Gait and Mild Cognitive Impairment: How spatiotemporal parameters and gait variability are affected in MCI

Stephanie Gravett
First, I would like to thank everyone at the Healthy Ageing Initiative, for the possibility to take part of your research, as well as for your dedication to contribute to the health of our elderly. I would also like to express my gratitude towards Anna Sundström and Nils Berginström. Both of you have guided and helped me through this challenging task. Thank you for all your comments, constructive criticism and support.

Brief explanation of gait terms used in the thesis

Step: A step is movement from one foot to the opposite foot.

Stride: A stride is two consecutive steps; movement from one foot, to the opposite, and back to the initial foot.

Swing: Swing is a phase of the walking cycle, when only one foot is in contact with the ground, and the opposite leg is swung forward.

Double support: Double support is the phase of the gait cycle when both feet are in the ground simultaneously.
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Previous research has found a connection between gait and cognitive function. However, the relationship between mild cognitive impairment (MCI) and gait has not been fully explored. Thus, the aim of this study was to examine how spatiotemporal gait parameters, and gait variability, are affected in people with MCI compared to cognitively healthy individuals (CHI). The study was carried out in cooperation with the Healthy Ageing Initiative research project, Umeå University, Sweden. A total of 1937 participants were included in the study. All participants were 70-years old and residents of the municipality Umeå. A total of 112 participants were classified as having MCI, as measured with the Mini-Mental State Examination (MMSE). Gait analysis was performed with the GAITRite® system, and participants performed four trials: preferred pace, fast pace, cognitive dual task and motor dual task. Results showed group differences in both spatial and temporal aspects of gait, especially during the first three trials. For example, participants with MCI walked more slowly, had shorter steps and strides, as well as a longer duration of the double support phase and lower duration of the swing phase. Participants with MCI revealed higher gait variability during cognitive dual task. Several of these variability variables, as well as spatiotemporal variables, could predict probability of having MCI, as seen through logistic regression. Results indicate that the gait observed in MCI could be related to a higher risk of falling.

Mild Cognitive Impairment (MCI) is the early decline of cognitive functions. It can be defined as the early stage of oncoming dementia, or a transitional zone in regards of cognitive function between a normal ageing process and early dementia (Petersen, 2004). The characteristics of MCI can be very subtle and the patient’s activities of daily living are generally relatively intact (Tomoeda & Bayles, 2013). It usually affects one or several domains out of memory, executive functions, attention, language and visuospatial skills. Severity must surpass what can be expected from normal ageing. Furthermore, the diagnosis excludes patients who are considered demented (Petersen, 2004). It can however be difficult to differentiate between MCI and early stages of dementia. Some even suggest that MCI is actually a form of mild, first stage dementia (Morris et al., 2001).
There are several different subtypes of MCI, for example amnestic MCI (a-MCI) in which memory deterioration is the primary symptom, and non-amnestic MCI (na-MCI), in which other cognitive domains are primarily affected. It is also suggested that MCI should be categorized as either single or multiple domain, depending on how many cognitive domains are affected (Petersen, 2004). This means that MCI is a diverse disorder (see Figure 1).

**Figure 1.** Categorization of MCI subtypes and domains (as proposed by Petersen, 2004).

Prevalence of MCI in older populations aged 65 years and over (65+) have been reported from anywhere between 3%-16% (Petersen et al., 2010; Solfrizzi et al., 2004). Progression rates have also been reported at a wide range. Petersen et al. (1999) found that their participants with MCI progressed into dementia with an annual rate of 12%, compared to control groups with a conversion rate of 1-2%. Solfrizzi et al. (2004) found an annual progression from MCI to dementia at 3.8%. These differences in progression rates are probably due to different diagnostic measures, small samples and different age groups. Not every case of suspected MCI will progress into dementia, and some patients remain stable or improve (Petersen, 2004). Still, individuals with MCI are at larger risk of developing dementia than a normal population.

Gait in dementia and MCI

Since MCI is a risk factor for dementia, it is important to explore this cognitive disorder further. In recent years, gait has become subject of interest in dementia and MCI. Gait is the act of walking, and the pattern in movement of limbs. There are both spatial (movement in space) and temporal (movement in time) aspects of gait. The variables are collectively called spatiotemporal parameters (Hollman, McDade, & Petersen, 2011).

Disturbances in gait have been found to correlate with cognitive disorders such as dementia and MCI (Allan, Ballard, Burn, & Kenny, 2005; Verghese et al., 2008). These findings are somewhat inconclusive, especially in relation to MCI and early stages of dementia, and it is still unclear how this relationship can be observed or used clinically. There are also different hypotheses as to why this relationship is prevalent. Some have found a relationship between brain structures, cognitive impairment, and gait dysfunction (Annweiler et al., 2012). Others hypothesize that gait may not be as automatic as previously thought, and that walking may be dependent on cognitive functions (Hausdorff, Yogev, Springer, Simon, & Giladi, 2005).

When examining gait, two different conditions are commonly used: Single task and dual task. Single task is simply walking without another task, often either at preferred pace or at fast pace. Dual task is walking while performing a given task, for example counting backwards from 100 in increments of 1. These tasks are often cognitively demanding, and research has shown that individuals with MCI have a higher dual task cost than cognitively healthy individuals (CHI). Dual task cost is the relative difference in spatiotemporal parameters between single task and dual task conditions (Muir et al., 2012). While gait differences between MCI and CHI can be prevalent during single task conditions (Bahureksa et al., 2017), differences are more prominent
during cognitively demanding dual task conditions and more spatiotemporal parameters are affected (Montero-Odasso, Muir, & Speechley, 2012; Muir et al., 2012).

A meta-analysis of 14 studies on gait and MCI provide some useful guidelines when deciding what aspects of gait can discriminate MCI from CHI (Bahureksa et al., 2017). The authors found that participants with MCI during single task walking presented a slower gait speed. During dual task walking, individuals with MCI presented slower gait speed, increased stride time, decreased stride length, and increased stride time variability compared to CHI. They found that stride time variability during dual task conditions shows significant effect size when discriminating between MCI and CHI.

Stride time variability has been suggested to be a biomarker for MCI (Beauchet et al., 2014). Variability (Coefficient of Variation, CoV) of gait parameters shows the standard deviation as a percentage of the mean. It has been described as a measure of symmetry and rhythm in gait, as well as level of control (Beauchet et al., 2009). Beauchet et al. (2014) found that stride time variability was higher in MCI than in CHI, and that stride time variability correlated with level of cognitive decline. The authors suggest that higher stride time variability is a motor phenotype of cognitive impairment. This has been supported by other research as well (Beauchet, Allali, Launay, Herrmann, & Annweiler, 2013; Muir et al., 2012). Montero-Odasso et al. (2014) found that a-MCI had higher stride time variability than na-MCI which suggests a diversity of gait disturbances within MCI.

Slow gait speed may also be a biomarker for MCI (Bahureksa et al., 2017). Individuals with MCI have shown significantly decreased gait speed compared to CHI, especially during dual tasking (Beauchet et al., 2013; Doi et al., 2014; Montero-Odasso et al., 2014). Slower gait speed has also been found to correlate with lesser cognitive performance across several domains, such as attention, language, memory and visuospatial skills (Savica et al., 2017). However, Montero-Odasso et al. (2014) also found that individuals with a-MCI had significantly decreased gait speed compared to na-MCI.

Several other spatiotemporal parameters of gait have been found to correlate with cognitive decline. Savica et al. (2017) found that longer double support time was associated with lower cognitive performance. Higher variability in stride length and swing time was also associated with worse cognitive performance along several domains. Longitudinally, these parameters were found to predict cognitive decline. Other studies have found that slow gait and impaired gait symmetry is correlated to a higher risk of progression to dementia, as well as a higher risk for disability (Doi et al., 2015; Gillain et al., 2016). These results suggest that it might be possible to predict the prognosis of MCI through gait analysis, which further emphasizes the importance of exploring the relationship between MCI and gait.

Previous evidence has been somewhat inconsistent in what aspects of gait are affected in individuals with MCI. This might be partly due to small sample sizes and there is need for a larger study. There are also differences in what type of gait parameters are included, making it difficult to compare studies and fully understand how gait is affected in MCI. Thus, the aim of this study was to further examine how gait, measured in spatiotemporal parameters and gait variability, is affected in individuals with MCI compared to the cognitively healthy. Additionally, this study aimed to explore the relationship between gait and MCI during cognitive dual task, since previous research has found this condition to be especially challenging for individuals with MCI.

More specifically, this study aimed to:
1. Explore group differences in spatiotemporal gait parameters between MCI and CHI when walking at preferred speed, fast pace, during cognitive dual task and motor dual task.
2. Explore group differences in gait variability between MCI and CHI when walking at preferred speed, fast pace, during cognitive dual task and motor dual task.
3. Explore if gait during cognitive dual task can predict probability of an individual having MCI, when controlling for possible covariates.

Based on previous research presented here, it was hypothesized that there would be differences between groups, especially slower gait speed and higher gait variability in MCI, and that cognitive dual tasking would reveal more differences between groups.
Method

Participants

This cross-sectional observational study analyses data from an ongoing project at Umeå University, Sweden, called the Healthy Ageing Initiative (HAI; www.healthyageinginitiative.com) The aim of HAI is to examine risk factors for dementia, cardiovascular disease, and falls in 70-year-old men and women. The inclusion criteria are: 1) 70 years of age at the time of contact, and 2) current residency in the municipality of Umeå, Sweden. There are no exclusion criteria. Contact information was drawn from population registers and participants received written information about the project. Shortly thereafter, telephone contact was made and eligible participants could either accept or decline the offer. The sample for the current study was selected out of the first 2159 participants who underwent the examination. At that time, the participation rate was close to 73%.

Procedure

Participants were invited to the laboratory of the Sports Medicine Unit (Department of community medicine and rehabilitation) or the laboratory of the Behavioral Medicine Unit, to perform a number of tests. They arrived fasted, and gave their oral and written consent to participate. The full procedure took around three hours and was performed by trained medical professionals. First, participants underwent a physical examination including body composition scans, bone mineral density testing, and blood sampling. After this, participants had a snack break while filling out a questionnaire about lifestyle, medical history, food-intake, and depressive symptoms. MMSE-testing was usually carried out right after the break, and was followed by testing of gait, balance and grip strength. One week after the first visit, participants were asked to return and were given feedback on their results, as well as possible lifestyle changes to maintain or improve health. A selection of the performed tests is included in this study and is presented below.

Instruments

Cognitive function. The Mini-Mental State Examination (MMSE) is one of the most widely used tests to screen for cognitive impairment. It has a maximum score of 30, and the test is divided into six domains: Orientation to time and place, Registration and learning, Attention, Memory, Language, and Visuospatial ability (Folstein, Folstein & McHugh, 1975). It takes about 10–15 minutes to administer. A cut-off at <26 has been suggested to indicate cognitive impairment, with a sensitivity of 72.5 % and a specificity of 91.3 % (Schultz-Larsen, Lomholt, & Kreiner, 2007). In this study, a score of 21-25 has been used to indicate mild cognitive impairment. This is according to research which has shown that a score <21 can indicate moderate to severe dementia (Pernezcky et al., 2006). A score of 26 or more has been used to indicate cognitive intactness in this study.

Gait. Gait analysis was performed with the GAITRite® system (CIR Systems, Sparta, NJ, USA, www.gaitrite.com). It is an 8.6-meter-long and 0.88-meter-wide electronic walkway with sensors 1.27 cm apart. Measurement is initiated when the sensors detect the first footfall, and terminates at last contact. A large amount of different spatial and temporal parameters is measured. The parameters chosen in this study have been strategically chosen to give a representative overview of gait, including both temporal and spatial aspects. The parameters have been described elsewhere (Hollman et al., 2011). Data is transmitted to the application software for processing. The software calculates means and standard deviations of gait parameters for each trial with separate values for the left and right legs, and combined means and standard deviations for both legs were calculated manually. Coefficients of variance (CoVs; [(SD/M) × 100]) were also calculated manually for all gait parameters.

Participants removed footwear and were instructed to start each trial 1 meter from the walkway to reduce acceleration effects. The participants performed four progressively challenging gait trials. During the first trial, participants were asked to walk at their own
preferred pace. In the second trial, participants were told to walk as fast as possible while maintaining control and a safe gait. During the third trial, dual tasking was introduced. Participants were asked to walk at a self-selected pace while simultaneously counting backwards from 100 in increments of 1. In the fourth trial, participants were asked to balance a small glass marble on a larger tray. The objective was to keep the marble in the middle of the tray. The parameters chosen in this study have been strategically chosen to give a full picture of gait, including both temporal and spatial aspects. Included were parameters from all five domains suggested by Hollman et al. (2011), namely rhythm, phases, variability, pace and base of support.

**Covariates.** Height (m) and weight (kg) were measured with a gauge and a scale. Body Mass Index (BMI) was calculated as [weight/(height²)]. Participants reported smoking, as well as medical history of stroke, cardiovascular disease, and diabetes, both type 1 and 2. These variables are coded as yes or no. Participants filled out the Geriatric Depression Scale 15 (GDS-15), a widely used self-reporting form to screen for depression in the elderly. It is a short form version of the original 30 item version (Sheikli & Yesavage, 1986). It consists of 15 questions with yes or no options. One point is given for each answer pointing towards depression, and the maximum score is 15. Questions concern for example mood, loss of interest, boredom and feelings of hopelessness and worthlessness. In this study, the Swedish version was administered (Gottfries, Noltorp, & Norgaard, 1997). The 15-item version has not been validated in Swedish, however the English version has reported a Cronbach’s alpha around 0.8 (Almeida & Almeida, 1999). A cut-off at ≥5 has been used in this study to indicate depression with a sensitivity of 89.3% and a specificity of 65.3% (Friedman, Heisel, & Delavan, 2005). Grip strength was measured with the JAMAR® Hydraulic Hand Dynamometer (Patterson Medical, Warrenville, IL, USA, www.pattersonmedical.com). Participants were asked to keep their non-dominant upper arm along the torso, while flexing the elbow 90 degrees. Then, they were asked to press the dynamometer as hard as they could. This has been proven to be a reliable way of measuring grip strength and the JAMAR® Hydraulic Hand Dynamometer has a satisfactory test-retest reliability in the elderly with ICC reported around 0.92 (Bohannon & Schaubert, 2005).

**Statistical analysis**

The sample was divided into two groups based on MMSE-scores; 21-25 was labeled MCI and 26-30 was labeled CHI. First, between-group differences in gait parameters for all four conditions were examined. Second, the same tests were performed for CoV of parameters to examine variability.

Group differences between the two groups were calculated with independent t-tests for continuous variables and Chi-square tests or Fischer’s exact test when needed for grouping variables. Significance level was set at p <.05.

To explore the relationship between gait and MCI during cognitive dual task, logistic regression was chosen. It predicts probability of outcome on the dependent variable and can control for several covariates. The spatiotemporal parameters and the CoV’s for parameters which differed significantly between groups were calculated as z-scores to facilitate interpretation of regression. Logistic regression analysis was then performed for each of those variables, with MCI (coded as 0 for not prevalent and 1 for prevalent) as the dependent variable. The analyses were performed in two steps. First, each variable was tested as a single independent variable. Second, covariates were added to the models. The variables controlled for were sex, BMI, grip strength, depression, stroke, cardiovascular disease, diabetes and height. SPSS Statistics 24.0 (IBM Corporation, Armonk, New York) was used for all analysis.

**Ethical considerations**

The research project has been approved by the local ethics committee of Umeå University, as well as the National board of Health and Welfare in Sweden. All participants were thoroughly informed about the project, and provided oral and written consent before participating. They also received information about their individual health status approximately one week after the examination.
Results

Characteristics of sample

Out of the 2 159 participants who were originally eligible for inclusion in this study, 114 participants did not have MMSE data, 94 participants did not complete the gait analysis, and 10 participants completed none of the two. They were all excluded from this study. Participants with MMSE scores <21 (n = 4) were also excluded. Participants were included if they had completed the first, normal walking speed trial. The current sample consisted of 1 937 participants, 991 men and 946 women. 42 participants did not complete all four walking trials; however, they were included in the sample and contributed to the analyses of trials they did complete. 5 CHI participants only completed the first walking trial. Another 16 terminated after the second trial (15 CHI, 1 MCI), and 21 additional participants terminated after the third trial (16 CHI, 5 MCI.) Reasons for this were predominantly a sense of instability or the use of a walking aid. If participants had any missing values on any of the other variables except MMSE or the first gait trial, they were excluded for those specific analyses only.

A total of 112 participants were classified as having MCI in this study (5.8% of sample). There were no significant differences between the MCI and CHI groups regarding sex, height, weight, BMI, grip strength, GDS-15 scores, or in prevalence of depression. Stroke was more prevalent in the MCI group than in CHI (p = 0.001), but prevalence of cardiovascular disease and diabetes as well as smoking habits did not differ significantly. Characteristics are presented in table 1.

Table 1. Characteristics of the sample and between groups comparison of cognitively healthy individuals and mild cognitive impairment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total N = 1937</th>
<th>CHI N = 1825</th>
<th>MCI N = 112</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>991/946</td>
<td>925/900</td>
<td>66/46</td>
<td>0.090</td>
</tr>
<tr>
<td>Height m</td>
<td>1.70 (0.09)</td>
<td>1.70 (0.09)</td>
<td>1.70 (0.09)</td>
<td>0.826</td>
</tr>
<tr>
<td>Weight kg</td>
<td>77.04 (13.98)</td>
<td>77.03 (14.04)</td>
<td>77.15 (13.08)</td>
<td>0.935</td>
</tr>
<tr>
<td>BMI</td>
<td>26.55 (4.05)</td>
<td>26.54 (4.05)</td>
<td>26.67 (4.05)</td>
<td>0.739</td>
</tr>
<tr>
<td>Grip strength</td>
<td>34.55 (10.85)</td>
<td>34.54 (10.91)</td>
<td>34.71 (9.90)</td>
<td>0.867</td>
</tr>
<tr>
<td>GDS-15 total</td>
<td>1.19 (1.61)</td>
<td>1.19 (1.62)</td>
<td>1.29 (1.54)</td>
<td>0.504</td>
</tr>
<tr>
<td>Depression</td>
<td>4.7 %</td>
<td>4.8 %</td>
<td>4.6 %</td>
<td>0.938</td>
</tr>
<tr>
<td>Smoker</td>
<td>5.7 %</td>
<td>5.7 %</td>
<td>7.1 %</td>
<td>0.512</td>
</tr>
<tr>
<td>Prevalent disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>3.7 %</td>
<td>3.3 %</td>
<td>10.7 %</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8.7 %</td>
<td>8.8 %</td>
<td>7.2 %</td>
<td>0.594</td>
</tr>
</tbody>
</table>

NOTE. Results are presented as numbers, means (standard deviations), or percentages, with p-values. Bolded p-values are smaller than the pre-set significance level 0.05.

CHI = Cognitively healthy individuals, MCI = Mild cognitive impairment, kg = Kilograms, m = meters, BMI = Body Mass Index, GDS-15 = Geriatric Depression Scale 15, Depression = GDS-15 score ≥5. Missing values in the sample: grip strength (n = 1), GDS-15 (n = 60), smoker (n = 4), Cardiovascular Disease (n = 5), stroke (n = 53), diabetes (n = 60).

Spatiotemporal gait differences

In the normal speed trial (condition 1), the MCI group had significantly decreased step length (t(1935) = 2.45, p = 0.014), step width (t(1935) = 2.41, p = 0.016), and stride length (t(1935) = 2.48, p = 0.013) compared to CHI. They also had a slower gait velocity (t(1935) = 2.32, p = 0.020), higher double support phase (t(1935) = -3.10, p = 0.002), and lower swing phase (t(1935) = 2.86, p = 0.004) than CHI.
During the fast speed trial (condition 2), the MCI group still had slower gait velocity (t(1930) = 3.59, p < 0.001), higher double support time phase (t(1930) = -2.44, p = 0.015), and lower swing phase than CHI (t(1930) = 2.30, p = 0.022) Stride time (t(118.10) = -2.20, p = 0.030), and step time (t(124.56) = -2.03, p = 0.044) were higher in MCI than CHI. Step length (t(120.47) = 2.38, p = 0.019), step width (t(120.73) = 2.42, p = 0.017), and stride length (t(120.48) = 2.40, p = 0.018) continued to be decreased in MCI compared to CHI.

While counting backwards from 100 (condition 3), the MCI group had significantly slower gait velocity (t(120.36) = 5.03, p < 0.001), higher double support phase (t(116.90) = -3.54, p = 0.001), lower swing phase (t(117.08) = 2.16, p = 0.033), and higher stride time (t(1914) = -2.64, p = 0.008) compared to CHI. Step length (t(117.96) = 2.47, p = 0.015), step width (t(118.22) = 2.34, p = 0.021), and stride length (t(118.04) = 2.478, p = 0.015) were still significantly lower in MCI compared to CHI.

When balancing a marble on a tray (condition 4), participants with MCI had slower gait velocity than CHI (t(1893) = 2.28, p = 0.023). No other spatiotemporal parameters differed significantly between groups. Means and standard deviations for gait parameters are presented in table 2.

Gait variability differences

Regarding variability, there were no significant differences between groups during either the first normal speed trial, the second fast speed trial, or the fourth marble/tray trial. During the third trial, the MCI group had significantly higher CoV’s for stride velocity (t(114.71) = 2.40, p = 0.018), stride time (t(120.26) = -2.18, p = 0.031), stride length (t(114.34) = -2.96, p = 0.004), step time (t(122.13) = -2.33, p = 0.022), step width (t(114.63) = -3.11, p = 0.002), step length (t(113.81) = -3.00, p = 0.003), and swing time (t(112.48) = -2.78, p = 0.006) compared to CHI. Stride width and double support time did not significantly differ between groups in this trial. Means and standard deviations are presented in table 3.

Logistic regression

In unadjusted (with no covariates) logistic regression analyses, the spatiotemporal parameters during cognitive dual task showed significant association with MCI, except for the variable stride time (see table 4). The unadjusted odds ratios showed that higher gait velocity (OR 0.59, CI 95% 0.49-0.71), stride length (OR 0.75, CI 95% 0.62-0.90), step length (OR 0.75, CI 95% 0.62-0.90), step width (OR 0.76, CI 95% 0.63-0.91), and swing phase (OR 0.80, CI 95% 0.68-0.93) was associated with a lower probability of having MCI. In addition, higher double support phase (OR 1.40, CI 95% 1.21-1.62) was associated with higher probability of having MCI.

In the adjusted models, the differences persisted and higher gait velocity (OR 0.56, CI 95% 0.46-0.66), stride length (OR 0.71, CI 95% 0.57-0.88), step length (OR 0.71, CI 95% 0.57-0.88), step width (OR 0.71, CI 95% 0.57-0.88), and swing phase (OR 0.78, CI 95% 0.66-0.93) was still associated with a lower probability of having MCI. Furthermore, the association between longer double support phase and MCI remained after multivariable adjustment (OR 1.46, CI 95% 1.24-1.72).

In the unadjusted analyses of gait variability, all variability variables showed significant association with MCI (see table 5). Variability of step time (OR 1.21, CI 95% 1.01-1.25), step length (OR 1.32, CI 95% 1.17-1.49), stride length (OR 1.29, CI 95% 1.15-1.45), stride time (OR 1.13, CI 95% 1.01-1.25), swing time (OR 1.31, CI 95% 1.17-1.47), stride velocity (OR 1.27, CI 95% 1.12-1.45) and step width (OR 1.31, CI 95% 1.16-1.48) indicated that higher variability was associated with higher probability of having MCI.

In the multivariable adjustment, variability of step length (OR 1.28, CI 95% 1.12-1.45), stride length (OR 1.26, CI 95% 1.12-1.43), swing time (OR 1.32, CI 95% 1.17-1.48), stride velocity (OR 1.26, CI 95% 1.10-1.45) and step width (OR 1.26, CI 95% 1.11-1.43) were significantly associated with MCI. The odds ratios indicated that higher variability was associated with higher probability of having MCI. However, after adjustment the difference between MCI and CHI on step- and stride time was no longer significant.
Table 2.
Spatiotemporal gait parameters during all four trials and comparisons between groups cognitively healthy individuals and mild cognitive impairment.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHI</td>
<td>MCI</td>
<td>p-value</td>
<td>CHI</td>
</tr>
<tr>
<td>GaITV</td>
<td>117.29 (19.27)</td>
<td>112.88 (23.05)</td>
<td><strong>0.020</strong></td>
<td>167.60 (26.64)</td>
</tr>
<tr>
<td>StrideT</td>
<td>1.10 (0.12)</td>
<td>1.12 (0.14)</td>
<td>0.154</td>
<td>0.90 (0.10)</td>
</tr>
<tr>
<td>StrideL</td>
<td>128.23 (15.00)</td>
<td>124.55 (18.38)</td>
<td><strong>0.013</strong></td>
<td>150.19 (18.27)</td>
</tr>
<tr>
<td>StrideW</td>
<td>11.38 (3.10)</td>
<td>11.66 (3.37)</td>
<td>0.358</td>
<td>11.39 (3.20)</td>
</tr>
<tr>
<td>StepT</td>
<td>0.55 (0.08)</td>
<td>0.56 (0.07)</td>
<td>0.306</td>
<td>0.45 (0.07)</td>
</tr>
<tr>
<td>StepL</td>
<td>63.92 (7.49)</td>
<td>62.11 (9.20)</td>
<td><strong>0.014</strong></td>
<td>74.86 (9.13)</td>
</tr>
<tr>
<td>StepW</td>
<td>65.09 (7.25)</td>
<td>63.37 (8.84)</td>
<td><strong>0.016</strong></td>
<td>75.02 (8.98)</td>
</tr>
<tr>
<td>DS Ph</td>
<td>23.58 (3.50)</td>
<td>24.64 (3.93)</td>
<td><strong>0.002</strong></td>
<td>19.75 (3.63)</td>
</tr>
<tr>
<td>SwingPh</td>
<td>38.19 (1.78)</td>
<td>37.69 (1.91)</td>
<td><strong>0.004</strong></td>
<td>40.14 (1.81)</td>
</tr>
</tbody>
</table>

Results are presented as means (standard deviations) and p-values. Bolded p-values are smaller than the pre-set significance level 0.05. CHI = Cognitively healthy individual, MCI = Mild cognitive impairment, V = Velocity in cm/s, T = Time in sec, L = Length in cm, W = Width in cm, DS = Double support, Ph = Phase, a percentage of the full gait cycle.

Table 3.
Gait variability as coefficient of variation for gait variables during all four trials and comparisons between groups cognitively healthy individuals and mild cognitive impairment.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHI</td>
<td>MCI</td>
<td>p-value</td>
<td>CHI</td>
</tr>
<tr>
<td>StrideV CoV</td>
<td>3.47 (1.78)</td>
<td>3.40 (1.79)</td>
<td>0.662</td>
<td>3.11 (2.39)</td>
</tr>
<tr>
<td>StrideT CoV</td>
<td>2.30 (3.99)</td>
<td>2.00 (0.98)</td>
<td>0.433</td>
<td>2.27 (3.04)</td>
</tr>
<tr>
<td>StrideL CoV</td>
<td>2.44 (1.50)</td>
<td>2.51 (1.55)</td>
<td>0.616</td>
<td>2.23 (2.10)</td>
</tr>
<tr>
<td>StrideW CoV</td>
<td>17.11 (9.21)</td>
<td>17.20 (8.92)</td>
<td>0.923</td>
<td>17.38 (10.06)</td>
</tr>
<tr>
<td>StepT CoV</td>
<td>3.34 (4.91)</td>
<td>3.06 (1.38)</td>
<td>0.543</td>
<td>3.32 (4.19)</td>
</tr>
<tr>
<td>StepL CoV</td>
<td>3.34 (2.35)</td>
<td>3.40 (1.82)</td>
<td>0.813</td>
<td>3.13 (2.27)</td>
</tr>
<tr>
<td>StepW CoV</td>
<td>3.83 (2.54)</td>
<td>3.80 (1.98)</td>
<td>0.901</td>
<td>3.72 (2.79)</td>
</tr>
<tr>
<td>DST CoV</td>
<td>7.35 (3.40)</td>
<td>6.85 (2.98)</td>
<td>0.124</td>
<td>9.08 (7.02)</td>
</tr>
<tr>
<td>SwingT CoV</td>
<td>3.75 (2.10)</td>
<td>3.59 (1.81)</td>
<td>0.429</td>
<td>3.69 (2.96)</td>
</tr>
</tbody>
</table>

NOTE: Results are presented as means (standard deviations) and p-values. Bolded p-values are smaller than the pre-set significance level 0.05. CHI = Cognitively healthy individuals, MCI = Mild cognitive impairment, V = Velocity, T = Time, L = Length, W = Width, DST = Double support time, CoV= Coefficient of variation.
Table 4. Logistic regressions for each of the spatiotemporal gait parameters during cognitive dual task, with Mild cognitive impairment as the dependent variable.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 (Unadjusted)</th>
<th></th>
<th>Model 2* (Adjusted)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Wald</td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>GaitV3</td>
<td>-0.53</td>
<td>31.61</td>
<td>0.59 (0.49 - 0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>StrideT3</td>
<td>0.09</td>
<td>2.95</td>
<td>1.10 (0.99 - 1.22)</td>
<td>0.086</td>
</tr>
<tr>
<td>StrideL3</td>
<td>-0.29</td>
<td>9.77</td>
<td>0.75 (0.62 - 0.90)</td>
<td>0.002</td>
</tr>
<tr>
<td>StepL3</td>
<td>-0.29</td>
<td>9.750</td>
<td>0.75 (0.62 - 0.90)</td>
<td>0.002</td>
</tr>
<tr>
<td>StepW3</td>
<td>-0.28</td>
<td>8.56</td>
<td>0.76 (0.63 - 0.91)</td>
<td>0.003</td>
</tr>
<tr>
<td>DS Ph3</td>
<td>0.34</td>
<td>20.21</td>
<td>1.40 (1.21 - 1.62)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Swing Ph3</td>
<td>-0.23</td>
<td>8.20</td>
<td>0.80 (0.68 - 0.93)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

NOTE: V = Velocity in cm/s, T = Time in sec, L = Length in cm, W = Width in cm, DS = Double support, Ph = Phase, a percentage of the full gait cycle, 3 = trial 3, cognitive dual task.

*Model 2: corrected for sex, BMI, grip strength, cardiovascular disease, stroke, diabetes, smoking, depression, and height. OR’s for these covariates are not presented in this report. Logistic regression has been performed for each of the spatiotemporal parameters independently. Every row in the table is one unadjusted model and adjusted model. The gait variables have not been included in the same models.

Table 5. Logistic regressions for each of the gait variability variables during cognitive dual task, with Mild cognitive impairment as the dependent variable.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 (Unadjusted)</th>
<th></th>
<th>Model 2* (Adjusted)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Wald</td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>StepT CoV3</td>
<td>0.11</td>
<td>4.44</td>
<td>1.12 (1.01 - 1.25)</td>
<td>0.035</td>
</tr>
<tr>
<td>StepL CoV3</td>
<td>0.28</td>
<td>19.86</td>
<td>1.32 (1.17 - 1.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>StrideL CoV3</td>
<td>0.26</td>
<td>17.49</td>
<td>1.29 (1.15 - 1.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>StrideT CoV3</td>
<td>0.12</td>
<td>4.50</td>
<td>1.13 (1.01 - 1.25)</td>
<td>0.034</td>
</tr>
<tr>
<td>SwingT CoV3</td>
<td>0.27</td>
<td>21.30</td>
<td>1.31 (1.17 - 1.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>StrideV CoV3</td>
<td>0.24</td>
<td>13.01</td>
<td>1.27 (1.12 - 1.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>StepW CoV3</td>
<td>0.27</td>
<td>18.21</td>
<td>1.31 (1.16 - 1.48)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

NOTE: V = Velocity in cm/s, T = Time in sec, L = Length in cm, W = Width in cm, CoV3 = Coefficient of variation, trial 3 (cognitive dual task).

*Model 2: corrected for sex, BMI, grip strength, cardiovascular disease, stroke, diabetes, smoking, depression, and height. OR’s for these covariates are not presented in this report. Logistic regression has been performed for each of the variability measurements independently. Every row in the table is one unadjusted model and adjusted model. The gait variability variables have not been included in the same models.
Discussion

The objective of this study was to explore how gait is affected in MCI compared to CHI. Both individuals with MCI and cognitively healthy individuals performed four walking trials: normal speed, fast speed, cognitive dual task and motor dual task. In addition, both spatiotemporal parameters and gait variability were explored. The results showed that most of the spatiotemporal parameters were affected in MCI compared to CHI in the first three trials, but not in the fourth, motor dual task. During cognitive dual task, most spatiotemporal parameters were significantly associated with MCI even when controlling for possible covariates. Gait variability was only higher in group MCI compared to CHI in the cognitive dual task trial. However, after adjustment for several potential covariates, stride time variability was no longer significantly associated with MCI. For swing time-, step width- and step length variability the difference between groups MCI and CHI persisted when controlling for covariates.

The results showed that, in general, the MCI group walked slower than healthy controls. They had narrower steps, shorter steps and strides, and they spent more time with both feet on the ground than in swing, in comparison to CHI. There were significant differences between groups MCI and CHI in gait during all four conditions, however, in trials 1-3 many more spatiotemporal parameters differed compared to trial 4. The only parameter which was consistently affected in the MCI group over all four trials was gait velocity, which gives further support to the suggestion that slow gait is a biomarker for MCI (Bahureksa et al., 2017).

During the fourth trial, only gait velocity was affected in the MCI group compared to CHI. One reason for this might be that the task was motorically rather than cognitively demanding. This suggests that motor dual tasking does not affect gait in individuals with MCI more than it affects the cognitively healthy.

During cognitive dual task, higher gait velocity, longer strides and steps, wider steps and a longer swing phase were associated with a lower probability of having MCI. A one standard deviation increase from the sample mean of these variables was associated with a 21-41 % lower probability of having MCI. A higher double support phase was associated with higher probability of having MCI. These associations were not largely affected by adding possible covariates to the models, suggesting that there might be an independent relationship between gait and MCI.Stride time could not reliably predict probability of MCI.

Previous research has found a connection between MCI and increased double support time and stride time, as well as decreased stride length during cognitive dual tasking (Bahureksa et al., 2017; Savica et al., 2017). Interesting findings of this study are that step width, step length and duration of swing phase were lower in the MCI group compared to CHI during preferred pace, fast pace, and cognitive dual task. Another important finding of this study is the fact that both single task trials revealed numerous group differences in spatiotemporal parameters, somewhat contradictory to previous research. Bahureksa et al. (2017) found that gait velocity was slower in MCI during single task, but that other parameters did not differ. The discrepancies observed between this study and previous ones could be due to the difference in parameters observed. Most prior studies have included a much smaller number of parameters than the present study.

Interestingly, variability of gait parameters was significantly larger in MCI participants during the cognitively demanding trial, except for the parameters stride width and double support time. Velocity from stride to stride differed, as well as stride length, step length, step width, and swing time, suggesting that MCI participants have a more staggering gait, compared to cognitively healthy individuals, when performing a cognitive task. The gait in the MCI group when performing this cognitive task can be described as more inconsistent and less fluent or rhythmic compared to CHI. Hence, the results of this study imply that cognitive dual tasking puts a strain on the cognitively impaired that in turn impairs their gait symmetry.

Higher variability in step time, step length, step width, stride time, stride length, stride velocity and swing time all had significant associations with MCI. A one standard deviation increase from the sample mean in variability of these variables was associated with a 12 – 32 % higher probability of having MCI. When adjusting for covariates, step time variability and stride time variability could no longer reliably predict probability of having MCI. The other variability variables were quite stable in the adjusted models.

Step time variability and stride time variability do not seem to be independently related to MCI in this sample. Though they could predict MCI in the unadjusted models, it seems this
relationship is influenced by other factors. This finding is quite contradictory to previous studies, which have suggested stride time variability as a biomarker for MCI (Beauchet et al., 2014). While the p-value for stride time variability (0.052) was just above the pre-set significance level, other variability variables showed stronger, more reliable associations with MCI. This result is not cause to reject the hypothesis that stride time variability is related to MCI, but it implies that other variables of gait variability should be examined further.

The findings of the relationship between gait variability and MCI during cognitive dual task are partly in accordance with previous research, specifically in regards of cognitive dual tasking revealing differences between groups MCI and CHI (Montero-Odasso et al., 2012; Muir et al., 2012). However, there are some discrepancies between the present study and previous ones. It seems that many more parameters, both spatial and temporal, are affected than simply stride time variability. Though higher variability in swing time and step length have previously been found to correlate with cognitive impairment (Savica et al., 2017), the results of this study indicate that gait variability of several additional spatiotemporal parameters during cognitive dual task are affected in individuals with MCI.

The results of this study show that it is possible to predict probability of having MCI from some gait variables during cognitive dual task. Furthermore, the results indicate that the relationship between gait and MCI is not largely affected by the possible covariates controlled for. This gives further support to hypotheses of gait and cognitive function being related to each other; either directly or through shared brain structures (Annweiler et al., 2012; Hausdorff et al., 2005).

Slow gait speed, an increased double support phase and a decreased swing phase have all been related to a higher risk of falling in elderly populations (Verghe, Holtzer, Lipton, & Wang, 2009). Higher variability during dual tasking has also been found to predict falls in the elders (Johansson, Nordström, & Nordström, 2016). It seems the gait type for MCI found in this study, especially during cognitive dual task, might be related to a higher risk of falling. The observed relationship in this study between double support and swing is similar to a finding in Multiple Sclerosis (MS) patients (Comber, Galvin, & Coote, 2017). The authors describe the increased double support as a compensation for lack of balance and control. The consequence is a hastened swing, which leads to more instability. While MS and MCI are separate conditions, this similarity in gait is interesting when trying to understand this gait type. The findings of the present study could possibly yield further understanding as to why risk of falling is doubled to tripled in people with MCI and dementia compared to cognitively healthy individuals (Härlein, Dassen, Halfens, & Heinze, 2009). This also suggests that individuals with MCI or dementia should take caution while walking to lower the risk of falling. They should try to avoid cognitive tasks while walking, and focus on maintaining control.

This study has limitations. The MMSE is a widely-used tool to detect cognitive impairment in clinical and research settings. Therefore, it is possible to compare results between studies. There are however some issues with this instrument. For example there are no predetermined cut-offs to detect cognitive impairment and different ones are used even within this specific research area (Bahureksa et al., 2017). In this study, it means that the MCI group may possibly contain both cognitively healthy individuals as well as demented participants. Furthermore, we cannot rule out completely that the CHI group could have included some participants with MCI or even early dementia. However, these issues were partly controlled for by using a lower cutoff of 21 to exclude demented individuals, as well as a higher cut-off of 25 for the MCI group, which has quite satisfactory sensitivity and specificity (Perneczky et al., 2006; Schultz-Larsen et al., 2007). Still, it is difficult to differentiate between MCI and early stages of dementia (Morris et al., 2001). In conclusion, the results of this study should be interpreted with some caution in regard to the concept MCI.

Another limitation in this study is the lack of specified MCI subtypes (subtypes as shown in Figure 1). Studies have shown that there are differences in gait between a-MCI and na-MCI, for example significantly lower gait velocity and larger stride time variability in individuals with a-MCI (Montero-Odasso et al., 2014). In this study, it was not possible to explore these in-group differences, however the author suggests that future studies take this into account. Due to the educational level was not available for the sample. Research has shown that MMSE scores correlate positively with higher levels of education. It is proposed that norms based on education be used when using cut-offs for cognitive impairment or dementia (Schultz-Larsen et al., 2007). Additionally, research has shown that people with higher levels of education show...
fewer cognitive symptoms of dementia (Stern, 2009). It would have been preferred to control for level of education.

Lastly, there are some issues with doing multiple comparisons. With an alpha level of 0.05, there is a 5% risk of making a type 1 error for every individual test. The probability of making such an error is larger when performing many tests. A correction of this problem can lead to extremely conservative alpha levels, making the risk of type 2 errors very probable (Rothman, 1990). It was therefore not done in this study. It was decided that the gains to be made from exploring gait more fully than previous studies was greater than the risk of finding a few differences that cannot be generalized to the larger population. It is however important to keep in mind that some of the group differences found in this study could be present due to chance.

While there are limitations to this study, there are also strengths. The sample was large compared to many studies in this research area. Because this was a population-based sample, every 70-year-old resident of the municipality of Umeå was offered participation. This combined with the high participation rate makes the results of this study more generalizable to the larger population. Lastly, this study examined many spatiotemporal parameters, giving an overview of gait rather than a selection of a few parameters.

For future research the author suggests more studies, with more extensive cognitive data, examining swing phase, double support phase, as well as swing time variability. Examination of these parameters has been limited previously in relation to MCI, but could offer understanding of the higher risk of falling in the cognitively impaired. Additional longitudinal studies are also of great value. Dementia is associated with high dependence and high societal costs, as well as low life quality (Tomoeda & Bayles, 2013). If gait could be used in a clinical setting for early detection and risk assessment of MCI, it would certainly be helpful.

In summary, there are aspects of gait affected in individuals with MCI when compared to healthy controls. In this study, gait velocity was generally decreased in the MCI group and several different spatial and temporal parameters differed between groups when walking at preferred pace, walking at fast pace and when performing a cognitive task. Cognitive dual tasking revealed higher gait variability in MCI than in CHI. Motor dual task did not affect gait in participants with MCI more than it affects the cognitively healthy. Several spatiotemporal gait parameters and gait variability variables during cognitive dual tasking could predict probability of having MCI, and could do so even when adjusting for several possible covariates. The gait pattern presented by individuals with MCI, especially during cognitive dual task, could be related to a higher risk of falling.

References


