Accepted Manuscript

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PII: S1064-7481(14)00135-3

DOI: [10.1016/j.jagp.2014.04.005](https://doi.org/10.1016/j.jagp.2014.04.005)

Reference: AMGP 369

To appear in: *The American Journal of Geriatric Psychiatry*

Received Date: 13 November 2013

Revised Date: 14 April 2014

Accepted Date: 15 April 2014

Please cite this article as: O.A. Donoghue, C. O'Hare, B. King-Kallimanis, R.A. Kenny, Anti-depressants are independently associated with gait deficits in single and dual task conditions, *The American Journal of Geriatric Psychiatry* (2014), doi: 10.1016/j.jagp.2014.04.005.

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Anti-depressants are independently associated with gait deficits in single and dual task conditions

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Conflict of interest: No conflicts of interest.

Acknowledgement: The authors would like to acknowledge the contribution of the TILDA participants and research team. Financial support was provided by Irish Life plc, the Irish Government and the Atlantic Philanthropies. These funders had no involvement in analysis and preparation of this paper.

Key words: depression, walking, falls, medication

Abstract

Objectives: This study examined the relationships between late-onset depressive symptoms, antidepressants and single and dual task gait in older adults.

Design: Cross-sectional study.

Setting: The Irish Longitudinal Study of Ageing (TILDA), a nationally representative cohort study.

Participants: Community-dwelling adults aged ≥ 60 years, with Mini-Mental State Examination score ≥ 24 , no history of Parkinson's disease or early onset depression and unaided completion of a gait assessment ($n=1998$). This study compared participants with and without potentially clinically relevant depressive symptoms (i.e. ≥ 16 on the Centre for Epidemiological Studies Depression scale) and (ii) participants who were and were not on anti-depressant therapy.

Measurements: Gait measures were obtained during single and dual task (reciting alternate letters of alphabet, A-C-E) walking using a 4.88 m GAITRite® walkway. Regression analysis was used to examine the associations between each group and gait adjusting for socio-demographics and health.

Results: In the unadjusted models, depressive symptoms and anti-depressant use were associated with gait deficits. After adjusting for covariates, anti-depressant use was associated with reduced gait speed and stride length in single and dual task walking, however depressive symptoms were not associated with any deficits.

Conclusions: As gait impairments are associated with an increased risk of adverse outcomes including falls, clinicians should be aware of the impact of anti-depressants on gait in older adults. Subsequent to this, interventions aimed at improving physical function which is a known precursor to falls and functional disability should be recommended.

Key words: depression; walking; falls; medication

OBJECTIVE

Falls are highly prevalent in older adults, have multiple underlying factors and can have a major impact on health, quality of life, and independence (1). Major depressive disorder is also common, affecting about 3% of community-dwelling older adults in the past year (2) while about 9% experience clinically relevant depressive symptoms (3). Depressive symptoms have been associated with an increased fall risk (4, 5) and fallers with high depression scores are twice as likely to report a decline in functional status, social or physical activities as a direct consequence of the fall (6). Iaboni et al. (7) present a model describing the complex and bidirectional relationship between depression and falls which includes common risk factors, factors relating to depression and the anti-depressant based treatment of depression, consequences of falls and subsequent effects on mood.

Gait impairments are recognised as one of the biggest risk factors for falls (8). In a clinical setting, gait is often assessed visually or a stopwatch is used to measure gait speed. In research based settings, computerised and sensed gait mats are often available and provide more detailed spatiotemporal measures. Deficits such as reduced gait speed (9-14), reduced step or stride length (9, 10, 15), increased double support phase (9, 10, 15), cycle duration (9) and swing time variability (10, 16) and other kinematic and postural effects (12) have been observed in individuals with depressive symptoms and major depressive disorder. However, the few studies that adjusted for confounders such as socio-demographics, cognitive function and health (10, 11, 13) found that independent effects were limited to reduced gait speed and stride length and increased swing time variability (10, 13). Anti-depressants are commonly prescribed to older adults and are associated with an increased fall risk independent of depressive symptoms (5, 17). This increased risk may be mediated by gait impairments, however, the effect of anti-depressant use on gait is conflicting and limited to a few studies with sample sizes of less than twenty (9, 18, 19).

All of the studies outlined above examined participants walking in single task conditions i.e. walking normally. Dual task conditions increase attentional demands as an individual must walk while simultaneously performing a cognitive or manual task. Gait impairments during dual task conditions are also associated with an increased fall risk (20). However, these tests have rarely been examined in those with depressive symptoms despite the fact that executive dysfunction and decreased processing speed are common in this group (11, 21). Again, the limited findings are conflicting – Wright et al. (22) found that depressed individuals especially those on anti-depressants walked slower during the more cognitively challenging tasks compared to the non-depressed group while van Iersel et al. (15) reported no differences between healthy older adults and those with mild to moderate depressive symptoms or diagnosed depression.

Based on existing research, the independent associations between late-onset depressive symptoms, anti-depressant use and gait are inconclusive and further studies using larger sample sizes are required. Therefore, this study examined the relationship between late-onset depressive symptoms, anti-depressants and spatiotemporal gait in single and dual task conditions using data from a nationally representative, community-dwelling older population. There were two parts to the analysis (i) a comparison of participants with and without potentially clinically relevant depressive symptoms and (ii) a comparison of participants who were and were not on anti-depressant therapy (ADT).

METHODS

Study Design

The Irish Longitudinal Study on Ageing (TILDA) is a large prospective cohort study of the social, economic and health circumstances of community-dwelling older adults in Ireland. This analysis is based on the first wave of data collected between January 2009 and July 2011. The sampling frame is the Irish Geodirectory, a listing of all residential addresses in the Republic of Ireland. A clustered

sample of addresses was chosen, and household residents aged ≥ 50 years and their spouses/partners (of any age) were eligible to participate in the study. Ethical approval was obtained from the Trinity College Dublin Research Ethics Committee and written informed consent was obtained from 8504 participants.

The study design has been described previously (23). Briefly, data collection involved (i) a computer-assisted personal interview (CAPI) that included detailed questions on socio-demographics, wealth, health, lifestyle, social support and participation, use of health and social care and attitudes to ageing, (ii) a self-completion questionnaire and (iii) a health assessment carried out by research nurses. Inclusion criteria for the present analysis was age ≥ 60 years, no history of Parkinson's disease, no self-reported doctor diagnosis of depression before age 60 as early onset and late onset depression may have different underlying mechanisms (24), Mini-Mental State Examination (MMSE) score ≥ 24 , participation in a health centre assessment and unaided completion of either the single or dual task gait assessment with a minimum of 8 steps (explained further below) leaving 1998 eligible participants (Figure 1).

Measures

Depression: Depressive symptoms were assessed using the 20-item Centre for Epidemiological Studies Depression (CES-D) scale where scores of ≥ 16 (out of 60) represent potentially clinically relevant symptoms (25). Medications were coded using the World Health Organization's Anatomical Therapeutic Chemical (ATC) codes. Anti-depressant use was identified where the first four digits of an ATC code was "N06A".

Gait: Gait assessment took place using a computerised walkway (4.88 m active area) with embedded pressure sensors (GAITRite®, CIR Systems Inc, New York, USA). Participants performed two walks at their normal pace followed by two walks under cognitive dual task conditions (reciting alternate

letters of the alphabet i.e. A-C-E, etc). The number of letters attempted and stated correctly was recorded. Participants started and finished 2.5 m before and 2 m after the walkway to allow for acceleration and deceleration. Mean gait speed, stride length, cadence, step width and double support phase were obtained along with standard deviations (SD) of stride length and stride time. As the SDs were related to the mean values for each variable, the coefficient of variation (CV) was calculated ($SD/mean \times 100$) and used to indicate stride-to-stride variability in stride length and stride time. These gait variables were chosen for analysis because of their associations with adverse outcomes such as falls in older adults. Stride parameters include data for the left step followed by the right step (or vice versa) and therefore they are not affected by asymmetrical gait patterns. As there is little variation between right and left stride-based data, we combined data for the right and left strides for analysis. Participants with a minimum of 8 steps in either walk (range 8-28 steps for normal walk; 8-26 steps for cognitive walk) were included in this study. This provided a minimum of 6 strides for analysis (n=1905 for normal walk; n=1954 for cognitive walk). Notably, the same results were obtained when data from all participants was analysed regardless of step count.

Falls and fear of falling: The number of falls in the last 12 months was recorded and categorised as 0, 1 or ≥ 2 falls. Fear of falling was assessed using the dichotomous question "Are you afraid of falling?". If a participant answered yes, they were asked to indicate if they were somewhat or very much afraid. This allowed us to categorise fear of falling into three levels for analysis (none, somewhat, very much).

Demographic: Age, sex and education were collected. Educational level was defined as primary, secondary or tertiary corresponding to ≤ 8 , 9-13 and >13 years of education respectively. Participants also indicated their living status (living alone/living with others).

Covariates: Global cognition was assessed using the MMSE. The number of doctor diagnosed chronic conditions was obtained from the following list: angina, heart attack, heart failure, stroke, transient ischemic attack, heart murmur, high blood pressure or hypertension, high cholesterol, diabetes, cataracts, chronic lung disease, asthma, arthritis, osteoporosis, cancer, stomach ulcer and hip fracture. This was then used as an indicator of co-morbidity where participants were classified as having 0, 1, 2 or ≥ 3 chronic conditions. Participants were asked to self-rate their vision and their answers were dichotomised as excellent/very good/good or fair/poor/registered blind. Chronic pain was assessed by asking participants if they often suffered from pain and if so, if this pain was mild, moderate or severe, most of the time. This variable was dichotomised into none/mild pain and moderate/severe pain. Polypharmacy was defined as using ≥ 5 medications. Anti-depressants were not counted in the polypharmacy measure as they were included as a covariate (when comparing those with and without depressive symptoms) and used to define the ADT group for comparison to the non-ADT group.

Grip strength was measured using a Baseline® hydraulic hand dynamometer. Two measurements were taken on the dominant hand and the average value was used in the analysis. Physical activity was measured using the International Physical Activity Questionnaire (26). Participants indicated the frequency and duration that they took part in walking, moderate and vigorous physical activity. Their answers were used to categorise them into low, moderate or high levels of physical activity.

Statistical Analysis

Statistical analysis was conducted using Stata v12 (StataCorp LP, Texas, USA). All analyses were weighted with respect to age, sex and education to the Quarterly National Household Survey (2010) to ensure that data were nationally representative. Data were further weighted by health status and socio-demographic factors to account for those who did not attend a health assessment. Baseline characteristics and mean gait variables were compared in those with and without potentially

clinically relevant depressive symptoms and also in respondents who were and were not on anti-depressant therapy (ADT).

Mean gait variables were normally distributed and linear regression analysis was used to examine differences between groups stratified by depressive symptoms and ADT. Gait variability measures were positively skewed, therefore quantile regression was used to estimate the differences in the medians and minimise the influence of high values. An additional advantage of this approach over transformations is that it keeps the coefficients in their original units allowing a more intuitive interpretation. For each gait parameter, the estimated model was adjusted for age, sex, height, weight, education, living status, MMSE, co-morbidity, self-rated vision, chronic pain, history of falls in the previous year, fear of falling, polypharmacy, grip strength and physical activity level. In addition, the depressive symptoms model was adjusted for anti-depressant use while the anti-depressant model was adjusted for level of depressive symptoms (i.e. CES-D score) to examine potential dose-response effects. Complete covariate data was available for 1853 (97.4%) and 1901 (97.4%) participants for the normal and dual task walk respectively (depressive symptoms comparison) and 1825 (95.9%) and 1876 (96.1%) participants for the normal and dual task walk respectively (ADT comparison). Complete case analysis was used for multivariate analyses i.e. all missing data were treated as missing completely at random. Significance level was set at $p < 0.05$.

RESULTS

In this population-based sample of older adults (mean age 68.2 years; range 60-93 years), 7.8% ($n=145$) had clinically relevant depressive symptoms while 4.9% ($n=82$) were on ADT. Baseline characteristics for each group are provided in Table 1.

Respondents scoring ≥ 16 on the CES-D were more likely to be females, recurrent fallers, very much afraid of falling, have at least three chronic conditions, be on at least five medications excluding anti-

depressants, have moderate/severe chronic pain, poor self-reported vision, poorer grip strength and low physical activity compared to those scoring <16. The ADT group were more likely to have at least three chronic conditions, moderate to severe chronic pain, low physical activity and lower grip strength compared to those who were not on ADT. Of these participants, 43 (52.4%) were taking selective serotonin reuptake inhibitors, 13 (15.9%) were taking serotonin-norepinephrine reuptake inhibitors, 21 (25.6%) were taking tricyclics and 5 (6.1%) were taking other antidepressants.

Table 2 provides the spatiotemporal gait characteristics stratified by presence of potentially clinically relevant depressive symptoms and use of anti-depressants. Respondents with depressive symptoms walked 7 cm/s and 4 cm/s slower in the single and dual task walks respectively compared to those without depressive symptoms. The ADT group displayed even larger deficits in gait speed (14 cm/s slower in both walks) compared to the non-ADT group. Other observed differences associated with depressive symptoms and ADT include reduced stride length and increased double support phase.

Table 3 provides the beta coefficients from the regression analysis used to examine the associations between depressive symptoms and gait, and ADT and gait in single and dual task conditions.

Depressive symptoms were not associated with any gait deficits after adjusting for covariates. In contrast, ADT was independently associated with reduced gait speed ($\beta=-7.508$, $t(1801)=-3.65$, $p<0.001$) and stride length ($\beta=-6.784$, $t(1801)=-4.63$, $p<0.001$) during normal walking. Coefficients of a similar size were observed in the dual task walking condition for gait speed ($\beta=-7.331$, $t(1852)=-2.71$, $p<0.01$) and stride length ($\beta=-6.591$, $t(1852)=-3.60$, $p<0.001$).

Table 4 provides the coefficients for ADT and level of depressive symptoms (CES-D score) in this fully adjusted regression model (i.e. model examining the effect of anti-depressants on single and dual task gait speed). The results show that anti-depressant use had a more substantial effect on gait speed compared to the effect of depressive symptoms (CES-D score). There is a small dose-response

effect between CES-D score and gait speed in single task walking ($\beta=-0.147$ [-0.293,-0.002], $p=0.047$) but no effect for dual task gait speed. The low numbers in each ADT category meant that the effect of individual anti-depressants could not be analysed.

We also examined the potential mediating effect of cognitive function (i.e. mean reaction time and Colour Trail 2 time) in our adjusted models. While both tests were independently associated with gait performance, neither test was found to be independent mediator of the relationship between depressive symptoms and gait or between ADT and gait (results not shown).

It should be noted that data for one participant with depressive symptoms who paused substantially during the dual task walk was removed from the analysis. Including this participant resulted in an association between depressive symptoms and increased double support phase that was just outside significance, however we felt that this was not reflective of behaviour in the entire depressive symptoms group.

CONCLUSIONS

Anti-depressant use, but not clinically relevant depressive symptoms, was associated with gait deficits in community-dwelling older adults after adjusting for socio-demographic, cognitive and health variables. The specific deficits observed were decreased gait speed and stride length in both single and dual task walking conditions. Slow gait speed during normal walking is a risk factor for many adverse outcomes including falls, cognitive decline, hospitalization and mortality (27, 28). Dual task gait deficits predict falls (20), and are important as this task represents the complex but more realistic challenges encountered in daily life. Several studies have linked anti-depressant use to an increased risk of falls, fractures and frailty (5, 17, 29). Gait deficits associated with anti-depressant use could potentially mediate this relationship, and the paucity of current research highlights the need to examine this further.

Verghese et al. (28) reported a 7% increased risk of falls for each 10 cm/s decrease in gait speed, however the clinical implications of reduced gait speed will depend on the actual level of performance. A 1.0 m/s cut-off for usual gait speed is often used to identify older adults at risk of health-related outcomes (30) with those below 0.6 m/s at highest risk. Other studies present the risk associated with walking at the lowest speed quantile compared to the highest. For example, usual gait speed of ≤ 1.05 m/s was associated with an almost twofold increased risk of decline in cognitive function over 5 years compared to those with gait speed ≥ 1.35 m/s (31). In our study, 19% of the depressive symptoms group and 34% of the ADT group walked at ≤ 1.05 m/s compared to about 10% of those without depressive symptoms or who were not on ADT, highlighting the relatively higher risk for these participants.

The finding that anti-depressant use has a more substantial effect on gait compared to depressive symptoms adds to the limited and conflicting literature in this area. A previous study found that a single dose of amitriptyline (a tricyclic) was associated with reduced walking speed and impaired kinematics of the trailing limb when stepping over obstacles in healthy, older adults (19), however others reported no difference between depressed groups with and without medications (9), or small gait improvements with anti-depressant therapy (18) although this latter study did not include a control group. Different anti-depressants also have different side-effect profiles (32) and while participants in the current study were most commonly prescribed SSRIs, it was not possible to elucidate if these were more or less detrimental than other anti-depressants due to small numbers. However, the association with poorer mobility remained when we compared the SSRI group to the non-ADT group.

Previous research has reported that depressive symptoms and/or depression were independently associated with reduced gait speed and stride length and increased swing time variability (10, 13,

14). However, we found that all deficits were fully explained by socio-demographics, co-morbidities and other health factors in our multivariate analysis. There were differences in the analysis, for example we used a categorical rather than a continuous measure of depressive symptoms (10) and adjusted for different covariates such as anti-depressant use and chronic pain.

There are several potential explanations for the observed associations between anti-depressant use and gait impairments. Age-related physiological changes lead to different pharmacokinetics, which can alter plasma protein levels, increase toxicity and make older adults more sensitive to medications (33). Older populations especially those on ADT also have greater co-morbidity and are on more medications, which increases their susceptibility to side-effects and drug-drug interactions (34). Anti-depressant side-effects include extrapyramidal symptoms such as akinesia, bradykinesia and/or muscle rigidity (35), anticholinergic side-effects such as confusion and subtle cognitive impairment (36) and day time drowsiness due to sedation and sleep disturbances (37). All of these could feasibly lead to gait impairments.

Alternatively, anti-depressant use may be a proxy for more chronic or persistent depressive symptoms that required participants to seek medical attention. While their current level of symptoms is not above clinical thresholds (possibly due to the effects of medication), the underlying effects and potential risk of adverse outcomes associated with depression may still persist. To complicate this, anti-depressants can be prescribed in the treatment of other co-morbidities such as pain, which is also highly related to depression (38) and can also influence gait.

It is also possible that vascular pathology plays a role as white matter lesions have been associated with late-onset depression (39), gait and cognitive impairments (40). Hajjar et al. also found that impairments affecting mobility, cognitive function and mood were related to hypertension and mediated by white matter lesions (41). Interestingly in the context of our findings, anti-depressant

use was found to be associated with greater brain atrophy and white matter lesions while depressive symptoms were not (42). As the current protocol did not include MRI based brain measurements, potential associations with white matter lesions could not be confirmed.

To the authors' knowledge, this is the largest study to examine the effects of depressive symptoms and anti-depressant use on single and dual task walking in community-dwelling older adults. The strengths of the study include the large, nationally representative sample and the standardised assessment of depressive symptoms, anti-depressant use and gait in single and dual task conditions. A self-reported doctor diagnosis of depression was not used to classify groups as it was thought that it would underestimate the true prevalence. Instead, depressive symptoms were chosen due to their high prevalence, relevance to fall outcomes and potential for intervention. While information on the duration and dose of anti-depressants was not available, future research should examine this in detail. Co-morbid psychological conditions could also play a role in the observed relationship. To examine this, we adjusted for distress and worry, which reduced the coefficients but did not fully explain the independent effects observed. However, as this reduced our sample size substantially, we removed it from the analysis. Finally, as the data is cross-sectional, we are unable to determine the causal relationship between depressive symptoms, anti-depressants and gait impairment until future waves become available. Future work will also examine the incidence of prospective falls in older adults with depressive symptoms and those on anti-depressants and investigate whether gait impairments mediate this relationship.

Guidelines for the mental health assessment of older adults do not mention gait impairments (43, 44) despite the commonly observed association between depressive symptoms and falls. Our results suggest that a gait and falls assessment (45) may be a useful addition when assessing older adults with depressive symptoms, especially when anti-depressants are prescribed. This is particularly pertinent given the increased prevalence of anti-depressant treatment in recent years (46).

Clinicians should also be aware of the adverse outcomes associated with reduced gait speed.

Exercise interventions provide both psychological and physiological benefits and are important to maintain functional ability and prevent falls (45). Highlighting this may be especially important for older adults whose perception of quality of life is often affected more by their ability to maintain independence rather than the specific diseases they have (47).

In conclusion, anti-depressant use was independently associated with reduced gait speed and stride length during single and dual task walking; these impairments are associated with an increased risk of falls. The decision to prescribe anti-depressants depends on several factors and the potential benefits must be considered along with the risks. This paper adds to the available literature to help inform clinicians about the appropriateness of prescribing ADT in older adults. It also emphasizes the importance of basic clinical assessments of gait and fall risk and the potential benefit of multidisciplinary input (e.g. physiotherapy) in the care of older adults who often present with complex psychiatric and physical needs.

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Table 1: Baseline characteristics of each group.

	Depressive symptoms (≥ 16 on CES-D)		Anti-depressant therapy	
	No (n=1,852)	Yes (n=145)	No (n=1,915)	Yes (n=82)
<i>Sociodemographic variables</i>				
Age (years)	69.8 $\pm$ 7.1	68.7 $\pm$ 6.7	69.6 $\pm$ 7.1	71.5 $\pm$ 7.4
Sex (female)	1009 (55.1)	98 (71.1)	1052 (55.8)	55 (66.0)
Education				
Primary	530 (48.2)	52 (57.3)	547 (48.3)	35 (60.5)
Secondary	711 (36.6)	46 (29.6)	728 (36.4)	29 (30.3)
Tertiary	609 (15.2)	47 (13.1)	638 (15.3)	18 (9.2)
Height	1.64 $\pm$ 0.09	1.60 $\pm$ 0.09	1.64 $\pm$ 0.09	1.62 $\pm$ 0.09
Weight	77.9 $\pm$ 15.7	74.8 $\pm$ 15.4	77.8 $\pm$ 15.6	75.1 $\pm$ 16.1
Living status (alone)	380 (27.5)	50 (38.4)	403 (27.8)	27 (39.4)
<i>Physical, mental and cognitive health</i>				
MMSE	28.3 $\pm$ 1.6	27.8 $\pm$ 1.8	28.3 $\pm$ 1.6	27.7 $\pm$ 1.7
Co-morbidity				
0 conditions	283 (14.0)	18 (9.9)	296 (14.1)	5 (5.8)
1 condition	466 (23.4)	27 (17.8)	480 (23.3)	13 (16.6)
2 conditions	458 (24.1)	26 (16.6)	465 (23.7)	19 (19.5)
≥ 3 conditions	643 (38.5)	74 (55.7)	672 (38.9)	45 (58.1)
Chronic pain (moderate/severe)	442 (26.0)	64 (50.3)	469 (27.1)	37 (43.4)
Polypharmacy	440 (27.8)	51 (40.1)	448 (27.6)	43 (52.2)
Falls				
None	1462 (79.4)	94 (61.7)	1501 (78.5)	55 (67.1)
Single fall	277 (14.8)	26 (21.8)	288 (15.1)	15 (20.3)

Recurrent fall	113 (5.8)	24 (16.5)	125 (6.4)	12 (12.6)
Depressive symptoms (CES-D)	4.0 ± 3.9	23.6 ± 7.4	5.0 ± 6.0	10.3 ± 10.4
Antidepressant therapy	68 (4.2)	14 (13.3)	-	-
Fear of falling				
None	1407 (72.8)	89 (52.9)	1446 (71.8)	50 (59.7)
Somewhat	378 (23.0)	33 (28.6)	387 (23.0)	24 (32.0)
Very much	66 (4.2)	23 (18.5)	81 (5.2)	8 (8.3)
Mean grip strength	24.0 ± 9.3	20.1 ± 8.1	24.0 ± 9.3	20.6 ± 7.9
Self-rated vision				
(fair/poor/registered blind)	124 (8.9)	29 (30.7)	144 (10.2)	9 (18.0)
Physical activity level				
Low	494 (30.4)	68 (55.7)	525 (31.2)	37 (55.1)
Moderate	693 (36.1)	46 (28.7)	717 (36.2)	22 (21.9)
High	655 (33.5)	30 (15.6)	663 (32.5)	22 (22.9)

Notes: Data are weighted and presented as Mean ± SD for continuous variables; number (%) for categorical variables. CES-D, Centre for Epidemiological Studies Depression scale; MMSE, Mini-Mental State Examination

Table 2: Gait characteristics of each group in single and dual task walking conditions

	Depressive symptoms		Anti-depressant therapy	
	No	Yes	No	Yes
<i>Normal walk</i>				
Gait speed (cm/s)	126.56 ± 21.23	119.37 ± 25.97	126.67 ± 21.45	112.49 ± 22.80
Stride length (cm)	133.63 ± 18.51	125.16 ± 20.50	133.54 ± 18.69	121.39 ± 17.51
Cadence (steps/min)	113.70 ± 10.58	113.89 ± 13.13	113.87 ± 10.73	110.83 ± 11.82
Step width (cm)	8.83 ± 2.89	8.55 ± 2.98	8.80 ± 2.85	9.08 ± 3.77
Double support phase (%)	26.80 ± 4.51	27.87 ± 4.87	26.82 ± 4.56	28.19 ± 4.12
Stride length CV (%)	2.33 ± 1.38	2.48 ± 1.17	2.32 ± 1.34	2.84 ± 1.74
Stride time CV (%)	1.96 ± 1.07	2.16 ± 1.34	1.94 ± 1.05	2.68 ± 1.65
<i>Dual task walk</i>				
Gait speed (cm/s)	101.45 ± 25.98	97.54 ± 28.26	101.89 ± 25.94	87.26 ± 26.92
Stride length (cm)	124.23 ± 22.31	116.95 ± 22.29	124.32 ± 22.30	111.61 ± 20.69
Cadence (steps/min)	97.85 ± 17.11	99.75 ± 18.55	98.26 ± 17.12	93.03 ± 18.50
Step width (cm)	9.34 ± 3.49	8.94 ± 3.24	9.28 ± 3.40	10.04 ± 4.49
Double support phase (%)	28.59 ± 5.75	29.55 ± 5.09	28.59 ± 5.72	29.97 ± 5.35
Stride length CV (%)	3.75 ± 2.89	3.88 ± 2.44	3.75 ± 2.89	3.86 ± 1.98
Stride time CV (%)	4.92 ± 5.47	4.68 ± 4.46	4.91 ± 5.44	4.88 ± 4.62

Notes: Gait data are presented as Mean ± SD. CV, coefficient of variation.

Table 3: Results of the multivariate linear regression model examining the relationship between (i) depressive symptoms and (ii) anti-depressant therapy and gait characteristics during single and dual task walking conditions.

	Depressive symptoms			Anti-depressant therapy		
	Unadjusted model	Adjusted model ¹		Unadjusted model	Adjusted model ²	
	β [95% CI]	β [95% CI]	R ²	β [95% CI]	β [95% CI]	R ²
<i>Single task walk</i>						
Gait speed (cm/s)	-6.045 [-9.592,-2.498]***	-0.460 [-3.577,2.657]	31.87	-14.982 [-19.661,-10.303]***	-7.508 [-11.541,-3.475]***	33.03
Stride length (cm)	-7.069 [-10.160,-3.979]***	-0.951 [-3.170,1.269]	54.33	-14.317 [-18.397,-10.241]***	-6.784 [-9.660,-3.908]***	55.31
Cadence (steps/min)	0.301 [-1.526,2.127]	0.334 [-1.294,1.963]	29.89	-1.893 [-4.318,0.533]	-1.527 [-3.643,0.590]	29.99
Step width (cm)	0.064 [-0.434,0.563]	0.019 [-0.452,0.490]	20.25	0.426 [-0.236,1.088]	0.420 [-0.197,1.038]	20.05
Double support phase (%)	1.096 [0.346,1.845]**	0.363 [-0.316,1.042]	27.29	1.630 [0.635,2.625]**	0.616 [-0.268,1.500]	27.97
Stride length CV (%)	0.130 [-0.094,0.354]	0.015 [-0.192,0.221]	7.74	0.378 [0.0773,0.678]*	0.030 [-0.240,0.299]	7.89
Stride time CV (%)	0.037 [-0.132,0.207]	-0.142 [-0.313,0.028]	5.96	0.300 [0.0737,0.527]**	0.116 [-0.104,0.336]	5.95
<i>Dual task walk</i>						
Gait speed (cm/s)	-4.034 [-8.484,0.416]	0.779 [-3.463,5.021]	19.64	-14.675 [-20.290,-9.060]***	-7.419 [-12.72,-2.117]**	20.39
Stride length (cm)	-6.804 [-10.540,-3.066]***	-0.325 [-3.183,2.534]	48.39	-14.894 [-19.608,-10.180]***	-6.665 [-10.252,-3.078]***	48.87

Cadence (steps/min)	1.035 [-1.975,4.045]	0.913 [-2.067,3.892]	12.68	-3.481 [-7.298,0.336]	-2.766 [-6.496,0.964]	12.91
Step width (cm)	0.083 [-0.514,0.680]	0.138 [-0.421,0.698]	21.62	0.822 [0.065,1.579] [*]	0.522 [-0.183,1.228]	21.69
Double support phase (%)	1.255 [0.346,2.164] ^{**}	0.447 [-0.402,1.296]	22.94	1.703 [0.550,2.857] ^{**}	0.629 [-0.442,1.701]	23.13
Stride length CV (%)	-0.019 [-0.371,0.333]	0.129 [-0.240,0.497]	9.99	0.515 [0.078,0.952] [*]	-0.064 [-0.531,0.403]	9.87
Stride time CV (%)	-0.196 [-0.661,0.268]	0.037 [-0.469,0.544]	10.48	0.285 [-0.289,0.860]	-0.121 [-0.769,0.526]	10.42

Notes: Beta coefficients (β), 95% confidence intervals (CI) and R^2 from multivariate linear regression analysis; Pseudo- R^2 is presented for multivariate quantile regression analysis; ^{*} $p < 0.05$, ^{**} $p < 0.01$, ^{***} $p < 0.001$. CV, coefficient of variation.

Depressive symptoms: single task walk - unadjusted model (1901 *df*), adjusted model (1829 *df*); dual task walk - unadjusted model (1949 *df*), adjusted model (1876 *df*).

Anti-depressant therapy: single task walk - unadjusted model (1901 *df*), adjusted model (1801 *df*); dual task walk - unadjusted model (1949 *df*), adjusted model (1851 *df*).

¹ Model adjusted for age, sex, education, height, weight, living status, MMSE, co-morbidity, self-rated vision, chronic pain, polypharmacy, history of falls, fear of falling, grip strength, physical activity, use of anti-depressant medication.

² Model adjusted for age, sex, education, height, weight, living status, MMSE, co-morbidity, chronic pain, polypharmacy, history of falls, fear of falling, grip strength, self-rated vision, physical activity, level of depressive symptoms (CES-D score).

Gait variability measures were additionally adjusted for usual gait speed/dual task gait speed as appropriate.

Table 4: Results of the multivariate linear regression model showing the effect of depressive symptoms on the relationship between anti-depressant use and gait speed in single and dual task walking conditions.

	Model 1 - β [95% CI]	Model 2 - β [95% CI]
<i>Single task gait speed (cm/s)</i>		
Anti-depressant therapy	-13.096 [-17.775, -8.417]***	-7.508 [-11.541, -3.475]***
CES-D score	-0.480 [-0.638, -0.322]***	-0.147 [-0.293, -0.002]*
<i>Dual task gait speed (cm/s)</i>		
Anti-depressant therapy	-12.603 [-20.290, -9.060]***	-7.419 [-12.722, -2.117]**
CES-D score	-0.423 [-0.618, -0.228]***	-0.167 [-0.361, 0.026]

Notes: Beta coefficients (β) and 95% confidence intervals (CI) from multivariate linear regression analysis; *

$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Anti-depressant therapy: single task walk – Model 1 (1901 *df*), Model 2 (1801 *df*); dual task walk – Model 1 (1949 *df*), Model 2 (1851 *df*).

Model 1 included anti-depressant therapy and level of depressive symptoms (CES-D score).

Model 2 additionally adjusted for age, sex, education, height, weight, living status, MMSE, co-morbidity, chronic pain, polypharmacy, history of falls, fear of falling, grip strength, self-rated vision, physical activity.