Antidepressant use and functional limitations in U.S. older adults

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ABSTRACT

Objective: The upsurge in prevalence and long-term use of antidepressants among older adults might have profound health implications beyond depressive symptom management. This study examined the relationship between antidepressant use and functional limitation onset in U.S. older adults.
Methods: Study sample came from 2006 and 2008 waves of the Health and Retirement Study, in combination with data from 2005 and 2007 Prescription Drug Study. Self-reported antidepressant use was identified based on the therapeutic classification of Cerner Multum's Lexicon. Functional limitations were classified into those pertaining to physical mobility, large muscle function, activities of daily living, gross motor function, fine motor function, and instrumental activities of daily living. Cox proportional hazard models were performed to assess the effects of antidepressant use on future functional limitation onset by limitation category, antidepressant type, and length of use, adjusted by depression status and other individual characteristics.
Results: Antidepressant use for one year and longer was associated with an increase in the risk of functional limitation by 8% (95% confidence interval = 4%–12%), whereas the relationship between antidepressant use less than a year and function limitation was statistically nonsignificant. Antidepressant use was associated with an increase in the risk of functional limitation by 8% (3%–13%) among currently nondepressed participants but not currently depressed participants.
Conclusion: Long-term antidepressant use in older adults should be prudently evaluated and regularly monitored to reduce the risk of functional limitation. Future research is warranted to examine the health consequences of extended and/or off-label antidepressant use in absence of depressive symptoms.

Introduction

Antidepressants are one of the most commonly prescribed medications in the U.S. [1]. The prevalence of antidepressant use among Americans 12 years of age and above nearly quadrupled from 3% in 1988–1994 to 11% in 2005–2008 [2,3]. Older adults are substantially more likely to use antidepressants compared to younger adults. In 2005–2008, 14.5% of adults 60 years of age and above took antidepressants, compared to 6.1% among adults 18–39 years of age [1]. In addition, a large majority of older Americans taking antidepressants have taken the medication for one or more years [1].

The upsurge in prevalence and long-term use of antidepressants among older adults might profoundly impact many aspects of their physical and mental health beyond depressive symptom management. The side effects of antidepressant use have been extensively documented, which include nausea, sexual dysfunction, fatigue, drowsiness, insomnia, dry mouth, blurred vision, constipation, agitation, anxiety, increased appetite, and weight gain [4]. Older adults could be particularly vulnerable to these medication side effects due to compromised

cognitive and physical functioning. Long-term use of antidepressants that act on the serotonin system has been linked to reduced bone mineral density and osteoporosis [5,6], which is found to be associated with an elevated risk of fall and hip fractures in older antidepressant users [7,8].

The health implications of long-term antidepressant use among older adults can be substantial. Many of the medication side effects could potentially interfere with older adults' activities of daily living, increase the risk of functional limitations and disability, and reduce their health-related quality of life. However, to our knowledge, no study has prospectively assessed the impact of antidepressant use on functional limitations of various types in older adults. This study fills in the gap by examining the relationship between antidepressant use and functional limitations using data from a nationally representative sample of older adults.

Methods

Study setting

Individual-level data came from the Health and Retirement Study (HRS), an ongoing longitudinal study that surveys a representative

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sample of U.S. community-dwelling adults 50 years of age and above since 1992. Follow-up interviews are conducted every other year, with an overall response rate over 80% across waves. HRS collects rich information including income, employment, assets, pension plans, health insurance, disability, physical health and functioning, cognitive functioning, and health care expenditures. Survey design, questionnaires, and other details can be found on the HRS web portal (http://hrsonline.isr.umich.edu/). This study used data from HRS 2006 and 2008 waves that were cleaned and compiled by the RAND Corporation (RAND HRS enhanced fat files and longitudinal dataset version N), merged with data from HRS 2005 and 2007 Prescription Drug Study (PDS). This data arrangement allowed us to examine the effect of previous antidepressant use on current functional limitation onset (i.e., antidepressant use in 2005 and 2007 in relation to functional limitation incidents in 2006 and 2008).

HRS was approved by the University of Michigan Human Subjects Review Committee. The present study involved secondary-data analysis of de-identified, publicly available data, and was deemed exempt from human subjects review by the Institutional Review Board of the University of Illinois at Urbana-Champaign.

Antidepressant use

HRS 2005 and 2007 PDS were a two-wave mail survey designed to track changes in prescription medication utilization among U.S. older adults. At the PDS baseline in 2005, a sample of 5654 individuals was drawn from HRS 2004 wave participants, including those born in 1942 or earlier or already covered by Medicare or Medicaid at some time between 2002 and 2004. People lacking prescription medication coverage or having low income and wealth were oversampled.

PDS respondents were asked to list all medications prescribed, report length of use for each listed medication, and document the medication name from the label on the prescription bottle. Medications were then matched to the three-level nested therapeutic classification scheme of Cerner Multum's Lexicon [9]. Based on the definition for antidepressant use of the Centers for Disease Control and Prevention, respondents were considered to be taking antidepressant if any of their medications were matched to the second level of drug categorical codes, specifically code 249 [1]. We further classified antidepressants into six major types: tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), atypical antidepressants (Mirtazapine [Axit, Mirtaz, Mirtazon, Remeron, Remeron SolTab, Zispin], Bupropion [Aplenzin, Budeprion XL, Buproban, Wellbutrin, Zyban], Trazodone [Desyrel, Oleptro], Nefazodone [Serzone], Vilazodone [Viibryd], and Vortioxetine [Brintellix]), monoamine oxidase inhibitors (MAOIs), and pharmacotherapeutic combination antidepressants (Amitriptyline/Perphenazine [Triavil], Chlordiazepoxide/Amitriptyline [Limbitrol], Perphenazine/Amitriptyline [Etrafon], and Olanzapine/Fluoxetine [Symbyax]).

Functional limitations

Functional limitations in HRS were classified into six categories based on validated indices. These indices were adopted for their comparability with other studies that measured functional limitations, their validity and reliability, and consistency across survey waves [10,11]. The six categories of functional limitations include: physical mobility limitation, large muscle function limitation, activities of daily living limitation, gross motor function limitation, fine motor function limitation, and instrumental activities of daily living limitation. Each question asked whether a participant had any difficulty (coded as "yes" or "no") in performing a specific activity. Physical mobility consists of five activities: walking one block, walking several blocks, walking across a room, climbing one flight of stairs without resting, and climbing several flights of stairs without resting. Large muscle function consists of four

activities: sitting for about two hours, getting up from a chair after sitting for long periods, stooping or kneeling or crouching, and pulling or pushing large objects like a living room chair. Activities of daily living limitation consist of five activities: bathing or showering, eating, dressing, walking across a room, and getting in or out of bed. Gross motor function consists of four activities: walking one block, walking across a room, climbing one flight of stairs without resting, and bathing. Fine motor function consists of three activities: eating, dressing, and picking up a dime from a table. Instrumental activities of daily living consist of three activities: using a telephone, taking medication, and handling money. Functional limitation of a specific category is defined as having difficulty (i.e., an answer of "yes") in performing at least one of the activities included in that category. Any functional limitation is defined as having one or more of the functional limitations in these six categories.

Depression

Depressive symptoms were measured by the eight-item Center for Epidemiologic Studies Depression Scale (CES-D), a shortened version of the 20-item CES-D [12]. Participants were asked whether ("yes" or "no") they felt depressed, felt that everything was an effort, slept restlessly, could not get going, felt sad, felt lonely, enjoyed life, and were happy in the past week. The two positive items (i.e., "enjoyed life" and "was happy") are reverse-coded, so that a higher score indicates a more depressed mood. The eight-item CES-D total score, ranging from zero to eight, sums up the presence of (coded as one) or absence (coded as zero) from each of the eight feelings. Melchior et al. (1993) reported that the eight-item and 20-item CES-D scales were highly correlated ($r = 0.93$) and had comparable discriminant validity [13]. A cut-off score of three has been suggested by previous validation studies to indicate clinically relevant depressive symptoms [14]. This cut-off score has a sensitivity of 0.71 and a specificity of 0.79 to predict major depressive episodes [14]. A participant was classified as having a depression onset in a survey wave if one scored three or above on the eight-item CES-D in that wave.

Other individual characteristics

We controlled both wave-invariant and wave-variant individual characteristics in the regression analyses. Wave-invariant covariates include gender, race/ethnicity (non-Hispanic white, non-Hispanic African American, non-Hispanic other race or multi-race, and Hispanic), and education (education less than high school, high school, college, and education higher than college). Wave-variant covariates include age in years, marital status (married or living with partner, and unmarried, divorced, separated, or widowed), household net wealth (divided into four quartiles based on the wealth distribution in each survey wave), current smoking status, heavy drinking status (defined as one or more drink per day on average or four or more drinks on any occasion in the past three months for women, and two or more drinks per day on average or four or more drinks on any occasion in the past three months for men), depression status (CES-D score of three and above), diagnosis of a chronic condition (hypertension, diabetes, heart disease, stroke, lung disease, arthritis, cancer, and memory related disease), residential census region (Midwest, Northeast, South, and West), and body weight status. Body mass index (BMI) was calculated from self-reported height and weight. Body weight status was classified into four categories based on the international classification of adult BMI values – underweight ($BMI < 18.5 \text{ kg/m}^2$), normal weight ($18.5 \text{ kg/m}^2 \leq BMI < 25 \text{ kg/m}^2$), overweight ($25 \text{ kg/m}^2 \leq BMI < 30 \text{ kg/m}^2$), and obesity ($BMI \geq 30 \text{ kg/m}^2$) [15].

Study sample

PDS 2005 wave data were merged to HRS 2006 wave data, and PDS 2007 wave data were merged to HRS 2008 wave data, both using personal identifiers that uniquely identified each study participant.