CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Antidepressant Use and Cognitive Decline: The Health and Retirement Study

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ABSTRACT

BACKGROUND: Depression is associated with cognitive impairment and dementia, but whether treatment for depression with antidepressants reduces the risk for cognitive decline is unclear. We assessed the association between antidepressant use and cognitive decline over 6 years.

METHODS: Participants were 3714 adults aged 50 years or more who were enrolled in the nationally representative Health and Retirement Study and had self-reported antidepressant use. Depressive symptoms were assessed using the 8-item Center for Epidemiologic Studies Depression Scale. Cognitive function was assessed at 4 time points (2004, 2006, 2008, 2010) using a validated 27-point scale. Change in cognitive function over the 6-year follow-up period was examined using linear growth models, adjusted for demographics, depressive symptoms, comorbidities, functional limitations, and antidepressant anticholinergic activity load.

RESULTS: At baseline, cognitive function did not differ significantly between the 445 (12.1%) participants taking antidepressants and those not taking antidepressants (mean, 14.9%; 95% confidence interval, 14.3-15.4 vs mean, 15.1%; 95% confidence interval, 14.9-15.3). During the 6-year follow up period, cognition declined in both users and nonusers of antidepressants, ranging from −1.4 change in mean score in those with high depressive symptoms and taking antidepressants to −0.5 change in mean score in those with high depressive symptoms and not taking antidepressants. In adjusted models, cognition declined in people taking antidepressants at the same rate as those not taking antidepressants. Results remained consistent across different levels of baseline cognitive function, age, and duration of antidepressant use (prolonged vs short-term).

CONCLUSIONS: Antidepressant use did not modify the course of 6-year cognitive change in this nationally representative sample.

 • *The American Journal of Medicine (2015) 128, 739-746*

KEYWORDS: Antidepressants; Cognition; Depression; Epidemiology

Depression is associated consistently with cognitive impairment and an increased risk for dementia in clinical and epidemiologic studies of older adults.[1-8] A meta-analysis of case-control and prospective studies concluded that a history of depression approximately doubled the risk for dementia.[1] However, whether treatment for depression can reduce the rate of cognitive impairment and dementia is unclear.[9-17]

Funding: See last page of article.

Conflict of Interest: See last page of article.

Authorship: See last page of article.

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0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2015.01.007

Research to date on the effects of antidepressants on the rate of decline in cognitive function has been limited by small sample sizes (<100 patients), short (<12 months) follow-up, lack of a comparison group, and selected subgroups of patients, such as those who responded to therapy (ie, those whose depressive symptoms decreased after treatment).[11-17] A number of studies have also examined whether antidepressant treatment can slow the rate of cognitive decline or progression of dementia among patients with preexisting cognitive impairments or dementia.[15,18-20] From these studies, it has been difficult to disentangle the association between antidepressant treatment and long-term cognitive outcomes in a broadly representative population of individuals with a wide range of cognitive function, from nonimpaired to moderately impaired, when depression is assessed.

CLINICAL SIGNIFICANCE

- Cognitive function did not differ at baseline between antidepressant users and nonusers.
- Rate of decline in cognitive function over 6 years did not differ between antidepressant users and nonusers.
- Treatment with antidepressant medication use does not seem to modify the well-established association between depression and cognitive decline.

Little work has been done on the relationship between antidepressant use and cognition in population-based samples. One study of 595 patients found that antidepressant use was associated with an increased risk of cognitive decline over 4.5 years among depressed patients without cognitive impairment.[10] Within the Women's Health Initiative Memory Study, antidepressant use was associated with a 70% increased risk of incident mild cognitive impairment over 7.5 years.[9] Of note, although the Women's Health Initiative Memory Study collected information on the type of antidepressant taken, neither study assessed the anticholinergic activity of antidepressants. Medications with anticholinergic effects, including amitriptyline, doxepin, paroxetine, and nortriptyline among others, can block muscarinic receptors causing impairment in various cognitive functions, including memory, executive function, and processing speed.[21]

We examined whether antidepressant use was associated with cognitive decline over a 6-year period using data from the nationally representative Health and Retirement Study (HRS) and the HRS Prescription Drug Study (PDS), which include serial assessments of cognitive function, depressive symptoms, and antidepressant treatment. We hypothesized that treatment with antidepressant medications would be associated with slower rates of cognitive decline.

MATERIALS AND METHODS

Data Source

Study data were drawn from the 2004, 2006, 2008, and 2010 waves of the HRS, and from the 2005 and 2007 waves of the PDS. The HRS is a longitudinal, nationally representative survey of US residents aged 51 years and older that includes assessments of depressive symptoms and cognitive function. The HRS began in 1992, and participants are re-interviewed every 2 years with high follow-up rates (90%-95%).[22] The PDS was a mail survey distributed to a subsample of the HRS, drawn from respondents to the 2004 HRS wave, designed to track changes in prescription drug use among beneficiaries as Medicare Part D was phased in. The PDS sample includes HRS respondents born in 1942 or earlier (age ≥65 years in 2007) or those who were already covered by Medicare or Medicaid between 2002 and 2004. This analysis starts with the 2004 data to correspond with the first wave of the PDS. This study was approved by the University of Michigan Institutional Review Board; participants provided informed consent at enrollment.

The current study included all PDS respondents born before 1943 who were community dwelling, self-respondents providing cognitive function and depressive symptom assessments in the 2004 HRS interview. Participants' cognitive function was assessed at each wave through the 2010 survey, with up to 4 total assessments. Our primary analyses focus on change in cognitive function in patients who were, compared with those who were not, taking antidepressants according to the PDS.

Assessment of Cognitive Function

At each HRS wave, cognitive function was assessed using a previously described and validated 27-point scale based on a battery of tests that included tests of memory, serial 7 subtractions, and naming.[23] This battery is a subset of an expanded battery (range, 0-35) administered to participants aged ≥65 years in the HRS; the expanded battery includes measures of orientation.[24] Participants requiring proxy interviews (because of cognitive or physical impairments that limited their ability to self-respond) were excluded from this analysis. Cut points for cognitive function were based on prior studies with the HRS data,[25,26] as well as methods used for the Aging, Demographics, and Memory Study, a supplemental study of dementia in the HRS.[27] These cut points defined a level of cognitive function that was generally consistent with normal function (12-27 points), cognitive impairment but no dementia (7-11 points), and dementia (0-6 points).[28]

Assessment of Depression

Baseline depression status was based on the 2004 wave of the HRS using an 8-item version of the Center for Epidemiologic Studies Depression Scale.[29,30] This version of the