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Authors

Besser, Lilah M
Litvan, Irene
Monsell, Sarah E
et al.

Publication Date

2016-06-01

DOI

10.1016/j.parkreldis.2016.04.007

Peer reviewed

HHS Public Access

Author manuscript

Parkinsonism Relat Disord. Author manuscript; available in PMC 2017 June 01.

Published in final edited form as:

Parkinsonism Relat Disord. 2016 June ; 27: 54–60. doi:10.1016/j.parkreldis.2016.04.007.

Mild cognitive impairment in Parkinson's disease versus Alzheimer's disease

Lilah M. Besser, MSPH[1,*], **Irene Litvan, MD**[2], **Sarah E. Monsell, MS**[1], **Charles Mock, MD, PhD**[1], **Sandra Weintraub, MD**[3], **Xiao-Hua Zhou, PhD**[1], and **Walter Kukull, PhD**[1]

[1] National Alzheimer's Coordinating Center, University of Washington, 4311 11th Ave NE, Suite 300, Seattle, WA 98105

[2] University of California San Diego, Department of Neurosciences, National Parkinson Foundation Movement Disorder Center of Excellence, 8950 Villa La Jolla Drive, Suite C112, La Jolla, CA 92037

[3] Cognitive Neurology and Alzheimer's Disease Center, and Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, 320 E Superior, Searle 11-467, Chicago, IL 60611

Abstract

Introduction—No known studies have compared longitudinal characteristics between individuals with incident mild cognitive impairment due to Parkinson's disease (PD-MCI) versus Alzheimer's Disease (AD-MCI).

[*]**Corresponding Author Contact:** Lilah Besser, 4311 11th Ave NE, Suite 300, Seattle, WA 98105; Phone: 206-616-5759; Fax: 206-616-5927; ; Email: lmbesser@uw.edu
Co-authors:
Irene Litvan, ilitvan@ucsd.edu
Sarah Monsell, smonsell@uw.edu
Charles Mock, cmock@u.washington.edu
Sandra Weintraub, sweintraub@northwestern.edu
Xiao-Hua Zhou, azhou@u.washington.edu
Walter Kukull, Kukull@uw.edu

Statistical Analysis completed by: Lilah Besser, University of Washington

Author Contributions

Lilah Besser was responsible for the study design and analyses, and was the primary author of the manuscript.
Irene Litvan was responsible for study design and content and editing of the manuscript for intellectual content.
Sarah Monsell was responsible for advising on study design and analysis and editing of the manuscript for intellectual content.
Charles Mock was responsible for editing of the manuscript for intellectual content.
Sandra Weintraub was responsible for editing of the manuscript for intellectual content.
Andrew Zhou provided advice on analysis and interpretation of the data.
Walter Kukull was responsible for editing the manuscript for intellectual content.

Disclosures

Lilah Besser reports no disclosures.
Sarah Monsell reports no disclosures.
Charles Mock reports no disclosures.
Xiao-Hua Zhou reports no disclosures.
Walter Kukull reports no disclosures.

Methods—We used longitudinal data from the National Alzheimer's Coordinating Center's Uniform Data Set to compare 41 PD-MCI and 191 AD-MCI participants according to their demographics, presence of ≥1 APOE e4 allele, and baseline and change over time in clinical characteristics, neuropsychological test scores, and Clinical Dementia Rating sum of boxes (CDR-SB). Multivariable linear regression models with generalized estimating equations were used to account for clustered data and to test for baseline and longitudinal differences in neuropsychological test scores.

Results—PD-MCI and AD-MCI participants differed by many demographic and clinical characteristics. Significantly fewer PD-MCI participants developed dementia over one year. Compared to AD-MCI participants, PD-MCI participants performed better at baseline and over time on a global measure of cognition (Mini Mental State Exam), memory measures (immediate and delayed Logical Memory), and a language measure (Boston Naming Test), and additionally performed better over time on an attention measure (Digit Span Forward), a language measure (Vegetable List), a processing speed measure (Digit Symbol), and an overall measure of memory and functional impairment (CDR-SB).

Conclusion—Our study provides further evidence that PD-MCI is clinically distinct from AD-MCI and requires different tools for diagnosis and monitoring clinical progression. More importantly, this study suggests that PD-MCI takes longer to convert into dementia than AD-MCI, findings that require replication by other studies.

Keywords

Parkinson's disease; mild cognitive impairment; Alzheimer's disease; neuropsychological assessment; clinical progression

1. Introduction

Approximately 27% of non-demented individuals with Parkinson's disease have mild cognitive impairment (PD-MCI), and up to 60% with PD-MCI convert to PD dementia within four years [1-5]. While some studies have found that PD-MCI participants often have non-amnestic, single domain MCI with deficits in attention, visuospatial function, and executive functioning, other studies have found amnestic presentations of PD-MCI [5]. Although PD-MCI appears to be heterogenous [1-10], previous studies also suggest that the clinical and neuropsychological features are distinct from MCI due to other etiologies, such as Alzheimer's disease (AD-MCI).

In 2012, the Movement Disorders Society (MDS) published PD-MCI diagnostic criteria [11] that were designed primarily to capture and diagnose PD-MCI as a transition state between normal cognition and dementia among participants with PD. Although the MDS developed the new criteria based on an understanding of the typical differences between PD-MCI and MCI due to other etiologies, to our knowledge no studies have compared the longitudinal differences in clinical characteristics and neuropsychological test scores between participants with PD-MCI and AD-MCI. Therefore, our primary aim was to characterize longitudinal changes in participants with incident PD-MCI compared to AD-MCI, the more common MCI etiology.

2. Methods

2.1. Participants

We used longitudinal data collected between September 2005 and March 2015 from the National Alzheimer's Coordinating Center's (NACC) Uniform Data Set (UDS) to study participants at 31 past and present U.S. Alzheimer's Disease Centers (ADC). ADCs have collected demographic, clinical, diagnostic, neuropsychological, and neuropathology data on UDS participants with normal cognition, mild cognitive impairment (MCI), and dementia approximately annually since 2005. UDS participants come from clinic samples, public recruitment efforts, participant referrals, other ongoing studies, and occasionally population-based samples. Because recruitment methods vary, UDS participants are best described as a clinical case series. Additional details about the UDS sample are found elsewhere [12,13].

2.2. Inclusion and exclusion criteria for main sample

We defined MCI in both groups according to the Petersen criteria [14] (the UDS neuropsychological tests limited our ability to define PD-MCI according to the new MDS criteria [11]). The PD-MCI participants had a primary diagnosis of PD (i.e., met the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria for PD) and MCI for ≥1 visit. The AD-MCI participants had primary probable AD as the suspected etiology at the incident MCI diagnosis and at their last UDS visit, and no contributing etiologic diagnosis at any UDS visit. ADCs are required to provide a suspected etiologic diagnosis for participants diagnosed with MCI. We restricted our analyses to incident MCI cases to help reduce clinical or neuropsychological score differences in the groups due simply to differences in time elapsed since diagnosis. We required all participants to have normal cognition or some impairment (impaired not MCI) but not MCI at their initial UDS visit. Impaired not MCI was diagnosed by clinicians as some cognitive impairment not meeting the Petersen criteria for MCI. The first follow-up visit with an incident MCI diagnosis was the starting point for inclusion in this study and is termed the baseline visit. Only participants with at least one UDS visit completed after their baseline MCI visit were included in our analyses.

Among the 31,872 participants in the UDS as of March 2015, 216 met our PD-MCI criteria and 1,065 met our AD-MCI criteria. We excluded those without an incident MCI diagnosis during UDS follow-up and without at least one visit following the baseline visit, resulting in the final sample of 41 PD-MCI and 191 AD-MCI participants.

2.3. Standard protocol approvals, registrations, and patient consents

Research using the NACC database was approved by the University of Washington Institutional Review Board. Informed consent was obtained at the individual ADCs. The NACC data were de-identified.

2.4. Demographic, clinical, and neuropsychological variables

At each UDS visit, information was collected on demographics, self-reported health history, clinical symptoms, and medication use, and participants were evaluated using the standardized UDS neuropsychological test battery and clinical exam. The Unified Parkinson's Disease Rating Scale [UPDRS] was used to measure motor disturbances [15].

The UDS neuropsychological battery [19] contains the Mini-Mental State Examination (MMSE), measuring global cognitive function; Digit Span Forward and Digit Span Backward (Wechsler Memory Scale-Revised [WMS-R]), measuring attention; Digit Symbol (Wechsler Adult Intelligence Scale-Revised [WAIS-R]) and Trail Making Test Part A, measuring processing speed; Trail Making Test Part B, measuring executive function; Immediate and Delayed Logical Memory (WMS-R), measuring episodic memory; and Animal list generation, Vegetable list generation, and the Boston Naming Test (BNT), measuring language. Visuospatial function was measured using the MMSE pentagon score (1=correct, 0=incorrect).

Participants (and their co-participants) reported any prescription medication use within two weeks preceding the UDS visit. We created variables to indicate use of: 1) anticholinergics, 2) amantadine, 3) dopaminergics, 4) memantine, 5) cholinesterase inhibitors, and 6) RBD medications (drug list, Supplemental Table 1). We used existing NACC variables to assess use of antipsychotics and antidepressants (NACC's derived variables documentation [17]). The Clinical Dementia Rating (CDR) was conducted at each visit. The CDR sum of boxes (CDR-SB) is a summary measure of scores for memory, orientation, judgment, community affairs, home and hobbies, and personal care, and ranges from 0 (no impairment) to 18 (greatest impairment). During the neurological exam, clinicians determine whether one or more of the following domains are affected: memory, language, attention, executive function, and visuospatial function. Dementia was diagnosed by meeting the standard criteria for dementia of the Alzheimer's type or for other non-Alzheimer's dementing disorders. Diagnoses were made by a single qualified clinician or through consensus by a team of clinicians.

2.5. Neuropathology data sample

The standardized Neuropathology Form and Coding Guidebook were used to collect neuropathological examination data [18,19]. Our analysis focused on neuropathology was restricted to participants with MCI, a clinical diagnosis primary PD, and no contributing AD diagnosis at their last visit before death. AD-MCI participants had MCI, an etiologic diagnosis of primary probable AD, and no contributing diagnoses at the last visit before death. Most of the participants in the main sample (n=235) (described above) were not in the neuropathology sample (n=38), and only 11 of the 38 participants with neuropathology data were in the main sample.

Neuropathological diagnoses were not used when defining the two groups because we aimed to describe the underlying neuropathology among those with clinical PD-MCI compared with clinical AD-MCI. The two groups were compared according to the neuritic plaque density (none, sparse, moderate, frequent), Braak stage for neurofibrillary degeneration (Stages 0, I/II, III/IV, V/VI), Lewy body (LB) pathology (no pathology, brainstem predominant, limbic, neocortical, or other/unspecified region) and presence of cerebrovascular disease (large artery infarct or lacune, microinfarct [cortical infarcts observed only through a microscope], cerebral hemorrhage or microbleed).

2.6. Main sample data analyses

We compared AD-MCI and PD-MCI groups by age, education, sex, race, ≥1 APOE e4 allele, affected cognitive domains (e.g., neurological assessment of whether visuospatial domain affected), and vascular risk factors. The two groups were then compared at baseline and one year later by an incident diagnosis of dementia, CDR-SB, impaired visuospatial function (MMSE pentagon score), motor symptoms, depressive symptoms, hallucinations, RBD, UPDRS scores (total motor score, postural instability gait disorder [PIGD] score [20], and tremor score [20]), and medication use. Approximately 62% of AD-MCI participants were missing part or all of the UPDRS; therefore, we were not able to test for statistically significant differences in UPDRS scores between the PD-MCI and AD-MCI participants. We focused on changes over one year because not all participants had a third follow-up visit and because one-year change can be a clinically useful measure. Differences were tested using the Pearson chi-squared test (categorical variables) or the t-test or Wilcoxon-Mann-Whitney test (normal or non-normal continuous variables). The Fisher's exact test was used when at least one comparison group included <10 participants. For all results, statistical significance was based on an alpha level of 0.05 [21].

Neuropsychological test scores (all except CDR-SB) were transformed into z-scores. Participants with normal cognition at their initial visit (normal cognition diagnosis and global CDR=0) served as the reference group in calculating z-scores (n=10,680).

Twelve separate linear regression models were run using generalized estimating equations (GEE) to test for differences in the baseline neuropsychological test z-scores. GEE accounted for Center clustering. For most tests, <11% of the participants were missing z-scores at baseline and none were missing CDR-SB. The models were first run without adjusting for covariates and were re-run controlling for baseline age, sex, and education.

Unadjusted and multivariable linear regression models with GEE were used to compare mean annual change in z-scores in the two groups. Using SAS PROC GENMOD, we first ran the multivariable models adjusting for baseline age, education, and sex, and then additionally adjusting for ≥1 APOE e4 allele.

2.7. Analysis of the neuropathology sample

We compared the demographic, clinical, and neuropathological characteristics between participants who were diagnosed with PD-MCI and AD-MCI at their last visit before death. Differences were tested using the Fisher's exact test (categorical variables) or Wilcoxon-Mann-Whitney test (non-normal continuous variables).

2.8. Post-hoc analyses

In post-hoc analyses we tested whether certain characteristics (visuospatial function, depression, RBD, use of cholinesterase inhibitors, antipsychotics, and RBD medications) changed from baseline to one year later within each diagnostic group. Six unadjusted logistic regression models (using GEE) were run to test whether those characteristics changed over one year in the two groups separately.

3. Results

3.1. Baseline demographic and clinical characteristics

Compared to AD-MCI participants, PD-MCI participants were younger at MCI diagnosis, younger at initial cognitive decline onset (occurred a few years earlier than the MCI diagnosis), had better memory but were more often affected in the attention and executive function domains, and less often had ≥1 APOE e4 allele ($p<0.05$) (Table 1). PD-MCI participants reported a history of heart disease, heart procedure or stroke significantly more often than AD-MCI participants ($p<0.05$) (Supplemental Table 2).

3.2. Clinical characteristics at baseline and one year later

Compared to AD-MCI participants, PD-MCI participants were less often diagnosed with dementia one year after baseline (Table 2). Depressive symptoms and RBD were more frequent in PD-MCI participants than AD-MCI participants. The one-year change in participants experiencing depressive symptoms and RBD was not significant in either group, whereas the percent with impaired visuospatial function increased over one year among AD-MCI participants ($p<0.05$).

Over one year, the percent using antipsychotics, antidepressants, or RBD medications did not significantly change in either group ($p>0.05$), however the percent of AD-MCI participants using cholinesterase inhibitors increased ($p<0.05$). Most PD-MCI participants reported using dopaminergics at baseline, and more PD-MCI participants than AD-MCI participants used antipsychotics and antidepressants at baseline and one year later.

3.3. Differences in baseline neuropsychological test scores

In unadjusted analyses, PD-MCI participants performed better than AD-MCI participants at baseline on the MMSE, immediate and delayed Logical Memory, Digit Span Forward, Animals list generation, and BNT (Table 3). After adjusting for age, sex, and education, PD-MCI participants performed better at baseline on the MMSE, immediate and delayed Logical Memory, and the BNT (Table 3).

3.4. Differences in annual change in neuropsychological test scores

In the unadjusted analysis and the multivariable analysis controlling for age, sex, and education, PD-MCI participants performed better over time than AD-MCI participants on the MMSE, immediate and delayed Logical Memory, Digit Span Forward, Vegetable List generation, BNT, Digit Symbol, and CDR-SB (Table 4). After additionally controlling for ≥1 APOE e4 alleles, the findings were essentially unchanged (Supplemental Table 3).

3.5. Neuropathological findings

LB pathology was present in all PD-MCI participants and 22% of AD-MCI participants (Supplemental Table 4). The majority of PD-MCI participants had low neurofibrillary degeneration (Braak stages 0-II), whereas the majority of AD-MCI participants had high neurofibrillary degeneration (Braak stages III-VI). Cerebrovascular pathology was not statistically significantly different in the two groups.

4. Discussion

This is the first study to assess the longitudinal differences in clinical and neuropathological features between PD-MCI and AD-MCI. We had several interesting findings. First, PD-MCI participants were less likely than AD-MCI participants to develop dementia one year after their incident MCI diagnosis. Second, PD-MCI participants performed better over time on a global cognition measure (MMSE), memory measures (immediate and delayed Logical Memory), an attention measure (Digit Span Forward), language measures (Vegetable list generation, BNT), a processing speed measure (Digit Symbol), and a global measure of memory and functional impairment (CDR-SB). Third, while there were no between-group differences in the cholinesterase inhibitor use at baseline, there was a higher proportion of AD-MCI participants taking them one year later. Fourth, all PD-MCI participants had LB pathology, but Lewy bodies were also found in a minority of AD-MCI participants. On the other hand, less neurofibrillary degeneration was present in the majority of PD-MCI participants.

The percent of PD-MCI participants progressing to dementia was low one year after baseline. Our findings are supported by another study that found that 8% of incident PD-MCI subjects developed dementia over two years [1]. On the other hand, our findings differ from those of another previous study that reported that 62% of PD-MCI participants developed dementia within 4 years [3]. Differences in findings may be explained by the fact that our study included incident cases followed for a shorter period of time.

The majority of the PD-MCI participants experienced memory problems. While many studies suggest that PD-MCI is typically non-amnestic [8,22], others have found PD-MCI to be amnestic [7,10]. ADCs have often focused recruitment on AD and memory impairment; therefore, it is not surprising that most PD-MCI participants had memory problems. A population-based study would better address the prevalence of affected domains among PD-MCI and AD-MCI participants.

Some studies have indicated that visuospatial abilities are impaired in the earlier stages of AD [23], and our limited analysis using the MMSE pentagon test suggests that this extends to AD-MCI participants. Most of our PD-MCI participants did not have impaired visuospatial function, which is consistent with previous studies suggesting visuospatial function is not always impaired in PD participants [24,25].

Among the clinical characteristics examined, RBD was present in approximately one-third of PD-MCI participants, consistent with previous prevalence estimates [26], and was rarely experienced by AD-MCI participants. Motor symptoms were present in all of the PD-MCI participants and approximately 20% of AD-MCI participants at baseline and one year after baseline. Motor symptoms are not that uncommon in the earlier stages of AD and have been suggested to be associated with undiagnosed LB disease or a previous infarct [27]. However, other studies suggest that different motor symptoms in AD may be due to differing mechanisms that have yet to be explained [28]. In our study, few in the AD-MCI group had LB pathology and they less often had infarcts compared to the PD-MCI group. Therefore, research is needed to investigate the underlying cause of motor symptoms in AD-MCI.

Our findings suggest that cholinesterase inhibitors are not often being prescribed to treat the cognitive symptoms of PD-MCI participants. Approximately 20% of both PD-MCI and AD-MCI participants reported using these medications. Some drug trials have indicated that their use could improve cognition among participants with Parkinson's disease dementia and dementia with Lewy bodies [29]. However, improved cognition in PD through the use of cholinesterase inhibitors can be accompanied by the increased tremor and adverse drug reactions [30].

The neuropathological results were consistent with expectations in which PD-MCI participants would have more LBD pathology and less AD neuropathology than AD-MCI participants. However, some PD-MCI participants had substantial AD neuropathology. Although not statistically significant, possibly due to a small sample size, the PD-MCI participants more often had infarcts or lacunes than the AD-MCI participants, whereas the AD-MCI participants more often had microinfarcts than the PD-MCI participants. Additional studies with larger autopsy samples of PD-MCI are needed to assess the heterogeneity in neuropathology and how it relates to clinical symptoms and subtypes of PD-MCI.

Strengths of our study include the use of prospectively collected clinical and neuropsychological data by the ADCs. Another strength of our study is the focus on participants with incident MCI, allowing us to provide clinically relevant estimates of progression and symptoms in the year following the initial diagnosis of MCI, which could be useful when advising patients on expected clinical progression.

Our study has limitations, including the potential lack of generalizability given the varying methods of recruitment at the ADCs and the higher education levels of the sample. Also, we were limited to using the Petersen MCI criteria instead of the MDS PD-MCI criteria. While we were able to detect significant between-group differences, the small sample size of incident PD-MCI participants may have limited our ability to detect true differences in some of the examined characteristics. Additionally, the number of AD-MCI and PD-MCI participants with an autopsy-confirmed diagnosis was too small to include in our study; therefore, it is possible that some of the participants were misdiagnosed with PD or AD. In addition, the MMSE pentagon test is not the best measure of visuospatial function, but it was all that was available. Finally, to assess the impact of test score data missing >1 year after the baseline visit (due to staggered enrollment dates or attrition), we conducted a sensitivity analysis using linear mixed models to account for data missing at random. The results were very similar with the exception that Vegetable List generation was not significantly different between the two groups (beta estimate: 0.06; 95% CI: −0.04, 0.17). Further studies are needed to replicate our findings.

Our study is the first known paper to examine clinical, neuropathological, and longitudinal differences among participants with a clinical diagnosis of incident PD-MCI and AD-MCI. Given the potential lack of generalizability and the number of other potential limitations, additional studies are needed to replicate our findings. Future work could address the longitudinal differences in PD-MCI and AD-MCI by factors common to both, such as depression, medication use, and vascular comorbidities. Additionally, future work could

examine longitudinal progression of different subtypes of incident PD-MCI, as defined by cognitive domains and non-cognitive clinical features. The results from our study provide further evidence that PD-MCI is clinically very different than AD-MCI, and may require different clinical and neuropsychological instruments to diagnose and monitor clinical progression as well as different therapeutic management strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The NACC database is funded by NIA/NIH Grant U01 AG016976. NACC data are contributed by the NIA-funded ADCs (listed individually in the Supplement). The authors thankfully acknowledge the patients and families enrolled at the ADCs who contributed data to the UDS and the faculty and staff of the ADCs who conducted the evaluations and collected the data used in these analyses. The authors would also like to thank the NIA, which provided support for the ADCs and NACC, as well as NACC staff (Duane Beekly, George Thomas, Mark Bollenbeck, Janene Hubbard, Mary Jacka, Joylee Wu, Elizabeth Robichaud, Nicole Barlow, Merilee Teylan, and Margaret Dean), without whom this research would not be possible.

Study funding: The National Alzheimer's Coordinating Center is funded by NIH U01 AG016976.

Irene Litvan was member of the Advisory Board or consultant for Pfizer, TEVA, MERZ, Northera, Bristol-Myers Squibb and UCB. Her research is funded by the National Institutes of Health 5P50 AG005131-31, 5T35HL007491, 1U01NS086659, 1U54NS092089-01, Parkinson Study Group, Michael J Fox Foundation, CBD Solutions-CurePSP, Teva Pharmaceuticals and AVID Pharmaceuticals.

Sandra Weintraub has research support from grant AG13854 (Alzheimer Disease Center) from the National Institute on Aging and grant DC008552 from the National Institute on Deafness and Communication Disorders.

This study is not industry sponsored.

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- Our findings suggest that cognitive decline and progression to dementia is slower in PD-MCI than AD-MCI subjects after the incident diagnosis.
- We found many differences in baseline and longitudinal characteristics in the two groups.
- Overall, our study provides further support for the distinction between PD-MCI and AD-MCI.
- Future work is needed to replicate our findings, especially regarding the slower progression to dementia in PD-MCI than AD-MCI.
- New studies could expand upon our findings to examine longitudinal changes in clinical and neuropsychological characteristics by PD-MCI subtypes.

Table 1

Characteristics of Uniform Data Set sample at baseline

Characteristics at baseline visit *	PD-MCI n=41	AD-MCI n=191	p-value
Number of visits, mean (SD)	3.5 (1.5)	3.3 (1.3)	0.51
Age at baseline (years), mean (SD)	70.2 (8.5)	79.1 (10.3)	<.001
Education (years), mean (SD)	16.0 (2.5)	15.6 (3.1)	0.40
Male, n (%)	25 (61.0%)	95 (49.7%)	0.19
Non-white race, n (%)	3 (7.3%)	34 (18.0%)	0.10
Age of cognitive decline onset, mean (SD)	67.6 (9.3)	76.5 (10.8)	<.001
Memory domain affected †	26 (63.4%)	182 (95.3%)	<.001
Language domain affected †	2 (4.9%)	29 (15.2%)	0.13
Attention domain affected †	16 (39.0%)	16 (8.4%)	<.001
Executive function domain affected †	24 (58.5%)	65 (34.0%)	0.003
Visuospatial domain affected †	5 (12.2%)	10 (5.2%)	0.10
≥1 APOE e4 allele, n (%)	7 (20.6%)	64 (41.8%)	0.02
Age at PD diagnosis, mean (SD)	62.2 (9.9)	NA	NA

Abbreviations: PD-MCI = mild cognitive impairment due to Parkinson's disease; AD-MCI = mild cognitive impairment due to Alzheimer's disease; SD = standard deviation; APOE = apolipoprotein E; PD = Parkinson's disease; NA = Not applicable

* Number of participants missing data (PD-MCI, AD-MCI): Education (0,1), race (0,2), age of cognitive decline onset (0,19), APOE genotype (7,38), age of PD diagnosis (3,not applicable)

† based on clinician's assessment

Table 2

Change in clinical characteristics from baseline to one year following baseline

Characteristics*	Baseline visit			One year after baseline visit		
	PD-MCI	AD-MCI	p-value	PD-MCI	AD-MCI	p-value
Diagnosis of dementia, n (%)	NA	NA	NA	2 (4.9%)	51 (26.7%)	0.002
CDR sum of boxes, mean (SD)	1.4 (1.2)	1.1 (1.0)	0.13	1.3 (1.2)	1.8 (1.5)	0.06
Depressive symptoms, n (%)	11 (31.4%)	17 (11.9%)	0.004	9 (28.1%)	26 (16.6%)	0.13
Visual or auditory hallucinations, n (%)	2 (5.7%)	0 (0.0%)	0.04	1 (3.1%)	1 (0.6%)	0.31
REM sleep behavior disorder (RBD), n (%)	10 (33.3%)	2 (1.5%)	<.001	7 (21.9%)	3 (1.9%)	<.001
Impaired visuospatial function†, n (%)	3 (10.3%)	26 (16.1%)	0.60	5 (14.7%)	44 (26.4%)	0.15
Motor symptoms‡, n (%)	35 (100.0%)	27 (18.8%)	<.001	32 (100.0%)	35 (22.2%)	<.001
UPDRS motor score (range: 0-108), mean (SD)	19.3 (8.8)	4.7 (3.8)	NC	20.0 (9.5)	6.7 (6.4)	NC
UPDRS PIGD score (range: 0-16), mean (SD)	3.2 (2.6)	1.7 (2.2)	NC	3.7 (2.6)	1.9 (2.5)	NC
UPDRS tremor score (range: 0-28), mean (SD)	2.7 (2.8)	0.8 (1.3)	NC	2.6 (2.7)	1.1 (1.7)	NC
Anticholinergic use, n (%)	3 (7.3%)	2 (1.1%)	0.05	4 (9.8%)	0 (0.0%)	0.001
Amantadine use, n (%)	9 (22.0%)	0 (0.0%)	<.001	9 (22.0%)	0 (0.0%)	<.001
Dopaminergic use, n (%)	38 (92.7%)	2 (1.2%)	<.001	38 (92.7%)	2 (1.1%)	<.001
Cholinesterase inhibitor use, n (%)	7 (17.1%)	33 (18.5%)	0.83	9 (22.0%)	49 (27.5%)	0.47
Memantine use, n (%)	0 (0.0%)	12 (6.7%)	0.13	0 (0.0%)	16 (9.0%)	0.05
Antipsychotic use, n (%)	2 (4.9%)	0 (0.0%)	0.03	4 (9.8%)	1 (0.6%)	0.005
RBD medication use, n (%)	4 (9.8%)	4 (2.3%)	0.04	7 (17.1%)	4 (2.3%)	<.001
Antidepressant use, n (%)	14 (34.2%)	31 (17.4%)	0.02	14 (34.2%)	33 (18.5%)	0.03

Abbreviations: PD-MCI = mild cognitive impairment due to Parkinson's disease; AD-MCI = mild cognitive impairment due to Alzheimer's disease; CDR = Clinical Dementia Rating; SD = standard deviation; REM = rapid eye movement; UPDRS = Uniform Parkinson's Disease Rating Scale; PIGD = postural instability/gait disorder; NC = Not calculated (insufficient sample size)

*Number of participants missing data (baseline visit, one year later): Impaired visuospatial function: PD (12,7), AD (29,24); Depression: PD (6,9), AD (48,34); Hallucinations: PD (6,9), AD (47,33); RBD: PD (11,9), AD (57,36); Any motor symptoms PD (6, 9), AD (,); UPDRS motor score: PD (0,2), AD (118,114); UPDRS PIGD: PD (0,2), AD (116,114); UPDRS tremor: PD (0,1), AD (114,112); Anticholinergics: PD (0,0), AD (13,13); Amantadine: PD (0,0), AD (13,13); Dopaminergics: PD (0,0), AD (13,13); Antipsychotics: PD (0,0), AD (13,13); RBD medications: PD (0,0), AD (13,13); Antidepressants: PD (0,0), AD (13,13)

†Did not answer the MMSE pentagon test correctly

‡Gait disorder, tremor, falls, or bradykinesia

Table 3

Mean neuropsychological test z-scores at baseline

	Unadjusted beta (SE)			Adjusted beta (SE)*	
Test	**PD-MCI**	**AD-MCI**	**p-Value**	**Group difference†**	**p-Value**
MMSE total	−0.28 (0.13)	−1.47 (0.18)	<0.001	0.87 (0.30)	0.003
Logical Memory Immediate	−0.81 (0.00)	−1.20 (0.09)	<0.001	0.47 (0.16)	0.004
Logical Memory Delayed	−0.53 (0.00)	−1.39 (0.10)	<0.001	0.72 (0.15)	<.001
Digit Span Forward	−0.22 (0.09)	−0.44 (0.08)	0.02	0.19 (0.10)	0.06
Digit Span Backward	−0.41 (0.05)	−0.45 (0.08)	0.88	−0.04 (0.09)	0.68
Animals list generation	−0.19 (0.19)	−0.74 (0.05)	0.005	0.35 (0.21)	0.09
Vegetables list generation	−0.50 (0.14)	−0.88 (0.09)	0.26	0.16 (0.18)	0.36
Boston Naming Test	0.35 (0.08)	−0.45 (0.10)	<0.001	0.59 (0.15)	<.001
Trail Making Test A‡	−0.57 (0.13)	−0.38 (0.11)	0.30	−0.32 (0.19)	0.10
Trail Making Test B‡	−0.96 (0.25)	−0.99 (0.13)	0.97	−0.27 (0.26)	0.29
Digit symbol	−0.79 (0.11)	−0.77 (0.10)	0.69	−0.23 (0.13)	0.08
CDR sum of boxes (raw score)	1.43 (0.23)	1.16 (0.10)	0.31	0.25 (0.30)	0.41

Abbreviations: PD-MCI = mild cognitive impairment due to Parkinson's disease; AD-MCI = mild cognitive impairment due to Alzheimer's disease; MMSE = Mini Mental State Exam; CDR = Clinical Dementia Rating

*Adjusted for age at baseline (years), sex, and education (years)

†An estimate >0 means that the PD-MCI participants performed better at baseline than the AD-MCI participants

‡For the Trail Making Tests A and B, a higher score means worse performance; therefore, the Trail Making z-scores have been inverted to be consistent with the other tests, in which a negative score means scoring worse than controls

Table 4

Annual change in neuropsychological test z-scores

	Unadjusted beta (SE)			Adjusted beta (95% CI)*	
Test	**MCI-PD**	**MCI-AD**	**p-Value**	**Group difference†**	**p-Value**
MMSE total	−0.08 (0.04)	−0.67 (0.13)	<.001	0.61 (0.34, 0.88)	<.001
Logical Memory Immediate	0.14 (0.06)	−0.19 (0.03)	<.001	0.34 (0.22, 0.46)	<.001
Logical Memory Delayed	0.16 (0.05)	−0.16 (0.03)	<.001	0.33 (0.20, 0.45)	<.001
Digit Span Forward	−0.04 (0.03)	−0.11 (0.02)	0.03	0.08 (0.01, 0.15)	0.02
Digit Span Backward	−0.05 (0.03)	−0.09 (0.02)	0.18	0.05 (-0.02, 0.13)	0.17
Animals list generation	−0.13 (0.03)	−0.17 (0.02)	0.45	0.03 (-0.05, 0.12)	0.42
Vegetables list generation	−0.07 (0.04)	−0.21 (0.03)	0.002	0.14 (0.05, 0.23)	0.003
Boston Naming Test	−0.06 (0.04)	−0.25 (0.06)	<.001	0.21 (0.09, 0.33)	<.001
Trail Making Test A‡	−0.13 (0.08)	−0.25 (0.05)	0.20	0.12 (-0.06, 0.30)	0.19
Trail Making Test B‡	−0.06 (0.09)	−0.22 (0.05)	0.19	0.15 (-0.07, 0.37)	0.18
Digit Symbol	−0.01 (0.03)	−0.13 (0.03)	0.01	0.12 (0.03, 0.20)	0.01
CDR sum of boxes (raw score)‡	−0.03 (0.06)	−0.92 (0.11)	<.001	0.88 (0.63, 1.12)	<.001

Abbreviations: PD-MCI = mild cognitive impairment due to Parkinson's disease; AD-MCI = mild cognitive impairment due to Alzheimer's disease; MMSE = Mini Mental State Exam; CDR = Clinical Dementia Rating

*Adjusted for age at baseline (years), education (years), sex

†An estimate >0 means that the PD-MCI participants performed better over time than the AD-MCI participants

‡For the Trail Making Tests A and B and CDR sum of boxes, a higher score means worse performance; therefore, z-scores have been inverted to be consistent with the other tests, where a negative score means scoring worse than controls