Journals of Gerontology: Medical Sciences
cite as: J Gerontol A Biol Sci Med Sci, 2018, Vol. 73, No. 12, 1682–1687
doi:10.1093/gerona/glx133
Advance Access publication June 27, 2017

Research Article

Physical Activity in Older Adults With Mild Parkinsonian Signs: A Cohort Study

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Received: February 21, 2017; Editorial Decision Date: June 7, 2017

Decision Editor: Anne Newman, MD, MPH

Abstract

Background: Physical activity regimens are beneficial for older adults with Parkinson's disease; however, their beneficial effect on individuals with mild parkinsonian signs (MPS) who do not meet criteria for Parkinson's disease is not established. The current observational study aims to determine the cognitive and motor impact of physical activity in older adults with MPS over a 1-year period.
Methods: Three hundred and forty-one individuals underwent medical and neurologic assessment of MPS at baseline. MPS was diagnosed using the motor portion of the Unified Parkinson Disease Rating Scale. Physical activity frequency (days/month) were recorded at baseline and 1-year follow-up along with Repeatable Battery for Assessment of Neuropsychological Status (RBANS) score and gait velocity during normal walking (NW) and walking while talking (WWT) conditions. Associations over the 1-year period were assessed using linear regressions controlling for key covariates.
Results: One hundred and thirty (38.1%) participants met criteria for MPS. These participants demonstrated significant associations between physical activity and gait velocity at baseline (NW: $p < .01$; WWT: $p = .03$) and follow-up (NW: $p < .01$; WWT: $p = .02$). Physical activity was also associated with RBANS total score ($p < .01$) at follow-up. Increases in physical activity frequency over 1 year were associated with increases in NW velocity ($p = .02$), WWT velocity ($p < .01$), and RBANS total score ($p < .01$).
Conclusions: Among older adults with MPS, increased frequency of physical activity is associated with decreased risk of cognitive and motor decline. Our results highlight the importance of participation in physical activities on maintaining motor and cognitive functioning in older adults with MPS.

Keywords: MPS, Gait, Exercise, Cognition

Mild parkinsonian signs (MPS) represents an intermediate state between normal and pathological aging that could potentially be reversible (1). MPS have been commonly described in older adults without known neurological disease (1–8), affecting 15% to 52% of older adults (3,5). Individuals with MPS also have increased rates of depression (9), vascular risk factors (10), functional disability (7), and mortality (5). Although MPS may represent the milder end of a disease spectrum; it is unclear whether MPS reflects an age-associated decline in motor function or early stages of neurodegenerative or cerebrovascular disease (8).

Previous studies have linked MPS to both motor and cognitive deficits, including greater impairments in balance and gait (1), as well as higher incidence of dementia and mild cognitive impairment syndrome (MCI)(3,4,6). Physical activity regimens, which have beneficial effects for healthy older adults (11,12), have also been linked to improvements in motor and cognitive performance among patients with neurodegenerative disease, including Parkinson's disease (PD) (13–16), Alzheimer's disease (17), and other forms of dementia (18). Although the beneficial effect of physical activity on older adults with similar mild neurologic symptomatology such as MCI, has been reported (19), to date the effect of physical activity on individuals with MPS has not been established.

To address this knowledge gap, we conducted an observational study in a large cohort of community residing nondemented older adults. Given that MPS may be reversible (1), we hypothesized that greater frequency of participation in physical activity would be associated with better cognitive and motor outcomes among individuals with MPS. Establishing the association of physical activities with better health outcomes in older adults with MPS might provide valuable insights into potential preventive interventions for this population.

Methods

Participants

Five hundred and forty-three nondemented adults aged 65 years and older were recruited from an ongoing cohort study entitled the Central Control of Mobility in Aging (CCMA; see ref. (20)) from June 2011 to March 2016, and of whom 432 completed a 1-year follow-up visit. Participants were further excluded from this analysis if: they did not have a complete neurological examination at baseline (n = 42), did not complete the physical activity questionnaire at baseline (n = 18) or at follow-up (n = 16), did not complete the motor tasks at baseline (n = 7) or at follow-up (n = 6), reported physician diagnosed PD (n = 1), or were prescribed dopamine-blocking agents/neuroleptics (n = 1).

Following exclusions, 341 nondemented older adults were evaluated for MPS, of which 130 (38.1%) met criteria (see below). The primary aim of the CCMA study is to determine cognitive and brain predictors of mobility in healthy aging. However, the primary aim of the current study is to determine the specific impact of physical activity in older adults with MPS. The institutional review board of the Albert Einstein College of Medicine approved the experimental procedures and all participants provided written informed consent in accordance with the tenets of the Declaration of Helsinki.

Neurological and Clinical Evaluation

Participants received comprehensive neurological and clinical in-house evaluations at baseline as well as at annual follow-up visits. Neurological examinations were conducted by trained clinicians (see ref. (8)). MPS diagnosis and MPS severity were systematically ascertained using the motor evaluation portion (Part III) of the original Unified Parkinson's Disease Rating Scale (UPDRS), a standardized examination protocol with moderate reliability and validity (21).

In brief, the four major functional domains from the UPDRS that are relevant for a diagnosis of MPS are: bradykinesia, rigidity, tremor, and postural instability. Severity for each of these domains was calculated by summing the clinician's ratings (0–4; absent to severe) across each of the items within the given domain: (i) *bradykinesia* in extremities (peripheral) was assessed with finger tapping, hand movements, rapid alternating hand movements, and leg agility (UPDRS items #23–26) and body (general or axial) bradykinesia was assessed by combining, slowness, hesitancy, decreased arm swing, small amplitude, and poverty of movement in general (UPDRS item #31); (ii) *rigidity* in extremities (peripheral) and neck (axial) were judged on passive movement of major joints with patients relaxed in sitting position while cogwheeling was ignored (UPDRS item #22); (iii) occurrence of *tremor* at rest was only assessed in extremities (UPDRS item#20); and (iv) *postural instability* was assessed with the observed absence of postural response to a sudden, strong postural displacement produced by a pull on the shoulders while standing prepared, erect, with eyes open, and feet slightly apart (UPDRS item #30).

Diagnosis of MPS has been variably defined by different research groups (3,8). In order to best differentiate participants with a mild disease from those merely exhibiting transient signs of normal aging (1), we applied previously established criteria outlined by Louis and colleagues (3). Participants were considered to have MPS if any of the following three conditions were met: (i) two or more UPDRS ratings on the four selected signs = 1; (ii) one UPDRS rating on any one of the fours signs ≥ 2; or (iii) UPDRS rest tremor rating ≥ 1.

Global health status (GHS; range 0–10) was obtained from dichotomous rating (presence or absence) of physician diagnosed medical illnesses including: diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, PD, chronic obstructive pulmonary disease, angina, and myocardial infarction (22,23). Depression was measured using the 30-item Geriatric Depression Scale (GDS) and a cutoff score >9 was used to define presence of significant depression symptomology (24).

Physical Activity

We implemented a modified version of Verghese and colleagues' validated physical activity scale (25) to determine individuals' physical activity level by asking participants: "how many days have you engaged in any physical activity during the previous month" (range 0–30 days). Utilization of this scale provides consistent levels of participation with good test–retest reliability for scores on entry and at 1-year follow-up (Spearman r = .410, p = .001) (25). In the current study, physical activity frequency (days/month) were also assessed at baseline and at 1-year follow-up. This questionnaire was administered as part of a larger cognitive and motor test battery as part of the standardized procedures of the CCMA study.

Motor and Cognitive Measures

Quantitative gait assessments were conducted by research assistants blinded to participants' MPS status as described in our previous studies (22,26,27). Gait velocity (cm/s) during normal walk (NW) was examined as the primary motor outcome, and was measured using a 20-foot instrumented walkway with embedded pressure sensors (GAITRite, CIR Systems, and Havertown, PA). The GAITRite system is widely used in clinical and research settings and has excellent psychometric properties (23). Participants were asked to walk on the computerized mat at their "normal walking speed" in a quiet and well-lit room as previously described (28).

Global cognition was examined as the primary cognitive outcome, and was assessed using the Repeatable Battery for Assessment of Neuropsychological Status (RBANS). The RBANS is a brief cognitive test with several alternate forms that measure five individual cognitive domains among attention, language, delayed memory, visual–spatial skills, and immediate memory. Each of these indices is scored independently. The RBANS also provides a total index score, which provides an overall assessment of global cognitive function. The RBANS is a well-validated exam of cognition with established test–retest reliability and has published age-appropriate normative data (29).

Cognitive-motor dual-tasking was examined using the walking while talking (WWT) task, validated in our previous studies (23,30). Participants were asked to walk on the computerized mat while reciting alternate letters of the alphabet (skipping the letter in between). Participants were asked to pay equal attention to their walking and their talking to avoid task prioritization (23). Gait velocity (cm/s) while performing this task was examined as the primary outcome.

Statistics

Associations between reported physical activity frequency (independent variable) and preidentified motor and cognitive outcomes (dependent variables) were examined using linear regression analyses adjusted for age, gender, Global Health score, Geriatric Depression Scale values, severity of MPS, and number of education years. Associations among changes were also adjusted for baseline task values. Participants were additionally divided into high and low physical activity subgroups based on the median frequency of physical activity at baseline (Figure 1a) and follow-up (Figure 1b), as well as the median change in frequency of physical activity over the 1-year period (Figure 2). Since median change was 0 over the 1-year period, this final subgroup illustrates the comparison between participants who reported maintaining or increasing their physical activity frequency from baseline to follow-up versus those who simply reported decreasing their physical activity frequency. Differences in outcomes among these subgroups were examined using one-way ANOVAs. All data analyses were conducted using SPSS Version 21 and corrections for multiple comparisons were applied when necessary (31).

Results

Baseline characteristics of the sample for individuals diagnosed with MPS (n = 130) are provided in Table 1. While 49.1% of the sample presented with at least one Parkinsonian sign, only 38.1% met study criteria for MPS. Among participants with MPS, rigidity was the most common feature (56.4%), followed by bradykinesia (35.8%), postural instability (23.0%), and tremor (13.3%).

At baseline, participants with MPS reported participating in 13.35 days ± 10.96 of physical activity per month on average. Physical activity days were associated with NW velocity (p < .01) as well as WWT velocity (p = .03), but not with RBANS total score (Table 2, Figure 1a). At follow-up, reported physical activity (12.02 days/mo ± 10.55 on average) was significantly associated with all three measures (NW velocity p < .01, WWT velocity p = .02, RBANS total score p < .01) (Table 2, Figure 1b).

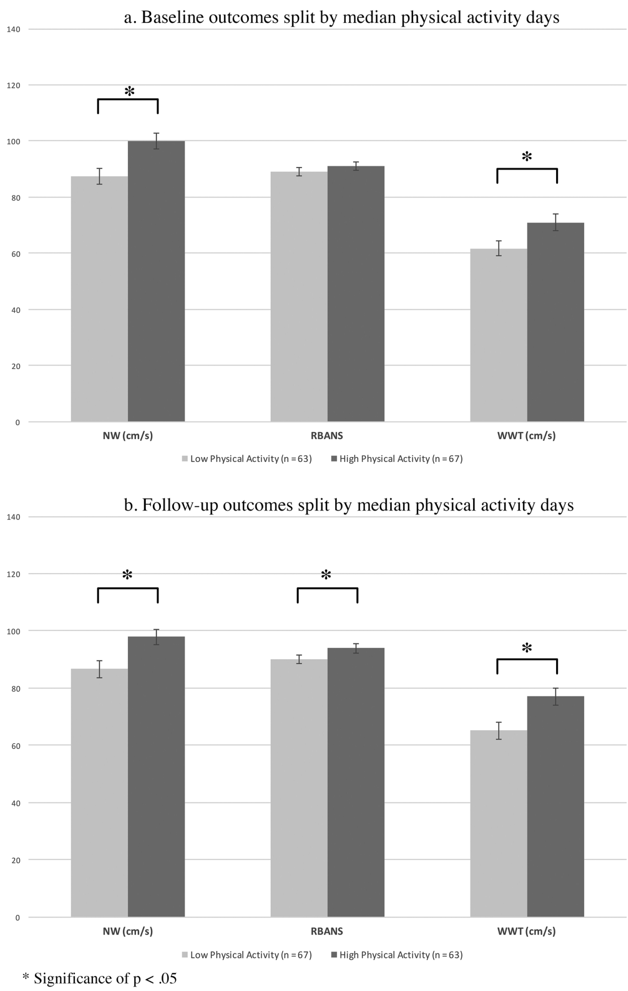

Figure 1. Comparison of outcome measures when participants are dichotomized by the median split in physical activity days. (**a**) Participants who reported engaging in at least the median physical activity frequency at baseline (12 days/mo; n = 67), demonstrated significantly higher normal walking (NW) velocity (p < .01) and WWT velocity (p = .01), but not RBANS total score when compared to those who did not. (**b**) Participants who reported engaging in greater than the median physical activity frequency at follow-up (8 days/mo; n = 63), demonstrated significantly higher NW velocity (p < .01), RBANS total score (p < .05), and WWT velocity (p < .01) when compared to those who did not. NW = Normal walking; RBANS = Repeatable Battery for Assessment of Neuropsychological Status; WWT = Walking while talking.

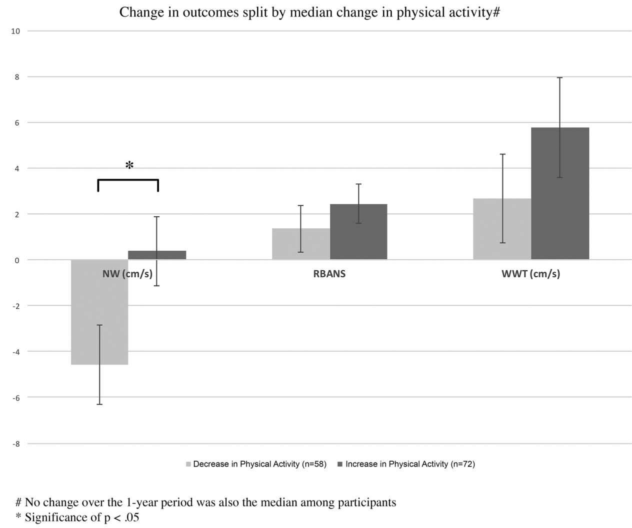

Figure 2. Comparison of changes in outcome measures when participants are dichotomized according to the median change in physical activity days over the 1-year period. Since median change was 0 over the 1-year period, this figure illustrates the comparison between participants who maintained or increased their physical activity level *vs.* those who simply decreased their physical activity frequency. While those participants who maintained or increased their physical activity frequency increased their NW velocity on average, participants who decreased their physical activity demonstrated a significant decrease in NW velocity (p = .01). Additionally, participants who decreased their physical activity frequency demonstrated less improvement on RBANS total score and WWT velocity, although nonsignificant. NW = Normal walking; RBANS = Repeatable Battery for Assessment of Neuropsychological Status; WWT = Walking while talking.

Table 1. Sample Characteristics With Average Physical Activity and Outcome Measures at Baseline

Demographics	Age (years)	78.45 (7.06)
	% Female	50.77%
	GHS Score (0–10)	1.83 (0.99)
	GDS Score (0–30)	4.93 (3.87)
	Education Years	14.68 (2.68)
	MPS Severity (0–36)	5.64 (4.12)
Physical activity	Days (0–30)	13.35 (10.96)
Motor	NW velocity (cm/s)	93.91 (23.00)
Cognitive	RBANS Total Score	90.03 (11.85)
Combined	WWT velocity (cm/s)	66.53 (23.36)

Note: Mean (SD) unless otherwise noted. GDS = Geriatric depression scale; GHS = Global health score; MPS = Mild parkinsonian signs; NW = Normal walking; RBANS = Repeatable Battery for Assessment of Neuropsychological Status; WWT = Walking while talking.

Compared to baseline, participants reported engaging in less physical activity at 1-year follow-up (−1.33 ± 12.79 days/mo). Participants on average also decreased (worsened) in NW velocity (−1.84 ± 13.26 cm/s) at 1-year follow-up, but on average increased (improved) in RBANS total score (1.96 ± 7.53) and WWT velocity (4.39 ± 16.99 cm/s).

Increases in physical activity level over the 1-year follow-up period were significantly associated with increases in NW velocity (p = .02) and WWT velocity (p < .01) (Table 3). Increases in physical activity over 1 year were also significantly associated with increases in global cognition as assessed by RBANS total score (p < .01). Specifically, increases in physical activity level were associated with increases in the attention (p < .01), immediate memory (p < .01), and delayed memory (p = .02) indices of the RBANS (Table 3). Participants who reported a decrease in their physical activity level at follow-up (44.6%, mean decrease 11.9 days/mo) demonstrated significantly decreased NW velocity over the 1-year period (p = .01) compared to those who reported maintaining (20%) or increasing (36.5%, mean increase 11.3 days/mo) their physical activity level over the 1-year period (Figure 2).

Discussion

Our study reveals that higher frequency of physical activity at baseline as well as longitudinally is associated with higher cognitive and motor performance in individuals with MPS. Specifically, individuals that reported engaging in more physical activities over 1 year demonstrated better gait performance, global cognitive functioning, and dual-tasking.

Previous studies have identified that among patients with other neurodegenerative diseases, such as PD, Alzheimer's, and MCI, exercise has been shown to provide a higher quality of life, improved cognitive function, and sustainable motor improvement (13–15,19). While the etiopathogenesis of MPS among the elderly adults remains uncertain, MPS diagnosis may nonetheless characterize a pathological form of aging. Previous studies have identified that the presence of MPS in older adults is associated with an increased incidence of dementia (3,6) and symptomatic MPS may in fact represent a marker for either early neurodegenerative diseases such as PD (32) or cerebrovascular disease (10).

Increases in physical activity levels were associated with increases in gait velocity during normal walking (NW) and walking while

Table 2. Physical Activity vs Task Outcome at Baseline and Follow-up

Baseline		β	95% Confidence Interval		p Value
			Lower Bound	Upper Bound	
Motor	NW velocity (cm/s)	0.54	0.20	0.86	<.01
Cognitive[a]	RBANS Total Score	0.01	−0.18	0.21	NS
Combined[a]	WWT velocity (cm/s)	0.38	0.04	0.73	.03
Follow-up					
Motor	NW velocity (cm/s)	0.49	0.13	0.84	<.01
Cognitive[a]	RBANS Total Score	0.35	0.13	0.56	<.01
	Attention	0.42	0.19	0.66	<.01
	Immediate memory	0.22	0.01	0.43	<.05
	Delayed memory	0.24	0.02	0.46	.04
	Language	0.20	0.04	0.35	.01
	Visuospatial	0.20	−0.05	0.45	NS
Combined[a]	WWT velocity (cm/s)	0.47	0.06	0.87	.02

Note: All Linear Models control for Age, Gender, GHS, GDS, and MPS Severity. β = regression coefficient for change in exercise day. GDS = Geriatric depression scale; GHS = Global health score; MPS = Mild parkinsonian signs; NW = Normal walking; RBANS = Repeatable Battery for Assessment of Neuropsychological Status; WWT = Walking while talking.

[a]Linear Models involving Cognitive Measures also control for education level.

Table 3. Change in Physical Activity vs Change in Task Outcome

		β	95% Confidence Interval		p Value
			Lower Bound	Upper Bound	
Motor	NW velocity (cm/s)	0.27	0.04	0.49	.02
Cognitive[a]	RBANS Total Score	0.24	0.11	0.37	<.01
	Attention	0.25	0.05	0.42	<.01
	Immediate Memory	0.25	0.08	0.42	<.01
	Delayed Memory	0.19	0.03	0.35	.02
	Language	0.14	−0.01	0.26	NS
	Visuospatial	0.17	−0.03	0.38	NS
Combined[a]	WWT velocity (cm/s)	0.40	0.11	0.70	<.01

Note: All Linear Models control for Age, Gender, GHS, GDS, MPS Severity, and Baseline values. β = regression coefficient for change in exercise days. GDS = Geriatric depression scale; GHS = Global health score; MPS = Mild parkinsonian signs; NW = Normal walking; RBANS = Repeatable Battery for Assessment of Neuropsychological Status; WWT = Walking while talking.

[a]Linear models involving cognitive measures control for education years.

talking (WWT) conditions. Gait velocity is a well-established marker of aging, associated with onset of dementia and increased risk of falls (33). Among individuals with MPS, gait impairment has been specifically related to increased mortality (34). On average, individuals with MPS had slower NW velocity over the course of 1 year. However, those individuals with MPS that maintained or increased their physical activity regimen increased their NW gait velocity; and similarly, increases in physical activity level were associated with further increases in NW gait velocity.

On average, individuals with MPS increased their total RBANS score over the 1-year period. While the increase in score may be due to a practice effect often seen in repeated cognitive testing (35), increases in physical activity levels were associated with increases in specific RBANS subscores, specifically in the areas of attention and memory; supporting a discrete effect of physical activity on cognitive domains rather than a global learning effect. Nevertheless, our participants do receive alternate forms across testing visits. Our results are supported by previous studies in disease populations. Patients who exercise more have demonstrated improvement in attention and memory in both MCI and Alzheimer's disease (11,17,19), and studies involving physical activity regimens among poststroke patients reveal increased functional rehabilitation with increased physical activity (11,36). These benefits may be attributed to increases in neuroplasticity initiated by physical activity (37). Similarly, increases in neuroplasticity may intensify the resulting practice effect in older individuals. Thus, future studies are warranted to parse apart improvements owed to increases in neuroplasticity from those due to a practice effect.

Impairments in both cognition and gait have been shown to be prominent risk factors for falls in older adults (30,33,38). Previous research has identified that walking is a complex task requiring higher order executive function (39), specifically related to attention and memory (38). The walking while talking (WWT) paradigm for this reason has been studied as a real-world test of divided attention to better examine the cognitive-motor interactions in older adults (23), specifically in reference to risk of falling (30). Our findings that increased physical activity levels are associated with increased WWT velocity (ie, better performance), along with increased NW velocity and increased attention and memory function, support prior research while strengthening the argument that physical activity is paramount for improved motor function and ambulation in this high-risk population.

This study is not without its limitations. Although the UPDRS is a reliable protocol for diagnosing PD, it's validity for defining MPS among normal aging adults has not been established. Additionally, we did not account for MPS localization among participants. Further studies may be warranted to ascertain differences between axial and peripheral MPS. Since our study involved self-reported physical activity levels, the actual amount of physical activities performed on a monthly basis could not be quantified objectively in the same manner as participant's motor and cognitive abilities. Though high correlation between validated activity scales and objective activity measurements have been reported (40), duration of activity done was not known. Furthermore, what we considered physical activity was not standardized among participants and comprised of a wide range of activities. In order to best establish therapeutic guideline for patients with MPS, further interventional studies involving controlled, standardized exercise regimens should be conducted to determine their direct influence on these patients.

In conclusion, greater physical activity was associated with better cognitive and motor outcomes in older adults with MPS. Additionally, increases in physical activity frequency were associated with decreased risk of cognitive and motor decline in older adults with MPS. Our results indicate that physical activity may be a beneficial intervention for individuals with MPS, and should be tested in future trials. These findings may be indicative of the increased neuroprotective and therapeutic role of maintaining or initiating physical activity among patients with MPS. Additionally, our results may be associated with the fact that MPS are reversible, however, further studies will be required to test this hypothesis directly.

Funding

This research is supported by NIA grants (R01AG036921 [PI: Holtzer] and R01AG044007 [PI: Verghese]) and an intramural grant from the Resnick Gerontology Center, Albert Einstein College of Medicine, Bronx, NY. D.S. is supported by the Albert Einstein College of Medicine Senior Research Fellowship grant.

Acknowledgments

The authors would like to thank the participants for their time and CCMA research assistants for their assistance with data collection.

Conflict of Interest

None reported.

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