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Gait Dysfunction in Mild Cognitive Impairment Syndromes

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Abstract

OBJECTIVES—To conduct a systematic clinical and quantitative assessment of gait in older adults with mild cognitive impairment (MCI) syndromes.

DESIGN—Cross-sectional.

SETTING—Einstein Aging Study, a community-based longitudinal aging study.

PARTICIPANTS—Fifty-four individuals with amnestic MCI (a-MCI), 62 with nonamnestic-MCI (na-MCI), and 295 healthy controls identified from the Einstein Aging Study participants.

MEASUREMENTS—Comparison of clinical and quantitative gait performance in subjects with MCI subtypes with that of cognitively normal older adults.

RESULTS—Neurological gaits were more common in a-MCI (31.5%, $P = .008$) but not in na-MCI (19.4%, $P = .55$), than in controls (16.3%). Quantitative gait in multiple parameters was worse in both MCI subtypes than in controls. Factor analysis revealed three independent factors representing pace, rhythm, and variability. Subjects with a-MCI had worse rhythm and variability scores than those with na-MCI and controls. Subjects with na-MCI had worse performance on the pace domain than the other two groups. Subjects with MCI and gait abnormalities had higher disability scores than subjects with MCI without gait abnormalities.

CONCLUSION—Gait dysfunction is common in older individuals with amnestic and nonamnestic subtypes of MCI.

Keywords

Gait; cognition; MCI

Mild cognitive impairment (MCI) syndrome is conceptualized as a transition state between cognitive normalcy and dementia in older adults.[1] Initially considered an amnestic syndrome,[2] the concept of MCI has been expanded to include impairments in nonamnestic cognitive

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domains such as executive function.[3] Although neuropsychological characteristics of the MCI syndromes are well known,[1-3] other behavioral markers are not well established. Recently, some but not all studies have suggested that gait disturbances are present in the earliest stages of dementia, including MCI.[4-15] Gait dysfunction has been reported to predict progression to dementia in cognitively normal older adults as well as those with MCI,[11-15] but there are limited studies of gait function in MCI,[4,7,8] especially using quantitative methods.[10,15]

Gait was assessed in participants in the Einstein Aging Study using a well-established clinical rating scale, as well as an instrumented walkway that generates eight individual gait parameters.[15-18] MCI was defined using current conceptualizations of this syndrome as amnestic (a-MCI) and nonamnestic (na-MCI) subtypes.[3] In prior work,[15] factor analysis of the eight individual gait variables revealed three orthogonal factors that measure the domains of pace, rhythm, and variability. The pace factor was associated with longitudinal decline on executive function, whereas the rhythm factor was associated with memory decline.[15] Based on these findings, it was predicted that pace would be associated with na-MCI and rhythm with a-MCI. Herein, overall gait performance and domain specific scores of older adults with amnestic and nonamnestic subtypes of MCI are compared with those of older adults without cognitive complaints or impairments. Given the high risk of conversion to dementia in older adults who meet criteria for MCI,[1-3] it is essential to characterize clinical and behavioral features of the various MCI syndromes, including gait dysfunction. A systematic examination of gait in MCI might provide a window into another aspect of brain function during the preclinical onset of dementia.

METHODS

Study Population

Gait was examined in participants with and without MCI in the Einstein Aging Study.[16-18] The primary aim of the Einstein Aging Study is to identify risk factors for dementia. Study design and methods have been previously reported.[16-18] In brief, potential subjects (aged 70 and older) identified from population lists of Bronx County were contacted by letter explaining the purpose and nature of the study and then by telephone. The telephone interview included verbal consent, medical history questionnaire, and cognitive screening tests.[17] Exclusion criteria included presence of severe audiovisual loss, being bed bound, and institutionalization.[16,17] After the interview, an age-stratified sample of subjects who matched on a computerized randomization procedure was invited for further evaluation at the Albert Einstein College of Medicine. Informed consent was obtained at enrollment according to protocols approved by the local institutional review board. Subjects returned yearly.

Between September 2004 and November 2006, 527 (86.4%) of 610 Einstein Aging Study participants seen during this period received detailed clinical and quantitative motoric assessments as part of a gait and mobility sub-study.[15,16] Reasons for not obtaining assessments included clinician or tester unavailability for conducting motoric assessments (n = 73), subject illness (n = 12), or subject refusal (n = 18). Subjects who did and did not receive the study assessments were similar in terms of age, sex, and cognitive status at enrollment.

Clinical Gait

Study neurologists (JV) determined whether gaits were neurologically normal or abnormal after visual inspection of gait patterns and turns while subjects walked up and down a well-lit hallway at their normal pace, as previously described.[14-16] Neurological gaits were subtyped as unsteady, ataxic, frontal, parkinsonian, neuropathic, hemiparetic, and spastic, as previously described (see reference [14] for detailed description and Web links to videos of neurological gait subtypes).[14-16] Gait abnormalities were graded as mild (walks unassisted), moderate (uses

walking aids), or severe (wheelchair-bound or stands with assistance).[16] Eighty-nine percent agreement (kappa 0.6) was reported on classifying gait as neurological or nonneurological on evaluations 1 year apart in 189 subjects in the Bronx Aging Study.[14] Interrater reliability, studied prospectively, between two study clinicians who independently assessed gait (normal vs abnormal) in 30 subjects from the present cohort was very good (kappa 0.8).[15,18]

Quantitative Gait

Research assistants conducted quantitative gait studies, independent of clinicians' evaluations or knowledge of cognitive status, using a computerized walkway (180 × 35.5 × 0.25 inches) with embedded pressure sensors (GAITRite, CIR Systems, Havertown, PA).[19] Subjects were asked to walk on the mat at their normal pace for two trials in a quiet well-lit hallway wearing comfortable footwear and without any attached monitoring devices. White lines on the floor marked start and stop points, and included 3 feet from the walkway edge for initial acceleration and terminal deceleration. Based on the footfalls recorded on the walkway, the software automatically computes gait parameters as the mean of two trials. The following eight gait variables that have been reported to have associations with cognitive function and dementia in aging studies were selected:[13,15] velocity (cm/s), cadence (steps/min), swing phase (seconds), stance phase (seconds), double support phase (seconds), stride length variability, and swing time variability. Variability is reported as coefficient of variation, which is the ratio of the standard deviation (SD) to the mean. The GAI-TRite system is widely used in clinical and research settings, and excellent reliability has been reported.[19,20]

Cognitive Assessments

An extensive neuropsychological test battery validated in aging populations was administered at all visits to all subjects, as described previously.[14-17] General cognition was assessed using the Blessed Information-Memory-Concentration test,[21] which has a high test–retest reliability and correlates well with Alzheimer's pathology.[22] Specific cognitive domains studied included verbal memory (free recall from the Free and Cued Selective Reminding Test [23]), executive function (Digit Symbol Substitution Test,[24] Block Design Test,[24] Trail-Making Test Part B (TMT-B),[25] and the Letter Fluency Test[26]), attention (TMT-A25 and Digit Span forwards[24]), and language (15-item Boston Naming Test[27]).

Other Variables

Subjects and caregivers were interviewed at each visit about sociodemographic variables, medical illnesses, medications, and depressive symptoms.[14-19,28] Seven activities of daily living were assessed using a disability scale developed for use in community-based cohorts:[29] bathing, dressing, grooming, feeding, toileting, walking around home, and getting up from a chair. Subjects were asked whether they were able to perform an activity unassisted (0 points) or unassisted but with difficulty (1 point) or whether they required assistance or were unable to do the activity (2 points). A summary disability score was then computed (range 0–14, with higher values indicating worse disability).[29] Study clinicians also ascertained functional status during their evaluation.[14-19] Additional sources consulted included medical records and primary care providers.

Diagnostic Procedures

The study neurologist (JV) and neuropsychologist assigned a diagnosis of MCI after reviewing all available clinical and neuropsychological information for each subject. Raters were blinded to gait measures. MCI was diagnosed if subjects met the following four criteria.

1. Presence of spontaneous cognitive complaints by the subject or self-rating by subject of memory being fair or poor. Forty (34.5%) of 116 subjects who met MCI criteria

reported living alone. Hence, absence of an informant was not used to exclude subjects.

2. Objective cognitive impairment in the following four cognitive domains: memory, executive function, attention, and language. Current recommendations do not specify tests or cutscores to define cognitive impairment.[1-3] Based on previous studies,[1-7] impairment in neuropsychological test performance in a cognitive domain was defined as a score 1.5 SDs or more below the age-appropriate mean, derived from baseline assessments in the cohort. Many cognitive processes are grouped under the rubric of executive function and attention. Hence, performance at or below the cutscore on any one of the tests in these domains was considered abnormal. Subjects diagnosed with a-MCI had impairment of verbal memory and were further subtyped as a-MCI single domain if they had impairment only on the memory test and a-MCI multiple domains if they had impairments on another cognitive domain in addition to memory. Subjects subtyped as na-MCI had impairment in one or more nonmemory tests but scored within the 1.5-SD range in the memory test. Subjects with na-MCI were also subtyped as involving single or multiple domains.

3. Preserved activities of daily living on the disability scale[29] and during the study clinicians interviews.[14-18]

4. Absence of dementia. Dementia was diagnosed, as previously described,[14,15,17] using the criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,*[30] at consensus case conferences attended by the study neurologists, neuropsychologist, and social worker (JV, MZ, RBL).

Data Analysis

Demographic characteristics and variables of interest were tabulated per diagnostic group and compared using analysis of variance and chi-square tests.[31] Quantitative gait variables were examined using analysis of covariance to compare performance across the two MCI subtypes and controls, adjusting for effects of age, sex, and education.[31] *P*-values are indicated for individual gait variables that remained significant (Table 3) using a previously developed approach[32] to control the false discovery rate. A subgroup analysis of individual gait variables was also conducted excluding subjects with neurological gaits.

As a complementary statistical approach, factor analysis using the principal component method was performed on the eight individual gait variables.[15,33] The initial factors were then subjected to an orthogonal Varimax rotation to reduce the larger number of highly correlated variables to a smaller number of uncorrelated independent predictors. The factors representing independent gait domains were then compared across groups. This approach has previously been used to identify distinct gait domains, and describe their association with cognitive decline in our cohort.[15]

Sensitivity analyses were conducted to account for the influence of diagnostic classifications on quantitative gait differences between diagnostic groups. The prevalence of two variables that can be easily assessed in clinical settings (neurological gait abnormality and slow gait) and their association with functional status were also examined using the disability scale.

Study Population

Of the 527 subjects who received cognitive and gait evaluations over the same days during the 15-month study period, 116 met MCI criteria.[3] Fifty-four were subtyped as a-MCI (27 single domain and 27 multiple domains) and 62 as na-MCI (26 single domain and 36 multiple domains).[3] Of the remaining 411 subjects, 26 with prevalent dementia, eight subjects with

objective cognitive impairment but no subjective cognitive complaints, and seven subjects with missing data were excluded.

Older adults with memory complaints, especially corroborated by informants,[3] are reported to be at greater risk of cognitive decline.[34,35] Hence, 75 subjects with subjective memory complaints but with deficits on cognitive testing not severe enough to meet the study criteria for objective cognitive impairment were also excluded. Thus, 295 healthy older controls were included in the main analyses, although analyses including the 75 subjects with subjective memory complaints but with deficits on cognitive testing in the control group were also conducted (n = 370).

RESULTS

Baseline demographic and medical characteristics are presented in Table 1. There were more women in the na-MCI group (71%) than in the a-MCI group (50%). Subjects with na-MCI had lower education than those with a-MCI and controls. Subjects with a-MCI and na-MCI were older than controls. Subjects with a-MCI had higher prevalence of diabetes mellitus than controls (22% vs 11%). Subjects with na-MCI had a higher prevalence of hypertension than controls (66% vs 49%). There were no group differences in prevalence of falls and other chronic illnesses. There were no group differences in disability scores (Table 1). Gait velocity was associated with disability scores in linear regression analyses adjusted for age, sex, and education in the overall group ($\beta = -0.441$, 95% confidence interval (CI) = −0.026 to −0.017, $P < .001$), as well as when the analysis was restricted to the 116 MCI subjects ($\beta = -0.479$, 95% CI = −0.36 to −0.16, $P < .001$).

Table 2 presents neuropsychological test performance in the groups without adjustments or corrections,[32] because it was not the dependent variable, but group differences were significant even after adjustments for age, sex, and education (data not shown). Both MCI subtypes had worse performance on most neuropsychological tests than controls. Subjects with a-MCI had more depressive symptoms[28] (but not major depression) than controls. Subjects with a-MCI had worse verbal memory (Free and Cued Selective Reminding Test) than those with na-MCI, whereas subjects with na-MCI had worse executive function (Digit Symbol Substitution Test and TMT-B), attention (TMT-A), and language (Boston Naming Test) than those with a-MCI.

Clinical Gait

Overall, 77 subjects were diagnosed with neurological gaits.[14-16] These subjects had slower gait (82.0 ± 22.8 vs 98.8 ± 22.4 cm/s, $P < .001$) than those with normal gaits. Severity of gait abnormalities was rated as mild (walks unassisted) in most subjects (75%). Neurological gaits were diagnosed in 17 subjects with a-MCI (31.5%, P vs controls = .008), 12 with na-MCI (19.4%, P vs controls = .56), and 48 controls (16.3%). There were no significant group differences comparing MCI subtypes with each other or with controls in the frequency of various neurological gait subtypes, including parkinsonian gaits.

Quantitative Gait

Table 3 shows that subjects with both MCI subtypes had worse performance on most gait variables than controls. Velocity and stride length were worse in both MCI subtypes than in controls. Subjects with a-MCI had worse gait variability measures than controls. Subjects with na-MCI had worse cadence, swing time, and double support time than controls. Subjects with a-MCI had worse swing time and stride length variability than subjects with na-MCI.

Gait Domains

Factor analysis with Varimax rotation yielded exactly three independent orthogonal factors accounting for 87.2% of the overall variance in quantitative gait performance in this sample (Table 4). The factor that explained most of the variance had strong loading according to velocity and stride length, and was termed the "pace" factor. The second loaded on variables reflected gait rhythm such as swing and cadence and was termed the "rhythm" factor. The final factor loaded heavily on gait "variability" measures.[15] The factor structure was similar to that obtained in a previous study.[15] The mean factor score was 0 ± 1. The factors can be conceptualized as summary risk scores, with higher scores denoting worse performance.

Table 5 shows that subjects with a-MCI and na-MCI had worse pace factor scores than controls. Subjects with a-MCI also had worse rhythm factor scores than controls and worse variability factor scores than subjects with na-MCI and controls.

Sensitivity Analyses

Table 3 shows that group differences were not materially different when the 77 subjects diagnosed with neurological gaits were excluded.

Seventy-five subjects with subjective memory complaints and mild cognitive impairments that did not meet the study criteria for objective cognitive impairment were excluded. These 75 subjects were older (81.6 ± 5.4 vs 79.3 ± 4.7, P =.002) and had worse cognition (Blessed scores 2.3 ± 2.4 vs 1.4 ± 1.5, P <.001) than the 295 normal controls, although group differences in quantitative gait were unchanged even when these subjects were included in the control group. For instance, mean velocity (98.3 ± 21.3 cm/s) was higher in the combined control group (n = 370) than in subjects with a-MCI (P <.001) or na-MCI (P <.001).

There were no quantitative gait differences within MCI subtypes when divided by single- or multiple-domain involvement (data not shown).[3]

Clinical Measures

Two variables that can be easily assessed in clinical settings were selected: neurological gait based on clinician's evaluation and slow gait (defined as velocity ≤70 cm/s based on previous studies[36,37]). Prevalence of neurological gait or slow gait or both was higher in subjects with MCI (46.6%) than controls (23.7%) (OR = 2.80, 95% CI = 1.78–4.40). These variables were not significantly different between MCI subtypes. Subjects with MCI and any one of these abnormalities had worse disability scores than subjects with MCI without these abnormalities (1.2 ± 1.8 vs 0.3 ± 0.6, P <.001).

DISCUSSION

These findings show that gait dysfunction is common in older adults diagnosed with MCI in a large well-characterized community-based cohort. Recent MCI criteria recommendations,[1,3] used herein, have expanded the cognitive profile to include amnestic and nonamnestic impairments. Quantitative testing (blinded to cognitive assessments and MCI diagnosis), which have been lacking in previous studies, revealed more gait dysfunction in subjects with amnestic and nonamnestic MCI subtypes than in healthy controls even after accounting for potential confounders and applying statistical corrections.

These findings are consistent with prior studies, suggesting that motoric impairment occurs early in the course of cognitive decline.[4-9,14,15] Quantitative gait dysfunction was seen in subjects with MCI even after excluding those with neurological gaits. Worse fine and complex motor skills, equilibrium, and limb coordination have been reported in older adults with MCI

than in normal controls,[8,9] although another study reported no differences in multiple motor measures in subjects with MCI and controls.[10] This study was modest in sample size and included patients presenting to a memory clinic with memory complaints; differences in study samples may help account for differences in results.

The complementary statistical approach using factor analysis revealed three gait domains: pace, rhythm, and variability. It was recently reported that worse performance on the pace factor was associated with longitudinal decline in executive function in this cohort, whereas worse performance on the rhythm factor was associated with memory decline.[15] Baseline variability and rhythm factor scores predicted risk of incident dementia.[15] Subjects with a-MCI, a precursor state to Alzheimer's disease,[1-3] in the current study had poor rhythm. Subjects with na-MCI had poor performance on the pace factor. The pace factor loads highly on velocity and stride length, which are associated with executive attention processes in individuals without dementia,[38] as well as with cerebrovascular pathology on imaging studies.[39]

Loss of functional independence, falls, and disability are major noncognitive outcomes in older adults, with a higher risk seen in individuals with cognitive impairment states such as MCI or dementia.[1,13,16,40] Gait disturbances not only are a marker of functional status in older adults, but also predict greater risk of disability.[16] Subjects with MCI do not have functional decline, by definition, although a range of function is expected. However, gait dysfunction in subjects with MCI was strongly associated with worse disability levels within this normal range. Clinical gait abnormalities in older adults without dementia predicted risk of institutionalization and death in this cohort.[16] Defining gait function in MCI may therefore have utility in clinical settings to help identify people at higher risk of developing noncognitive outcomes such as disability or falls, which may be similar to the association noted in subjects without dementia.[16]

Performance on individual gait variables and on independent gait domains distinguished older adults with a-MCI from those with na-MCI. Subjects with a-MCI had worse swing time and stride length variability than those with na-MCI. Subjects with a-MCI had worse performance on rhythm and variability gait domains than controls and those with na-MCI. Neurological gaits were more common in subjects with a-MCI. Parkinsonian signs in MCI were related to the severity and type of cognitive impairment in another elderly cohort.[6] Gait was worse in subjects with na-MCI than in those with a-MCI in that cohort. Unlike in the current study, in which a neurologist individually classified subjects' gaits, the study nurse derived a composite gait score irrespective of whether subjects would be clinically diagnosed with parkinsonian gait.[4-6] Another community-based study reported that mild parkinsonian signs were associated with a-MCI but not na-MCI.[7]

The findings of the current study that link motoric and cognitive impairment in MCI raise the possibility of shared pathogeneses, including Alzheimer's pathology, Lewy body pathology, and vascular disease. Cerebrovascular lesions, which may result in specific neurological gaits,[14] have been reported to be common in a-MCI and na-MCI.[41] Cerebrovascular disease has also been linked to quantitative gait measures in older adults.[39,41] Conversely, correlations between temporal lobe atrophy and poor mobility independent of cerebrovascular disease have been reported.[42] Parkinsonian gait in the absence of idiopathic Parkinson's disease has been correlated with substantia nigra neurofibrillary tangles even in cases without clinical Alzheimer's disease or low-level Alzheimer's pathology.[43] Vascular or neurodegenerative mechanisms or both may mediate concurrent motor and cognitive decline.

The utility of gait measures such as neurological gaits and gait velocity that do not require elaborate equipment were explored. Clinical gait assessment is a part of routine clinical

evaluation, and slow gait can be easily measured using a stopwatch.[13-15,36,37] Presence of neurological or slow gait was overrepresented (OR = 2.8) in subjects MCI and was associated with worse disability scores than in subjects with MCI without these abnormalities. Although quantitative gait assessments are dependent on availability of equipment, these measures can be easily and quickly collected without requiring attachment of monitoring devices and do not require extensive training or specialized personnel. Gait velocity is commonly used in clinical setting to assess health,[36,37] although the findings of the current study with respect to other gait variables and domains favors further exploration of the utility of these quantitative techniques in various clinical settings. Quantitative gait dysfunction may also help provide insights into potential interventions for MCI.

This and other studies support a role for quantitative assessments in predicting cognitive decline. Quantitative gait dysfunction predicted dementia and cognitive decline in the same cohort.[15] Lower extremity dysfunction and parkinsonian gait have been reported to predict risk of developing Alzheimer's disease in MCI.[4,7] There is no pathological or imaging confirmation of these findings. Neuroimaging studies were not routinely obtained in subjects diagnosed with MCI.[14-18] It was possible to locate reports of brain imaging studies done in 27 subjects (50%) with a-MCI and 29 with na-MCI (47%) as part of evaluations done by their primary care providers for investigation of cognitive complaints or other neurological symptoms. Findings in the 27 subjects with a-MCI included strokes (n = 7), lacunar infarctions (n = 7), leukoaraiosis (n = 4), moderate to severe cortical atrophy (n = 7), and no abnormalities (n = 8). Findings in the 29 subjects with na-MCI included strokes (n = 8), lacunar infarctions (n = 11), leukoaraiosis (n = 15), moderate to severe cortical atrophy (n = 6), and no abnormalities (n = 5). Hence, cerebrovascular disease is common in a-MCI and na-MCI, although the selection bias inherent in this subgroup limits formal comparisons. Prevalence of diabetes mellitus in subjects with a-MCI and hypertension in subjects with na-MCI was higher than in controls, although adjusting for hypertension or diabetes mellitus did not influence the results. Imaging and other objective vascular correlates of motoric dysfunction need to be further explored in future studies.

Strengths of this study include the large sample size with systematic gait assessments, validated diagnostic procedures, and application of updated MCI criteria independent of gait assessments. Although diagnostic misclassification is possible, corroboration of cognitive complaints by informants and overall neuropsychological test profiles (irrespective of cutscores), which support amnestic and nonamnestic distinctions, increase confidence in the MCI subtyping. A number of sensitivity analyses were also conducted to corroborate the findings. For instance, the results were unchanged when subjects with cognitive complaints, who had worse cognitive status than controls, were included in the reference group.

The findings show that clinical and quantitative gait impairments are common in amnestic and nonamnestic subtypes of MCI and are associated with worse functional status. Assessment of gait in older adults may provide a window on brain function that complements current definitions of MCI and usefully predicts dementia and other outcomes of interest.

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Table 1

Baseline Characteristics According to Cognitive Status

Variable	Normal (n = 295)	a-MCI (n = 54)	na-MCI (n = 62)	*P*-Value*		
				a-MCI versus Normal	na-MCI versus Normal	a-MCI versus na-MCI
Age, mean ± SD	79.3 ± 4.7	82.6 ± 5.7	81.8 ± 6.2	<.001	.002	.68
Female, n (%)	184 (62.4)	26 (48.1)	44 (70.9)	.07	.25	.01
Education, years, mean ± SD	14.6 ± 3.1	13.7 ± 2.9	11.5 ± 4.0	.17	<.001	.002
Falls previous year, n (%)	40 (13.6)	11 (20.4)	10 (16.1)	.40	.43	1.00
Neurological gaits, n (%)	42 (14.2)	14 (25.9)	12 (19.4)	.04	.33	.50
Systolic blood pressure, mmHg, mean ± SD	137.9 ± 17.7	139.7 ± 14.3	142.4 ± 21.3	.82	.23	.73
Diastolic blood pressure, mmHg, mean ± SD	77.4 ± 8.6	75.9 ± 8.1	78.3 ± 8.3	.50	.78	.34
Disability score, mean ± SD (range 0–14)	0.6 ± 1.0	0.7 ± 1.5	0.8 ± 1.2	.76	.32	.85
Medical illness, n (%)						
Diabetes mellitus	33 (11.2)	12 (22.2)	11 (17.7)	.04	.33	.64
Hypertension	144 (48.8)	28 (51.8)	41 (66.1)	.77	.02	.13
Cardiac failure	7 (2.4)	2 (3.7)	2 (3.2)	.23	.28	1.00
Previous myocardial infarction	25 (8.5)	1 (1.8)	5 (8.1)	.15	1.00	.21
Angina pectoris	29 (9.8)	3 (5.6)	4 (6.5)	.44	.48	1.00
Stroke	18 (6.1)	6 (11.1)	4 (6.5)	.24	1.00	.51
Parkinson's disease	2 (0.7)	3 (5.6)	4 (6.5)	.29	.08	1.00
Chronic obstructive pulmonary disease	36 (12.2)	7 (12.9)	7 (11.3)	.83	.27	.34
Depression	39 (13.2)	5 (9.3)	5 (8.1)	.51	.39	1.00

**P*-values refer to comparisons using descriptive statistics (see Methods).

a-MCI = amnestic mild cognitive impairment; na = MCI = nonamnestic mild cognitive impairment; SD = standard deviation.

Table 2

Neuropsychological Performance According to Cognitive Status

Domain	Variable	Normal (n = 295)	a-MCI (n = 54)	na-MCI (n = 62)	a-MCI versus Normal	na-MCI versus Normal	a-MCI versus na-MCI
		Mean ± Standard Deviation			*P*-Value		
General cognition	Blessed Test score	1.4 ± 1.5	3.1 ± 2.3	2.6 ± 2.1	<.001	<.001	.131
Mood	15-item Geriatric Depression Scale, score	2.1 ± 2.0	2.7 ± 2.2	2.1 ± 1.9	.03	.96	.08
Memory	Free and Cued Selective Reminding Test, free recall score	33.4 ± 4.4	20.7 ± 3.0	31.5 ± 4.4	<.001	.001	<.001
Executive function	Digit Symbol Substitution Test score	50.9 ± 11.7	39.6 ± 15.9	33.4 ± 15.8	<.001	<.001	.009
	Block Design score	25.9 ± 8.9	20.9 ± 8.5	18.7 ± 8.6	<.001	<.001	.19
	Trail-Making Test Part B, seconds	113.4 ± 42.4	164.9 ± 94.5	211.8 ± 98.4	<.001	<.001	<.001
	Letter fluency score	40.7 ± 8.2	30.8 ± 9.5	28.4 ± 11.3	<.001	<.001	.25
Attention	Trail-Making Test Part A, seconds	47.9 ± 13.6	65.7 ± 25.4	78.4 ± 31.1	<.001	<.001	<.001
	Digit Span Forward, score	5.6 ± 4.2	5.3 ± 1.1	4.7 ± 0.9	.40	<.001	<.001
Language	Boston naming test (15-item), total correct	12.9 ± 1.7	11.4 ± 2.7	9.4 ± 2.8	<.001	<.001	<.001

a-MCI = amnestic mild cognitive impairment; na = MCI = nonamnestic mild cognitive impairment.

Table 3

Motor Performance According to Cognitive Status in the Overall Group and in the Subgroup without Neurological Gait Abnormalities

Variable	Normal	a-MCI	na-MCI	*P*-Value a-MCI versus Normal	*P*-Value na-MCI versus Normal	*P*-Value a-MCI versus na-MCI
Overall cohort, n	295	54	62			
Velocity, cm/s	99.7 ± 21.7	87.3 ± 25.4	83.2 ± 24.0	.002†	<.001†	.52
Cadence, steps/min	103.1 ± 11.3	102.3 ± 13.0	98.3 ± 12.9	.89	.006†	.04
Stride length, cm	115.5 ± 19.5	101.4 ± 23.4	101.5 ± 22.3	<.001†	<.001†	.49
Stance, seconds	0.75 ± 0.12	0.78 ± 0.16	0.81 ± 0.13	.25	.01†	.28
Swing, seconds	0.43 ± 0.05	0.42 ± 0.05	0.44 ± 0.05	.047	.23	.01†
Double support time, sec	0.32 ± 0.11	0.35 ± 0.17	0.36 ± 0.11	.05	.02	.82
Stride length variability, COV	0.04 ± 0.03	0.06 ± 0.05	0.04 ± 0.02	<.001†	.32	.003†
Swing time variability, COV	0.06 ± 0.05	0.09 ± 0.13	0.06 ± 0.04	.003†	.77	.03
Normal clinical gaits cohort (excluding neurological gaits), n	247	37	50			
Velocity, cm/s	102.3 ± 20.5	93.9 ± 25.4	85.0 ± 23.5	.06	<.001†	.14
Cadence, steps/min	103.7 ± 11.2	103.9 ± 13.6	97.7 ± 12.6	.90	.001†	.01†
Stride length, cm	118.2 ± 18.6	107.1 ± 21.4	103.9 ± 21.0	.003†	<.001†	.96
Stance, seconds	0.75 ± 0.12	0.77 ± 0.18	0.81 ± 0.13	.36	.005†	.19
Swing, seconds	0.43 ± 0.05	0.41 ± 0.05	0.44 ± 0.05	.07	.10	.007†
Double support time, seconds	0.32 ± 0.10	0.35 ± 0.20	0.36 ± 0.11	.10	.02†	.68
Stride length variability, COV	0.04 ± 0.03	0.05 ± 0.05	0.04 ± 0.02	.003†	.35	.08
Swing time variability, COV	0.05 ± 0.04	0.09 ± 0.16	0.06 ± 0.04	.001†	.72	.01†

† Indicates significant *P*-value (<.05) after applying correction for multiple comparisons (see Methods for description).

a-MCI = amnestic mild cognitive impairment; na = MCI = nonamnestic mild cognitive impairment; COV = coefficient of variation (ratio of the standard deviation to the mean).

Table 4

Factor Loading of Eight Quantitative Variables on the Three Independent Gait Factors Rotated and Extracted According to Factor Analysis

Gait Variable	Pace Factor	Rhythm Factor	Variability Factor
Velocity, cm/s	−0.879	0.360	−0.258
Stride length, cm	−0.948	−0.005	−0.238
Cadence, steps/min	−0.358	0.870	−0.279
Double support time, seconds	0.552	−0.430	0.570
Swing time, seconds	−0.039	−0.909	-0.083
Stance time, seconds	0.478	−0.678	0.473
Stride length variability, COV	0.280	0.000	0.773
Swing time variability, COV	0.143	−0.140	0.891
Variance explained, %	30.5	29.8	26.9

COV = coefficient of variation (ratio of the standard deviation to the mean).

Table 5

Gait Domains (Derived from Factor Analysis) According to Cognitive Status

Variable	Normal (n = 295)	a-MCI (n = 54)	na-MCI (n = 62)	a-MCI versus Normal	na-MCI versus Normal	a-MCI versus na-MCI
	Mean ± Standard Deviation			*P*-Value		
Pace factor	−0.18 ± 0.95	0.35 ± 0.98	0.54 ± 1.01	.001	<.001	.66
Rhythm factor	−0.02 ± 0.98	0.31 ± 0.95	−0.19 ± 1.07	.02	.10	.002
Variability factor	−0.06 ± 0.75	0.45 ± 2.00	−0.12 ± 0.57	<.001	.77	.002

P-values are derived from analysis of covariance adjusted for age, sex, and years of education. Higher factor scores denote worse performance.

a-MCI = amnestic mild cognitive impairment; na = MCI = nonamnestic mild cognitive impairment