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Clinical differences among mild cognitive impairment subtypes in Parkinson's disease

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Abstract

Background—Mild cognitive impairment is increasingly recognized as a construct in Parkinson's disease (PD) and occurs in about 25% of non-demented PD patients. Although executive dysfunction is the most frequent type of cognitive deficit in PD, the cognitive phenotype of PD mild cognitive impairment (PD-MCI) is broad. PD-MCI subtypes are represented by amnestic and nonamnestic domain impairment as well as single- and multiple-domain impairment. However, it is unclear whether patients with different PD-MCI subtypes also differ in other clinical characteristics besides cognitive profile.

Methods—We studied 128 PD-MCI subjects at our Movement Disorders center, comparing clinical, motor, and behavioral characteristics across the PD-MCI subtypes.

Results—We found varying proportions of impairment subtypes: nonamnestic single-domain (47.7%), amnestic multiple-domain (24.2%), amnestic single-domain (18.8%), and nonamnestic multiple-domain (9.5%). Attentional/executive functioning and visuospatial abilities were the most frequently impaired domains. PD-MCI subtypes differed in their motor features with nonamnestic multiple-domain PD-MCI subjects showing particularly pronounced problems with postural instability and gait. Differences among PD-MCI subtypes in age, PD duration, medication use, mood or behavioral disturbances, or vascular disease were not significant.

Conclusions—In addition to differing cognitive profiles, PD-MCI subtypes differ in motor phenotype and severity but not in mood, behavioral, or vascular co-morbidities. Greater postural instability and gait disturbances in the nonamnestic multiple-domain subtype emphasize shared non-dopaminergic neural substrates of gait and cognition in PD. Furthermore, increased burden of cognitive dysfunction, rather than type of cognitive deficit, may be associated with greater motor impairment in PD-MCI.

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Keywords

amnestic; dementia; gait; mild cognitive impairment; nonamnestic

Introduction

Mild cognitive impairment in PD (PD-MCI) has become increasingly recognized as a distinct entity that signifies a state of cognitive decline in clinically diagnosed PD patients that is not normal for age, but does not significantly impair functional activities, and does not meet criteria for PD dementia (PDD) [1–3]. While rooted in studies of aging and Alzheimer's Disease (AD), [4, 5] the construct of MCI recently has been applied to PD. In PD, MCI may represent the earliest stage of cognitive decline and a risk factor for PDD [6, 7], a frequent complication [8, 9] associated with poor outcomes [10, 11] and lacking effective treatments [12]. Greater understanding of PD-MCI and its subtypes may lead to earlier detection of patients at risk of dementia and ultimately, therapies to halt or slow the progression of PD-MCI and PDD.

PD-MCI is frequent, occurring in about 25% of non-demented PD patients (range 19–55%) [1, 6, 13–21] and even in newly diagnosed, untreated PD patients [13, 16, 18]. To date, many, but not all, PD-MCI studies have applied MCI criteria and subtyping proposed by Petersen et al [5] and Winblad et al [22]. In the latter, MCI is further categorized into four subtypes depending on the presence of memory impairment and number of cognitive domains impaired: amnestic MCI single-domain, amnestic MCI multiple-domain, nonamnestic MCI single-domain, or nonamnestic MCI multiple-domain. Recently, PD-MCI diagnostic criteria have been developed by a Movement Disorder Society (MDS) Task Force [2]. While nonamnestic single-domain impairment, particularly affecting executive function, predominates in PD-MCI, [6, 13, 15, 16, 18, 19] the PD-MCI cognitive phenotype is heterogeneous with some patients exhibiting posterior cortical-type profiles [7], and others, greater amnestic deficits [14, 23–25]. This heterogeneity may reflect methodological differences between studies [1, 20, 21], but also differences in the neurobiological substrates of MCI subtypes.

Few studies, however, have examined whether PD-MCI subtypes differ in characteristics besides cognitive phenotype. Moreover, sample sizes of most PD-MCI cohorts have been relatively small (range 18–72), thereby precluding comparisons across subtypes, with the exception of one large multi-center study in which amnestic and nonamnestic multiple-domain PD-MCI had worse motor symptoms than those with single-domain PD-MCI [14]. Differences in motor severity, mood or behavioral disorders, or other co-morbidities among PD-MCI subtypes would be important information to acquire because such differences may affect rates of progression and potentially influence treatment strategies.

Accordingly, the purpose of our study was to examine the clinical characteristics of PD-MCI subtypes (amnestic single-domain, amnestic multiple-domain, nonamnestic single-domain, nonamnestic multiple-domain) and determine whether PD-MCI subtypes, while distinct in their cognitive phenotype, differ regarding other clinical aspects and co-morbidities.

Methods

Subjects and evaluations

We studied 128 PD-MCI subjects drawn from a larger, prospective study involving a cross-sectional cohort of 350 consecutive PD patients evaluated at the Rush University Movement Disorders Center over a 2 ½-year period. All PD subjects met United Kingdom PD Society

Brain Bank criteria [26] and were examined by movement disorders neurologists. We excluded those with atypical or secondary parkinsonism, known causes of dementia, and prior neurosurgery. The study was approved by the Rush University Institutional Review Board, Chicago, IL.

The clinical evaluation assessed: demographics, medical co-morbidities, medications, and disease-related features including the Unified PD Rating Scale (UPDRS) Part III motor score, Hoehn and Yahr stage, and UPDRS Part I Thought Disorder score [27]. PD medications were converted to levodopa equivalent daily doses (LEDD) [28]. To identify associations of clinically distinct motor elements of the UPDRS Part III with PD-MCI subtypes, individual motor item scores were converted to six factors (i.e., axial functioning/gait, rest tremor, rigidity, left bradykinesia, right bradykinesia, and postural tremor), using previously published weighted factor loadings [29]. Composite vascular risk factor scores (0–5) were calculated based on the dichotomized presence or absence of hypertension, hypercholesterolemia, diabetes mellitus, cardiovascular or cerebrovascular disease [30].

The neuropsychological evaluation included: 1) MiniMental State Examination (MMSE), [31] Hamilton Depression Rating Scale, [32] and individual cognitive tests grouped conceptually into following four cognitive domains – (a) attentional/executive function (Digit span forwards and backwards [33]; oral version of the Symbol Digit Modalities Test [34], category fluency test of animal naming in 1 minute [35]), (b) declarative memory (3 trials of word list learning and delayed recall from the Consortium to Establish a Registry for AD [CERAD] [35]), (c) language (Boston Naming Test [36]; Similarities [33]), and (d) visuospatial function (Judgment of Line Orientation [37], intersecting pentagon drawing item from the MMSE using an ordinal 6 point scale [38, 39]), 2) a semi-structured interview with the subject and/or informant, and 3) clinical impression of the subject's general cognitive function.

Cognitive classification

Raw scores for cognitive tests were transformed to z-scores based upon normative data [40, 41]. Cognitive domain scores were calculated by averaging z -scores for neuropsychological tests within specific domains, thereby accounting for any unequal distribution of tests per domain. Impairment was defined as a z-score of ≤ -1.5 for a given domain. The MMSE, except for intersecting pentagons, was used only for descriptive purposes.

PD subjects were classified as having PD-MCI if they had a decline in cognition as assessed during the neuropsychological evaluation, had a z-score of ≤ -1.5 on at least one of four cognitive domains, and did not meet MDS-PDD criteria [3]. Subjective cognitive complaints were not required for the definition of PD-MCI but were endorsed by 83% of PD-MCI subjects. Of the 350 consecutive PD subjects, PD subjects with dementia (n=34) or normal cognition (n=188) were excluded.

Subtyping of PD-MCI subjects

Using these methods, PD-MCI subjects were categorized in one of the following four subtypes: amnestic single-domain (only memory domain impaired), amnestic multiple-domain (memory plus one or more other domains impaired), nonamnestic single-domain (one non-memory domain impaired), or nonamnestic multiple-domain (more than one non-memory domain impaired) [22].

Statistical analyses

Statistical analyses were performed using SPSS 18.0 (PASW 18, Chicago, IL).

Demographic- and disease-related variables were compared across PD-MCI subtypes using one-way analysis of variance (ANOVA) or for categorical variables, Kruskal-Wallis tests. Levene's test was used to assess homogeneity of variance of the variables; continuous variables demonstrating unequal variances were analyzed using non-parametric tests. Analyses were adjusted for multiple comparisons using Bonferroni corrections, which are also valid for unequal samples. Single- and multiple-domain PD-MCI subtypes were compared using independent t-tests or Chi-square tests. Predictors of PD-MCI subtype were examined using multinominal logistic regressions with variables entered stepwise and nonamnestic single-domain subtype as the reference category. Statistical significance was set at $p<0.05$.

Results

Cognitive profile of PD-MCI subjects

All four MCI subtypes were represented: 47.7% had nonamnestic single-domain impairment, 24.2% amnestic multiple-domain impairment, 18.8% amnestic single-domain impairment, and 9.5% nonamnestic multiple-domain impairment. Overall, nonamnestic deficits predominated, occurring in 57%. Two-thirds of the PD-MCI group had single-domain impairment, either amnestic or nonamnestic subtypes. Within nonamnestic single-domain impairment, visuospatial deficits were frequent (73.8%), followed by attentional/executive dysfunction (18%), and language deficits (8.2%). When multiple domains were impaired, 76.7% had two domains involved, 23.3% had three domains affected, but none had all four domains impaired (Figure 1).

Comparison of PD-MCI subtypes

There were no significant differences across PD-MCI subtypes regarding age, gender, or education (Table 1). PD duration, LEDD, vascular risk factors, and UPDRS Part III motor scores also did not differ significantly among PD-MCI subtypes, though mean UPDRS motor scores were higher in both multiple-domain groups compared to single-domain subtypes. Motor function as measured by Hoehn and Yahr stage, however, differed significantly among PD-MCI subtypes (χ^2 [3, N=128]=8.15, p=0.04). More advanced Hoehn and Yahr stages occurred in nonamnestic multiple-domain PD-MCI subjects, compared to amnestic single-domain PD-MCI (p=0.036, corrected for multiple comparisons). Moreover, axial functioning/gait, one of the six clinically distinct UPDRS factors, differed significantly among PD-MCI subtypes (F [3, 117] 2.73, p=0.047), with worse axial function in nonamnestic multiple-domain subjects compared to nonamnestic single-domain subjects (p=0.05) (Table 2).

Regarding non-motor features, PD-MCI subtypes did not differ in depression or psychosis. Amnestic multiple-domain PD-MCI subjects were treated more frequently with antidepressants or anxiolytics, compared to nonamnestic multiple-domain PD-MCI subjects. As defined, PD-MCI subtypes differed significantly in cognitive and MMSE scores (F [3, 124] 18.86, p<0.0001), with the lowest MMSE scores in nonamnestic multiple-domain PD-MCI subjects (Table 3, Supplemental table). There was a trend for greater use of cognitive medications (i.e., cholinesterase inhibitors or memantine) in amnestic multiple-domain PD-MCI subjects (χ^2 [3, N=128]=7.49, p=0.06).

We also compared single- and multiple-domain PD-MCI subtypes to examine differences related to degree of cognitive dysfunction rather than qualitative categorization as amnestic or nonamnestic. Compared to single-domain PD-MCI subjects, multiple-domain PD-MCI subjects had significantly worse MMSE scores (t [126] = 5.11, p<0.001) and more frequent cognitive complaints (t [126] = 2.17, p=0.03). Multiple-domain PD-MCI subjects had worse

motor function as measured by Hoehn and Yahr stage (t [126] = 1.96, p=0.05) and UPDRS factors reflecting axial/gait function (t [119] = 2.31, p=0.02) and left-sided bradykinesia (t [119] = 2.09, p=0.04).

Predictors of PD-MCI subtype

We assessed predictors of PD-MCI subtypes using multinominal logistic regression models with age, PD duration, LEDD, Hamilton Depression Rating score, vascular risk factor score, and motor severity (Hoehn and Yahr staging, UPDRS motor factors, or UPDRS total motor score) as predictors and PD-MCI subtype as the dependent variable. Hoehn and Yahr stage contributed significantly to the model (χ^2 = 10.58, df 3, p = 0.01), with significant differences in nonamnestic multiple-domain PD-MCI compared to amnestic single-domain PD-MCI (Wald 8.89, p=0.003). Of the UPDRS motor factors, only axial functioning/gait contributed significantly (χ^2 = 8.33, df 3, p = 0.04), with significant differences between nonamnestic multiple-domain and amnestic single-domain PD-MCI (Wald 5.92, p=0.02). Age, PD duration, LEDD, depression, vascular factors, or UPDRS total motor scores did not predict PD-MCI subtype.

Discussion

The main finding of our study was that PD-MCI subtypes differed in motor stage and axial functioning/gait, in addition to cognitive phenotype. Our findings suggest a link between nonamnestic multiple-domain PD-MCI and motor impairment, particularly axial functioning/gait disturbances. Few studies have examined PD-MCI subtypes and their motor features, and to our knowledge, none has described discrete UPDRS motor factors. In the largest reported PD-MCI cohort (n=1346) drawn from eight centers, amnestic and nonamnestic multiple-domain PD-MCI subtypes had worse motor symptoms than single-domain PD-MCI subjects, but additional details regarding motor phenotype were not presented [14]. Other studies included small PD-MCI cohorts. In a longitudinal study of 38 PD-MCI subjects, at baseline examination, those with multiple nonamnestic domains "slightly impaired" (n=15) had higher mean Hoehn and Yahr stages than those with amnestic impairment (n=6) [6]. In a retrospective chart review of 38 PD-MCI subjects, comparison of single-domain vs. multiple-domain, or amnestic vs. nonamnestic subtypes did not reveal statistically significant differences in motor characteristics, though details were not given and subject numbers, small [19].

Greater motor severity and worse cognitive function have been associated with shared neural substrates, increased dementia risk, and earlier dementia onset [6–8, 42, 43]. Specifically, the axial motor phenotype, characterized by postural instability and gait disturbance, may be linked to cognitive impairment in PD [44, 45]. Cholinergic deficits in the pedunculopontine nucleus and neocortex may underlie PD-related postural instability and gait disturbances [46, 47] and in basal forebrain nuclei, prefrontal and temporal regions, may impair attentional/executive function and memory in PD [46, 48]. Increased fall risk in PD may be associated with worse performance on frontal lobe tasks [49, 50]; PD patients with attentional/executive dysfunction demonstrate variable gait and slower speeds when simultaneously walking and performing cognitive tasks [51, 52].

Vascular risk factors, which have been associated with cognitive and gait impairment, were low in our PD-MCI cohort overall. Nonamnestic multiple-domain PD-MCI had higher median scores, though not statistically significant. White matter lesions on brain magnetic resonance imaging (MRI) [53–55] have been associated with increased gait variability [56] and falls [57] in older adults and in one PD study, the postural instability/gait difficulty-dominant phenotype [54]. Neuroimaging may help elucidate the relationships between PD-MCI subtypes, gait impairment, and vascular burden.

The cognitive profile of our PD-MCI cohort featured predominantly nonamnestic deficits and single-domain phenotype, similar to other studies [1, 13, 15, 16, 18]. Of the nonamnestic domains impaired, attentional/executive function and visuospatial abilities were primarily affected. The high rate of visuospatial impairment may signify greater posterior-cortical impairment, which in some studies confers an increased dementia risk [7, 58, 59]. In our cohort, both multiple-domain PD-MCI subtypes had prominent visuospatial deficits. Multiple-domain PD-MCI subtypes demonstrated a greater burden of cognitive dysfunction (i.e., lower MMSE and other cognitive scores) compared to single-domain PD-MCI, and thereby reflect a gradient of cognitive severity and a progressive distribution of neuroanatomical regions involved in cognitive deficits. Similarly, greater postural instability may signal advancing motor severity and non-dopaminergic involvement. Of particular interest in our cohort, however, was that the two multiple-domain PD-MCI subtypes differed in motor profile, with only nonamnestic multiple-domain PD-MCI exhibiting significantly worse axial functioning/gait. Distinct cognitive and motor phenotypes within multiple-domain subtypes may indicate different contributions from PD, coexistent AD, vascular disease, or other neuropathologies. Longitudinal follow-up studies of our PD-MCI cohort will permit investigations of cognitive and motor progression.

With growing recognition of PD-MCI as a construct and pre-dementia state, a greater understanding of PD-MCI subtypes, their neurobiology, and progression is paramount to advancing our treatments for cognitive decline. In non-PD populations, MCI subtypes may differ in etiologies and conversion rates to dementia. Amnestic subtypes (in non-PD) are more likely to convert to AD; nonamnestic subtypes typically develop non-AD dementias or depression [4, 5, 60, 61]. MCI subtypes vary in their progression; some MCI patients even improve to normal cognition at follow-up, while others remain stable or decline. Higher rates of improvement in nonamnestic single-domain impairment MCI and higher rates of decline in multiple-domain impairment or amnestic subtypes have been reported at follow-up [60, 62–64]. Additionally, MCI subtypes may have different functional consequences [65, 66], with worse financial management abilities in amnestic MCI and worse performance on health and safety measures in nonamnestic MCI.

In PD, there is increasing evidence from neuroimaging, genetics, and neuropathology that different cognitive phenotypes reflect different neurobiological substrates. Compared to amnestic MCI patients without PD, amnestic PD-MCI (single- and multiple-domain impairment) patients exhibited prefrontal and temporal lobe atrophy [67] and hypoperfusion in parieto-occipital regions on neuroimaging studies [68]. Single-domain PD-MCI patients also demonstrated prefrontal and parietal lobe atrophy, regions similarly affected in multiple-domain PD-MCI but to a greater extent [67, 69]. Genetic studies suggest dissociations between fronto-striatal and posterior-cortical dysfunction in PD. Catechol-O-methyl transferase Val158Met gene polymorphisms, linked to executive functions, were not associated with dementia over 5-year follow-up of an incident PD cohort [58], whereas microtubule-associated protein tau H1/H1 genotypes, associated with posterior-cortical functions, were [58 70]. The neurochemistry of cognitive processes, however, is complex, involving dopaminergic and non-dopaminergic neurotransmitters with direct, indirect, and modulating effects. Classic dopaminergic deficits associated with PD executive function may depend on disease duration and stage; [71] executive functions also have monoaminergic and cholinergic influences [72, 73], and dopamine plays a role in learning and memory [74]. With neuropathological examination of eight PD-MCI cases (mixed subtypes) revealing mixed Lewy bodies, AD, and cerebrovascular pathologies [75], future biomarker and post-mortem studies of nonamnestic and amnestic PD-MCI subtypes are needed to delineate the neural substrates of these heterogeneous clinical phenotypes and identify cases with co-existent PD and AD pathology.

Our study's strengths include a large, well-defined PD cohort, diagnosis by Movement Disorder specialists, and detailed motor and cognitive characterizations including factors (e.g., medications, mood, disorders, and vascular disease), which can affect cognitive function. As diagnostic criteria specifically for MCI in PD have only been recently developed [2], we utilized well-recognized classification schema for MCI and its subtyping [5, 22] and excluded PDD using currently recommended MDS-PDD criteria [3]. Our rationale for amnestic/nonamnestic MCI subtyping was rooted not only in historical AD and MCI literature and PD-MCI studies to date, but also in our investigation of distinct clinical and neurobiological substrates in amnestic and nonamnestic phenotypes. With large PD-MCI cohorts and collaborative efforts, future studies can compare PD-MCI subtypes across individual cognitive domains and using recently proposed MDS PD-MCI criteria.

Limitations include our university setting and relatively highly educated subjects, which may diminish the direct extrapolation of our findings to a general population. A number of neuropsychological decisions (e.g., selection and number of tests administered, classification of tests in cognitive domains, and cut-off scores for defining MCI) were anchored in frequently used neuropsychological schemas and our own experience, [1, 20, 21] and thus, could lead to over- or under-estimations of PD-MCI and its subtypes. In the evolving area of PD-MCI, definitive guidelines for these issues have not yet been established, and recently published MDS PD-MCI criteria await validation. In the absence of large samples suitable for factor analyses of cognitive domains [76], we followed general neuropsychological principles and previous literature in classifying neuropsychological tests into cognitive domains. With this methodology, our concept of an executive system encompassed executive functions and attentional roles [77–79]. Neuropsychological tests can be grouped into cognitive domains differently; some tests have overlapping features (e.g., executive components of visuospatial tests), and others may be sensitive to deficits in more than one area (e.g., category fluency and temporal and frontal dysfunction). Also, although our PD-MCI cohort was relatively large (n=128), the nonamnestic multiple-domain subtype was the smallest. Although we assessed and controlled for this statistically, non-balanced groups may affect results, and findings related to the smaller group will require replication in larger samples. Lastly, our motor evaluation focused specifically on the UPDRS Part III (total score and component factor analyses) and Hoehn and Yahr staging, but future studies incorporating dual-tasking paradigms or other motor analyses may clarify the motor associations of attentional/executive dysfunction.

We conclude that besides the heterogeneous cognitive phenotype of PD-MCI, PD-MCI subtypes may be distinguished by their motor profile. These findings suggest the association of nonamnestic multiple-domain PD-MCI and greater axial/gait dysfunction. Longitudinal studies of large, well-defined PD-MCI cohorts will be needed to determine the progression and prognoses of different PD-MCI subtypes and to compare effects of increased burden of cognitive dysfunction (i.e., multiple-domains affected) and type of cognitive deficit (i.e., amnestic or nonamnestic deficits) on the risk of dementia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

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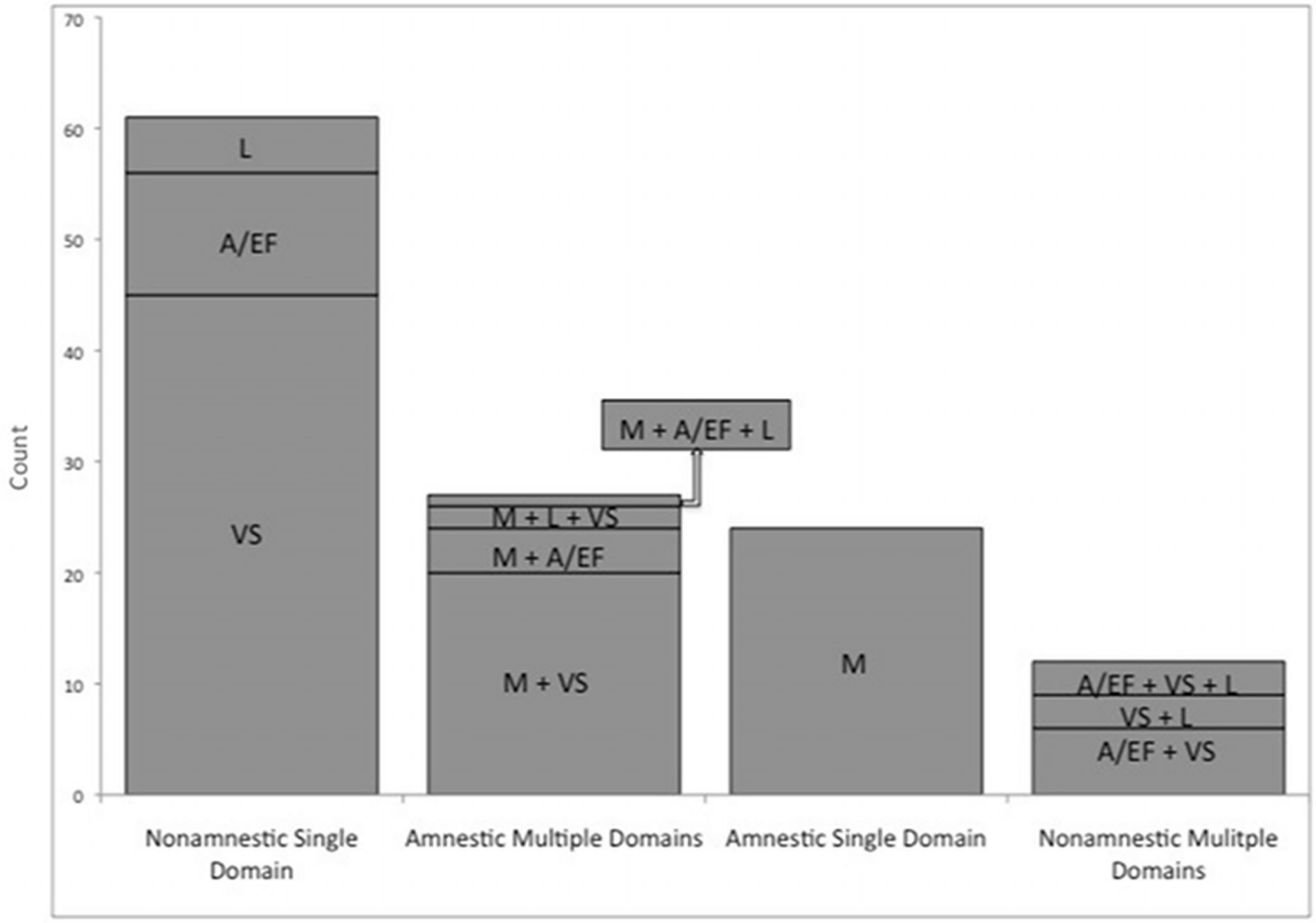

Figure 1.

Table 1

Clinical characteristics of PD-MCI subtypes

	Amnestic Single-domain N=24	**Amnestic Multiple-domain N=31**	**Nonamnestic Single-domain N=61**	**Nonamnestic Multiple-domain N=12**	**p value**
Age, years	72.79 (10.57)	71.81 (6.83)	70.51 (10.88)	76.50 (6.01)	0.24
Male, n (%)	16 (66.7)	20 (64.5)	32 (52.5)	8 (66.7)	0.51
Education, years	15.50 (3.67)	14.39 (3.01)	14.26 (2.48)	15.25 (3.02)	0.37
PD duration, years	5.54 (4.13)	7.06 (4.04)	7.64 (5.16)	9.04 (7.18)	0.19
UPDRS total motor score	28.43 (11.46)	31.83 (11.07)	29.97 (12.08)	36.42 (11.07)	0.24
Hoehn & Yahr stage (median, range)	2.0, 2–4	2.0, 2–5	3, 1–4	3, 2–5 *	0.04
Vascular risk factor score (median, range)	1.0, 0–5	1.0, 0–4	1.0, 0–4	1.5, 0–3	0.57
LEDD, mg/d	375.63 (308.42)	524.84 (368.89)	550.33 (552.65)	753.96 (438.20)	0.14
Agonist, n (%)	6 (25.0)	10 (32.3)	24 (39.3)	4 (33.3)	0.65
Mood medication (antidepressant/anxiolytic), n (%)	8 (33.3)	14 (45.2)	21 (34.4)	0 (0) +	0.05
Sleep medication, n (%)	4 (16.7)	5 (16.1)	9 (14.8)	3 (25.0)	0.86
Antipsychotic, n (%)	3 (12.5)	3 (9.7)	1 (1.6)	1 (8.3)	0.21
Cognitive medication, n (%)	2 (8.3)	7 (22.6)	4 (6.6)	0 (0)	0.06

Data presented as mean (SD), unless otherwise noted.

Abbreviations: LEDD, levodopa equivalent daily doses; UPDRS, Unified Parkinson's Disease Rating Scale.

* Nonamnestic multiple-domain vs. Amnestic single-domain PD-MCI, p=0.04;

+ Nonamnestic multiple-domain vs. Amnestic multiple-domain PD-MCI, p=0.03

Table 2

UPDRS factor scores for PD-MCI subtypes

	Amnestic Single-domain N=24	**Amnestic Multiple-domain N=31**	**Nonamnestic Single-domain N=61**	**Nonamnestic Multiple-domain N=12**	**p value**
Axial functioning/gait	5.90 (2.87)	6.89 (3.54)	5.97 (3.32)	8.84 (4.12) *	0.05
Rest tremor	1.48 (1.82)	1.78 (2.22)	1.43 (2.22)	1.17 (2.05)	0.83
Rigidity	5.17 (2.41)	4.96 (2.41)	5.35 (2.57)	6.08 (1.72)	0.59
Left side bradykinesia	3.96 (2.41)	4.79 (2.02)	4.29 (1.90)	5.53 (1.83)	0.12
Right side bradykinesia	3.54 (1.86)	4.27 (2.02)	4.01 (2.14)	4.84 (1.49)	0.30
Postural tremor	1.13 (1.20)	1.14 (1.16)	1.27 (1.18)	0.74 (1.13)	0.56

Data presented as mean (SD), unless otherwise noted.

* Nonamnestic multiple-domain vs. nonamnestic single-domain, p=0.05

Table 3

Neuropsychological features and cognitive domain scores for PD-MCI subtypes

	Amnestic Single-domain N=24	**Amnestic Multiple-domain N=31**	**Nonamnestic Single-domain N=61**	**Nonamnestic Multiple-domain N=12**	**p value**
MMSE	27.88 (1.92) *	26.39 (1.91)	27.87 (1.48) ^	25.08 (3.45)	<0.0001
Cognitive complaints, n (%)	18 (75)	31 (100) †	48 (78.7)	9 (75)	0.04
Hamilton Depression rating scale	5.61 (3.24)	7.61 (4.36)	7.39 (4.16)	7.33 (3.75)	0.26
UPDRS Thought disorder score (median, range)	0, 0–3	0.5, 0–4	0.5, 0–3	0.5, 0–1	0.84
Cognitive domain z-scores					
Attentional/Executive Function	−0.70 (0.58)	−1.17 (0.57)	−0.82 (0.70)	−1.58 (0.50)	<0.0001
Memory	−1.95 (0.31)	−1.97 (0.40)	−0.60 (0.59)	−0.82 (0.54)	<0.0001
Language	0.89 (1.23)	0.25 (1.48)	0.55 (1.33)	−1.47 (2.44)	0.02
Visuospatial	−0.78 (0.71)	−2.95 (3.13)	−1.91 (1.66)	−2.77 (0.95)	<0.0001

Data presented as mean (SD), unless otherwise noted.

Abbreviations: MMSE, MiniMental State Examination; UPDRS, Unified Parkinson's Disease Rating Scale.

* Amnestic single-domain vs. Amnestic multiple-domain, p=0.03; vs. Nonamnestic multiple-domain, p<0.0001;

^ Nonamnestic single-domain vs. Amnestic multiple-domain, p=0.004; vs. Nonamnestic multiple-domain, p<0.0001;

† Amnestic multiple-domain vs. Amnestic single-domain, p=0.02; vs. Nonamnestic single-domain, p=0.04; vs. Nonamnestic multiple-domain, p=0.02