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Author(s): Rantakokko, Merja; Iwarsson, Susanne; Slaug, Björn; Nilsson, Maria H.

Title: Life-space mobility in Parkinson's disease : associations with motor and non-motor symptoms

Life-space mobility in Parkinson's disease: Associations with motor and non-motor symptoms.

Merja Rantakokko, PhD[1], Susanne Iwarsson, PhD [2], Björn Slaug, PhD [2], Maria H. Nilsson, PhD [2,3]

[1] Gerontology Research Center, Faculty of Sport and Health Sciences, University of Jyvaskyla, Finland

[2] Department of Health Sciences, Lund University, Sweden.

[3] Memory Clinic, Skåne University Hospital, Malmö, Sweden.

Corresponding author:

Merja Rantakokko, PhD

Gerontology Research Center, Faculty of Sport and Health Sciences

P.O.Box 35 (viv)

40014 University of Jyvaskyla,

Jyvaskyla, Finland

Tel. +358 805 3589

Email: Merja.rantakokko@jyu.fi

ABSTRACT

Background: To describe life-space mobility and explore associations of motor and non-motor symptoms with life-space mobility in people with Parkinson's disease (PD).

Methods: 164 community-dwelling persons with PD (mean age 71.6 years, 64.6% men) received a postal survey and a subsequent home visit. Motor assessments included perceived walking difficulties (Walk-12G), mobility (Timed Up and Go test), motor symptoms (UPDRS-III) and freezing of gait (item 3, FOG-Qsa). Non-motor symptoms included depressive symptoms (GDS-15), pain, fatigue (NHP-EN) and global cognition (MoCA). Life-space mobility was assessed with the life-space assessment (LSA). Calculations included composite score (range 0-120; higher indicating better life-space mobility), independent life-space (range 0-5), assisted life-space (range 0-5), and maximal life-space (range 0-5). Associations were analyzed with linear regression models, adjusted for age, sex, and PD severity (Hoehn and Yahr).

Results: Mean life-space mobility score was 72.3 (SD 28.8). Almost all participants (90 %) reached the highest life-space level (beyond town). Half of these reached this level independently, while one-third were unable to move outside their bedroom without assistive devices or personal help. When adjusted for confounders, depressive symptoms, pain, and perceived walking difficulties was negatively associated with life-space mobility. In the multivariable model, only perceived walking difficulties was associated with life-space mobility.

Conclusions: Our findings indicate that perceived walking difficulties should be targeted to maintain or improve life-space mobility in people with PD. Depressive symptoms and pain may also merit consideration. More research is needed to elucidate the role of environmental and personal factors for life-space mobility in PD.

INTRODUCTION

Participation in out-of-home activities is a prerequisite for independent living and an important determinant of quality of life (1). Life-space mobility is an indicator of participation in different life situations outside the home. It refers to the area in which a person moves in daily life, taking into account where, how often, and with what kind of help people move about (2). Life-space mobility includes all forms of transportation and reflects what people actually do, not what they are capable of doing.

In general population samples of older people, life-space mobility correlates with, for example, lower extremity functioning (3), depressive symptoms (4) and cognitive functioning (5). It has been strongly correlated with quality of life in both cross-sectional and longitudinal studies (1, 6). Life-space mobility has been investigated in people with specific diagnoses such as heart failure (7), cystic fibrosis (8) and mild cognitive impairment (9). To the best of our knowledge, life-space assessment (2) has not been used in research targeting people ageing with Parkinson's disease (PD). Liddle et al (2014) assessed life-space among people with PD using GPS in smartphones and focusing on the size of the area. They found that with increasing symptoms of PD there was a slight trend of decreasing life-space area. (10)

For people with PD, the possibility to move outside their home may be compromised early on, especially among those with gait and balance impairments (11). PD is often characterized by both motor (e.g., walking difficulties, freezing of gait, tremor) and non-motor (e.g., depressive symptoms, fatigue, pain) symptoms. These symptoms separately or in combination create difficulties in daily life and impose restrictions on participation in activities outside the home (12). This was also found in a study of a personalized coaching program among sedentary Parkinson patients, which showed that time spent outdoors correlated strongly with several health-related

outcomes (13). So far, no study has investigated how motor and non-motors symptoms are associated with life-space mobility in PD. We hypothesized that several motor and non-motor symptoms would be associated with life-space mobility among people with PD.

Knowledge on life-space mobility in PD is important for designing interventions aiming at improving the possibilities for social participation and living an active life, despite of the presence of this chronic and progressive disease. This study aimed to describe life-space mobility among people with PD and explore the associations of motor and non-motor symptoms with life-space mobility in people with PD.

METHODS

Participants and study design

This study is part of the longitudinal project "Home and Health in People Ageing with PD" (14). We used data collected at the first follow-up, that is, three years after baseline, when questions on life-space mobility were added to the data collection. The data collection included a self-administered postal survey and a subsequent home visit that involved interview-administered questions/questionnaires and clinical assessments. The two data collectors were both registered occupational therapists and had undergone project specific training.

At baseline, participants were recruited from three hospitals in southern Sweden. To be included, participants were required to have a diagnosis of PD (ICD-10: G20.9) for at least one year, and be willing to participate. Exclusion criteria were difficulties in understanding/speaking Swedish, severe cognitive difficulties (evaluated by specialist PD-nurses and screening of medical records), other reasons (e.g., hallucinations, a recent stroke) and residing outside southern Sweden that prevented

the individual from providing an informed consent or participating in most of the data collection phases. At baseline, the sample comprised 255 participants. Details of the recruitment, data collection and procedures have been published previously (14, 15). All those who had agreed to be contacted again were considered eligible for the 3-year follow-up. At the 3-year follow-up, four individuals no longer had a diagnosis of PD, 22 were deceased and 12 were unreachable or had relocated away from southern Sweden. Fifty-one declined to participate, one participant was excluded due to extensive missing data and another because the self-administered questionnaires had been answered by someone else. Hence, the follow-up sample contained 164 participants. Their mean age was 71.6 (SD 8.9); 64.6 % were men. See Table 1 and Supplementary material 1 for further descriptive information.

The project was conducted in accordance with the Helsinki Declaration and was approved by the Regional Ethical Review Board in Lund, Sweden (Nos. 2012/558, 2015/611). All participants provided a written informed consent.

Life-space mobility

Life-space mobility was assessed using the Swedish version of the University of Alabama at Birmingham (UAB) Study of Aging Life-Space Assessment (LSA) (2, 16). The LSA targets movement in six specific life-space areas (bedroom, home, outside home, neighbourhood, town, beyond town). Participants were asked to state how many times a week (daily, 4-6 times, 1-3 times, less than once a week) they had moved in each area, and whether they had needed help from another person or assistive devices. Four indicators of life-space were calculated: 1) Independent life-space (LSA-I), indicating the life-space attained without help from any assistive devices or another person (range 0-5 according to life-space areas); 2) Life-space using assistive devices (LSA-A), indicating the life-space attained with the help of assistive devices if needed but not the

help of another person (range 0-5 according to life-space areas); 3) Maximal life-space (LSA-M), indicating the greatest distance attained with the help of assistive devices and/or another person if needed (range 0-5 according to life-space areas) and; 4) Life-space mobility composite score (LSA-C), which ranges from 0 to 120 (higher scores= better life-space mobility). Four participants had missing information on life-space mobility and were thus excluded from the regression analyses. The test-retest reliability of the Swedish version of LSA has been found to be good for total score (ICC 0.84), LSA-I (Weighted Kappa 0.94) and LSA-A (Weighted Kappa 0.86), but slightly compromised for LSA-M (Weighted Kappa 0.50) (16).

Motor symptoms

Motor symptoms were assessed with the motor examination of the Unified Parkinson's Disease Rating Scale (UPDRS part III, scored 0-108; higher=worse) (17). Mobility was assessed with the Timed Up & Go (TUG) test at a comfortable gait speed; the best value of three trials was used (18). Fourteen % (n=21) of the participants used mobility devices while performing TUG, most commonly rollator (n=13). Freezing of gait (FOG) was assessed with item 3 (i.e., freezing, scored 0-4) of the self-administered version (19) of the FOG Questionnaire (FOGQsa)(20). Those who scored ≥ 1 were classified as having FOG (21). Perceived walking difficulties in daily life was assessed by using the self-administered generic walking scale, Walk-12G (scored 0-42; higher=worse) (22).

Non-motor symptoms

Assessments of non-motor symptoms included cognition, fatigue, depressive symptoms and pain. Cognitive functioning was assessed with the Montreal Cognitive Assessment (MoCA), scored 0-30 (higher = better) (23). Fatigue was assessed with the self-administered Energy subscale of the Nottingham Health Profile (NHP-EN) (24); those who affirmed at least one out of three dichotomous (Yes/No) questions (tired all the time, everything is an effort, soon out of energy)

were classified as having fatigue (25). Pain was assessed by the dichotomous (No/Yes) question "Are you bothered by pain?" Depressive symptoms were assessed with the 15-item Geriatric Depression Scale (GDS-15, interview-administered, scored 0-15; higher = worse) (26).

Confounders

Confounders included age, sex and PD severity, which was clinically assessed according to Hoehn & Yahr (score range, I-V; higher = worse) (27).

Descriptive data

PD duration, education level, cultural background, use of mobility devices indoors and outdoors and living status (alone/with someone and rural/urban) were self-reported and used for descriptive purposes. *(See Supplementary material).*

Statistical analyses

Participant characteristics are described as means and standard deviations, or frequencies and percentages. Data was reviewed for outliers. Proportions of participants reaching different life-space levels are described as cumulative percentages starting from the lowest life-space area (bedroom). Correlations between variables were assessed with Spearman correlation coefficients (r_s). Associations of motor and non-motor symptoms with life-space mobility were studied with linear regression analyses. First, crude associations were studied. Second, associations were adjusted for confounders (age, sex, PD severity). The number of participants in each model varied due to missing information in the explanatory variables; the number of missing values are shown in Table 1. In the final multivariable model, all the variables were included simultaneously and adjusted for confounders. Complete data on all variables were available for 122 participants.

This sample size of 122 yields a power of approximately 90% to show a contribution to the explained variance of 15 % in a linear regression model with 10 predictors (including interactions, but not constant) if the probability level (alpha) is set at 0.05.

The appropriateness of linear regression models was assessed by examining residuals. The residuals were normally distributed, indicating good fit of the model to the data. The analyses were conducted with SPSS 24.0. The level of statistical significance was set to $P<.05$.

RESULTS

The mean life-space mobility score (LSA-C) was 72.3 (SD 28.7, range 4-120). Those with the mildest stage of PD had the highest life-space mobility score (HY I: LS mean score 95.3), which decreased steadily as the severity of PD increased (HY II: 92.0; HY III: 69.2; HY IV: 43.8; HY 5: 26.1). As shown in Table 2, less than half of the participants (47.5%) reached the highest life-space area (i.e. beyond town) independently, that is without using any assistive devices or personal help (LSA-I). Close to three out of four (73.1%) reached the life-space of their home independently, indicating that one out of four (26.9 %) was not able to move outside their bedroom without assistive devices or personal help. Nearly 60 % reached the highest life-space level using assistive devices if needed, but without personal help (LSA-A). However, almost all (90%) participants reached the highest life-space area (i.e. beyond town) (LSA-M), with assistive devices or personal help if needed. For further details, see Table 2.

Correlations between motor and non-motor symptoms and life-space mobility are shown in supplementary material 2. In the crude linear regression models, all the motor and non-motor symptoms were significantly associated with life-space mobility (all $p<.001-.003$). Having walking

difficulties (Walk-12G), slower mobility (TUG), more motor symptoms (UPDRS III) and experiencing FOG were negatively associated with life-space mobility. Of the non-motor symptoms, depressive symptoms, pain and fatigue were negatively associated with life-space mobility. Better cognitive functioning was positively associated with life-space mobility *(not shown in Table)*.

The results of the adjusted linear regression analyses are presented in Table 3. When adjusted for age, sex and PD severity, perceived walking difficulties was the only motor symptom that was statistically significantly associated with life-space mobility. Of the non-motor symptoms, depressive symptoms and pain were statistically significantly associated with life-space mobility after adjustments.

In the multivariable model that included all motor and non-motor symptoms, perceived walking difficulties was the only variable that was independently associated with life-space mobility.

DISCUSSION

This is the first study to describe life-space mobility (2) and examine the associations with motor and non-motor symptoms in people with PD. The findings show that almost all participants reached the highest life-space level, but only half did so without any assistance from a mobility device or another person. We hypothesized that several motor and non-motor symptoms would be associated with life-space mobility. Of the motor and non-motor symptoms in PD, only perceived walking difficulties, depressive symptoms and pain were associated with life-space mobility when adjusted for confounders. Notably, perceived walking difficulties stood out as the only variable that was independently associated with life-space mobility.

Our findings suggest that to maintain or improve life-space mobility in people with PD, it is important to address perceived walking difficulties. Several evidence-based interventions such as cueing or treadmill exercise (28, 29) have significantly improved walking in people PD. However, to the best of our knowledge, such intervention studies have not yet used life-space mobility as their primary outcome. Hence further research on whether interventions that improve walking capacity or performance would also improve life-space mobility is warranted.

The Walk-12G reflects perceived walking difficulties in everyday life and includes items such as difficulties in negotiating stairs and limitations in how far a person is able to walk (22). Stair climbing is often necessary for getting outdoors, especially for people living in a house with entrance stairs but without an elevator or ramp. Difficulties in negotiating stairs and when walking around in the neighborhood can be early signs of declining function in people with PD who have postural instability-gait difficulties (11). Changes in gait (pace, variability and postural control) may also be signs of decline in cognitive functions (30), which influence also on life-space mobility (31). Seen in this light, the impact of walking difficulties on life-space mobility is not a surprising finding. In addition, even though life-space mobility includes the use of varied modes of transport, some amount of walking is usually needed for making transitions from indoors to outdoors and vice versa. It is therefore not surprising that perceived walking difficulties is independently associated with life-space mobility while non-motor symptoms are not.

Life-space mobility reflects the actual behavior of a person and provides valuable information on people's possibilities to participate in community activities. The possibility to go outdoors is essential for continuing to engage in valued activities outside the home. Despite of their chronic and progressive illness, most participants reached the highest life-space level (beyond town) and had better life-space mobility than in a Swedish sample of people aged 75-90 years, as our study

participants had life-space mobility score 72.3 (SD 28.7) vs. 65.1 (SD 22.4) (16). This may be partly due to age range, as our study sample was somewhat younger. In the present study, this finding was related to the availability of personal assistance; that is, someone else helped the person with PD to move in this life-space area. However, a large proportion of the participants reached this level without personal assistance but with help from assistive devices. This facet of the findings indicates that people with PD are able, with assistive devices, to compensate for their functional decline and thus maintain their life-space mobility, and ultimately, participation in the community. Actually, as clearly shown in Table 2, there are marked differences in life-space mobility depending on which indicator was used. This supports that life-space mobility is strongly influenced by environmental factors. As shown in a prior study, the physical and social environments also influence participation among people with PD (32). It is possible that participation restrictions on out-of-home activities may be resolved by provision of assistive devices, removal of physical and social environmental barriers and improving access to transportation, even in people with unremitting motor symptoms. Thus, more research examining the influence of environmental factors on life-space mobility among people with PD is called for. Future research should also consider addressing personal factors shown to be associated with perceived walking difficulties, for example, general self-efficacy (15).

The finding that depressive symptoms were associated with life-space mobility in the bivariable but not in the multivariable analyses merits comment. In this, as in previous studies, significant associations were found between depressive symptoms and life-space mobility in general populations of older adults (4, 33). However, the present discrepancy between the bivariable and multivariable results highlights the importance of studying sub-groups of the ageing population, not least those with specific diagnoses. In older adults in general, walking difficulties may partially mediate the association between depressive symptoms and life-space mobility (4). In the present study, depressive symptoms also correlated with other motor aspects besides walking difficulties

(i.e. UPDRS part III scores and TUG) and may therefore not be independently associated with life-space mobility among people with PD.

It should be noted that in the multivariable model, pain was almost statistically significantly (p=.054) associated with life-space mobility. Pain influences daily life in older age, especially in people with chronic conditions (34). The association between pain and life-space mobility has not been widely studied, but older people with chronic pain reduce their activity levels to prevent exacerbation of pain (34). It is possible that pain was well managed among our participants and thus not as restrictive on life-space mobility as perceived walking difficulties. As we lack information on pain treatment, this is mere speculations. As the used indicator of pain was rather crude, more research on the association between pain and life-space mobility is needed.

Strengths and limitations

A major strength of this study is the introduction of a novel concept in research on an important subgroup of the ageing population: life-space mobility in persons with PD. Moreover, we used data collected from a large sample of people with PD, including data on physical performance, symptoms and life-space mobility. We do consider it plausible that other variables may also be of importance for life space mobility among people with PD. Our access to a variety of data puts us in a strong position to initiate further research on the associations found so far.

The study also has its limitations. The cross-sectional design does not allow us to draw causal inferences on the direction of the associations, and thus longitudinal studies are needed. Our sample ranged rather widely in age, disease duration and PD severity, all of which may have influenced the associations with life-space mobility. Unfortunately, the sample was too small for stratified analyses; however, we adjusted the models for age and PD severity. Nevertheless, owing to the large variation in the study sample, we cannot rule out the possibility of residual confounding,

which may lead to biased effect estimates. A further possible limitation is that while the LSA (2, 16, 35) has been validated among older people, it has not been validated among people with PD. Since validity and reliability are sample-dependent (36), psychometric studies of the LSA are needed in PD samples. In addition, in line with a previous study (16), we found a ceiling effect in measure of maximal life-space, which suggests that other indicators of life-space would be better to detect variation in life-space mobility in this population. With respect to the Walk-12G (22), it should be noted that it includes two items on the need of support when moving indoors (e.g., holding on to furniture, using a cane) and outdoors (e.g., using a cane, rollator). Although the LSA addresses the use of assistive devices when moving in certain life-space areas, the correlation (0.644) between these two instruments did not show any overlapping association of concern. Turning to another kind of possible limitation, the number of missing values for explanatory variables may lead to underestimation of the results. That is, with data on only 122 of the participants in the multivariable model, the statistical power of the analyses may not be sufficient to detect all the possible associations.

Conclusions

Addressing the concept of life-space mobility, the results of this study indicate the importance of understanding the prerequisites for participation among people with PD. Our findings suggest that perceived walking difficulties, in particular, should be addressed to maintain or improve life-space mobility in this subgroup of the ageing population. Depressive symptoms and pain may also warrant attention. More research is needed to elucidate the role of environmental and personal factors in life-space mobility in people with PD.

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Table 1. Life-space mobility and motor and non-motor symptoms of the participants (N=164).

	Mean (SD) or % (n)	Range	Missing, n
Life-space mobility, score	72.3 (28.7)	4-120	4
Motor Symptoms			
Mobility (TUG), sec.	18.1 (15.4)	7.5-102.8	16
Walking difficulties (Walk-12G)	18.4 (12.1)	0-42	13
PD motor symptoms (UPDRS III)	31.4 (16.7)	3-85	10
Freezing of gait (item 3, FOG-Qsa), % (n)	58.4 (94)		3
Non-motor symptoms			
Depressive symptoms (GDS-15)	3.4 (3.0)	0-15	6
Cognition (MoCA)	25.1 (4.0)	6-30	13
Fatigue (NHP Energy), % (n)	58.6 (95)		2
Pain, % (n)	64.6 (106)		1
Confounders			
Age	71.5 (8.8)	48-94	
Sex, men % (n)	64.6 (106)		
Hoehn & Yahr scale, % (n)			
I: "unilateral"	6.1 (10)		
II: "bilateral"	42.1 (69)		
III: uni- or bilateral and postural	22.0 (37)		
IV: severe	23.8 (39)		
V: wheelchair bound	6.1 (10)		

PD, Parkinson's disease; TUG, Timed Up and Go; FOG-Qsa, Freezing of gait questionnaire

UPDRS, Unified Parkinson's disease rating scale; GDS-15, Geriatric Depression Scale; MoCA,

Montreal Cognitive Assessment; NHP Energy, Energy subscale of the Nottingham Health Profile

Table 2. The life-space areas reached in people with Parkinson's Disease (n=160).

Life-space area reached	Independent life-space Cumulative % (n)	Assisted life-space Cumulative % (n)	Maximal life-space Cumulative % (n)
Bedroom	100.0 (160)	100.0 (160)	100.0 (160)
Home	73.1 (117)	90.6 (145)	100.0 (160)
Outside home	68.8 (110)	86.8 (139)	98.8 (158)
Neighbourhood	57.5 (92)	80.0 (128)	98.8 (158)
Town	55.0 (88)	71.2 (114)	96.9 (155)
Beyond town	47.5 (76)	58.8 (94)	90.0 (144)

Independent life-space, i.e. area reached without assistive device or personal help

Assisted life-space, i.e. area reached with assistive device if needed, but without personal help

Maximal life-space, i.e. area reached with assistive device and/or personal help if needed

Table 3. Associations between motor and non-motor symptoms with life-space mobility in people with Parkinson's disease.

	MODEL 1		MODEL 2	
	Stand. Beta (s.e.)	P-value	Stand. Beta (s.e.)	P-value
Motor Symptoms				
Walking difficulties (Walk-12G)	-.24 (.16)	<.001	-.19 (.20)	.036
Mobility (TUG)	-.11 (.12)	.134	-.12 (.13)	.139
PD motor symptoms (UPDRS III)	-.09 (.14)	.270	.08 (.19)	.409
Freezing of gait (FOG-Qsa, item3)	-.03 (3.14)	.584	.02 (3.40)	.784
Non-motor symptoms				
Depressive symptoms (GDS-15)	-.12 (.49)	.028	-.10 (.59)	.161
Pain	-.12 (2.97)	.013	-.13 (3.48)	.054
Fatigue (NHP Energy)	-.09 (2.98)	.074	-.04 (3.79)	.631
Cognition (MoCA)	.06 (.41)	.282	-.06 (.49)	.450

Model 1, bivariate associations, adjusted for confounders: age, gender, and disease severity.

Model 2, Multivariable model, all variables included simultaneously, adjusted for confounders.

Walk-12G, generic walking scale; TUG, Timed Up and Go; UPDRS III, Part III the Unified Parkinson's disease rating scale; FOG-Qsa, Freezing of gait questionnaire; GDS-15, Geriatric Depression Scale;

MoCA, Montreal Cognitive Assessment;

NHP Energy, Energy subscale of the Nottingham Health Profile

Note: Number of participants in Models 1 and 2 varies due to missing information (see Table 1), in Model 2 n=122.