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A longitudinal study of gait function and characteristics of gait disturbance in individuals with Alzheimer's disease

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ABSTRACT

Walking in daily life places high demands on the interplay between cognitive and motor functions. A well-functioning dual-tasking ability is thus essential for walking safely. The aims were to study longitudinal changes in gait function during single- and dual-tasking over a period of two years among people with initially mild AD (n = 21). Data were collected on three occasions, twelve months apart. An optical motion capture system was used for three-dimensional gait analysis. Gait parameters were examined at comfortable gait speed during single-tasking, dual-tasking naming names, and naming animals. The dual-task cost for gait speed was pronounced at baseline (names 26%, animals 35%), and remained so during the study period. A significant (p < 0.05) longitudinal decline in gait speed and step length during single- and dual-tasking was observed, whereas double support time, step width and step height showed inconsistent results. Systematic visual examination of the motion capture files revealed that dual-tasking frequently resulted in gait disturbances. Three main characteristics of such disturbances were identified: Temporal disturbance, Spatial disturbance and Instability in single stance. These aberrant gait performances may affect gait stability and increase the risk of falling. Furthermore, the observed gait disturbances can contribute to understanding and explaining previous reported gait variability among individuals with AD. However, the role that dual-task testing and aberrant dual-task gait performance play in the identification of individuals with early signs of cognitive impairment and in predicting fall risk in AD remains to be studied.

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1. Introduction

Considering the benefits of maintaining walking capacity and, thereby, independence and well-being during the progression of Alzheimer's disease (AD) [1-3], it is important to clarify the natural course of gait deterioration and its relation to declining cognitive function in AD. In a number of cross-sectional studies [4-9], impairments in temporal and spatial gait parameters, including step-to-step variability, have been reported among individuals in the early stages of AD. Executive and attention dysfunctions have

E-mail addresses: ylva.cedervall@pubcare.uu.se (Y. Cedervall), kjartan.halvorsen@it.uu.se (K. Halvorsen), anna.cristina.aberg@pubcare.uu.se (A.C. Åberg). been suggested to be the main cause of these early gait disturbances, which, in turn, may be risk factors for falls [10–13].

Walking in constructed and natural environments places high demands on the interplay between cognitive (i.e. executive and attention functions) and motor functions. There is, for example, a constant need to adapt body movements to rapidly evolving situations related to crowded places and traffic. Additionally, environmental factors such as curbs, uneven surfaces, and weather conditions can aggravate walking and cause fall incidences [1,14-16]. A well-functioning ability to sustain, shift, and divide attention between environmental and body function factors is thus essential for walking safely in everyday life. Therefore, in recent dementia research, much attention has been placed upon studying gait function using the dual-task paradigm [4,6,17,18]. Dual-tasking here refers to the (dis)ability to maintain walking when a cognitive task is performed simultaneously. The intention is to mimic walking in everyday life where the requirements on executive and attention functions are commonly high.

To our knowledge, however, there is a lack of studies on longitudinal changes in gait function under both single- and dualtask conditions in AD. By studying how gait function is affected longitudinally during single- and dual-tasking in the early years of





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AD, it may be possible to clarify why the fall risk occurs, and at which point in the course of AD fall accidents increase. The identification of changes in gait function during dual-tasking may additionally guide the design of interventions aimed at promoting physical function and independence, among individuals with AD. The aim was, therefore, to study longitudinal changes in gait function under single- and dual-task conditions during a period of two years among people who initially had mild AD.

2. Methods

2.1. Participants

Twenty-five participants with mild AD were recruited consecutively from an outpatient memory clinic at a university hospital in Sweden. They were included in an extensive longitudinal project exploring different aspects of physical activity in individuals with AD. The present study is a sub-study of this longitudinal project. The inclusion procedure is described in detail elsewhere [19]. Individuals were diagnosed as AD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [20] and of the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) [21]. The inclusion criteria were: age <80 years, a Mini Mental State Examination (MMSE) [22] score of 20-30 points, ability to walk 10 m without a walking aid, and community-dwelling with a spouse. Exclusion criteria were other illnesses or injuries that affect the ability to move, and treatment by anti-psychotics.

Twenty-one of the participants completed the present substudy. Reasons for discontinuation during the study period were: severe illness other than AD (n = 2), cohabitant's occupation (n = 1) and withdrawal by the participant's spouse due to severity of dementia (n = 1). The longitudinal results in the present study were, therefore, based on a group of 21 participants with initial mild AD. Participants' characteristics are displayed in Table 1. The Research Ethics Committee at Uppsala University approved the study. All participants gave their informed consent to participate.

2.2. Apparatus

An optical motion capture system (ProReflex, Qualisys AB, Gothenburg, Sweden) was used for three-dimensional gait analysis. Eighteen reflecting markers were applied on defined anatomical landmarks according to the marker setup, developed at the Lundberg Laboratory, Sweden (Appendix A). Six cameras recorded the position of the markers. Marker data were sampled at 240 Hz and low-pass-filtered with a cutoff frequency of 6 Hz. Data were processed using the software Visual 3D (C-Motion Inc., Germantown, DM, USA).

2.3. Procedure

The participants underwent gait analysis on three occasions, 12 months apart. In connection with the gait testing, measurements of height and weight were performed. Cognitive function, walking capacity, and functional status (Table 1) were measured two weeks before each occasion for practical reasons and to minimize the risk of exhaustion of the participants. In addition, a 14-day physical activity diary for recording health-promoting physical activity was distributed, and data on falls over the last year was collected.

During the gait tests, the participants walked barefoot, men wore shorts, and women shorts and a bra. Instructions on how to walk were initially given in a narrative way, and then followed by standardized instructions (Appendix B). If necessary, the instructions were repeated to ensure that the participant had understood and remembered.

2.4. Data analysis

The following temporal and spatial gait parameters were computed: gait speed (m/s), step width (m), step length (m), step height (m), and double support time (s). All gait parameters were examined at the participant's comfortable gait speed under three different conditions and in the following order: five single-task trials, three dual-task trials naming names, and three dual-task trials naming animals. The participants were instructed to

Table 1

Characteristics of the 21 participants with Alzheimer's disease at baseline and 1- and 2-year follow-up. Longitudinal changes were calculated by the use of Friedman's test due to non-normal distributions.

	Baseline	n	1-year follow-up	п	2-year follow-up	n	p-value
Baseline parameters							
Gender, male/female	10/11	21					
Age (yrs), Md (range)	72 (55–78)	21					
Education, university studies (number)	10	21					
Height (cm), Md (range)	169 (153–184)	21					
Weight (kg), Md (range)	73 (55–89)	21	71 (55–89)	21	72 (54–87)	21	0.988
Functional status							
Functional Assessment Staging $(0-7 p)^a$, Md (range)	4 (4-4)	21	4 (4-6)	21	4 (4-7)	21	0.001
Cognitive function							
Mini Mental State Examination (0–30 p) ^b , Md (range)	25 (21-30)	21	22 (16-29)	21	20 (9-28)	21	< 0.001
Clock drawing test (0–7 p) ^b , Md (range)	4 (0-7)	21	4 (0-7)	19	2 (0-7)	17	0.009
Verbal fluency (number) ^b , Md (range)	16 (7-25)	21	12 (4-18)	21	9 (2-20)	20	< 0.001
Trail Making Test A (0–240 s) ^a , Md (range)	69 (40-240)	21	84 (46-240)	20	111 (47-240)	17	< 0.001
Walking capacity							
6-min walk test (m), Md (range)	498 (344-712)	21	446 (340-703)	21	430 (260-616)	21	< 0.001
Walking performance ^c							
Physical activity level (minutes/week), Md (range)	330 (8-945)	20	272 (10-670)	21	270 (10-600)	21	0.698

The Mini Mental State Examination is a composite screening test of cognitive function, the Clock drawing test assesses visuospatial function, semantic memory and planning, the Verbal fluency test assesses semantic memory and language, and the Trail Making Test A, assesses visual attention and executive function (mental speed and flexibility). The 6-minute walk test is a test of walking endurance. Median and ranges are displayed due to non-normal distributions.

^a Higher values indicate more severe cognitive impairment.

^b Higher values indicate better cognitive function.

^c The public health recommendation for physical (aerobic) activity of moderate intensity is \geq 150 min per week.

Table 2

Differences in gait parameters measured at comfortable gait speed in 21 subjects with Alzheimer's disease at baseline and 1- and 2-year follow-up. Repeated measures ANOVA was used for all parameters except double support where Friedman's test was used due to non-normal distribution. Effect sizes were calculated between baseline and 2-year follow-ups.

Gait parameters	Baseline (mean \pm SD)	1-yr follow-up (mean \pm SD)	2-yr follow-up (mean \pm SD)	p-value	Effect size (Cohen's d)
Single tasks					
Gait speed (m/s)	1.14 ± 0.14	1.10 ± 0.15	1.01 ± 0.20	0.009 ^a	0.77
Step length (m)	0.62 ± 0.07	0.60 ± 0.07	0.57 ± 0.09	0.006 ^a	0.64
Step width (m)	$\textbf{0.08} \pm \textbf{0.02}$	0.08 ± 0.02	0.09 ± 0.02	0.801	0.51
Double support (s)	0.27 ± 0.06	0.26 ± 0.07	0.29 ± 0.08	0.001 ^b	0.03
Step height (m)	0.22 ± 0.02	0.21 ± 0.02	0.21 ± 0.02	0.007 ^a	0.51
Dual tasks					
Gait speed names (m/s)	0.84 ± 0.22	0.84 ± 0.25	0.75 ± 0.26	0.01 ^a	0.38
Gait speed animals (m/s)	0.74 ± 0.22	0.76 ± 0.27	0.64 ± 0.22	$< 0.001^{a}$	0.47
Step length names (m)	$\textbf{0.59} \pm \textbf{0.08}$	0.58 ± 0.08	0.53 ± 0.13	0.043 ^a	0.57
Step length animals (m)	0.57 ± 0.09	0.55 ± 0.09	0.51 ± 0.11	0.014 ^a	0.61
Step width names (m)	$\textbf{0.09} \pm \textbf{0.03}$	0.09 ± 0.03	0.10 ± 0.03	0.205	0.34
Step width animals (m)	$\textbf{0.09} \pm \textbf{0.03}$	0.09 ± 0.04	0.10 ± 0.03	0.117	0.34
Double support names (s)	0.42 ± 0.18	0.38 ± 0.17	0.40 ± 0.14	0.268	0.13
Double support animals (s)	0.50 ± 0.32	0.43 ± 0.19	0.49 ± 0.18	0.014 ^b	0.04
Step height names (m)	0.21 ± 0.02	0.21 ± 0.02	0.20 ± 0.03	0.106	0.40
Step height animals (m)	0.21 ± 0.02	0.20 ± 0.02	0.20 ± 0.03	0.006 ^a	0.40

^a p < 0.05, significant differences by post hoc test between the 1-year and the 2-year follow-ups (corrected for multiple comparisons by Bonferroni).

 b p < 0.025, significant differences by post hoc tests for double support between the 1-year and the 2-year follow-ups (corrected for multiple comparisons by the Wilcoxon's signed rank test). Non-significant *p*-values are calculated from the overall repeated measures ANOVA. Significant *p*-values are calculated from pairwise post hoc tests.

prioritize the walking task. To avoid the inclusion of acceleration and retardation phases, we analyzed three to four steps in the middle part of the seven-metre trial. The first single-task trial was considered as a practice round and, therefore, excluded from analysis. Results for each participant at each occasion were based on means of four single-task trials, three dual-task trials naming names and three dual-task trials naming animals. In addition to the quantitative gait analysis, a systematic visual examination of the motion capture files was performed to identify characteristics of aberrant gait performance due to the dual-task conditions.

2.4.1. Statistical analysis

Descriptive statistics were calculated for participant characteristics, cognitive function, falls and gait parameters. All gait parameters, except double support time, were normally distributed. Therefore, parametric statistics (repeated measures ANOVA) were used for longitudinal differences in gait speed, step width, length, and height. Non-parametric statistics (Friedman's test) were used for calculating longitudinal differences in double support time. The dual-task cost per cent was calculated for gait [((single-task speed value – dual-task value)/single-task value) \times 100]. The paired samples *t*-test was used for crosssectional analysis of differences between single- and dual-task normally distributed gait parameters, and the Wilcoxon's signed rank test was used for double support time. Correlations between gait parameters and cognitive function were assessed by Spearman's rank correlation coefficient. All tests were two-tailed. The level of significance was set at p < 0.05 for longitudinal changes. The Bonferroni method was used to correct for multiple comparisons. For post hoc tests of double support time, the Wilcoxon's signed rank test was used and significance was set at p < 0.025 to adjust for the two relevant comparisons. Significance for correlations was set at p < 0.01 to minimize the risk of type-1 error due to multiple testing. Cohen's d was used to calculate effect sizes. All calculations were performed with the Statistical Package for the Social Sciences, version 20.

The systematic visual examination comprised repeated scrutinizing of all motion capture files to identify aberrant gait performance due to the dual-task conditions. After a preliminary classification by the first author, the motion capture files were scrutinized again, the characteristics of different gait performances were compared with each other and the preliminary classification was refined [23]. Peer debriefings were held between the authors at which the motion capture files were reviewed. Finally, the classification was determined.

3. Results

During the two-year follow-up period, there was a significant (p < 0.05) decline in gait speed and step length under all three investigated conditions (i.e. single-task, dual-task names and dual-task animals) (Table 2). Furthermore, step height and double support time deteriorated significantly (p < 0.05) for single- and dual-task animals, but not for dual-task names. Post hoc tests revealed that the significant differences for all gait parameters occurred between the 1- and the 2-year follow-ups.

In contrast, dual-task cost was pronounced at baseline, but seemed to remain on a stable level during the same period. The dual-task costs for gait speed at baseline, the 1-, and the 2-year follow-ups were 26%, 24%, and 26% for naming names, and 35%, 31%, and 37% for naming animals. The cross-sectional differences between single- and dual-task gait parameters were significant for 9/10 comparisons at baseline (all but step width/names), 8/10 at 1-year follow-up (all but step width/names and step width/animals), and 9/10 at the 2-year follow-up (all but step length/names). It is notable that gait speed was significantly lower (p < 0.05) during the dual-task animals than during the dual-task names on all three occasions (Fig. 1).

Correlations between gait parameters and cognitive function were calculated cross-sectionally at baseline, at the 1-, and at the 2-year follow-ups. Significant moderate correlation was found at the 1-year follow-up between double support time and the Trail Making Test A (p = 0.009, r = 0.565). No significant correlations between gait parameters and cognitive tests were found at baseline or at the 2-year follow-up.

Systematic visual examinations of the motion capture files identified three different characteristics of aberrant gait performance due to dual-tasking: (1) *Temporal disturbance*, (2) *Spatial disturbance*, and (3) *Instability in single stance*. *Temporal disturbance* comprised occasional stops in single or double stance, Spatial *disturbance*: variable step length, step width or deviating direction, and *Instability in single stance*: correction of the stance foot position



Fig. 1. The cross-sectional differences between gait speed single-task, dual-task names and animals. The differences are significant for comparisons between single- and dual-task names, single- and dual-task animals, and dual-task names and dual-task animals on all three occasions.

in single stance. Illustrations of the identified characteristics of aberrant gait performances are enclosed as video files. (Table 3, video 1–5). Twelve participants exhibited at least one distinct feature of gait disturbance at baseline, but the number did not increase during the study period (n = 10, n = 10). However, there was a tendency of an increase of gait disturbance features during the follow-up period (16/15/18) (see Supplementary data). No longitudinal increase of reported falls was shown.

4. Discussion

The main finding in the present study was that a simultaneous cognitive task appears to have a distinct impact on gait function already in mild AD. The dual-task cost for gait speed was pronounced at baseline in comparison with age-matched reference values [7], but remained relatively stable during the follow-up period. However, gait speed and step length during both singleand dual-tasking deteriorated as the AD progressed, whereas double support time, step width and step height showed inconsistent results. Interestingly, whilst all participants had a stable gait during single-tasking, during dual-tasking however, aberrant gait performances were frequent and showed different characteristics of disturbance. A trend towards an increase in dualtask gait disturbances was observed during the 2-year study period.

In older adults, a strategy to adapt to declining walking capacity is to slow down gait speed, shorten step length, and increase the time spent in double support [24]. These changes may be indicators of instability [25]. The extreme of this strategy is to stop walking in a cognitively demanding situation. In 1997, Lundin-Olsson [26] reported that older people with an increased fall risk stopped walking when talking during a spontaneous conversation [27]. However, a "stops-walking-while-taking-strategy" indicates some ability to adapt walking to a reduced cognitive reserve, and to environmental demands. In contrast, frail older people with dementia can tend to walk too fast in relation to their walking capacity and environment [28]. These results illustrate two different gait strategies related to impaired dual-tasking, the first "secure" and the latter more "risky", both, however, predicative of falls.

In the present study, we identified signs of both these gait strategies among the participants. At first sight, the calculated decrease of gait speed during dual-tasking could be interpreted as an adaptation by a general slowed, steady speed, including shorter step length. However, when scrutinizing the motion files, only nine

Table 3

The main types (I–III) of aberrant gait performance during dual-tasking are illustrated by video file examples. The presentations are based on the skin marker setup of the Qualisys motion capture system. The impact of dual-tasking on gait in each video file, first shows the subject in sagittal and frontal views during single-task gait, and then during dual-task gait.

Sagittal view



Example of single-task gait Frontal view



Example of single-task gait

(I) Temporal disturbance	
Occasional stops in single stance	VIDEO 1
Occasional stops in double stance	VIDEO 2
(II) Spatial disturbance	
Variable step length	VIDEO 3
Variable step width/deviating direction	VIDEO 4
(III) Instability in single stance	
Stance foot correction	VIDEO 5

participants showed a stable dual-task gait performance at baseline, whereas seven demonstrated temporal disturbances that slowed the average gait speed. Occasional stops in double stance were most common, and possess similarities with a "stopswalking-while-talking-strategy". Stops in single stance also occurred, but must obviously be viewed as a more hazardous performance, along with other types of gait disturbances such as variable step width [25,29] and stance foot correction in single stance. Further, four had distinct variable step length. The analysis of motion capture files by visual examination hence demonstrated that dual-task gait disturbances (i.e. irregularities), can affect calculated means of gait parameters and contribute to explain why double support time, step width and height provided inconsistent longitudinal results in the present study.

During the 2-year study period, there was a tendency that the observed number of gait disturbance features increased, as well as participants who exhibited two or more characteristics of gait disturbance (see Supplementary data). Notable is that combinations of "secure" and "risky" gait performances could occur in the same participant at the same or at different occasions, indicating that presence of any gait disturbance due to dual-tasking may be important in detecting those at higher risk of future falls. However, the importance of the different characteristics of gait disturbance as predictors for future falls and rapidly declining physical function in AD remains to be studied.

The dual-task cost of gait speed in the study group was increased compared with healthy controls at baseline (35% vs. 9%) and is comparable with results from previous cross-sectional studies in individuals with mild AD [7]. Unexpectedly, the dualtask cost did not change significantly during the study period. One may speculate if this could be explained as the early signs of a "walking-too-fast-strategy" [28], reflecting a lack of insight into declining executive and attention functions, and resulting in an impaired ability to adapt gait to a cognitively demanding situation. This conclusion is supported by a tendency that "risky" dual-task gait performances increased as the AD progressed. On the other hand, the participants might not have experienced their performance as hazardous. In daily life, people are exposed to activities that challenge postural control. A majority of the participants in the present study were physically active on a health-promoting level (Table 1) and had been diagnosed with AD for only a short period of time. They might therefore have been used to challenge their postural limits, and had to this point not sustained more falls than healthy controls [19].

The number of reported falls among the participants in our study was low at baseline and did not increase longitudinally. This is in line with previous research [30] and may reflect that in the early years of AD the fall risk is increased, but not necessarily the number of sustained falls. Another aspect is the difficulty to obtain a correct falls registration among individuals with mild to moderate AD who, in part, live an independent life and spend time on their own. If they fall when alone, they may not mention the accident. Methods for correct fall registration in the early stages of dementia need to be developed to improve the understanding of why and when individuals with early AD are more prone to sustain falls.

4.1. Methodological considerations and clinical implications

The major limitation was that the data collection method consisting of three to four consecutive steps per trial did not enable statistical calculations of step-to-step variability of gait parameters [31]. Aberrant gait performances were therefore identified, solely by visual examination of motion capture files. This method lacks in objectivity, but allows repeated inspections of each gait trial.

Reporting the performance on the cognitive tasks during walking and when sitting, could have complemented the interpretations. Comparison with a healthy control group could also have been of benefit. However, our focus was to study longitudinal changes of gait function in individuals with mild AD and previous studies have already shown that gait function is significantly deteriorated in mild AD, in comparison to that of healthy controls [6,7,18,30]. The group size was small, but comparable to previous laboratory-based studies [6,7,30]. Nevertheless, the sample size and the dropouts of participants unable to perform the Trail Making Test A and the Clock drawing test as the dementia progressed may have contributed to the lack of correlations between gait parameters and the cognitive test.

Our results support previous research where naming animals combined with walking [7] was feasible to detect impairments in dual-tasking in individuals with mild AD and mild cognitive impairment [7]. A benefit of using animal naming is that it seems to affect gait more than naming names. A possible reason for this is that participants tended to choose family members' names during the naming-task, which appeared an easier task than randomly naming animals. However, if the purpose is to detect individuals with early signs of cognitive impairments, we propose that naming animals is combined with a more complex motor task (e.g. Timed Up-and-Go test) [19], or that a comfortable gait be combined with a more demanding cognitive task (e.g. counting backwards) [7].

The longitudinal design combining laboratory-based gait analysis and the systematic visual examination of gait performance during single- and dual-tasking is the main strength of our study. This approach yielded a comprehensive picture and new insight into gait disturbance and increased fall risk in the early years of AD.

5. Conclusions

In mild AD, a simple cognitive task, such as naming animals, can have a distinct impact on gait function. The dual-task cost appears to be pronounced, but seems to remain stable during the early years of AD whereas both single- and dual-task gait speed and step length deteriorate significantly. Moreover, dual-tasking can result in observable gait disturbances of different characteristics, which may help to explain previously reported gait variability in AD. A limited ability to prioritize during dual-tasking is assumed to cause these aberrant gait performances, which in turn may affect stability and increase the risk of falling. Visual examination of motion capture files can constitute a complement to statistical calculations of gait variability to facilitate understanding and communication of gait disturbances in AD to clinicians, researchers, patients and significant others. However, the role that dualtask testing and aberrant dual-task gait performance play in the identification of individuals with early signs of cognitive impairment and in predicting fall risk in AD remains to be studied.

Conflicts of interest statement

There are no conflicts of interest concerning this study.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.gaitpost.2013. 12.026.

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