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Fall Risk in Relation to Individual Physical Activity Exposure in Patients with Different Neurodegenerative Diseases: a Pilot Study

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Abstract

Falls in patients with neurodegenerative diseases (NDDs) have enormous detrimental consequences. A better understanding of the interplay between physical activity (PA) and fall risk might help to reduce fall frequency. We aimed to investigate the association between sensor-based PA and fall risk in NDDs, using "falls per individual PA exposure time" as a novel measure. Eighty-eight subjects ($n = 31$ degenerative ataxia (DA), $n = 14$ Parkinson's disease (PD), $n = 12$ progressive supranuclear palsy (PSP) and 31 healthy controls) were included in this pilot study. PA was recorded in free-living environments with three-axial accelerometers (activPAL™) over 7 days. Falls were prospectively assessed over 12 months. Fall incidence was calculated by (i) absolute number of falls per person years (py) and (ii) falls per exposure to individual PA. Absolute fall incidence was high in all three NDDs, with differing levels (DA, 9 falls/py; PD, 14 falls/py; PSP, 29 falls/py). Providing a more fine-grained view on fall risk, correction for individual exposure to PA revealed that measures of low walking PA were associated with higher fall incidence in all three NDDs. Additionally, higher fall incidence was associated with more sit-to-stand transfers in PD and longer walking bouts in PSP. Our results suggest that *low* walking PA is a risk factor for falls in DA, PD and PSP, indicating the potential benefit of increasing individual PA in these NDDs to reduce fall risk. Moreover, they show that correction for individual exposure to PA yields a more differentiated view on fall risk within and across NDDs.

Keywords Ataxia · Spinocerebellar ataxia · Exposure · Falls · Parkinson's disease · Physical activity · Progressive supranuclear palsy

Abbreviations

ADS	Allgemeine Depressions-Skala
CON	Healthy control subject
DA	Degenerative ataxia
DGI	Dynamic Gait Index
FES-I	Falls efficacy scale-international
MoCA	Montreal Cognitive Assessment
NDD	Neurodegenerative disease
PA	Physical activity
PD	Parkinson's disease
PSP	Progressive supranuclear palsy
UMSARS	Unified Multiple System Atrophy Rating Scale

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Introduction

Sufficient levels of physical activity (PA) are key for cognitive and neurological functioning, cardiovascular fitness, metabolism, emotional well-being and numerous other health-related outcomes. However, the recommendations and limitations of PA have not yet been studied in detail for neurodegenerative diseases (NDDs). In particular, a trade-off has to be made between the benefits of PA and the risks of inappropriate PA levels, which include the

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increased risk of falls in NDDs. High PA levels can be protective for maintaining and promoting physical function and have usually been associated with a reduced fall risk [1, 2]. However, higher PA levels can also increase fall frequency by increasing exposure to potentially fall-associated situations, particularly in subjects with reduced physical function [3] and/or behavioural disturbances (e.g. risk-taking behaviour) [4]. Thus, studies on the risks of falls in NDDs should also include individual PA exposure time as an incidence outcome.

Here, we used both incidence measures as outcome variables to study the relationship between PA and falls in NDDs: *falls per person year* and *falls per individual PA exposure time*. We studied this+ relationship in three paradigmatic NDDs known to have an increased risk of falls, namely Parkinson's disease (PD), degenerative ataxia (DA) and progressive supranuclear palsy (PSP). Up to 70% of patients with PD [5] and over 80% of patients with DA [6] fall at least once a year. Patients with PSP suffer from even higher fall frequencies [7]. We here aimed to determine (i) whether fall incidences (FI) differ between high vs. low PA groups in these three different NDDs, and (ii) whether correction towards individual PA exposure time can help to get a more differentiated view on fall risk. To determine PA in everyday real-life environment, we used body-worn sensors. Continuous recording here allows extraction of relative exposure times to different PAs and PA variables (such as walking activity or the number of transfers) which can be related to fall risk. We hypothesised that *low* walking activity in the NDD groups is associated with *higher* fall risk.

Patients and Methods

Subjects

Eighty-eight subjects (DA ($n = 31$), PSP ($n = 12$), PD ($n = 14$) and 31 healthy controls, CON) were recruited by movement disorder specialists at the Department of Neurodegenerative Diseases, Tübingen, and included in this pilot study. All PSP patients met the criteria for probable or possible PSP [8] and all PD patients met the UK Brain Bank Criteria for PD [9]. In DA (hereditary and sporadic), secondary causes of ataxia had been carefully excluded. Exclusion criteria for all participants were other neurological disorders, dementia, psychiatric disorders, drug abuse, ophthalmologic disorders other than supranuclear palsy, extremity prosthesis, arthritis or musculoskeletal injuries in the past 3 months. All patients provided written informed consent. The Ethics Committee of the University of Tübingen approved the study (application no. 602/2012BO1).

Clinical Assessment

Age, sex, age of disease onset, disease duration and body mass index were assessed. For comparison of motor performance across the disease groups, the Unified Multiple System Atrophy Rating Scale (UMSARS) [10] and the Dynamic Gait Index (DGI) [11] were used. Global cognition was tested using the Montreal Cognitive Assessment (MoCA) [12], executive functions were tested using the Trail Making Test (TMT) [13], mood disturbances were quantified with the Allgemeine Depressions-Skala (ADS) [14] and the falls efficacy scale-international (FES-I) assessed fall-related self-efficacy [15].

PA Assessment

PA was measured using a three-axial accelerometer (activPAL3, PAL Technologies Ltd., Glasgow, UK) [16] for seven consecutive days. The first and last days of the measurement were excluded from analysis as only days with circadian PA measurement over the full 24 h were considered eligible (see "Statistical Analysis"). The recorded data was processed with activPAL process and presentation V7.2.32 algorithm, detecting three PA categories: (1) lying or sitting, (2) standing and (3) walking [17]. For analysis, walking episodes and sit-to-stand transfers were considered.

Prospective Fall Assessment

All participants received a prospective 12-month fall protocol [18], developed and implemented by a consensus group of international experts in fall research (http://farseeingresearch.eu). A close monitoring of the completion and correctness of the filled in fall protocols was guaranteed by a study nurse.

Statistical Analysis

Analyses were performed using IBM SPSS Statistics 22.0. Characteristics of the participants and the FI were calculated for each disease group separately. Working days and weekends were considered separately, as previous analysis of our data showed that PA levels were different. Due to missing weekdays in some subjects, average daily estimates were calculated by weighting the available working days, the Saturday and the Sunday of each subject assuming a full 1-week measurement: (PA on Sunday + PA on Saturday + 5 × mean PA of working days) divided by 7. The following fall risk-associated PA parameters were calculated: walking duration (average daily total walking duration [min]), number of walking bouts (absolute number of walking bouts ≥ 10s), walking bout length (average walking bout length of bouts > 10s) and sit-to-stand transfers (the average daily number of sit-to-stand transfers). Each group was divided into two subgroups with the PA median as the cut-off. Negative binomial regression models were used to calculate incidence rates with 95%

confidence intervals (95%-CI) for each of the above-mentioned parameters stratified by disease group. To relate the FI to the quantity of performed PA, falls were corrected for exposure time [19]. Total exposure time was calculated for walking (i.e. hours walked, number of walking bouts ≥ 10s) and for transfers (i.e. number of transfers), respectively. The average daily total walking PA (i.e. average total daily walking duration of 7 days recorded by the activPAL) and the transfer PA (i.e. average total number of daily transfers during the 7 days recorded by the activPAL), respectively, were multiplied with the total number of observed days in the follow-up period of 12 months (i.e. 365 days) [19].

Results

Descriptive Variables

Demographic and clinical data are presented in Table 1. In line with previous work [20], DA patients presented with the youngest mean age, earliest mean age of onset and longest disease duration at study examination. PSP patients showed as expected [21] the most severe motor and cognitive impairment compared to that of the other groups.

Absolute FI and Overall Fall Risk Relative to Walking Exposure

Mean FI was 8.9 falls/py in DA, 13.9 falls/py in PD and 28.9 falls/py in PSP, all higher than those in CON (0.4 falls/py) (Table 1). Also, the fall risk relative to walking time differed largely between groups. While DA patients showed 4.5 falls/100 h walked, PSP patients exhibited 13.6 falls/100 h walked. All participants who were administered a sensor reported good tolerance of the sensor; 89% of the healthy control subjects showed complete data sets, 83% of the ataxia patients, 82% of the PD patients and 89% of the PSP patients.

Degenerative Ataxia (DA)

FI per py of Low vs. High PA Performers The group with low walking duration (median 49 min) showed higher FI (10.3 vs. 6.7 falls/py) than the high-activity group (median 86 min), not reaching statistical significance. The group with low number of walking bouts (median 78 bouts) showed an almost twofold higher FI (11 vs. 6 falls/py) than the high-activity group (median 142 bouts), although not reaching statistical significance. The group with low walking bout length (median 0.37 min) showed a significantly higher FI (12.5 vs. 4.4 falls/py) than the high-activity group (median 0.53 min). Although results of the parameters of walking duration and number of walking bouts did not reach significance, the consistency of results across the range of all walking-associated parameters suggests that low walking activity might be associated with high FI. There was no difference in FI between DA subjects with low vs. high number of sit-to-stand transfers (see Table 2).

FI per Exposure to PA of Low vs. High PA Performers The presumed association of lower walking activity levels with higher fall rate became more obvious when calculating *FI in relation to exposure time*. The DA group with low walking duration showed significantly higher FI (8 vs. 1 falls/100 walking hours), the DA group with low number of walking bouts showed significantly higher FI (0.8 vs. 0.1 falls/1000 bouts) and also the group with low walking bout length showed significantly higher FI (6 vs. 1 falls/walking hour) than the respective high-activity groups (see Table 3). There was no significant difference in FI between DA subjects with low vs. high number of sit-to-stand transfer (0.7 vs. 0.4 falls/1000 transfers) (see Table 3).

Parkinson's Disease (PD)

FI per py of low vs. high PA performers FI per py did not statistically differ for the groups with low vs. high walking duration or number of walking bouts (see Table 2). However, the group with low walking bout length (median 0.40 min) showed a significantly higher FI (25.4 vs. 2.4 falls/py) than the high-activity group (median 0.58 min). In contrast, a significantly higher FI was observed for the group with high number of sit-to-stand transfers (25.6 vs. 2.3 falls/py) compared to that for the low-activity group.

FI per exposure time to PA of low vs. high PA performers PD patients with low walking bout length showed significantly higher FI (11.1 vs. 0.7 falls/walking hour) than the high-activity group. In contrast, significantly higher FI was found in the group with high number of sit-to-stand transfers (0.9 vs. 0.1 falls/1000 transfers) (see Table 3). There was no significant difference in FI between PD subjects with low vs. high walking duration or number of walking bouts (see Table 3).

Progressive Supranuclear Palsy (PSP)

FI per py of Low vs. High PA Performers At first glance, a different phenomenon was observed in PSP as compared to DA and PD. The PSP group with high walking duration (median 112 min) showed a significantly higher FI (46.2 vs. 11.7 falls/py) than the low-activity group (median 13 min). In the same direction, but without reaching statistical significance, the group with the high number of walking bouts (median 148 bouts) showed higher FI (38.5 vs. 19.3 falls/py) than the low activity (median 16 bouts). The group with high walking bout length (median 0.88 min) showed a significantly higher FI (45.3 vs. 12.5 falls/py) than the low-activity group (median 0.45 min). The groups with a high vs. low number of sit-to-stand transfers did not differ in FI (see Table 2).

Table 1 Descriptive variable

	DA $n = 31$	PD $n = 14$	PSP $n = 12$	CON $n = 31$
Demographics				
Age [years]	58.2 ± 11.6 *	71.2 ± 6.1	65.9 ± 5.9	70.7 ± 4.0
Female [%]	51.6	57.1	41.7	48.4
Age of onset [years]	43.0 ± 16.3	61.4 ± 8.6	62.2 ± 6.9	n.a.
Disease duration [years]	15.2 ± 9.0	9.8 ± 6.1	3.8 ± 2.6	n.a.
Body mass index	25.4 ± 2.9	27.0 ± 4.5	27.9 ± 2.9	26.0 ± 4.3
Fall incidence – 12-month data (falls/person year)	8.5	13.9	28.9 *	0.4 ± 1.3
Motor performance				
Unified Multiple System Atrophy Rating Scale, score	14.9 ± 5.2 *	17.7 ± 7.3 *	24.5 ± 5.7 *	1.0 ± 1.2
Non-motor performance				
Montreal Cognitive Assessment, score	26.0 ± 3.2	26.9 ± 3.4	22.1 ± 3.9 *	27.6 ± 1.1
Trail Making Test A [performance time in s]	70.5 ± 36.3	64.1 ± 37.6	174.9 ± 130.1 *	36.3 ± 12.9
Trail Making Test B [performance time in s]	128.0 ± 64.9	163.3 ± 106.8	299.9 ± 169.8 *	93.2 ± 37.2
Allgemeine Depressions-Skala, score	13.2 ± 4.9	11.8 ± 6.3	11.7 ± 6.4	10.0 ± 4.5
Falls efficacy scale-international, score	15.8 ± 5.0 *	11.1 ± 3.2 *	17.9 ± 3.5 *	7.3 ± 0.7
Physical activity				
Average daily total walking duration [min]	68.8 ± 32.3 *	98.1 ± 37.2 *	63.8 ± 49.5 *	138.4 ± 40.4
Absolute number of walking bouts ≥ 10s	113.7 ± 53.1 *	153.3 ± 54.5	81.5 ± 64.6 *	185.4 ± 51.0
Average walking bout length of bouts > 10s [min]	0.45 ± 0.12 *	0.52 ± 0.17	0.67 ± 0.30	0.7 ± 0.3
Average daily number of sit-to-stand-transfers	46.3 ± 12.7	58.4 ± 13.3	41.2 ± 12.7 *	54.1 ± 14.9

Descriptive variables for patients with degenerative ataxia (*DA*), Parkinson's disease (*PD*), progressive supranuclear palsy (*PSP*) and healthy controls (*CON*). Group differences in demographical, clinical and physical activity variables were analysed using a x^2 or a one-way analysis of variance (ANOVA). Between group differences in performance in each single variable (dependent variables) was also analysed by an ANOVA with group membership as the independent factor and, when significant, was followed by subsequent post-hoc test of Bonferroni. Values are given in mean and standard deviation

*Significant compared with healthy

FI per exposure time to PA of low vs. high PA performers If adjusted for exposure time to individual PA, also in the PSP group, low walking PA was associated with high FI, with the exception of the parameter walking bout length (see Table 3). The PSP group with low walking duration showed a significantly higher FI (21.9 vs. 7.1 falls/100 walking hours) than the high-activity group. Moreover, the group with low number of walking bouts showed a higher FI (2.8 vs. 0.9 falls/1000 walking bouts) than the high-activity group, without reaching statistical significance. Interestingly, the group with high walking bout length showed a significantly higher FI (7.8 vs. 4.9 falls/walking hour) than the low-activity group. The groups with a high vs. low daily number of sit-to-stand transfers did not significantly differ in FI (2.7 vs. 1.4 falls/1000 transfers).

Discussion

This pilot study evaluated the relationship between sensor-based individual PA and prospectively assessed FI in three different paradigmatic NDDs. It provides a new perspective on fall risk in NDDs by using (i) objective 7-day sensor-based PA monitoring in association with prospectively assessed FI in DA, PSP and PD patients; and by using (ii) PA as an *exposure measure* for falls (=falls per exposure time to individual PA). Our results suggest that using a combination of both parameters (falls per py and falls per individual exposure time) allows a more fine-grained view on the relation between PA and fall risk in NDD. In summary, our findings indicate that several measures of low PA are associated with higher FIs in all NDD groups—when adjusted for individual exposure time to PA. Specifically, low walking duration (in DA and PSP), low number of walking bouts (DA) and low average walking bout length (in DA and PD) were associated with higher FI. Our results moreover indicate that, at least in some conditions, higher FIs might simply reflect the higher amount of walking PA, but not the higher risk to falls per se. Correction for individual PA exposure time here provides a more accurate view on this relationship. This is best illustrated for PSP: when calculating falls per py, subjects with high PA had a higher fall risk, but after correction, they had in fact a lower fall risk than the low-activity group.

Prospective FIs in NDDs

Our results showed high FI in all three NDDs (8.5 falls per py in DA, 13.9 falls per py in PD and 28.9 falls per py in PSP) during the observed period of 12 months.

Table 2 Fall incidence per person year during 12 months of follow-up and 95% confidence intervals according to disease group and low vs. high physical activity performers

	DA $n = 31$			PD $n = 14$			PSP $n = 12$		
	Median (Q1–Q3)	Fall incidence (CI)	Absolute number of falls	Median (Q1–Q3)	Fall incidence (CI)	Absolute number of falls	Median (Q1–Q3)	Fall incidence (CI)	Absolute number of falls
Activity related to walking duration									
Average daily total walking duration [min]									
Low activity group (median split)	49 (12–66)	10.3 (6.2;17.2)	165	64 (42–94)	11.6 (5.4;25.0)	81	13 (3–39)	*11.7 (5.1;26.9)*	70
High activity group (median split)	86 (67–136)	6.7 (3.9;11.6)	101	137 (103–156)	16.3 (7.6;35.0)	114	112 (72–133)	*46.2 (20.6;103.7)*	277
Activity related to walking composition									
Absolute number of walking bouts ≥ 10s									
Low-activity group (median split)	78 (18–110)	11.0 (6.6;18.4)	176	105 (77–144)	11.4 (5.3;24.8)	80	16 (5–61)	19.3 (8.5;43.9)	116
High-activity group (median split)	142 (113–227)	6.0 (3.5;10.4)	90	202 (173–233)	16.4 (7.7;35.2)	115	148 (84–173)	38.5 (17.1;86.6)	231
Average walking bout length of bouts > 10s [min]									
Low-activity group (median split)	0.37 (0.28–0.44)	*12.5 (7.5;20.8)*	200	0.40 (0.31–0.48)	*25.4 (12.0;54.1)*	178	0.45 (0.29–0.54)	*12.5 (5.4;28.7)*	75
High-activity group (median split)	0.53 (0.44–0.75)	*4.4 (2.5;7.7)*	66	0.58 (0.50–0.94)	*2.4 (1.0;5.9)*	17	0.88 (0.60–1.16)	*45.3 (20.2;101.8)*	272
Activity related to transfers									
Average daily number of sit-to-stand-transfers									
Low-activity group (median split)	39 (25–49)	9.0 (5.5;14.9)	153	49 (42–53)	*2.3 (0.9;5.6)*	16	34 (15–340)	33.0 (14.6;74.3)	198
High-activity group (median split)	55 (50–87)	8.1 (4.6;14.1)	113	66 (55–92)	*25.6 (12.0;54.4)*	179	51 (45–57)	24.8 (11.0;56.2)	149

DA, degenerative ataxia; *PD*, Parkinson's disease; *PSP*, progressive supranuclear palsy. Low-activity group, < median split of PA variable; high-activity group, > median split of PA variable; fall incidence is calculated using negative binomial regression model; values in italics indicate significant difference in fall incidence between low- and high-activity groups

Table 3 Falls per individual physical activity (PA) exposure during 12 months of follow-up and 95% confidence intervals according to disease group and low vs. high PA performers

	DA $n = 31$			PD $n = 14$			PSP $n = 12$		
	Median (Q1–Q3)	Fall incidence (CI)	Absolute number of falls	Median (Q1–Q3)	Fall incidence (CI)	Absolute number of falls	Median (Q1–Q3)	Fall incidence (CI)	Absolute number of falls
Activity related to walking duration									
Average daily total walking duration [min]									
Low-activity group (median split)	49 (12–66)	*8.0 (4.7;13.4)*	165	64 (42–94)	2.7 (1.2;5.8)	81	13 (3–39)	*21.9 (9.2;52.2)*	70
High-activity group (median split)	86 (67–136)	*1.3 (0.7;2.2)*	101	137 (103–156)	2.5 (1.2;5.4)	114	112 (72–133)	*7.1 (3.2;16.0)*	277
Activity related to walking composition									
Absolute number of walking bouts ≥ 10s									
Low-activity group (median split)	78 (18–110)	*0.8 (0.5;1.4)*	176	105 (77–144)	0.3 (0.1;0.6)	80	16 (5–61)	2.8 (1.2;6.4)	116
High-activity group (median split)	142 (113–227)	*0.1 (0.1;0.2)*	90	202 (173–233)	0.2 (0.1;0.5)	115	148 (84–173)	0.9 (0.4;2.0)	231
Average walking bout length of bouts > 10s [min]									
Low-activity group (median split)	0.37 (0.28–0.44)	*6.2 (3.7;10.3)*	200	0.40 (0.31–0.48)	*11.1 (5.2;23.7)*	178	0.45 (0.29–0.54)	*4.9 (2.2;11.5)*	75
High-activity group (median split)	0.53 (0.44–0.75)	*1.3 (0.8;2.3)*	66	0.58 (0.50–0.94)	*0.7 (0.3;1.7)*	17	0.88 (0.60–1.16)	*7.8 (3.5;17.5)*	272
Activity related to transfers									
Average daily number of sit-to-stand-transfers									
Low-activity group (median split)	39 (25–49)	0.7 (0.4;1.2)	153	49 (42–53)	*0.1 (0.1;0.3)*	16	34 (15–340)	2.7 (1.2;6.1)	198
High-activity group (median split)	55 (50–87)	0.4 (0.2;0.6)	113	66 (55–92)	*0.9 (0.4;2.0)*	179	51 (45–57)	1.4 (0.6;3.2)	149

DA, degenerative ataxia; *PD*, Parkinson's disease; *PSP*, progressive supranuclear palsy. Low-activity group, < median split of PA variable; high-activity group, > median split of PA variable; fall incidence is calculated using negative binomial regression model; values in italics indicate significant difference in fall incidence between low- and high-activity groups; average daily total walking duration: fall incidence = falls/100 walking hours; absolute number of walking bouts ≥ 10s : fall incidence = falls/1000 bouts; average walking bout length of bouts > 10s: fall incidence = falls/walking hour; average daily number of sit − to − stand transfers : fall incidence = falls/1000 transfers

Although falls are frequent in PSP, this is the first study with *prospective* data on FIs in PSP. In line with our findings, William and colleagues showed retrospectively that PSP patients have the highest FI (97.5% fallers; falls recorded in a dichotomous manner) among different NDD groups [7].

For DA, only one prospective fall study reported for the majority of patients to have fallen at least once a year (84.1%) [22] but without quantification of the exact number of falls. This result is now further differentiated by our numeric values of exact FIs.

PA and Falls

To date, studies on the relationship of PA and falls in DA and PSP are missing. Studies examining the relationship between PA and falls in PD [2, 23, 24] used total observation time to estimate fall risk, i.e. time to first fall or falls per py. However, our data suggest that FIs differ between high vs. low PA subjects in different NDDs. While DA and PD patients with low walking bout length show a high FI, PSP patients with a high walking bout length show a high FI. This difference might be due to a higher exposure to walking PA in the high PA groups, rather than a higher risk to fall per se. Therefore, our findings suggest measuring FI in relation to individual PA exposure time.

FI per Individual Exposure Time to PA

FI per individual walking or transfer PA considers PA as an exposure-related fall risk, and allows correcting for one's individual amount of performed PA. It proved to be a sensitive measure in a large cohort of older people [19] and in a group of people with dementia [25].

In the present study, the relative risk of falling varies between the NDD types: while DA patients showed a smaller fall risk per hour walked (4.5 falls/100 h walked) and per transfer (0.6 falls/1000 transfers), PSP patients showed the largest fall risk per hour walked (13.6 falls/100 h walked) and per transfer (2.0 falls/1000 transfers). This finding might reflect the higher walking- and transfer-related postural instability in PSP compared to that in DA.

When calculating FI adjusted for individual PA exposure time, low walking duration (in DA and PSP), low walking bout length (in DA and PD) and low number of walking bouts (PSP) were associated with higher FI. The relation between low PA level and a higher incidence of falls as well as the need for PA-exposure time correction is best exemplified by PSP. The low-activity PSP group showed the lowest walking duration (13 min) and, at the same time, the highest rates of falls per 100 h walked (21.9 falls/100 walking hours). In line with this finding, the ActiFE-Ulm study [19] found in older subjects the highest rates of falls per 100 h walked in the low-activity subjects. Therefore, a low PA level might be a *general* risk factor for falls in older subjects with and without NDDs.

Could an increase of PA thus reduce fall risk? A recently published intervention study found increased PA during exercise intervention to be associated with reduced number of falls in people with dementia [25]. This potentially beneficial effect of PA exposure argues for the promotion of PA in fall prevention interventions, as well as for the application of the novel concept of PA as an exposure measure, and might be transferred to other cohorts in future intervention studies.

Despite this association of low PA and high fall risk, the type of PA and NDD might play an important role in the relation between PA and fall risk. In PD, a high number of sit-to-stand transfers was accompanied by a high FI. This outstanding risk factor could be explained through electrophysiological knowledge on muscle activation and force production in PD patients [26]. In these electromyography analyses, PD patients were not able to produce constant equilateral force, when performing sit-to-stand transfer.

Interestingly, for PSP also, the group with high walking bout length showed a significantly higher FI than the low-activity group (7.8 falls/walking hour vs. 4.9 falls/walking hour), even if corrected for individual PA exposure time. Overestimation of physical abilities and risk-taking behaviour might explain why a higher activity level leads to higher fall frequency [4]. Butler et al. described that in contrast to older participants with good physical ability and low behavioural risk, subjects with poor physical ability took either no or very high behavioural risks.

In sum, applying the measure of exposure time to individual PA might provide a more differentiated view on fall risk in relation to PA within and across NDDs, and may serve as outcome parameters in future fall assessment and treatment trials.

Limitations

This is a pilot study. Therefore, the small sample size prevented examining the influence of confounders possibly contributing to falls. As this is an explorative study, designed to detect disease-specific patterns of PA, classical testing for significance and multiple comparisons were not applied. Moreover, extrapolation of PA measurement to 1 year could be improved by longer-term or multiple-point measurements in future studies. Further, longitudinal measures of disease progression as a potential risk factor for the risk of falling should be included in the follow-up study.

Falls per individual PA exposure time is a differentiated measure to individually quantify, evaluate and correct the relationship between PA and falls in NDD. By use of this novel exposure measure, low PA levels were associated with an increased fall risk and might thus present a general risk factor for falls in NDDs (and possibly also in elderly persons without

NDDs). Consequently, motivating patients to achieve a minimum PA level could potentially be beneficial.

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Dr. Klenk: design and conceptualization of the study, analysis of the data, revising the manuscript, final approval of the version to be submitted

Dr. Schwenk, Mrs. Schatton, Mrs. Teubner-Liepert, Mr. Schwickert, Mrs. Meyer, Mrs. K.C.: acquisition of data, analysis of the data, revising the manuscript, final approval of the version to be submitted

Prof. Maetzler, Prof. Becker: conceptualization of the study, analysis of the data, revising the manuscript, final approval of the version to be submitted

Dr. Synofzik: design and conceptualization of the study, acquisition of data, analysis of the data, drafting the manuscript, final approval of the version to be submitted

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Compliance with Ethical Standards

All patients provided written informed consent. The Ethics Committee of the University of Tübingen approved the study (application no. 602/2012BO1).

Conflict of Interest The authors declare that they have no competing interests.

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