RESEARCH ARTICLE

Gait Patterns in Parkinsonian Patients With or Without Mild Cognitive Impairment

Marianna Amboni, MD, PhD,[1,2] Paolo Barone, MD, PhD,[3]* Luigi Iuppariello, MS,[4] Ilaria Lista, PhD,[1] Riccardo Tranfaglia, PhD,[4] Alfonso Fasano, MD, PhD,[5] Marina Picillo, MD,[6] Carmine Vitale, MD, PhD,[1,2] Gabriella Santangelo, PhD,[7] Valeria Agosti, PhD,[1,2] Alessandro Iavarone, MD, PhD,[8] and Giuseppe Sorrentino, MD, PhD[1,2]

[1]*University of Naples Parthenope, Naples, Italy*
[2]*IDC Hermitage-Capodimonte, Naples, Italy*
[3]*Neurodegenerative Diseases Center, University of Salerno, Salerno, Italy*
[4]*Department of Biomedical Electronic Engineering, University of Naples Federico II, Naples, Italy*
[5]*Department of Neurology, Catholic University of Sacred Heart, Rome and Department of Neuroscience, AFaR-Fatebenefratelli Hospital, Rome, Italy*
[6]*Department of Neurological Sciences, University of Naples Federico II, Naples, Italy*
[7]*Department of Psychology, Second University of Naples, Caserta, Italy*
[8]*Neurological and Stroke Unit, CTO Hospital, AORN Ospedale dei Colli, Naples, Italy*

ABSTRACT: Although in recent years the relationship between cognition and gait in Parkinson's disease (PD) has received increasing attention, the specific connections between gait patterns and cognitive features are not fully understood. The objective of this study was to describe the gait patterns in patients affected by PD with or without mild cognitive impairment (MCI+ and MCI−, respectively). We also sought to find an association between gait patterns and specific cognitive profiles. Using a gait analysis system, we compared the gait patterns among MCI+ patients (n = 19), MCI− patients (n − 24), and age- and sex-matched healthy subjects (HS; n = 20) under the following conditions: (1) normal gait, (2) motor dual task, and (3) cognitive dual task. In PD patients, gait parameters were evaluated in both the off and on states. Memory, executive, and visuospatial domains were assessed using an extensive neuropsychological battery. Compared with MCI− PD and HS, MCI+ PD patients displayed reduced step length and swing time and impairment of measures of dynamic stability; these dysfunctions were only partially reversed by levodopa. We also found that dual-task conditions affected several walking parameters in MCI+ PD in the off and on states relative to MCI− PD and HS. Factor analysis revealed 2 independent factors, namely, pace and stability. The latter was strongly and directly correlated to the visuospatial domain. In conclusion, dysfunctions on specific gait parameters, which were poorly responsive to levodopa and highly sensitive to dual-task conditions, were associated with MCI in PD patients. Importantly, visuospatial impairment was strongly associated with the development of instability and more generally with the progression of PD.

Key Words: Parkinson's disease; cognition; gait

Over the last decade, the relationship between cognitive function and gait performances has received increasing attention. Gait is no longer considered merely an automated motor activity but an activity requiring executive function and attention as well as motivation and judgment of external and internal cues.[1]

Dysfunction in specific gait variables has been associated with an increased risk of cognitive decline and Alzheimer's disease.[2] Furthermore, in a large community-based cohort,[3] gait dysfunctions were reported to be frequent in older adults diagnosed with mild cognitive impairment (MCI).

Additional Supporting Information may be found in the online version of this article.

***Correspondence to:** Prof. Paolo Barone, Neurodegenerative Diseases Center, University of Salerno, Via Allende, Baronissi (Salerno), Italy; pbarone@unisa.it

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Originally, the construct of MCI was conceptualized as the transitional state between normalcy and Alzheimer's disease.[4] More recently, it has been used to identify a predementia state in patients with Parkinson's disease (PD).[5,6]

It has long been recognized that the "postural instability gait disorder" phenotype is associated with cognitive impairment in PD[7] and that axial symptoms such as gait disorders, postural instability,[8,9] and cognition[10] worsen as PD progresses. Moreover, these symptoms respond poorly to dopaminergic treatment, which may reflect the involvement of neurotransmitters systems other than dopamine.[11,12] Several studies[13–16] have assessed the levodopa effect on locomotion components with relatively inconsistent results, thus suggesting that several factors might play a role.

Previous studies have pointed out the key role played by executive functions and attention in gait performances in PD patients.[17,18] We recently showed that freezing of gait is associated with executive dysfunction[19] and with a worse progression of cognitive impairment in parkinsonian patients.[20] Conceivably, gait impairment in PD may reflect altered motor control and overload of frontal networks. This consistently affects the ability of PD patients to walk while performing another task (ie, dual task).[21,22] Rochester et al[23] observed that the magnitude of the dual-task effect in PD is related to age, cognition, motor performance, and affective status. Furthermore, PD patients with poor executive functions, especially with set-shifting ability impairment, have been found to be more sensitive to the dual-task effect, thus being at higher risk of falling.[24,25]

Very recently, PD patients with MCI in different domains have been reported to display higher postural instability and gait disorder subscale scores than cognitively normal PD patients,[26] thus suggesting that cognitive domains other than the executive one could be involved in balance and gait control. To our knowledge, no study has yet explored the relationship between quantitative gait variables and MCI in PD.

In the present study we objectively assessed the gait patterns of PD patients with MCI (MCI+) or without MCI (MCI−) in order to confirm the hypotheses that: (1) these 2 subgroups have different gait patterns during off conditions; (2) gait variables of MCI+ have a poorer response to levodopa than MCI− patients; (3) dual-task paradigms have different effects in MCI+ than in MCI− patients; and (4) specific gait components might correlate with specific cognitive domains. PD patients were also compared with healthy subjects (HS).

Patients and Methods

Study Population

Patients were screened from a series of consecutive outpatients at the Movement Disorders Unit of the University of Naples Federico II who had a diagnosis of PD according to the United Kingdom Parkinson's Disease Brain Bank criteria.[27]

Patients were classified as MCI+ if they had both (1) a cognitive deficit not causing a significant functional decline and (2) dysfunction in at least 1 cognitive domain as confirmed by a consistent pattern of impairment (at least 1.5 standard deviations below the expected age and education-corrected mean score) in the specific neuropsychological tests.[5] The 2 groups of patients were matched for age, sex, and disease duration.

HS were enrolled among volunteers who were age- and sex-matched to the patient population.

Further details on entry criteria are available online.

Clinical and Cognitive Evaluation

All subjects were evaluated using an extensive neuropsychological battery and a detailed clinical evaluation, including demographic and anthropometric data (see Supplemental Material). All neuropsychological tests were administered to patients during the on state. Tests scores were corrected for current normative values.

Gait Analysis

Gait was assessed with an optokinetic system (Qualisys, Sandvälen, Sweden) equipped with a set of 6 infrared cameras, a ProReflex Motion Capture Unit (MCU, CCD technology, 240-Hz sampling rate), and data acquisition software (Qualisys Track Manager). Patients' gait was assessed in both the off and on states and during 3 experimental conditions (each performed twice): (1) normal gait (normal walking; gait-off and gait-on); (2) motor dual-task (walking while carrying a tray with 2 glasses filled with water; Mot-off and Mot-on); and (3) cognitive dual task (walking while serially subtracting 7s starting from 100; Cog-off and Cog-on). The gait of HS was assessed in the same 3 conditions (each performed twice). Before the trials, all participants were instructed to walk at a normal pace at their usual speed and were not given any specific instruction regarding prioritization (walking or task).

For further details on gait analysis and walking parameters, refer to the online Supplemental Material.

Statistical Analysis

Differences in the distribution of categorical variables among groups were assessed by the chi-square test. To better avoid type 1 errors, all statistical analyses applied were nonparametric tests. Demographic, clinical, and gait continuous variables of MCI+ PD patients, MCI− PD patients, and HS were compared using the Kruskal–Wallis test. Multiple comparisons of gait variables between groups (MCI+ vs MCI− vs HS) were performed with the post hoc Dunnett test.

TABLE 1. Demographic and clinical features of PD patients with (MCI+) and without (MCI−) mild cognitive impairment and healthy subjects (mean ± standard deviation)

	PD MCI+ (n = 19)	PD MCI− (n = 24)	Healthy subjects (n = 20)	*P*
Age (y)	65.10 ± 6.85	64.08 ± 6.44	63.50 ± 3.14	.68
Sex (M/F)[a]	13/6	20/4	10/10	.061
Education (y)	9.00 ± 4.63	11.12 ± 4.52	12.00 ± 2.79	.071
Disease duration (y)	5.47 ± 2.71	5.42 ± 2.80	—	.947
H&Y stage	2.22 ± 0.43	2.23 ± 0.51	—	.962
Gait-Q score	11.53 ± 11.10	9.54 ± 9.96	—	.546
FOG-Q score	7.26 ± 6.17	5.83 ± 5.71	—	.441
UPDRS I	1.58 ± 1.30	1.79 ± 1.18	—	.583
UPDRS II	7.68 ± 3.99	7.71 ± 5.09	—	.986
UPDRS III in off state	23.63 ± 6.06	23.04 ± 6.91	—	.767
UPDRS III in on state	11.42 ± 3.72	10.83 ± 5.40	—	.676
UPDRS IV	2.89 ± 2.42	1.58 ± 1.72	—	.055
BDI	9.68 ± 4.89	9.79 ± 6.11	8.00 ± 5.79	.527
BMI (kg/m^2)	26.36 ± 3.74	26.91 ± 4.86	26.71 ± 3.50	.910
Trochanter-malleolus (cm)	74.79 ± 3.81	76.25 ± 4.68	75.12 ± 5.44	.571
Intermalleolus (cm)	7.47 ± 0.54	7.55 ± 0.64	7.19 ± 0.65	.527

H&Y stage, Hoehn & Yahr stage; Gait-Q, Gait Questionnaire; FOG-Q, Freezing of Gait Questionnaire; UPDRS, Unified Parkinson's Disease Rating Scale; BDI, Beck Depression Inventory; BMI, body mass index; trochanter-malleolus, distance between greater trochanter and lateral malleolus; intermalleolus:, distance between lateral and medial malleoli.
[a]Chi-square test.

The effects of dual-task conditions on gait parameters were evaluated by Friedman's ANOVA using the post hoc Dunnett test for multiple comparisons, assuming group (MCI+ PD vs MCI− PD vs HS) as the between factor and dual-task condition (normal gait parameters vs motor dual-task parameters vs cognitive dual-task parameters) as the within factor. To identify an association between the gait variables and any cognitive domain, factor analysis was performed (further details are available online).

Significance was set at $P = .05$. Computation was supported by SPSS version 16.0 (SPSS, Chicago, IL).

Results

Sixty-three subjects were evaluated: 43 PD patients and 20 HS. Nineteen patients were classified as MCI+ and 24 as MCI− The 3 groups did not differ on demographic and anthropometric variables. MCI+ PD and MCI− PD patients did not differ in any of the clinical variables (Table 1). The 2 groups differed significantly on several tests loading on memory, executive, and visuospatial domains (Table 2). Cognitive scores were normal in HS.

Gait variables comparisons among the 3 groups are reported in Table 3a. Post hoc multiple comparisons were performed only on the gait parameters that differed significantly among the 3 groups.

Gait Patterns during Off State

As expected, step length was shorter in all conditions in PD patients (both MCI+ and MCI−) than in HS (Table 3b and Fig. 1A).

Swing time was shorter in MCI+ PD patients than in HS in all conditions, whereas it was shorter in MCI− PD patients compared with HS only during the cognitive dual task (Table 3b and Fig. 1B).

The single/double support time ratio was lower in all conditions in MCI+ PD than in HS, whereas it did not differ between MCI− PD and HS in any condition (Table 3b and Fig. 1C). Furthermore, the single/double support time ratio was significantly lower in MCI+

TABLE 2. Data (mean ± standard deviation) from cognitive testing in PD patients with (MCI+) and without (MCI−) mild cognitive impairment and between-group comparisons (1-way ANOVA)

	MCI+ PD	MCI− PD	*P*
MMSE	26.57 ± 2.09	27.71 ± 1.72	NS
Episodic memory domain			
Rey 15 words, immediate recall	35.07 ± 6.28	41.31 ± 7.95	.01
Rey 15 words, delayed recall	7.27 ± 2.78	8.52 ± 2.33	NS
Executive domain			
Phonemic fluency	28.10 ± 10.24	36.88 ± 10.01	<.01
Frontal Assessment Battery	12.55 ± 2.03	15.14 ± 1.73	<.0001
Stroop, part II (color table)	31.63 ± 10.33[a]	35.59 ± .89[a]	NS
Stroop, part III (color/word table)	18.07 ± 5.10[a]	21.67 ± 5.36[a]	.03
Visuospatial domain			
Spatial span	4.23 ± 0.85	4.67 ± 0.70	NS
Constructive apraxia	10.46 ± 1.47	11.23 ± 1.31	NS
Raven's PM 47	23.07 ± 3.95	28.37 ± 4.35	.0001
Ten Point Clock test	4.10 ± 3.12	7.08 ± 3.12	.001

MMSE, Mini Mental State Examination; NS, not significant.
[a]Number of correct responses delivered in 30 seconds.

TABLE 3. Significance of gait variables in different conditions in PD patients with (MCI+) and without (MCI−) mild cognitive impairment and in healthy subjects (HS) (a) and multiple comparisons (b)

a)

	Gait conditions					
Gait variable	NG-off (*P*)	Mot-off (*P*)	Cog-off (*P*)	NG-on (*P*)	Mot-on (*P*)	Cog-on (*P*)
Step length	.001	.0001	.0001	.010	.005	.002
Stance phase	NS	NS	NS	NS	NS	NS
Swing phase	.025	.032	.013	.003	NS	.024
Single/double support T R	.001	.001	.0001	.009	.013	.002
Cadence	NS	NS	NS	NS	NS	NS
Velocity	.048	.045	.011	NS	NS	.041
Step length variability	.046	.004	NS	NS	.018	NS
Swing time variability	NS	NS	NS	NS	NS	NS

b)

	Gait conditions (off)					
	NG (*P*)		Mot (*P*)		Cog (*P*)	
Gait variable	MCI+ vs HS[a]	MCI− vs HS[a]	MCI+ vs HS[a]	MCI− vs HS[a]	MCI+ vs HS[a]	MCI− vs HS[a]
Step length	.003	.002	.0001	.002	.001	.004
Swing phase	.019	NS	.02	NS	.032	.0048
Single/double support T R	.0001	NS	.0001	NS	.0001	NS
Velocity	NS	NS	NS	NS	NS	NS
Step length variability	NS	NS	.018	NS	0.034	NS
	Gait conditions (on)					
Step length	.009	NS	.004	.019	.001	NS
Swing phase	.006	NS	NS	NS	NS	NS
Single/double support T R	.003	NS	.017	NS	.001	NS
Velocity	NS	NS	NS	NS	NS	NS
Step length variability	NS	NS	.013	NS	NS	NS

NG, normal gait; Mot, motor dual task; Cog, cognitive dual task; off, in off state; on, in on state; NS, not significant.
[a]For HS, motor condition (off/on) is not applicable.

PD than in MCI− PD during the cognitive dual task ($P = .022$; Fig. 1C).

Multiple comparisons did not reveal any difference between groups on gait velocity in any conditions (Table 3b).

Step length variability was increased in MCI+ PD compared with MCI− PD and HS, with a gradient of MCI+ PD > MCI− PD > HS in all conditions. Furthermore, step length variability was increased in MCI+ PD versus HS in both dual-task conditions, whereas it did not differ in MCI− PD versus HS in any condition (Table 3b and Fig. 1D).

Levodopa effect on Gait Patterns

After levodopa, step length was still shorter in MCI+ PD than in HS in all conditions, whereas it was shorter in MCI− PD than in HS only in the motor dual task (Table 3b and Fig. 1A). Swing time was shorter in MCI+ PD than in HS only during normal gait, whereas it did not differ between MCI− PD and HS in any condition (Table 3b and Fig. 1B). The single/double support time ratio was still lower in all conditions in MCI+ PD versus HS and did not differ between MCI− PD and HS in any condition (Table 3b and Fig. 1C). Furthermore, the single/double support time ratio was significantly lower in MCI+ PD versus MCI− PD during normal gait ($P = .045$; Fig. 1C).

Multiple comparisons did not reveal any difference between groups in gait velocity in any condition (Table 3b).

Step length variability was increased in MCI+ PD versus HS only during the motor dual task. Again, it did not differ in MCI− PD versus HS (Table 3b and Fig. 1D).

Dual-Task Effects on Gait Patterns

Dual tasks affected step length in the off state in both MCI+ PD ($P = .001$) and MCI− PD ($P = .002$) compared with HS. During the on state, this effect was still significant in MCI+ PD ($P = .001$) but not in MCI− PD. Dual-task paradigms affected swing time during both off ($P = .019$) and on ($P = .035$) states in

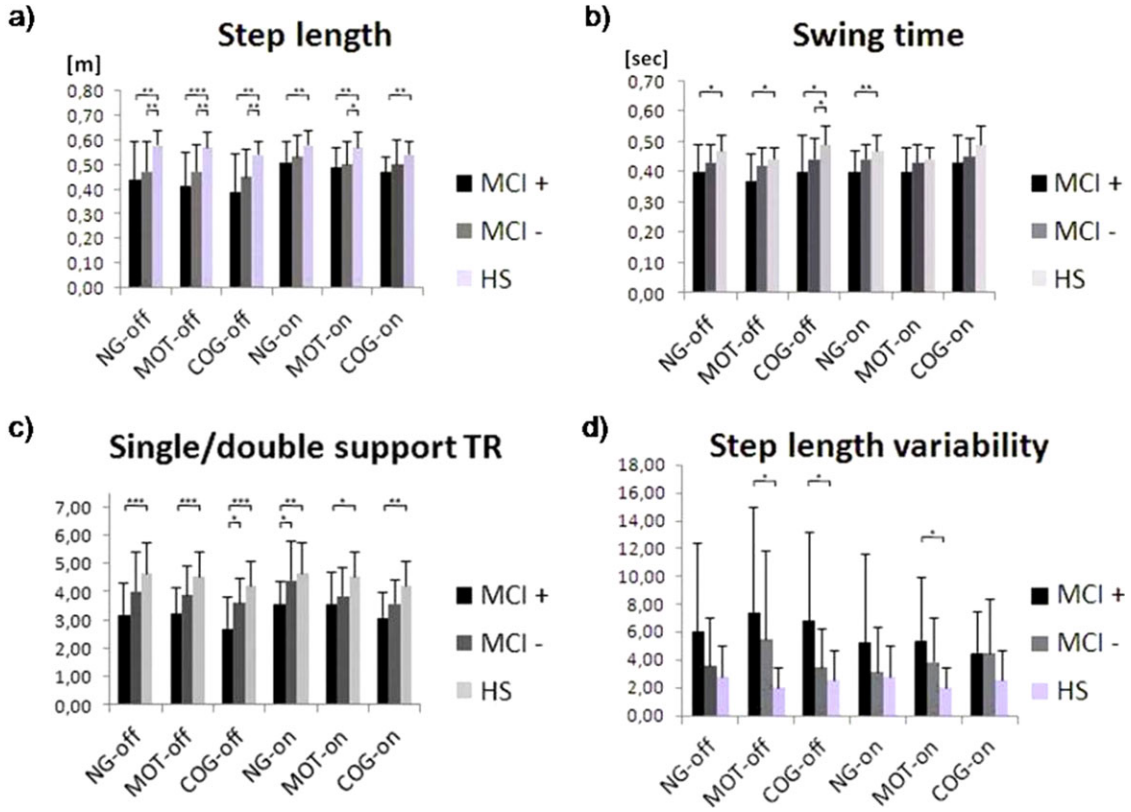

FIG. 1. Post hoc multiple comparison analysis of PD patients with (MCI+) and without (MCI−) mild cognitive impairment and healthy subjects (HS) on step length (**A**), swing time (**B**), single/double support time ratio (**C**), and step length variability (**D**). NG, normal gait; Mot, motor dual task; Cog, cognitive dual task; off, in off state; on, in on state; NS, not significant; $^{*}P < .05$; $^{**}P < .01$; $^{***}P < .001$.

MCI+ PD but not in MCI− PD with respect to HS. Dual tasks displayed a significant effect on the single/double support time ratio during both off ($P = .0001$) and on ($P = .0001$) states in MCI+ PD versus HS. The same effect was detected in MCI− PD patients during off time, with a trend toward significance ($P = .05$), but not during the on state. Dual-task conditions did not affect velocity in PD patients relative to HSs in either the off or the on states. Finally, dual tasks affected step length variability during both the off ($P = .018$) and on ($P = .008$) states in MCI+ PD but not in MCI− PD with respect to HS. We did not find any significant interaction between groups and dual task for any gait variable.

Gait Factors and Their Relationship with Cognitive Domains

The principal-component analysis had a Bartlett's chi square of 346.576 ($P < .0001$) and generated 2 factors that explained about 75% of the variance (Table 4). The first factor loaded on the following variables: stance phase, swing phase, cadence, and velocity. The second factor loaded on step length, single support/double support time ratio, step length variability, and swing time variability. In line with the reported locomotion components,[28] we named "pace" the first factor loading on variables related to initiation and maintenance of step rhythm, and we named "stability" the second factor loading on variables related to balance. The pace factor was not correlated with any cognitive or clinical variable (Table 5a, b). The stability factor was strongly and directly correlated with the visuospatial domain (Table 5a). Furthermore, the stability factor was also inversely

TABLE 4. Factor analysis of the 8 quantitative gait parameters

	Magnitude	Variance
Factor 1	3.842	0.480
Factor 2	2.169	0.271
Structure matrix of factor loading after rotation	Factor 1 (pace)	Factor 2 (stability)
Step length	0.006	*0.750*
Stance phase	*0.748*	−0.182
Swing phase	*0.960*	0.398
Single support/double support	0.401	*0.735*
Cadence	*−0.941*	−0.122
Velocity	*−0.705*	0.305
Step length variability	0.023	*−0.689*
Swing time variability	0.014	*−0.715*

Principal-component analysis with Varimax rotation. Method of extraction: roots > 1. Values > 0.50 in the structure matrix are italicized.

TABLE 5. Partial correlation of factor scores with cognitive cumulative scores (a) and main clinical measures (b)

	Factor 1 (pace)		Factor 2 (stability)	
a)				
Memory	0.163	NS	−0.157	NS
Executive	0.011	NS	0.0190	NS
Spatial	0.031	NS	0.412	(0.006)
b)				
Disease duration	0.166	NS	−0.259	NS
H&Y stage	0.209	NS	−0.430	(< 0.004)
Gait-Q	0.088	NS	−0.517	(0.0003)
FOG-Q	0.060	NS	−0.443	(< 0.003)
UPDRS III on	0.095	NS	−0.288	(0.06 — trend)

H&Y stage, Hoehn & Yahr stage; Gait-Q, Gait Questionnaire; FOG-Q, Freezing of Gait Questionnaire; UPDRS III on, Unified Parkinson's Disease Rating Scale part III in on state; NS, not significant.

correlated with almost all the main clinical measures of disease progression (Table 5b).

Discussion

To our knowledge, this is the first study evaluating the relationship between MCI, quantitative walking parameters, and the effect of dual tasks on gait in PD patients during both the off and on states compared with HS. It is also the first exploring the relationship between specific gait variables and the cognitive domains more commonly impaired in PD. Here we showed that, compared with MCI− patients and HS, MCI+ PD patients display specific gait features (ie, both reduced step length and swing time and impairment of dynamic stability), which are only partially reversed by levodopa. We also found that dual-task conditions affect several walking parameters in MCI+ PD in both the off and on states with respect to MCI− and HS. This finding supports evidence that cognitive loading exerts a detrimental effect on gait performance in PD patients,[17] the magnitude of which is related to the underlying cognitive dysfunction. Finally, we have shown that instability is specifically associated with both visuospatial impairment and clinical progression in PD .

Gait Patterns during Off State and Levodopa Effect

In agreement with previous findings,[14–16,29] during the off state, step length was shorter in PD patients than in HS. During the on state, step length did not improve significantly in MCI+ PD during any condition, whereas it increased in MCI− during both normal gait and the cognitive dual task but not during the motor dual task. The motor dual task could be more demanding in PD patients because it requires not only executive-attentional but also visuospatial skills,[30] which could explain the reduced effect of levodopa during performance of this task.

Similarly, during the off state, the single/double support time ratio was lower in MCI+ PD than in MCI− PD and HS and did not improve in the on state. The single/double support time ratio is a direct measure of dynamic stability.[31] By means of a quantitative gait assessment, our findings support the well-known relationship between cognitive impairment and increased instability in PD patients,[7,32,33] as well as the poor response of axial symptoms to levodopa.[11,34] Consistently, in the off state during dual-task conditions, step length variability was greater in MCI+ PD. This supports the finding that a dual task exerts a strong effect on variability measures of gait in PD patients with cognitive impairment.[22,24,35] Previous findings have reported inconsistent results on levodopa efficacy in reducing gait variability in PD,[13–16] suggesting that co-occurrence of other factors may account for such differences. In the present study, levodopa reduced step length variability during the cognitive dual task but not during the motor one. Again, this supports the concept that the motor dual task might be more demanding. Because increased step length variability is a measure of stability impairment[25] as well as both lower single/double support time ratio and shorter step length, our findings show a reduced response of instability to levodopa in MCI+ PD compared with MCI− PD, perhaps suggesting that dopa-resistant gait components and cognitive dysfunction might share common nondopaminergic network dysfunction.[11,34]

During the off state, swing time was shorter in MCI+ PD than in HS in all conditions and shorter in MCI− PD than in HS only during the cognitive dual task. During the on state, swing time increased in PD patients, although it remained shorter in MCI+ PD than in HS. Surprisingly, this difference was significant only during normal gait, which could indicate a reduced dual-task effect sensitivity of this parameter in patients with an underlying cognitive dysfunction.

Consistent with previous observations,[29] velocity was reduced in PD patients in both the off and on states with respect to HS. However, multiple comparisons did not reveal any significant difference in any condition, thus mirroring that velocity is a raw measure underlain by multiple gait adjustments, variably modulated by patients. Furthermore, it has been reported that cognition contributes poorly to gait speed in PD patients while both normal and dual-task walking.[23,36]

Dual-Task Effects on Gait Patterns

The lack of any significant interaction between group and dual-task conditions is partly in agreement with previous reports[17,37] and indicates that healthy

elderly subjects and PD patients tend to deteriorate gait performances under dual tasks. Nevertheless, this effect was significantly different in the comparisons of PD subgroups. In fact, dual-task conditions affected step length, swing time, single/double support time ratio, and step length variability in MCI+ PD patients in both the off and on states, whereas they exerted an effect on both step length and single/double support time ratio during the off but never during the on state in MCI− PD patients. These findings support the hypothesis of "wrong prioritization" (first task and then posture) when gait cortical control collapses under the dual-task overloading, thereby increasing the risk of falling in PD patients.[30] However, our comparison of PD patients with and without MCI during both the off and on states with HS demonstrates (1) that "wrong prioritization" mostly concerns MCI+ PD patients maybe mirroring impaired hazard estimation in such patients[38] and (2) that levodopa does not reduce increased sensitivity to dual tasks in MCI+ PD patients.

Gait Factors and Their Relationship with the Cognitive Domains

Previous studies have highlighted the crucial role of both attention and executive functions in gait control.[17,18,36] Nevertheless, these studies focused on frontal lobe–based cognitive abilities and did not assess more posterior cognitive skills as a visuospatial domain.

In our PD population, the stability factor was specifically correlated with visuospatial domain scores, whereas the executive domain did not correlate with any factor, maybe suggesting a more generalized role for executive functions on gait. A growing body of evidence has drawn attention to the importance of visual information processing during the generation of motor plans[39] and in the control of locomotion in PD.[40] Furthermore, recent studies evaluating the effect of space perception on gait in PD patients[41,42] have shown that visuospatial ability is more greatly affected in PD patients with freezing of gait than in those without. Very recently, UPDRS subscores for postural instability and gait disturbances were found to be associated with visuospatial functions in newly diagnosed PD patients.[43] On the one hand, our data confirmed the relationship between the visuospatial domain and gait, and on the other hand, they showed that a specific component of locomotion, namely the stability, is highly related with visuospatial processing. Interestingly, a reduced stability factor score was also inversely associated with higher H&Y stage, gait and freezing questionnaire scores, and motor UPDRS, suggesting a specific relationship among motor progression, instability, and visuospatial impairment in PD. Conceivably, the clinical impact of our results could be that PD patients with visuospatial impairment compared with PD patients with other cognitive dysfunction would display more instability and could be in at greater risk of falling.

Our study has several limitations. First, we know that clinical diagnostic criteria for MCI in PD were published very recently,[44] but because these criteria were lacking at the time of study enrollment, we referred to the arbitrary definition for MCI proposed by Caviness et al.[5] Nevertheless, the MCI criteria we used, based on consistent dysfunction in at least 1 cognitive domain not causing significant decline, are mostly in agreement with the recent PD-MCI criteria. Second, we identified off and on states according to widely used procedures, but we knew that motor states so identified could be biased by individual and pharmacological factors. Third, we are aware that our results could have been influenced by the small sample size, and therefore they should be regarded as preliminary. Fourth, another limitation was the relatively short duration over which gait was recorded. Finally, the main study limitation was probably relying on its cross-sectional design, which does not allow for inference about a causative relation between cognitive dysfunction and gait abnormalities. Further longitudinal studies are needed to elucidate any causative relationship between these aspects.

In conclusion, our data demonstrate that dysfunctions in specific gait parameters that are poorly responsive to levodopa and highly sensitive to dual-task conditions are associated with MCI in PD. Importantly, visuospatial impairment seems strongly associated with the development of instability and more generally with the progression of PD.

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