be a clinical scenario of depression being diagnosed and successfully treated, with the poor memory testing improving. Over time, the other dementia symptoms develop and a dementia is diagnosed.
- In very rare cases, an initial diagnosis of dementia is made based on the poor memory testing, and when the memory improves after depression treatment "pseudo-dementia" is diagnosed. Unfortunately, when followed over time many or most of these people actually do develop true dementia.

## Depression as One of the Behavioral and Psychological Symptoms of Dementia

- Behavioral and psychological symptoms of dementia (BPSD) include noncognitive symptoms and behaviors that commonly occur in patients with dementia
- Studies have reported that major and minor depressive symptoms are seen in approximately one-third to one-half of persons with dementia.
- Recent large study in US using Medical Expenditure Panel Survey (2002, 2004, 2006, 2008, 2010, and 2012) data showed prevalence of depression in dementia of 22%. Am J Geriatr Psychiatry 2017; 25:803–813
- Those with a family history of depression are at increased risk for developing major depressive episodes during the course of the disease process.

## Lack of Association Between ECT and the Development of Dementia

- There is no evidence that electroconvulsive therapy (ECT) results in a higher incidence of dementia in persons treated for depression

Osler, M., Rosing, M. P., Christensen, G. T., Andersen, P. K., & Jorgensen, M. B. (2018). Electroconvulsive therapy and risk of dementia in patients with affective disorders: a cohort study. *The Lancet. Psychiatry*, 5(4), 348–356. [http://doi.org/10.1016/S2215-0366\(18\)30056-7](http://doi.org/10.1016/S2215-0366(18)30056-7)

## Association Between Antidepressant Drugs and the Development of Dementia

- There is an association between use of antidepressant drugs and the development of dementia (odds ratio 2), especially for use that begins earlier than age 65.
- The authors of recent meta-analysis suggest this is likely a result of confounding (depression as a symptom of dementia) but biological mechanisms potentially linking antidepressant exposure to dementia have been described, so an etiological effect of antidepressants is possible.

Moraros, J., Nwankwo, C., Patten, S. B., & Mousseau, D. D. (2017). The association of antidepressant drug usage with cognitive impairment or dementia, including Alzheimer disease: A systematic review and meta-analysis. *Depression and Anxiety, 34*(3), 217–226. <http://doi.org/10.1002/da.22584>

## Association Between Antidepressant Drugs and the Development of Dementia

- Just to confuse you more, there is evidence that citalopram decreases CSF A $\beta$  production in healthy individuals and in transgenic AD mice

Sheline, Y. I., West, T., Yarasheski, K., Swarm, R., Jasielec, M. S., Fisher, J. R., et al. (2014). An antidepressant decreases CSF A $\beta$  production in healthy individuals and in transgenic AD mice. *Science Translational Medicine, 6*(236), 236re4. <http://doi.org/10.1126/scitranslmed.3008169>

- This received much national and international press in 2014 but remains to be repeated or shown to have clinical importance either as treatment or prophylaxis

# Evidence for Efficacy of Antidepressant Drugs in Persons With Dementia

- Meta-analysis of all published clinical trials of antidepressant drug therapy for persons with dementia shows no efficacy compared to placebo

Nelson, J. C., & Devanand, D. P. (2011). A Systematic Review and Meta-Analysis of Placebo-Controlled Antidepressant Studies in People with Depression and Dementia. *Journal of the American Geriatrics Society*, 59(4), 577–585. <http://doi.org/10.1111/j.1532-5415.2011.03355.x>

- The drugs are associated with significant side-effects, though.
- This presents a conflict between evidence-based medicine and our desires to provide treatment
- 88% of persons with dementia in the US who have diagnosis of depression are receiving antidepressants

Bhattacharjee, S., Oh, Y. M., Reiman, E. M., & Burke, W. J. (2017). Prevalence, Patterns, and Predictors of Depression Treatment among Community-Dwelling Elderly Individuals with Dementia in the United States. *The American Journal of Geriatric Psychiatry*, 25(7), 803–813. <http://doi.org/10.1016/j.jagp.2017.03.003>

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