Depression, Antidepressants, and Falls Among Community-Dwelling Elderly People: The MOBILIZE Boston Study

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Background. The mechanisms linking falls and depression are still unknown. The aim of the study is to examine the association between depression and antidepressants, with indoor and outdoor falls, and to investigate how antidepressants mediate this relationship.

Methods. The study included 763 men and women aged 70 and older with baseline measures for depression and antidepressant use are captured with prospective data on falls from the “Maintenance of Balance, Independent Living, Intellect and Zest in the Elderly” (MOBILIZE) Boston study, which is a population-based longitudinal study (from 2005 to 2009).

Results. Overall, the rate of falls was 26 falls/100 person-years. Seventeen percent of participants had clinically significant depressive symptoms (CSDS), and 12% used antidepressants. CSDS increased the risk of indoor and outdoor falls (incidence rate ratio [IRR] = 1.6, 95% confidence interval [CI] = 1.2–2.3, \( p < .01 \)). Antidepressant use increased the risk of outdoor falls by 70% and partially mediated the association between CSDS and outdoor falls (IRR = 1.7, 95% CI = 1.2–2.5, \( p < .05 \)). There was no relationship between antidepressant use and indoor falls. Similar results were observed when depression was considered as a continuous variable.

Conclusions. Depression increased the risk of indoor and outdoor falls. Antidepressant use among older adults with CSDS increased the risk of outdoor, but not indoor falls. Clinicians should carefully consider the role of antidepressants among older adults with CSDS and their potential increase for the risk of outdoor falls.

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endocrine stressors (9). Alternatively, depression may lead to falls via antidepressants, which can impair attention, gait, balance, and blood pressure regulation (1,10).

Some studies have found an association between antidepressants and falls (11,12), whereas other studies have not (13,14). A systematic review by Hartikainen and colleagues from 1996 to 2004 concluded that there was an inconsistent association between antidepressants and falls (15). Therefore, it remains unclear whether antidepressants help mitigate depressive symptoms and ultimately lower fall risk, or inadvertently increase the risk of falls (15).

Given the lack of data on the relationships between depression symptoms, antidepressants, and falls risk, our objective was to examine the associations between depression, antidepressants, and indoor or outdoor falls in a community-based study of older adults. Our secondary objective was to determine whether antidepressants mediate the relationship between depression symptoms and indoor and outdoor falls.

METHODS

Study Participants

Participants included 763 members of the “Maintenance of Balance, Independent living, Intellect and Zest in the Elderly” (MOBILIZE) Boston study, a population-based prospective longitudinal study designed to investigate novel risk factors for falls (16). Participants were recruited from September 2005 to April 2009. The sampling frame was obtained from the list of households with adults aged ≥ 70 years within a 5-mile radius of the Hebrew SeniorLife, Boston, MA. Inclusion criteria were that participants had to be ≥70 years and able to (i) communicate in English, (ii) walk independently across a small room either with or without the use of a walker or cane, and (iii) demonstrate no more than minimal cognitive impairment (mini-mental state examination ≥ 18) (17). Participants who planned to move to another state during the next 2 years, or suffered from terminal illness, or severe vision, or hearing deficits were excluded. The participation rate of MOBILIZE Boston was 58% (18,19). The study was approved by the Institutional Review Board of Hebrew SeniorLife for human participants research.

Falls

A fall was defined as unintentionally coming to rest on the floor, ground, or other lower surface (20). Falls were ascertained by self-report using falls calendar postcards and telephone interviews for participants who did not return the calendar. Any participant reporting a fall would receive a follow-up phone call to collect more information about the location and circumstances of the fall. An indoor fall was defined as one that occurred inside the participant’s home, inside someone else’s home, inside another building, or inside another location. Outdoor falls were those reported to have occurred anywhere outside (5).

Depression

The Center for Epidemiologic Studies Depression-Revised (CESD-R) scale, which is an updated version of the CESD scale (21), served as the measure of depression (22–25). The CESD-R consists of 20 items that cover all Diagnostic and Statistical Manual of Mental Disorders criteria for depression (26). The modified-CESD-R (m-CESD-R) scale was constructed using item response theory methods and rescaled to a mean of 50 and standard deviation of 10, with higher scores indicating worse depression. Because all persons who satisfy the Diagnostic and Statistical Manual of Mental Disorders criteria for major depression have a m-CESD-R score ≥ 60 (ie, 1 SD above the mean score in persons aged 70–74 years), we defined clinically significant depressive symptoms (CSDS) as a m-CESD-R score of ≥60. In a sensitivity analysis, we restricted the definition of depression to participants diagnosed with depression in the past year by a clinician.

Antidepressant Use

During the baseline home interview visit, participants were asked to show study interviewers all over-the-counter and prescription medications they used in the past 2 weeks. Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), or other antidepressants were classified based on the Iowa Drug Information System ingredient codes (27). Use of any antidepressant in the 2 weeks before the baseline interview was defined as antidepressant use.

Other Covariates

Height was measured in meters and weight was measured with light clothing in kilograms and used to calculate body mass index (kg/m²). Race and education were self-reported. Cognitive function was measured by the mini-mental state examination. Executive function was characterized using Trails B, with higher scores indicating slower (worse) cognitive function. Gait speed of participants during a 4-m walk was measured twice. The faster gait speed was used for analyses based on suggestion from previous studies (28). Comorbidities (ie, heart disease, hypertension, diabetes mellitus, spinal stenosis or disc disease, lung disease, stroke, arthritis, kidney disease, liver disease, ulcer or stomach disease, anemia, and cancer) were self-reported and summed to create a comorbidity index (range from 0 to 12) (29). Vision was measured with a Snellen eye chart at 20 ft and categorized by tertiles. Physical activity was measured by the validated Physical Activity Scale for the Elderly (30), a self-reported summary scale of participation in 10 common activities with higher scores indicating more activity. Blood pressure was measured while sitting.
and after standing at 1 and 3 minutes. A decline of 20 mm Hg in systolic blood pressure associated with standing was defined as systolic orthostatic hypotension. The number of times during a month participants walked for exercise in their neighborhood and engaged in sedentary activities, such as reading, watching TV, or doing handcrafts, was measured by self-administered questionnaire.

**Statistical Analysis**

Univariate analyses were conducted to check the distribution of each variable and to describe the characteristics of participants by CSDS status (Table 1). To describe the association between either depression or antidepressants and indoor and outdoor falls, incidence rate ratios (IRR) and 95% confidence intervals (CIs) were calculated using negative binomial regression models. Participants who experienced both an indoor and outdoor falls during follow-up were included in both indoor and outdoor models. Depression was considered as both a dichotomous variable (ie, yes vs no CSDS) and as a continuous variable (m-CESD-R scale). Fully adjusted models considered age, gender, race, education, body mass index, vision, comorbidities, physical activity, executive function, gait speed, and minimal state examination as covariates.

Using the definition of mediation from previous studies (31,32), we then tested whether the relationship between depressive and falls was explained by antidepressant use. A mediator effect was supported if the β coefficient for depressive was reduced by more than 10% when the mediator (ie, antidepressant use) was included in the models (33). All analyses were conducted in SAS, version 9.2 (34).

**Results**

Table 1 shows the baseline characteristics of the study population. The mean age of participants was 78 ± 5 years. Sixty-four percent were female participants, and 78% were white. The mean m-CESD-R score was 50 (range: 31–84). The prevalence of antidepressant use was 12% (7% SSRI, 2% TCA, and 3% other). Seventeen percent of participants had CSDS. Participants with CSDS tended to have a greater number of comorbidities, poor vision, cognitive impairment, and slower gait speed. Fifty-three percent of participants were prescribed an antidepressant and had no CSDS.

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**Table 1. Characteristics of 763 Participants of the Maintenance of Balance, Independent Living, Intellect and Zest in the Elderly (MOBILIZE) Boston Study, as Characterized by Clinically Significant Depressive Symptoms (CSDS) Status**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n = 763)</th>
<th>Non-CSDS (a) (n = 631)</th>
<th>CSDS (b) (n = 132)</th>
<th>p-Value (a vs b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year), M (SD)</td>
<td>78 (5)</td>
<td>78 (5)</td>
<td>78 (6)</td>
<td>.91</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>489 (64)</td>
<td>395 (63)</td>
<td>94 (71)</td>
<td>.06</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>593 (78)</td>
<td>497 (79)</td>
<td>96 (73)</td>
<td>.14</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school, n (%)</td>
<td>85 (11)</td>
<td>66 (11)</td>
<td>19 (14)</td>
<td>.40</td>
</tr>
<tr>
<td>High school/vocational training, n (%)</td>
<td>314 (41)</td>
<td>261 (4)</td>
<td>53 (40)</td>
<td></td>
</tr>
<tr>
<td>At least 4 y College/graduate education, n (%)</td>
<td>363 (48)</td>
<td>304 (48)</td>
<td>59 (45)</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²), M (SD)</td>
<td>27 (5)</td>
<td>27 (5)</td>
<td>27 (5)</td>
<td>.73</td>
</tr>
<tr>
<td>Comorbidity index (range: 0–12), M (SD)</td>
<td>3 (2)</td>
<td>3 (2)</td>
<td>4 (2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Vision</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vision &lt; 61, n (%)</td>
<td>249 (33)</td>
<td>198 (31)</td>
<td>51 (39)</td>
<td>.04</td>
</tr>
<tr>
<td>61 ≤ Vision &lt; 73, n (%)</td>
<td>243 (32)</td>
<td>207 (33)</td>
<td>36 (27)</td>
<td></td>
</tr>
<tr>
<td>Vision ≥ 73, n (%)</td>
<td>269 (35)</td>
<td>225 (36)</td>
<td>44 (33)</td>
<td></td>
</tr>
<tr>
<td>Physical activities (PASE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PASE &lt; 66, n (%)</td>
<td>248 (33)</td>
<td>194 (31)</td>
<td>54 (41)</td>
<td>.06</td>
</tr>
<tr>
<td>66 ≤ PASE &lt; 121, n (%)</td>
<td>250 (33)</td>
<td>208 (33)</td>
<td>42 (32)</td>
<td></td>
</tr>
<tr>
<td>PASE ≥ 66, n (%)</td>
<td>258 (34)</td>
<td>222 (36)</td>
<td>36 (27)</td>
<td></td>
</tr>
<tr>
<td>Executive function (Trails B, s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Trail B &lt; 91, n (%)</td>
<td>233 (31)</td>
<td>199 (32)</td>
<td>34 (26)</td>
<td>.04</td>
</tr>
<tr>
<td>91 ≤ Trail B &lt; 155, n (%)</td>
<td>233 (31)</td>
<td>201 (32)</td>
<td>32 (24)</td>
<td></td>
</tr>
<tr>
<td>Trail B ≥ 155, n (%)</td>
<td>246 (32)</td>
<td>193 (31)</td>
<td>53 (40)</td>
<td></td>
</tr>
<tr>
<td>Antidepressant use, n (%)</td>
<td>93 (12)</td>
<td>53 (8)</td>
<td>40 (30)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No use, n (%)</td>
<td>659 (86)</td>
<td>569 (90)</td>
<td>90 (68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>TCA, n (%)</td>
<td>18 (2)</td>
<td>14 (2)</td>
<td>4 (3)</td>
<td>.58</td>
</tr>
<tr>
<td>SSRI, n (%)</td>
<td>55 (7)</td>
<td>27 (4)</td>
<td>28 (21)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>23 (3)</td>
<td>14 (2)</td>
<td>19 (14)</td>
<td>.01</td>
</tr>
<tr>
<td>Follow-up time (y), M (SD)</td>
<td>2.3 (0.8)</td>
<td>2.3 (0.8)</td>
<td>2.2 (0.9)</td>
<td>.56</td>
</tr>
<tr>
<td>m-CESD-R, M (SD)</td>
<td>51 (10)</td>
<td>51 (8)</td>
<td>66 (5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gait speed (m/s), M (SD)</td>
<td>0.94 (0.26)</td>
<td>0.96 (0.25)</td>
<td>0.89 (0.26)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>MMSE score, M (SD)</td>
<td>25 (2.7)</td>
<td>27.2 (2.5)</td>
<td>24.3 (3.1)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

**Notes:** MMSE = mini-mental state examination; PASE = Physical Activity Scale for the Elderly; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant. m-CESD-R: depression scale, higher scores indicate more severe depressive symptoms.
Overall, the rate of falls was 26 falls/100 person-years (outdoor fall rate: 17/100 person-years and indoor fall rate: 18/100 person-years). The rate of falls resulting in an injury was 19/100 person-years regardless of location.

Table 2 indicates that CSDS increased the risk of indoor falls and outdoor falls by 62% and 60%, respectively, compared with participants without CSDS (indoor falls: IRR = 1.62, 95% CI = 1.16–2.26, p < .01; outdoor falls: IRR = 1.60, 95% CI = 1.17–2.20, p < .01). Antidepressant use increased the risk of outdoor falls by 70% compared with participants who did not use antidepressants (IRR = 1.70, 95% CI = 1.16–2.49, p < .05). SSRI use was associated with an increased risk of outdoor falls (IRR = 1.53, 95% CI = 1.05–2.25, p < .05). Antidepressant use was not associated with indoor falls (IRR = 0.94, 95% CI = 0.64–1.37, p = .74). When combining indoor and outdoor falls, both CSDS and antidepressant use were associated with an increased risk of falls. A sensitivity analysis using depression as diagnosed by a physician in the prior year yielded similar results. Further, the effect of CSDS on injurious falls was similar to the outdoor fall results (results not shown).

Figure 1 presents the rate of falls among participants according to CSDS and antidepressant use. Among participants with CSDS and antidepressant use, the rate of outdoor falls was higher than the rate of indoor falls (75 outdoor falls/100 person-years vs 71 indoor falls/100 person-years). In contrast, among participants with CSDS and no antidepressant use and participants without CSDS and antidepressant use, the rate of falls was similar, with indoor falls occurring more frequently than outdoor falls. The group without CSDS or antidepressant use had the lowest rate of indoor and outdoor falls (34 indoor falls/100 person-years and 35 outdoor falls/100 person-years, respectively).

Table 3 shows that the coefficient for CSDS decreased by >10% (~14%) when antidepressants were added to the model of outdoor falls, suggesting that the relationship between CSDS and outdoor falls is partially mediated by antidepressants. In contrast, the coefficient between CSDS and indoor falls did not change when antidepressants were added to the model. Similar results were obtained when depression was considered as a continuous variable.

Among participants with CSDS, antidepressant users had a higher prevalence of systolic orthostatic hypotension at 1 and 3 minutes than non-antidepressant users (15% vs 3%, p = .02 and 10% vs 1%, p = .02, respectively). Although not statistically significant, antidepressant users tended to walk for exercise in their neighborhood more often than participants who did not take antidepressants (5.5 times/mo vs 4.4 times/mo, p = .43) and spent fewer hours per week engaged in sedentary activities than non-antidepressant users (16.7 times/week vs 18.2 times/week, p = .02).
h/wk vs 18.9 h/wk, respectively, \( p = .24 \). However, neither orthostatic hypotension nor walking outside modified the association between antidepressants and outdoor falls.

**Discussion**

We found that depression was independently associated with an increased risk of indoor and outdoor falls. Antidepressant use was associated with an increased risk of outdoor, but not indoor falls. The association between depression and outdoor falls was at least partially mediated by antidepressant use. Based on this study, it is important that clinicians inform depressed patients of the risk of falls, especially of the risk of outdoor falls, when being treated for depression.

Our finding that depression is associated with an increased risk of falls is consistent with some of the prior literature (5). Depression may lead to an increased risk of falls through psychological, biological, or social mechanisms. For example, potential psychological mechanisms among severely depressed persons may lead people to be less focused and have poor medication adherence. Berry and coworkers (19) found that poor medication adherence is associated with falls. Potential biological mechanisms among persons with CSDS may include impaired neurological reflexes to coordinate the movement of the body (36), which compromises gait and balance. It is also possible that persons with CSDS tended to isolate themselves and that inactivity results in weakness and an increased risk of falls. Further, depression is often associated with cerebrovascular disease (vascular depression), which may simultaneously impair gait and mobility (37–39). We did not have data to validate these hypotheses.

To explore potential mechanisms by which antidepressants could mediate falls risks, we examined the differences in falls risk factors between antidepressant users and non-users among participants with CSDS. We speculate that our findings could be explained if treating depression with an antidepressant resulted in an increase in outdoor activity and more opportunity for outdoor falls. Given the small number of participants prescribed an antidepressant without depressive symptoms, we were unable to test this assumption. It is unclear if the increased exposure to outdoor activities would outweigh the protective effects of exercise. Nonetheless, environmental factors are also likely to play a mechanistic role in outdoor fall risk among individuals with CSDS who take antidepressants.

Another possible explanation for the association between antidepressant use and the increased risk of outdoor falls is orthostatic hypotension. We found that antidepressant users were more likely to have orthostatic hypotension compared with non-antidepressant users. This was somewhat surprising given the low utilization of TCAs in this study. Although newer SSRIs and serotonin–norepinephrine reuptake inhibitors are less often associated with postural changes in blood pressure, orthostatic hypotension has been reported with many of these drugs. If orthostatic hypotension was the mechanism through which antidepressants cause falls, one would expect to have found a relationship among these drugs and indoor falls. Surprisingly, we found that antidepressant use was associated with an increased risk of outdoor falls only, and thus, other mechanisms should be explored.

In addition to causing orthostatic hypotension, antidepressants could cause falls through other mechanisms. For example, TCAs have been associated with falls by causing blurred vision, dizziness, constipation, urinary retention, confusion, and cardiovascular problems among older adults (35). Although SSRIs may have less side effects and are better tolerated in older adults, they can cause nausea, dizziness, and anxiety (35) and may increase the risk of falls (12,35,40). Furthermore, monoamine oxidase inhibitors are prescribed to treat major depression, but they can cause hypotension and other adverse effects in older adults. In our study, there was a statistical association between SSRIs and outdoor falls. TCAs and other types of antidepressants were not statistically associated with either indoor or outdoor falls possibly due to the small number of users with insufficient statistical power to detect a difference in falls rate among users of these drugs.

Our results suggest that the risk of falls was greatest in persons with CSDS using antidepressants, and the risk was least in persons without CSDS or antidepressant use.
Interestingly using antidepressants without CSDS or CSDS with no antidepressant use conferred a similar risk of falls. This suggests that depressive symptoms and antidepressant use both contribute to fall risk.

The strengths of this study include its longitudinal design and population-based sample. In addition, falls were recorded daily using falls calendars. Antidepressant use in the past 2 weeks was recorded and gave an opportunity to examine whether antidepressants mediate the effect of CSDS on falls.

There are several limitations of this study. First, the dose and duration of use of antidepressants were not known. Second, time spent indoors or outdoors for each participant was not collected, so that indoor and outdoor fall rates may be different according to exposure time. Third, self-report on the number of falls may be susceptible to recall bias, although falls calendars are likely more accurate than historic recall. Fourth, information on antidepressant use was ascertained at baseline and it is likely that some participants’ exposure to antidepressants changed during follow-up. Finally, although we attempted to separate the effects of depressive symptoms on the risk of falls from the effects of antidepressants by using a mediation approach, some residual confounding by indication may remain.

In conclusion, these results provide evidence that depression significantly increased the risk of indoor and outdoor falls in older adults. The relationship between depression and outdoor falls was at least partially mediated by antidepressant use. No association between antidepressant use and indoor falls was found. Persons with CSDS need to be cautious about the increased risk of outdoor falls when taking antidepressants.

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