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The effect of functional-task training on activities of daily living for people with Parkinson`s disease, a systematic review with meta-analysis

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ABSTRACT

Objective: To evaluate the effect of functional-task training on activities of daily living (ADL) in people with Parkinson`s Disease.

Methods: We searched five databases (Cinahl, Embase, Medline, Pedro and CENTRAL). The included studies were assessed on therapeutic validity and risk of bias. We classified the quality of evidence according to the principles of the GRADE approach. All assessments were executed independently by two researchers. The results of included studies were pooled in a meta-analyses and heterogeneity was explored by meta-regression analysis.

Results: Out of 2546 identified studies, 69 full texts articles were checked for eligibility, of which ten were included in the systematic review. *Moderate* quality of evidence indicated that exercise interventions containing functional-task training had a positive effect on ADL performance scores on the Unified Parkinson's Disease Rating Scale (UPDRS) in people with Parkinson (pwp) directly after intervention (UPDRS = -2.62(-5.34;0.10)).

This effect improved, in favor of functional-task interventions, at the first follow-up (UPDRS = -4.0(-7.56;-0.4)). A post-hoc meta-regression analysis yielded a significant relationship between intensity rate (minutes/week) and the size of the (average) effect on ADL score.

Conclusion: Exercise interventions containing functional-task training have a clinically important positive effect on ADL performance in pwp directly after intervention and at first follow-up, compared to no intervention or placebo. The intensity rate of the functional-task training should be as intense as possible, within the capabilities of the person with PD. Future research is necessary to determine the exact amount of effect that can be contributed to functional-task training.

1. Introduction

Parkinson's Disease (PD) is the second most common neurodegenerative disorder after Alzheimer`s disease.[1] People with Parkinson (pwp) can experience difficulties with walking, balance, dual tasks and cognitive function as PD progresses.[2–5] The progression of the disease can be associated with loss of independence in basic Activities of Daily Living (ADL)(walking, transferring in/out bed, dressing) and Instrumental Activities of Daily Living (IADL)(housework, shopping, preparing a meal).[2] Treatment of people with Parkinson (pwp) aims to control symptoms, as optimizing ADL, participation and quality of life in all stages of the disease, rather than cure the disease.[6]

Previous studies show that exercise programs targeting gait, balance, transfers or physical capacity can reduce motor symptoms in pwp,[7–11] although there is a lack of evidence about the effects of these exercise programs on ADL or IADL. The European guideline for PD recommends physical therapists to focus exercise programs on functional-task training, in which those tasks will be trained that are aimed to be improved.[12] The authors of the guideline referred to a study that compared functional-task and resistance training in healthy elderly,[13] the effects on strength were equal, but functional-task training was more effective for ADL performance with longer lasting effect. The functional-task training consisted of exercises of diverse daily activities, which were executed with different attributes, with interaction with other persons in various environments. These variations aim to induce relatively permanent changes in the capability for movement, also known as motor learning.[14] In these processes, the fronto-parietal cortices, the basal ganglia and the cerebellum are involved.[15,16] Since

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the function of the basal ganglia is receding in pwp, motor learning might be impaired. Therefore, both the short as well as the long-term effects of functional-task training on ADL function in healthy elderly are not necessary generalizable to pwp.[17]

The results of studies with functional-task exercises as part of their exercise intervention with participants with PD and ADL performance as one of their outcome measurements, could solve the generalizability issue. Since the results of these studies were conflicting[18–20]; the effectiveness of functional-task exercises on ADL is unclear in pwp.

Therefore the aim of this systematic review is to summarize the best evidence for the effect of functional-task training, on ADL performance in pwp.

2. Methods

2.1. Search strategy

The protocol for this study was published in the Prospero database.[21] The protocol and reporting were based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement.[22] We searched Cinahl, Embase, Medline, Pedro and CENTRAL for articles from inception to 10 February 2016. Terms and free text words such as “function training”, “functional-task”, “task-related” were used in combination with terms for Parkinson’s disease. The detailed search strategy is presented in Appendix 1. There was no restriction on publication language.

2.2. Eligibility criteria

Functional-task training was defined here as repetitive training of ADL were trained during the exercise program. If activities were trained without the context in which they are necessary in daily living, e.g. walking on a treadmill, these were not labelled as functional-task training. Studies with functional-task training were considered eligible for inclusion if they met the following criteria:

1) Randomized Control Trial (RCT) or a cross-over trial, 2) Participants were diagnosed with Parkinson Disease stage 1–4 on the H &Y-scale,[23] 3) No cognitive impairment or comorbidity that is likely to influence the training effects., 4) Control groups consisted of no intervention, usual care (medication and other programs without focus on ADL training) or sham intervention (e.g. stretching or group education), 5) Outcomes included the performance of ADL relevant for IADL, measured with Unified Parkinson's Disease Rating Scale (UPDRS)-ADL or other ADL scales, 6) Outcomes were measured directly after the intervention or within 6 months.

2.3. Study selection

Study selection, data extraction and the assessment of therapeutic validity and risk of bias were carried out by two reviewers (SP, PN) independently. Disagreement was resolved by discussion or, if necessary, a third reviewer (CL) was consulted.

2.4. Therapeutic validity

Therapeutic validity of the functional-task training programs was assessed using the CONTENT-scale developed by Hoogeboom et al.[24] Total scores ranged from zero (worst) to nine (best). A score of six or higher was defined as high.[24]

2.5. Risk of bias

The studies were assessed on seven criteria recommended by the Cochrane Handbook for Systematic Review of Interventions.[25] These criteria included items for random sequence generation, allocation concealment, blinding of participants, professionals and outcome assessors, incomplete outcome data, selective reporting and other bias. Each item could be scored ‘yes’ (low risk of bias), ‘unclear’ or ‘no’ (high risk of bias).

2.6. Outcomes

The primary outcome was ADL performance measured by UPDRS-ADL, Self-Assessed Disability Scale (SAS), Nottingham Extended Activities of Daily Living index (NEADL), Functional Independence Measure (FIM) or Physical Performance Test (PPT). Outcome data were separated in two measurement moments, directly after intervention and/or at the first follow-up between one and six months.

The UPDRS-ADL scale is a validated scale to measure ADL in pwp.[26] The scale consists of 13 items and the score ranges from a minimum of zero (best) to 52 (worse). The Minimal Clinical Important Change (MCIC) was determined as a score between 2.3 and 2.7.[27] The other ADL scales, SAS and NEADL, are validated scales to measure ADL in pwp as well.[26] The FIM is recommended for measuring ADL, but not validated in a study with pwp.[26] The PPT is a performance test for physical functioning which is not validated in a population with pwp.[28]

2.7. Statistical analysis

ADL performance was measured by different scales. Therefore the mean difference was converted into the effect size Hedges`g (ˆg), which was computed as the mean change of the intervention group subtracted with the mean change of the control group, divided by the baseline pooled standard deviation.[25] A negative `g represents a beneficial improvement for ADL performance for functional-task training group. To compare the results to a minimal clinical important change (MCIC), `g is re-expressed into the UPDRS-ADL score using the pooled standard deviation at baseline of the studies.[25] If studies presented the median instead of the mean, the study was excluded from the meta-analysis.

We performed meta-analyses by pooling the study results into a weighted effect size direct after intervention and at first follow-up within six months. Since clinical heterogeneity was expected, we used a random effects model. The meta-analysis was performed in Review Manager (RevMan, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).[25]

We assessed heterogeneity by the I^2 and χ^2 statistics, and visual inspection of the overlap of 95% confidence interval (CI). When I^2 was lower than 30% it was considered as not important, 30%–60% as moderate and 60%–100% as substantial.[25]

Subgroup analyses were performed to differentiate between studies with high and low therapeutic validity. If five studies or more were included in one comparison and the heterogeneity was substantial, we performed a meta-regression analysis to explore the heterogeneity. The meta-regression analysis was performed in R-studio using the metafor-package.[29]

2.8. GRADE

The quality of evidence was evaluated according to the principles of the GRADE-approach.[25] Since only RCT`s were included, the evaluations started at the highest level of evidence and it was downgraded if there were serious (one level) or very serious (two levels) concerns about, risk of bias, inconsistency, imprecision, indirectness or publication bias.[25]

3. Results

3.1. Study selection

A total of 3384 citations were identified from the electronic databases (Fig. 1). After the duplicates were removed, 2546 titles and abstracts were screened and 2477 citations were excluded. We retrieved

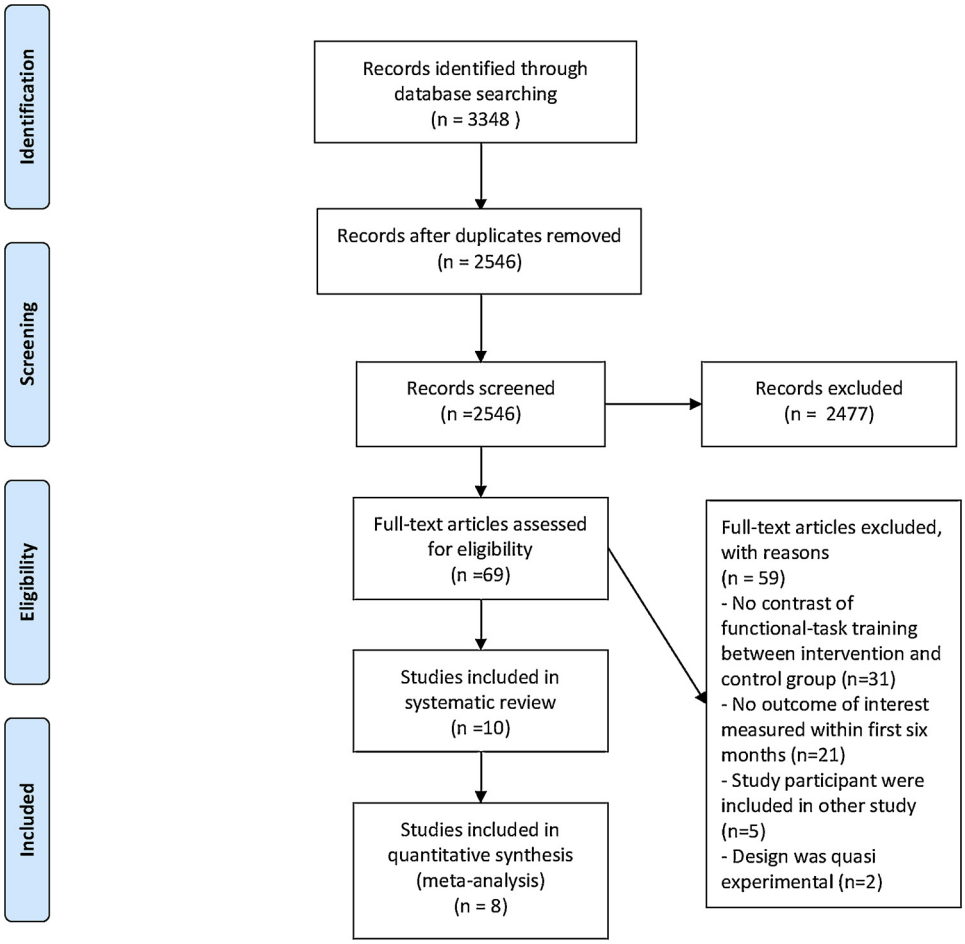

Fig. 1. Flowchart.

the full text articles of the remaining 69 studies. Absence of contrast in the amount of functional-task training between intervention and control group (n = 31) was the main reason for exclusion after assessing full text articles. For example the study of Lun et al.[30] compared functional-task training at home with and without the supervision of a physical therapist. Other reasons for exclusion were no outcome of interest measured within the first six months (n = 21), study participant were included in another study (n = 5) and a quasi-experimental study design (n = 2). Details for definitive exclusion for full text can be obtained from the first author.

Ten RCT`s were included in the systematic review (Table 1). Two studies used a cross-over design,[20,31] two studies had three intervention arms[32,33] and the other six studies were two arm parallel designs.[18,19,34–37]. We retrieved the data from the first period of the cross-over trails and the data from the functional-task training group and the control group in the three arm trials. This resulted in a total of 1015 pwp, their stadia on the H&Y-scale ranged from one to four. In all exercise interventions ADL tasks were trained repetitively under supervision of at least one physical therapist. The intensity rate (minutes trained/week) differed from 60 to 900 and the intervention period ranged from three to 26 weeks. In the exercise interventions functional-task exercises were combined with other content (Table 1). Four interventions were executed at home of the participants,[18,20,32,36] three were in a physical therapy practice[31,33,34] and the other three were incorporated in a multi-disciplinary program in a rehabilitation clinic.[19,35,37]

Eight studies were included in one of the meta-analyses. The studies of Nieuwboer et al.[20] and Stack et al.[36] could not be included, since their results were presented in medians with an interquartile range.

3.2. Therapeutic validity

Scores ranged from three points to eight on the CONTENT scale. Eight studies scored six or higher and were therefore assigned to the high therapeutic validity group (Table 2). Description of the training intensity (n = 3), the intervention rational (n = 4) and personalization (n = 5) were among the poorest reported items.

3.3. Risk of bias

The risk of bias of the eight studies included in the meta-analysis is presented in Fig. 2. The studies of Nieuwboer et al.[20] and Stack et al.[36] scored high risk on the item `blinding of participants and personnel'. Nieuwboer et al.[20] scored low on all other items, and Stack et al.[36] scored high risk on `attrition bias' because of their high lost to follow-up rate.

3.4. ADL performance directly after intervention

With the exception of the study of Frazitta et al.[35] all studies presented ADL performance measured directly after intervention. In the study of Nieuwboer et al.[20] the functional-task training group (n = 76) started with a NEADL (low = good) score of 41(32–53.8) and ended with 42.5(36–53) after the six weeks intervention. The controls (n = 77) had a baseline score of 40(35–51) and scored 46(34–51) after six weeks. The functional-task training group (n = 16) in the study of Stack et al.[36] started at baseline with a median SAS (low = good) score of 50(43–59), after four weeks intervention it decreased to a median score of 49(43–67). The control group (n = 18) increased from

Table 1
Characteristics of included studies.

Study	Design/Participants	Intervention	Intensity rate Duration	Control group	Outcomes (primary /secondary)
Ashburn et al 2007	• RCT/ 2 parallel groups • N = 142 • Hoehn and Yahr 2-4 • Independently mobile, living at home in the community, experiencing more than one fall in the previous 12 months.	• Individualized exercises chosen by a physical therapist. Exercises aimed to improve ADL at individual level. They were given at home and contains range of motion, strengthening, balance or walking exercises.	• 1 x 60 minutes a week • 6 weeks.	• The control group received usual care which, for the vast majority, comprised contact with a local PD nurse	• Differences in fall rates. • **SAS (six months)** • Berg Balance test • Functional rest test • QOL thermometer
Conradson et al 2015	• RCT/ 2 parallel groups. • N = 100 • Hoeyn and Yahr 2 and 3. • Based on assessment they included individuals with impaired balance, such as instability during postural transfers and gait impairments	• Highly challenging balance tasks exercises with progression in difficulty by adding extra tasks. • The training was performed in groups of 4 to 7 participants supervised by 2 physical therapist.	• 3 x 60 minutes a week • 10 weeks	• The participants in the control group were encouraged to maintain their normal physical activities and were not restricted from participation in ongoing rehabilitation programs	• Mini BEST test • Gait velocity. • FES • **UPDRS 2 (ADL) (no follow up)** • Physical activity level • Performance of cognitive talk while walking.
Ellis et al 2005	• RCT with a crossover design. • N = 68 • Hoehn en Yahr 2 and 3 • Participants were diagnosed with typical idiopathic PD.	• Functional strengthening, functional training, balance training, cueing and recreational games and relaxation. • Each sessions was led by a physical therapist and an assistant.	• 2 x 90 minutes a week • 6 weeks	• Waiting list (cross-over trial)	• The Sickness Impact Profile (SIP 68). • UPDRS 2 ADL (no follow up) • UPDRS total score
Frazzitta et al 2015	• RCT/ 2 parallel groups. • N = 40 • Hoeyn an Yahr 1 to 1,5. • Newly diagnosed PD patients.	• Multi-disciplinary rehab treatment (MIRT), including training of activities of daily living. • Three daily sessions: one functional task exercises, one balance and mobility last one was occupational therapy focused on ADL tasks.	• 15 x 60 minutes a week • 4 weeks	• Patients in the Control Group underwent only pharmacological treatment	• UPDRS 2 (ADL) (no measurement direct after intervention, six months) • UPDRS 3 • Six minute walk test • TUG • Dosage of levodopa
Monticoni et al 2015	• RCT/ 2 parallel groups. • N = 70 • Hoeyn and Yahr 2,5- 4. • A decline in function assessed by a physiatrist (eg, worsening of transfers and walking ability, frequent falls, risk of losing their independence).	• This program included motor training, cognitive training, and ergonomic education. Motor training, performed by physical therapist, involved task-oriented exercises, transfers, balance, and gait training. • Daily Physical training, including ADL tasks by a physical therapist, two times a week cognitive training by a psychologist and one time ergonomic education by an occupational therapist.	• 450 minutes a week • 8 weeks	• Program included neuromotor techniques, passive and active articular mobilization, strengthening and stretching of the spine and limbs, as well as balancing by means of proprioceptive training when standing, and walking exercises, mainly devoted to resistance and velocity training.	• UPDRS 3 (motor score). • **FIM (ADL scale) 12 months.** • Berg balance scale • PDQ 39
Morris et al 2015	• RCT/ 3 parallel groups • N = 210 • Hoehn and Yahr less than 5. • PD confirmed by a medical practitioner, and being medically able and safe to perform the interventions	• Fall prevention information program combined with movement strategy training. Strategies to prevent falls, improve mobility and balance during functional tasks, such as transfers. • Program was supervised by a physical therapist at home.	• 120 minutes a week • 8 weeks	• Life skill sessions given by physical therapists, occupational therapist or speech therapist. These included social activities, practical advice, information sessions and group discussions but not any content related to falls or mobility. • Progressive Resistance Strength Training*.	• Falls Rates During 12-Month Follow-up Period • **UPDRS 2 (ADL) (9 months)** • UPDRS 3 • PDQ 39 • EURP QOL 5d • Six meter walking test • TUG.
Nieuwboer et al 2007	• Single blind cross-over trial. • N = 153 • Hoehn and Yahr 2-4 • Patients with idiopathic Parkinson's disease.	• Cueing training in home situation delivered by a therapist. • Cued practice was applied during a variety of tasks and environmental situations.	• 3 x 30 minutes a week • 3 weeks	• Waiting list (cross-over trial)	• Posture and gait (PG) score, a composite score of gait and balance UPDRS items (13–15 and 29–30) • **NEADL (no follow up)** • Ten meter walk test • PDQ 39

(*continued on next page*)

Table 1 (*continued*)

Study	Design/Participants	Intervention	Intensity rate Duration	Control group	Outcomes (primary /secondary)
Schenkman et al 2012	• RCT/ 3 parallel groups • N = 121. • Hoehn and Yahr 1-3 • Lived in the community, and ambulated independently.	• Individualized spinal and extremity flexibility exercises supervised by a physical therapist followed by group balance/functional training.	• 3 x 30 minutes a week • 18 weeks	• Endurance group* • Fitness counts program (usual care) without any supervision or follow up. Program from 2012, version from 2014 is online available. [4]	• Physical function (CS-PFP) • Balance (FRT) • Walking economy (oxygen uptake (ml/kg/min)). • **UPDRS 2 (ADL) (six months** • UPDRS 3 (motor score) • PDQ 39
Stack et al 2012	• RCT/ 2 parallel groups. • N = 47 • Hoeyn and Yahr 1 to 4. • Patient diagnosed with PD and problems with chair transfers.	• A home physiotherapy program focused on chair transfers. Which contained supervised exercises, teaching movement strategies and included cueing. • A four weeks program with a maximum of one-hour per session three times a week.	• 3 x 60 minutes a week • 4 weeks	• Control group did not received any extra therapy.	• **SAS (one month)** • PAS sit to stand • Standing start 180 degree turn test • Functional reacht • UPDRS posture items • HR-QOL
Stozek et al 2015	• RCT/ 2 parallel groups. • N = 64 • Hoehn and Yahr 1,5-3. • Diagnosis of PD according to UKPD Society Brain Bank criteria.	• Rehabilitation training program focused on mobility, balance, gait and functional training exercises. • Four weeks program with 28 two-hour therapy sessions. Intervention was conducted in groups of two or three persons.	• 7 x 120 minutes a week • 4 weeks	• Participants in the control group received only medication therapy.	• **Nine item PPT test (one month)** • Tandem stance (balance) • Pastor test (balance) • Ten met walk test. • Spinal axial rotation

Bold outcomes: ADL performance.

Nottingham extented activities of living; index(Neadl); Parkinson`s disease questionnaire (PDQ-39); Functional independence measure (FIM); Self-Assessed Disability Scale(SAS); Physical Performance Test (PPT).

Table 2
Assessment of therapeutic validity per individual study per scale item.

	Patient eligibility			Rationale		Content				
Study	Described	Adequate	Setting and therapist	Study	Intervention	Intensity	Monitored	Personalized	Adherence	Total score
Ashburn et al. 2007	yes	yes	yes	yes	no	no	yes	yes	no	6
Conradson et al. 2015	yes	yes	yes	yes	yes	yes	yes	no	yes	8
Ellis et al. 2005	yes	yes	yes	yes	no	no	no	no	yes	5
Frazzitta et al. 2015	yes	no	yes	yes	yes	yes	yes	no	yes	7
Monticoni et al. 2015	yes	yes	yes	yes	no	no	yes	yes	yes	7
Morris et al. 2015	yes	no	yes	yes	no	no	yes	yes	yes	6
Nieuwboer et al. 2007	yes	yes	yes	yes	no	no	yes	yes	yes	7
Schenkman et al. 2012	yes	yes	yes	yes	yes	yes	yes	no	no	7
Stack et al. 2012	yes	yes	yes	yes	yes	no	yes	yes	no	7
Stozek et al 2015	yes	no	no	yes	no	no	yes	no	no	3

Bold outcomes: studies with a therapeutic validity score > 5.

52(40–64) to 59(45–71). The results of the seven other studies were included in the meta-analysis representing a total of 596 participants. The mean effect across the studies was `g = -0.63(-1.10;-0.16) (Fig. 2). The 0-hypothyses of homogeneity was rejected ($X^2$ = 46.85 df = 6 (p < 0.01)) and the $I^2$ total value was 87%. Therefore, heterogeneity was considered substantial. Within the high therapeutic validity subgroup, the mean effect across the studies was `g = -0.53(-1.08;0.02). Heterogeneity remained substantial, with an I^2 value of 88% in the high and 86% in the low subgroup.

The pooled standard deviation at baseline in the studies using the UPDRS-ADL was 4.94 points.[31–35] The result of `g -0.53(-1.08;0.02) is equal to a decrease of 2.62(-0.10;5.34) points on the UPDRS-ADL scale.[25]

A post-hoc meta-regression analysis yielded a significant

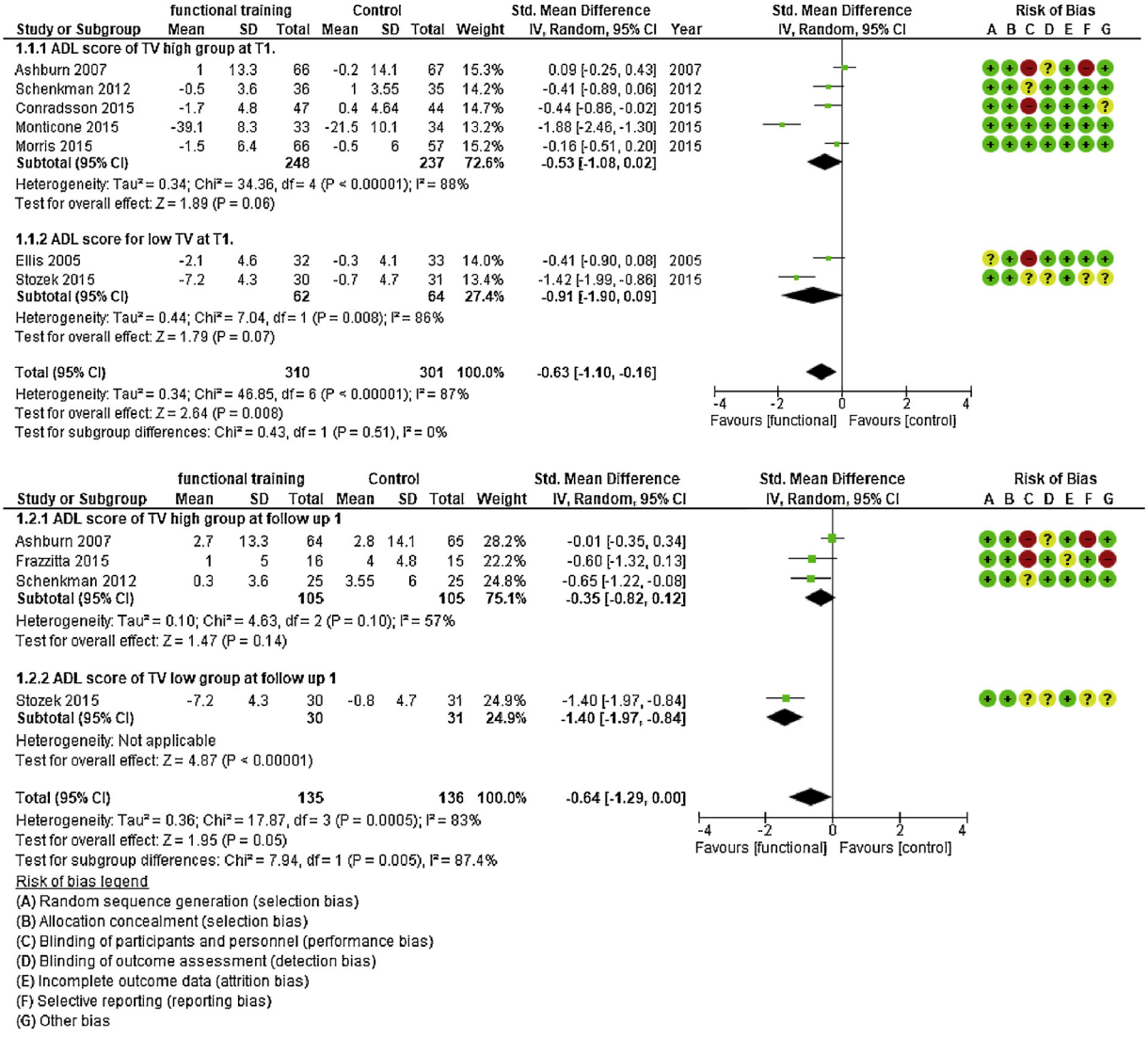

Fig. 2. ADL score directly after intervention and at first follow up.

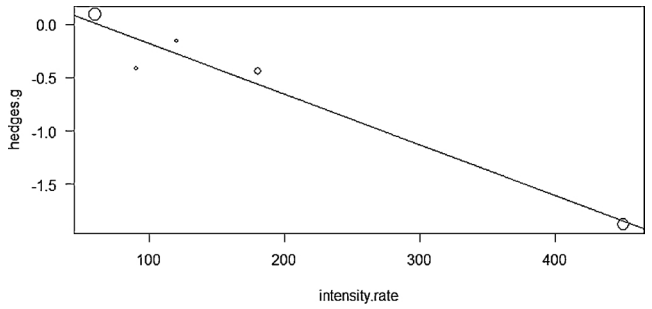

Fig. 3. Meta-regression analyses.
Post-hoc meta-regression analysis: relationship between intensity rate (minutes/week) and the size of the (average) effect on ADL score (intercept = 0.313, b = -0.005, S.E. = 0.001, p = < 0.001).

relationship between intensity rate (minutes/week) and the size of the (average) effect on ADL score (intercept = 0.313, b = -0.005, S.E. = 0.001, p = < 0.001) (Fig. 3). The amount of heterogeneity accounted for was 100%.

3.5. ADL performance measured at first follow-up

ADL performance measured at first follow-up after intervention and within six months was described in five studies.[18,33,35–37] Two studies had their first follow-up after more than six months, Morris et al.[32] and Monticone et al.[19] and were therefore excluded for the analysis at first follow-up. Stack`s functional-task group (n = 16) declined to 58(50–66) after four months, their control group (n = 18) scored 60(48–66).[36] The results of the other four studies were included in the meta-analysis, representing 271 participants (Fig. 2). The mean effect across the studies was `g = -0.64(-1.29;0.00). The 0-hypothyses of homogeneity was rejected (X^2 = 1787 df = 3 (p < 0.01)) and the I^2 total value was 83%. Therefore heterogeneity was considered substantial. I^2 decreased to 57% in the high subgroup and 0% within the low. With respectively a `g of -0.35(-0.82; 0.12) and -1.40(-1.97;-0.84). A sensitivity analysis with the results of Morris and Monticone changed the mean effect to `g of -0.90(-1.56;-0.25), and the high subgroup effect to -0.81(-1.53;-0.08). Which is equal to a decrease of 4.0(0.4;7.56) points at the UPDRS-ADL scale.[25]

3.6. GRADE

The quality of the evidence of the studies with a high therapeutic validity reporting ADL directly after intervention was *moderate* (Table 3). Only RCT`s were included, therefore the starting point of the evidence was *high* quality.[25] It was downgraded to *moderate* since performance bias occurred in the studies of Ashburn et al.[18] and Conradson et al.[34] At first follow-up within six months, the quality of evidence was downgraded twice ending *low* (Table 3). Besides performance bias, which could have occurred in of Ashburn et al.[18] and Frazitta et al.[35] the other reason for downgrading was lack of precision since the analysis had 210 participants.

4. Discussion

To our knowledge, this is the first systematic review that evaluated the effect of functional-task training on ADL performance in pwp. The results show that exercise interventions containing functional-task training have a positive effect on ADL performance for pwp directly after intervention. This effect remains at first follow-up. Since most of the exercise interventions were a combination of functional-task training and other content, we were not able to determine the exact effect of functional-task training.

Table 3
Summary of findings: Exercise interventions containing functional-task training compared to usual care/placebo for improvement of ADL performance in patients with Parkinson`s Disease.

Outcomes	Anticipated absolute effects* (95% CI) Change score of usual care/placebo	`g	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
ADL scales (UPDRS-adl, SAS, FIM). Low is good. Direct after intervention.	Decrease of 0.24 SD compared to baseline.	`g - 0.53(-1.08, 0.02)	485 (5 RCTs)	⊕⊕⊕◯ Moderate[1]	Nieuwboer NEADL (0-66,low = good) scores in mediaan(IQR). Functional; T0: 41(32-53) T1 42,5(36-53), controls;T0 40(35-61) T1 46(34-51). Stack; SAS(low = good), functional T0 50(43-59) T1 49(43-67) controls T0 52(40-64) T1 59(45-71).
ADL scales (UPDRS-adl, FIM). Follow up: range 1 months to 6 months	Increase of 0.38 SD compared to baseline.	`g -0.35(-0.82, 0.12)	210 (3 RCTs)	⊕⊕◯◯ LOW[2,3]	Stack: SAS(low = good) functional group: 58(50-66), control group: 60(48-66) measured 4 weeks after the intervention.

*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
`g: Hedges MD: Mean difference 95%CI: 95 % confidence interval.
GRADE Working Group grades of evidence.
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
Performance bias might have occurred in studies of Ashburn and Conradson.
Performance bias might have occurred in studies of Ashburn and Frazitta.
Confidence interval contains zero, lack of precision < 300 participants.

4.1. ADL performance directly after intervention

The positive effect of exercise interventions containing functional-task training was also found in the total group and in the studies which were not included in the meta-analysis.[20],[36] According to the GRADE recommendations, the quality of the evidence of the studies in the meta-analysis was *moderate*.

The heterogeneity of 86% in the total group could not be attributed to therapeutic validity (CONTENT scale). Further exploration of the heterogeneity showed a significant positive correlation between intensity rate and ADL performance (Fig. 2). These results suggest a dose-response relationship between functional-task training and ADL performance. Other potentially relevant covariates, such as the location of the intervention (at home, rehabilitation or physical therapy clinic) and the disciplines involved in the intervention, could not be studied due to the small number of included studies.

Compared to the MCIC, the mean effect of 2.62 lower score indicates a clinical important effect.[27]

The results of this review are in line with previous reviews, where the effect of functional-task training was evaluated within healthy elderly and people recovering from a stroke.[38],[39] Performing daily tasks, such as turning in bed or dressing, requires cooperation of multiple muscle groups and body motor elements to carry out these tasks. To execute a task, individuals need to control all elements. If training is focused on one of those element only, and ignores other elements, the effect on ADL may be compromised. When training the actual task in different contexts and environments, with different levels of resistance and different speeds, all the elements are trained in every repetition. Thus, motor learning could be established. This could explain why the effect of exercise interventions containing functional-task training on ADL is larger than the effects of physical therapy and external sensory cueingon ADL.[10],[40]

The importance of performing ADL was also recognized by a specific PD treatment regimen, Lee Silverman Voice Treatmant (LSVT-BIG).[41] In their exercise interventions, 50% of the time is spent on performing ADL using high amplitude (BIG) movements.[41],[42] If exercise interventions only focus on basic exercises aiming to improve speed, range of motion or strength, the effect on ADL might be a lot smaller.

4.2. ADL at first follow-up

The effect of exercise interventions containing functional-task training remains after first follow-up. The quality of the evidence on the ADL outcome after first follow-up was *low*, according to the GRADE recommendations. The effect was smaller than the MCIC reported by Schrag.[27] But if the results of Morris and Monticone were included in the meta-analysis, it would result in a 4.0 points lower score on the UPDRS-ADL scale, which indicates a clinical important effect.[27]

Since basal ganglia and cerebellum are involved in the motor learning process and these functions are declining in pwp it was questionable whether the short term results remained in the long-term.[14–17] Elements that could induce motor learning and therefore lead to a longer lasting effect are training the actual task, task variation and interaction with other persons.[13] Despite that these elements were present in the included interventions; relative permanent changes in the performance of ADL were only found in the studies of Monticone, Morris and Stozek.[19,32,37] Reason for these differences could be found in the intensity rate. This was at least 120 min a week (Table 1) in the intervention that showed permanent effects on ADL.

It was suggested earlier that a greater amount of practice increases learning.[43] This suggestion was evoked by Paul et al.[44] They found that there is a minimal amount of exercises challenging the gait and balance required, to reduce falling and improve gait.

Another way to enhance motor learning and therefore improve and retain performance of ADL might be the use of external rhythmical cues during training.[45] It has been hypothesized that external cues bypass the basal ganglia and use an alternative pathway to initiate movements.[40] Results of the review of Cassimatis et al.[40] describes a larger effect of external sensory cues on ADL presenting at first follow-up (3.57 points on UPDRS ADL) compared to the effect directly after intervention (2.27 points). Pwp were trained to implement external cues during their ADL activities. In the studies of Monticone, Morris and Stozek different forms of external cues were used during the exercise interventions. Whether the improvements are due to intensive training, or because of the use of external sensory cues requires further investigation.

4.3. Clinical implications

This review indicated that exercise interventions containing functional-task exercises have a positive effect on the ADL performance of pwp. There is a positive correlation between the size of the improvement and the intensity of training. Each person with PD consulting a physical therapist, is confronted with an unique ADL problem. Therefore the content of each program should be tailored for each person with PD. The ADL, which is experienced as a problem, should be trained as intense as possible, in various ways, in various environments and in combination with interaction with other persons.

4.4. Strengths and limitations

A strength of this review is that all included studies are judged on their risk of bias as well as their therapeutic validity. Therefore, the reader is able to get an overview of the therapeutic validity of the intervention according to the CONTENT scale.[24] This provides insight in the quality of the interventions, or at least the quality of reporting of the interventions.

Another strength is the exploration of the heterogeneity with a meta-regression analyses. After a random effects study the remaining heterogeneity should be explored.[25] The minimal number of studies recommended for a meta-regression analysis is five.[25]The number of studies within a meta-analysis is often lower than five, therefore the exploration using a meta-regression analysis is often lacking. We were able to perform a meta-regression analysis and attribute a large part of the heterogeneity due to the intensity of the training.

There were also a few limitations in this review. Firstly, the included studies had small sample sizes. Therefore, baseline differences of the outcome interest between intervention and control group occurred within the original studies. The use of `g resolved this problem and made it possible to compare studies measuring the same outcome with a different measurement scales. The downside of `g is that it is not possible to interpret it directly. There is no MCIC for this effect size, re-expressing the results to a known instrument was therefore necessary. We used the standard deviation of all the included studies to re-express the results. Although this is the recommended procedure,[25] it is not guaranteed that the results would be similar if the same instrument was used in all the studies.

A second limitation is the heterogeneity between the remaining parts of the interventions. Although in all interventions ADL were repetitively trained during the interventions, this was seldom the only content of the intervention. Differences in the content of the remaining parts of the interventions were described in Table 1. Since these remaining parts were the main interest for the original researchers they were not present in the control groups. Future research is necessary to determine the exact amount of effect which can be contributed to functional-task training.

Third limitation is that the small amount of studies limited the power of the meta-analysis and the number of covariates in the meta-regression analysis. Since this was a post-hoc analysis with the minimal amount of studies, the results have to be interpreted with caution.[25] We could not explore if there were differences in the other elements in the interventions that could explain the heterogeneity.

4.5. General conclusion

Moderate quality evidence showed that exercise interventions containing functional-task training have a clinically important positive effect on ADL performance for pwp directly after intervention as compared to no interventions, usual care, or forms of sham exercises. A higher intensity rate resulted in larger effects of functional-task training on ADL performance. According to *low* quality evidence, the effect remains positive at first follow-up after interventions within six months and is even larger in two studies with longer follow-up moments (nine and twelve months). The intensity rate of the interventions should probably be as intense as possible, within the capabilities of the person with PD. Future research is necessary to determine the exact amount of effect that can be contributed to functional-task training.

Conflict of interest

There were no conflicts of interest.

Sponsor`s role

None.

Appendix 1

Pubmed search date: 10-02-2016, 757 Hits.

("Parkinsonian Disorders"[Mesh] OR "Parkinson Disease"[Mesh] OR parkinson*[tiab]) AND ("Physical Therapy Modalities"[Mesh] OR "Motor Activity"[Mesh] OR "Task Performance and Analysis"[Mesh] OR "Exercise"[Mesh] OR "Physical Fitness"[Mesh] OR exercis*[tiab] OR physical activit*[tiab] OR fitness[tiab] OR physical conditioning*[tiab] OR circuit training[tiab] OR circuit class[tiab] OR task-related[tiab] OR sequential exercise[tiab] OR repetitive practice[tiab] OR functional task[tiab] OR training[tiab]) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT (animals[mh] AND humans[mh])))

Cochrane, same strategy and search date as pubmed; 863 HITS (RCT`s).

Embase search date: 10-02-2016, 1412 Hits

1. parkinsonism.mp.
2. Parkinson disease.mp.
3. parkinson*.ti,ab,kw.
4. 1 or 2 or 3
5. fitness.mp.
6. exp exercise/
7. exp motor activity/
8. functional training.mp.
9. (exercis* or physical activit* or fitness or physical conditioning* or circuit training or circuit class or task-related or sequential exercise or repetitive practice or functional task).mp. or training.ti,ab,kw. [mp = title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
10. 5 or 6 or 7 or 8 or 9
11. clinical trial/Insert Search Statement
12. randomized controlled trial/
13. exp randomization/
14. exp placebo effect/ or exp placebo/ or placebo.mp.
15. Randomized controlled trial$.tw.
16. Rct.tw.
17. Randomly.tw.
18. trial.ti.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. animal/ not (animal/ and human/)
21. 4 and 10 and 19
22. 21 not 20

Cinahl: 10-02-2016 316 Hits.

S21S13 AND S14 AND S20
S20S15 OR S16 OR S17 OR S18
S19("Rct") AND (S15 OR S16 OR S17 OR S18)
S18"Rct"
S17"randomization"
S16"randomized trial"
S15(MH "Clinical Trials+") OR "clinical trials" OR (MH "Randomized Controlled Trials")
S14S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
S13S1 OR S2 OR S3
S12("training program") AND (S1 OR S2 OR S3)
S11"training program"
S10(MH "Physical Therapy+") OR "physical therapy"
S9"physical conditioning"
S8"fitness"
S7"circuit training"
S6(MH "Group Exercise") OR (MH "Exercise+") OR "exercise" OR (MH "Therapeutic Exercise+")
S5"task exercise"
S4(MH "Functional Training") OR "functional training"
S3"parkinson"
S2"parkinsonism"
S1(MM "Parkinson Disease")

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