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ORIGINAL RESEARCH ARTICLE

Anticholinergic and Sedative Medications and Dynamic Gait Parameters in Older Patients

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Abstract

Background Anticholinergic and sedative medications are associated with poorer physical function in older age. Gait and physical function have traditionally been assessed with the time needed to execute objective function tests. Accelerometer-based gait parameters provide a precise capturing of gait dynamics and patterns and as such have added value.

Objectives This study examined the associations between cumulative exposure to anticholinergic and sedative medications and gait dimensions as assessed with accelerometer-based dynamic gait parameters.

Methods Data were collected from outpatients of a diagnostic geriatric day clinic who underwent a comprehensive geriatric assessment (CGA). Cumulative exposure to anticholinergic and sedative medications was quantified with the Drug Burden Index (DBI), a linear additive pharmacological dose–response model. From a total of 22 dynamic gait parameters, the gait dimensions 'Regularity', 'Complexity', 'Stability', 'Pace', and 'Postural Control' were derived using factor analysis (and standardized total scores for these dimensions were calculated accordingly). Data were analyzed with multivariable linear regression analysis, in which adjustment was made for the covariates age, gender, body mass index (BMI), Mini Mental State Examination (MMSE) score, Charlson Comorbidity Index (CCI) including dementia, and number of medications not included in the DBI.

Results A total of 184 patients participated, whose mean age was 79.8 years (± SD 5.8), of whom 110 (60%) were women and of whom 88 (48%) had polypharmacy (i.e., received treatment with ≥5 medications). Of the 893 medications that were prescribed in total, 157 medications (17.6%) had anticholinergic and/or sedative properties. Of the patients, 100 (54%) had no exposure (DBI = 0), 42 (23%) had moderate exposure (0 > DBI ≤ 1), while another 42 (23%) had high exposure (DBI >1) to anticholinergic and sedative medications. Findings showed that high cumulative exposure to anticholinergic and sedative medications was related with poorer function on the Regularity and Pace dimensions. Furthermore, moderate and high exposure were associated with poorer function on the Complexity dimension.

Conclusions These findings show that in older patients with comorbidities, cumulative anticholinergic and sedative exposure is associated with poorer function on multiple gait dimensions.

1 Introduction

Anticholinergic and sedative medications from different therapeutic classes are often prescribed in older patients. These medications are prescribed for psychiatric, respiratory, gastrointestinal, cardiovascular, and other conditions. However, there is increasing awareness among clinicians that exposure to anticholinergic and sedative medications is also associated with increased fall risk and poorer physical and cognitive function [1–5, 34]. Anticholinergic medications inhibit the binding of acetylcholine to muscarinic receptors in various brain areas. These include the corpus striatum, which plays a key role in movement, and other brain areas such as the hippocampus, the fusiform gyrus, and the inferior prefrontal cortex [6–8]. Peripheral anticholinergic effects such as the inhibition of acetylcholine-mediated muscle contractions are also common [6]. Medications with sedative properties, such as benzodiazepines, increase the inhibitory effects of GABAergic neurons in the central nervous system [9]. Because of comorbidities and the treatment of side effects of one medication with another medication, older patients often have polypharmacy (i.e., coincident prescribing of ≥ 5 medications). Consequently, older patients

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Key Points

Multiple medications given at once, especially medications with so-called sedative and anticholinergic effects, has been associated with mobility problems in older geriatric patients.

This study analyzed gait data (obtained with accelerometer devices) of patients with various levels of exposure to these drugs.

The associations found between exposure to these drugs and gait measures (regularity, pace, and complexity of walking) propagate an adoption of instrumented movement analysis in clinical geriatric practice. This will offer new possibilities to measure the effects of medication and effectiveness of medication reviews in an objective manner.

are often treated with multiple anticholinergic and sedative medications.

The Drug Burden Index (DBI) [10] was developed to quantify an individual older patient's cumulative exposure to medications with anticholinergic and sedative effects. Several findings sustained the predictive validity of the DBI. After adjusting for co-morbidity and other covariates, a higher DBI was found to be associated with increased mortality and hospitalization risk as well as an array of adverse outcomes including falls, mobility impairment, poorer balance, slower gait speed, decreased capacity to carry out activities of daily living (ADLs), and poorer cognitive function [11–13]. Although the associations of poorer balance and walking with a higher DBI were previously demonstrated on objective physical function tests [11], the execution time has merely been used as an outcome measure.

Sensitive parameters that capture the dynamics of gait more precisely than existing measures of physical function, henceforth called dynamic gait parameters, are likely to have additional value [14]. Dynamic gait parameters have been found to increase classification accuracy of older patients who experienced a fall [15, 16]. Furthermore, these dynamic gait parameters were previously found to predict future cognitive decline [17, 18], β-amyloid and white matter hyperintensities in the brain [19], and brain infarcts [20]. Dynamic gait parameters can be feasibly measured with an accelerometer during the conduct of a walking test. As such, dynamic gait parameters are likely to enrich the output of objective walking tests. From a clinical point of view, the importance of the dynamic gait parameters is that these are likely to provide insight into dysfunctional gait patterns that predispose older patients to falling. As such, dynamic gait parameters could serve as early warning signals.

Accordingly, the present study aims to examine associations between cumulative exposure to anticholinergic and sedative medications, as quantified with the DBI, and dynamic gait parameters.

2 Methods

2.1 Study Population

Data were collected between January 2012 and January 2017 at the diagnostic geriatric outpatient clinic of the Slotervaart Hospital, Amsterdam, the Netherlands. Patients were referred to the geriatrician, usually by the general practitioner because of undefinable age-related complaints. All referred patients underwent a comprehensive geriatric assessment including assessments of cognitive and physical function as part of clinical care. Data on medication use and demographic and clinical characteristics were extracted from patients' medical records. Dynamic gait parameters were calculated from the trunk accelerations measured with a wearable accelerometer. Exclusion criteria were inability to walk for three minutes without a walking aid, a diagnosis of Parkinson's disease, a history of stroke or other neurological conditions with specific gait disorders, having severe mobility impairment caused by pain and/or orthopedic conditions, and insufficient command of the Dutch language. Due to these strict criteria, a convenience sample of patients was adopted for this study. The study was performed in accordance with the Declaration of Helsinki. The Medical Ethical Committee of the Slotervaart hospital approved the study. All patients or their legal representatives (when patients had cognitive impairment) gave written informed consent.

2.2 Drug Burden Index

Medication use was established by cross-checking a patient's history, information from their pharmacy, and their general practitioner. The name, dose, and frequency of intake of every medication, and code of the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization [21] were registered. Over-the-counter medications were included if these had a known ATC code. Only medications used by the patient at the time of the examination were included. All doses were recalculated in milligrams. Cumulative exposure to anticholinergic and sedative medications was quantified with the DBI using the prescribed daily dose of each medication in the method proposed previously [10]:

$$\mathrm{DBI} = \sum \frac{D}{\delta + D}$$

where D stands for the prescribed daily dose of an individual drug (mg) and δ represents the DR_{50} or the dose (mg) that gives 50% of the maximum effect. In a systematic manner, we previously compiled a list of medications with anticholinergic and/or sedative properties [22, 35]. As the DR_{50} is unknown, it was substituted by the minimum daily oral dose according to Dutch prescribing guidelines.

2.3 Dynamic Gait Parameters

During a 3-min walking period, trunk accelerations in anterior-posterior (AP), medio-lateral (ML), and vertical (V) directions were measured with a wearable accelerometer. Data collected between 2012 and 2014 used a stand-alone accelerometer of the DynaPort hybrid unit (McRoberts BV, The Hague, the Netherlands; $N = 114$), while data collected between 2015 and 2017 used the iPod Touch G4 (iOS 6; Apple Inc.; $N = 70$), which has a built-in tri-axial acceleration sensor. Both devices were previously shown to generate comparable acceleration signals [23]. The devices were fixed with a belt near the level of lumbar segment L4. From the acceleration signals, a total of 22 dynamic gait parameters were calculated using custom-made algorithms in MATLAB (version 2015b; The MathWorks Inc.). These dynamic gait parameters did not rely on foot contact detection. This is an important advantage because older patients often have shuffling gait, which may make foot contact detection inaccurate in this patient group. Dynamic gait parameters can be classified into time-independent and time-dependent gait parameters. Time-independent parameters ignore the successive ordering of signals over time and quantify the magnitude of the variability around the mean (e.g., coefficient of variation). Time-dependent dynamic gait parameters take the ordering and possible dependence of successive signals into account and provide information about the dynamics of gait (e.g., sample entropy and maximal Lyapunov exponent) [24]. Table 1 provides an overview of the 22 dynamic gait parameters. Details about the calculation of these dynamic gait parameters have been described elsewhere [25–27]. To facilitate interpretation, dynamic gait parameters were rescored such that lower scores were indicative of more dysfunctional gait. As gait parameters often tend to be correlated, we subjected our dynamic gait parameters to a factor analysis ('varimax rotation') to identify distinct underlying gait dimensions. Factor analysis demonstrated that the 22 dynamic gait parameters represented the following five gait dimensions, which explained 72% of the variance (see Supplementary Information 1 in the electronic supplementary material [ESM] for factor loadings of dynamic gait parameters on these dimensions, and Table 1 for abbreviation definitions):

- 'Regularity': lower values indicate less regular stride accelerations (G-STR-AP and G-STR-V), less regular step accelerations (G-STE-AP and G-STE-V), less symmetry (GSY-AP and GSY-V) in anterior–posterior and vertical directions, and less predictable accelerations in the anterior–posterior direction (MSE-AP);
- 'Complexity': lower values indicate less predictable accelerations in the vertical direction (MSE-V) and more mutual predictability between accelerations of the anterior–posterior direction with those in the medio-lateral direction (CSE-AP-ML), between accelerations in the anterior-posterior direction with those in the vertical direction (CSE-AP-V), and between accelerations in the medio-lateral with those in the vertical direction (CSE-ML-V);
- 'Stability': lower values indicate greater sensitivity to local perturbations of accelerations in anterior–posterior, medio-lateral, and vertical directions (MLY-AP, MLY-ML, MLY-V);
- 'Pace': lower values indicate slower gait speed (GS), less variability of accelerations in anterior–posterior, medio-lateral, and vertical directions (RMS-AP, RMS-ML, RMS-V), less smoothness of gait in the vertical direction (IH-V), and less smoothness of accelerations in the anterior–posterior direction (IH-AP);
- 'Postural control': lower values indicate less predictable accelerations (MSE-ML) and less smoothness of accelerations (IH-ML) in the medio-lateral direction.

For each patient, gait parameters were summated according to these dimensions. The Regularity and Stability total scores were log-transformed to normalize their distributions. Total scores were standardized (z-scores).

2.4 Statistical Analysis

Descriptive statistics were calculated for demographic variables, body mass index (BMI), co-morbidities as assessed with the Charlson Comorbidity Index (CCI), total number of medications, and number of medications not included in the DBI, polypharmacy (i.e., treatment with ≥ 5 medications), cognitive status (Mini Mental State Examination, MMSE), as well as the clinical diagnosis of dementia or mild cognitive impairment (MCI). The clinical diagnosis of dementia was made using consensus criteria. We also compared patients with no exposure (DBI = 0), moderate exposure ($0 > \mathrm{DBI} \leq 1$), and high exposure (DBI > 1) to anticholinergic and sedative medications on the preceding variables.

Table 1 Overview of time-independent and time-dependent dynamic gait parameters

Outcome	Description	Original scoring	Scoring reversed (R)
Time-independent measures			
Gait speed (GS)	Distance walked	Meters per second	
Root mean squares for AP, ML, and V directions (RMS-AP, RMS-ML, RMS-V)	Magnitude of variability of the accelerations	Higher values are indicative of more variability	
Indices of harmonicity for AP, ML, and V directions (IH-AP, IH-ML, IH-V)	A frequency spectrum analysis of the acceleration and a measure for smoothness of gait	Values ranging from 0 to 1 (0, entirely uneven pattern; 1, perfectly smooth pattern)	
Time-dependent measures			
Multiscale entropies for AP, ML, and V directions (MSE-AP, MSE-ML, MSE-V)	Complexity of gait signals	Higher values denote less predictable gait pattern	R
Cross-sample entropies (CSE-AP-ML, CSE-AP-V, CSE-ML-V)	Quantifies the degree of synchronization or coupling between accelerations of AP with ML directions, AP with V directions, and ML with V directions	Higher values denote less mutual predictability between acceleration signals	
Maximal Lyapunov exponent for AP, ML, and V directions (MLY-AP, MLY-ML, MLY-V)	Calculated using Wolf's algorithm to quantify local trunk stability	Higher values indicate greater sensitivity to local perturbations (i.e., less stability)	R
Gait stride regularity in AP and V directions (G-STR-AP, G-STR-V)	Unbiased autocorrelation as a measure of regularity of gait stride	Higher values indicate more regular strides	
Gait step regularity for AP and V directions (G-STE-AP, G-STE-V)	Unbiased autocorrelation as a measure of regularity of gait step	Higher values indicate more regular steps	
Gait symmetry in AP and V directions (GSY-AP, GSY-V)	Difference between step and stride regularity expressed as a percentage	0% represents a perfectly symmetric gait pattern while higher percentages express less symmetry	R

AP anterior-posterior, *ML* medio-lateral, *V* vertical

A series of multivariable linear regression analyses were conducted to examine mean differences on the gait dimensions 'Regularity', 'Complexity', 'Stability', 'Pace', and 'Postural control' for the DBI categories (no exposure, moderate and high exposure). The gait dimensions (i.e., standardized total scores) were entered as the dependent variables. The DBI categories were represented by dummy variables and were entered as independent variables. Adjustment was made for the covariates age, gender, BMI, MMSE score, co-morbidities including dementia using the CCI, and number of medications not included in the DBI. We chose to exclude medications incorporated into the DBI to prevent collinearity.

To interpret the magnitude of the mean differences between the DBI categories (no exposure, moderate and high exposure), these were compared with the mean differences on the gait dimensions for patients aged 80 years and older versus patients younger than 80 years. Tests were two-tailed and statistical significance was set at $p < 0.05$ and 95% confidence intervals were calculated. Statistical analyses were performed with R version 3.5.1.

3 Results

3.1 Demographic and Clinical Characteristics

A total of 184 patients participated, whose mean age was 79.8 years (± SD 5.8), of whom 110 (60%) were women and of whom 88 (48%) had polypharmacy (i.e., received treatment with ≥ 5 medications). Of the patients, 100 (54%) had no exposure (DBI = 0), 42 (23%) had moderate exposure (0 > DBI ≤ 1), while another 42 (23%) had high exposure (DBI > 1) to anticholinergic and sedative medications (Table 2). Patients with moderate and high exposure were slightly more often female, while those with high exposure had a slightly higher BMI, more co-morbidity (i.e., a higher value on the CCI) and more often had polypharmacy.

Of the 893 medications that were prescribed in total, 157 medications (17.6%) had anticholinergic and/or sedative properties. These medications mainly included drugs for the central nervous system (psycholeptic drugs, 31%; psychoanaleptic drugs, 17%; or other CNS drugs, 8%), medications for the cardiovascular system (26%) and the respiratory system, including medications for obstructive airway disease (13%).

Table 2 Demographic and clinical characteristics of the total sample ($N = 184$) and three DBI groups

	Total sample ($N = 184$)	DBI exposure[a]		
		None ($n = 100$, 54%)	Moderate ($n = 42$, 23%)	High ($n = 42$, 23%)
Demographic characteristics				
Age (years, mean ± SD)	79.8 ± 5.8	80.4 ± 5.8	78.8 ± 5.7	79.3 ± 5.8
Gender (n, % female)	110 (59.8)	57 (57)	26 (62)	27 (64)
Physical health				
Body mass index	25.9 ± 4.1	25.6 ± 4.1	25.9 ± 3.2	26.5 ± 4.7
Charlson comorbidity index (mean ± SD)	1.6 ± 1.4	1.5 ± 1.4	1.5 ± 1.3	2.1 ± 1.5
Medication prescribing				
Total number (mean ± SD)	4.7 ± 3.6	3.0 ± 2.7	5.1 ± 3.2	8.1 ± 3.2
Number excluding DBI medications (mean ± SD)	3.7 ± 3.1	3.0 ± 2.8	3.7 ± 3.2	5.6 ± 2.9
Polypharmacy				
<5 medications	96 (52)	71 (71)	21 (50)	4 (10)
≥5 medications	88 (48)	29 (29)	21 (50)	38 (90)
Cognitive function				
MMSE (mean ± SD)	24.6 ± 4.1	24.6 ± 4.5	24.8 ± 3.5	24.4 ± 4.0
Dementia diagnosis (n, %)				
No dementia	92 (50)	49 (49)	23 (55)	20 (48)
MCI	64 (35)	35 (35)	14 (33)	15 (36)
Dementia	28 (15)	16 (16)	5 (12)	7 (16)

DBI Drug Burden Index, *MMSE* Mini Mental State Examination, *MCI* mild cognitive impairment

[a]None: DBI = 0; moderate: 0 > DBI ≤ 1; high: DBI > 1 exposure to anticholinergic and sedative medications

Table 3 Mean values (SD) of no exposure, moderate and high exposure (DBI) to anticholinergic and sedative medications on gait dimensions with adjusted regression coefficients and 95% confidence intervals

Gait dimensions	Mean	SD	Regression coefficient[a]	95% CI
Regularity				
No exposure (DBI = 0)	0.07	0.88	Reference	Reference
Moderate exposure (0 > DBI ≤ 1)	0.19	0.63	0.09	−0.27 to 0.44
High exposure (DBI >1)	−0.36	1.42	**−0.50**	**−0.88 to −0.12**
Complexity				
No exposure (DBI = 0)	0.18	1.05	Reference	Reference
Moderate exposure (0 > DBI ≤ 1)	−0.14	0.96	**−0.42**	**−0.76 to −0.07**
High exposure (DBI > 1)	−0.29	0.86	**−0.61**	**−0.98 to −0.24**
Stability				
No exposure (DBI = 0)	−0.09	1.13	Reference	Reference
Moderate exposure (0 > DBI ≤ 1)	0.06	0.88	0.15	−0.21 to 0.51
High exposure (DBI > 1)	0.17	0.74	0.30	−0.08 to 0.68
Pace				
No exposure (DBI = 0)	0.18	0.98	Reference	Reference
Moderate exposure (0 > DBI ≤ 1)	−0.03	1.04	−0.30	−0.64 to 0.05
High exposure (DBI > 1)	−0.38	0.91	**−0.60**	**−0.97 to −0.24**
Postural control				
No exposure (DBI = 0)	−0.01	0.95	Reference	Reference
Moderate exposure (0 > DBI ≤ 1)	−0.20	0.90	−0.18	−0.54 to 0.19
High exposure (DBI > 1)	0.23	1.17	0.29	−0.09 to 0.68

BMI body mass index, *CCI* Charlson Comorbidity Index, *CI* confidence interval, *DBI* Drug Burden Index, *MMSE* Mini Mental State Examination, *SD* standard deviation

[a]Adjusted for age, gender, BMI, MMSE score, co-morbidities including dementia using the CCI, and number of medications not included in the DBI

Values in bold indicate statistically significant $p < 0.05$.

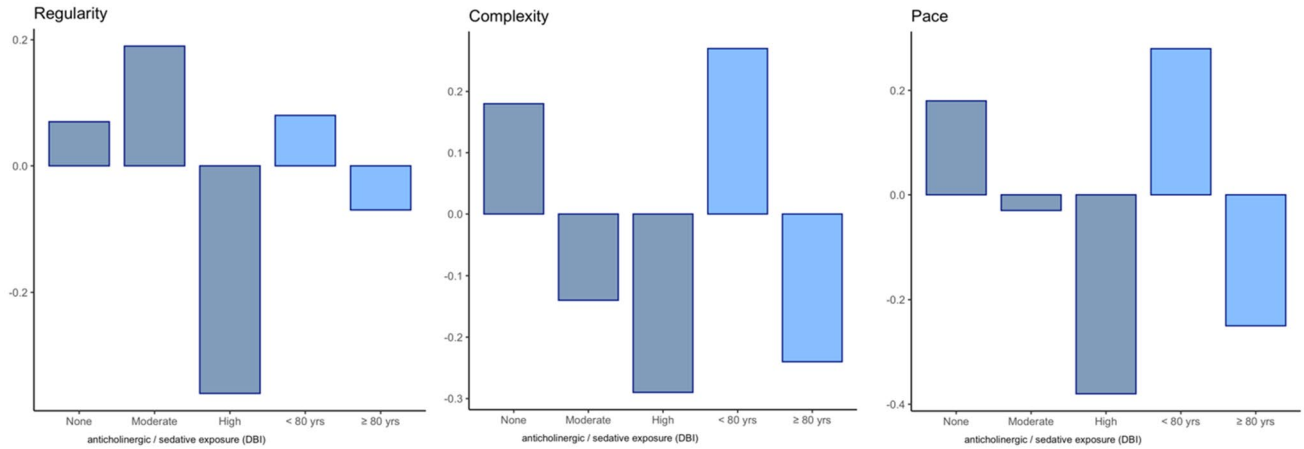

Fig. 1 Mean values on the gait dimensions Regularity, Complexity, and Pace for no, moderate, and high exposure to anticholinergic and sedative medications as measured with the Drug Burden Index (DBI) in comparison with the mean values of patients ≥ 80 years and < 80 years

3.2 Associations Between the DBI and Dynamic Gait Parameters

The multivariable linear regression analyses, in which adjustment was made for the covariates age, gender, BMI, MMSE, co-morbidities (CCI) including dementia, and number of medications not included in the DBI, demonstrated significant associations between anticholinergic and sedative exposure as measured with the DBI and the Regularity, Complexity, and Pace dimensions (Table 3). Compared

with patients without exposure, patients with high exposure had lower values on the Regularity dimension, that is, less regular stride accelerations and less regular step accelerations, less symmetry, and less predictable gait than patients without exposure. Likewise, patients with high exposure had also lower values than patients without exposure on the Pace dimension, that is, a slower gait speed, less variability in accelerations, less smoothness of gait in the vertical direction, and less smoothness of gait in the anterior–posterior direction than patients without exposure. Furthermore, patients with moderate and high exposure had lower values on the Complexity dimension than patients without exposure, that is, less predictable gait and more mutual predictability between accelerations in different directions than patients without exposure (see also explanation in the Methods Sect. 2.3 'Dynamic Gait Parameters').

To illustrate the magnitude of the mean differences for the DBI categories, we compared these with those for patients aged < 80 years (mean 74.8, SD 3.5) and those aged 80 years and older (mean 84.3, SD 3.2) (see Fig. 1). The mean difference on 'Regularity' between patients with a high DBI and patients without exposure was almost three times greater than that between patients ≥ 80 years and patients < 80 years. The mean differences on 'Complexity' of patients with moderate and high exposure compared with patients without exposure were, respectively, over half than and comparable with that between patients ≥ 80 years and patients < 80 years. Likewise, the mean difference on 'Pace' between patients with a high DBI and patients without exposure was comparable to that between patients aged ≥ 80 years and patients < 80 years.

4 Discussion

In this study of older patients with comorbidities, we examined associations between cumulative exposure to anticholinergic and sedative medications as measured with the DBI and gait as assessed with dynamic gait parameters. Using wearable accelerometers, we extracted 22 different dynamic gait parameters from 3D-acceleration signals during walking. Dynamic gait parameters were both time-independent (i.e., ignoring the time aspect, e.g., gait speed) and time-dependent (i.e., considering the dependence of successive steps, e.g., gait step regularity). Factor analysis demonstrated that these dynamic gait parameters reflected five overarching gait dimensions, namely 'Regularity', 'Complexity', 'Stability', 'Pace' and 'Postural control'.

High cumulative exposure to anticholinergic and sedative medications was related to lower values on the Regularity and Pace dimensions. Furthermore, both moderate and high exposure were associated with lower values on the Complexity dimension. Importantly, these associations were adjusted for the covariates age, gender, BMI, MMSE, co-morbidities (CCI) including dementia, and number of medications not included in the DBI.

We did not find associations of the DBI with the dimensions of 'Stability' and 'Postural control'. As patients with the greatest levels of gait impairment and gait problems (e.g., because of Parkinson's disease) were excluded, it is unlikely that advanced physical and cognitive decline and/or heterogeneity therein attenuated possible associations between the DBI and these dimensions. Participants of this study were also not older than participants from previous DBI studies. The mean age of the outpatients included in this analysis was about 80 years, which was in the center of the age distribution of participants in other DBI studies [11]. Our findings are consistent with other findings demonstrating associations between cumulative exposure to anticholinergic and sedative medications and impairments including slower gait [3, 28–31].

The findings of the present study have implications for research and practice. First, these dynamic gait patterns may provide insight into dysfunctional gait characteristics that predispose older patients for falling. Time-dependent dynamic gait parameters have been found to increase classification accuracy of older patients who experienced a fall incident [15, 16]. As such, dysfunctional gait characteristics as measured with accelerometer-based dynamic gait parameters could serve as early warning signals. As both are feasible to assess in clinical practice, the DBI and the dynamic gait parameters could aid geriatricians in deprescribing potentially inappropriate anticholinergic and sedative medications that are associated with an increased fall risk.

A number of methodological issues are worthwhile to consider. First of all, the dynamic gait parameters of this study are likely to have additive value. Although the DBI was previously examined in relation to physical function, our own and other reviews of the literature demonstrated that the mere completion time of objective functional tests and patient self-reported ability to carry out ADLs have been adopted as global measures of physical function [11, 32]. By contrast, the present study examined gait in a more detailed manner using accelerometer-based dynamic gait parameters that capture the dynamics and patterns of gait. A particular strength of the dynamic gait parameters examined in this study is that these are independent of foot contact detection, which is an advantage given the frequent shuffling gait of older patients. At the same time, and as in other studies that adopted accelerometers, we cannot rule out the possibility of reactivity to accelerometers which may have altered patients' walking behavior (i.e., a kind of Hawthorne effect). Dynamic gait parameters have also been found to predict future cognitive decline [17, 18]. In this regard, a limitation of the

current study is the cross-sectional design, that only allows us to assess associations between dynamic gait parameters and the DBI. Future studies should focus on monitoring changes over time in dynamic gait parameters to examine medication-induced deterioration and adverse reactions [36].

With regard to the DBI, there are possible advantages and disadvantages. The key advantage of the DBI, compared with studying associations of specific drugs with gait, is that the DBI offers a feasible formula to quantify the cumulative exposure to a variety of anticholinergic and sedative medications from different therapeutic classes. As such, the DBI better captures the clinical situation of older patients with comorbidities who often receive treatment with multiple medications. Two advantages of the DBI over related measures is that it includes sedative medications in addition to anticholinergic medications, and that it takes the dosages of medications into account. A potential disadvantage concerning the DBI and related scales is that there is no final international consensus on the list of anticholinergic or sedative medications between experts. Despite this possible limitation, the DBI remains a non-invasive tool for the screening of potentially harmful polypharmacy [33], especially anticholinergic and sedative drug burden in older patients.

5 Conclusion

Taken together, we conclude that in older patients with comorbidities, cumulative anticholinergic and sedative exposure is associated with poorer function on the gait dimensions 'Regularity', 'Complexity' and 'Pace'. As indicators of subtle gait impairment, these gait dimensions, calculated from accelerometer-based dynamic gait parameters, could be useful to aid the deprescribing of potentially inappropriate anticholinergic and sedative medications.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40266-021-00902-1.

Declarations

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Conflicts of interest HW, JPVC, MJK, LK, SNH, KT, HGVDM, and CJCL report no conflicts of interest.

Ethics approval The Medical Ethical Committee of the Slotervaart hospital approved the study. We certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate All patients or their legal representatives (when patients had cognitive impairment) gave written informed consent.

Consent for publication Not applicable.

Availability of data and material Data will be made available as Electronic Supplementary Material.

Code availability Not applicable.

Author contributions Concept/design: HW, JPVC, CJCL; acquisition of data collection from participants: JPVC, MJK, LK, CJCL; Data analysis: HW, CJCL; interpretation of data: HW, JPVC, LK, SNH, KT, HGVDM, CJCL; preparation of manuscript: HW, JPVC, MJK, LK, SNH, KT, HGVDM, CJCL. All authors have read and approved the final manuscript.

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