Does Cueing Training Improve Physical Activity in Patients With Parkinson's Disease?

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Abstract

Background. Patients with Parkinson's disease (PD) are encouraged to stay active to maintain their mobility. Ambulatory activity monitoring (AM) provides an objective way to determine type and amount of gait-related daily activities. *Objective*. To investigate the effects of a home cueing training program on functional walking activity in PD. *Methods*. In a single-blind, randomized crossover trial, PD patients allocated to early intervention received cueing training for 3 weeks, whereas the late intervention group received training in the following 3 weeks. Training was applied at home, using a prototype cueing device. AM was applied at baseline, 3, 6, and 12 weeks in the patient's home, to record body movements. Postures and motions were classified as percentage of total time spent on (*a*) static activity, further specified as % sitting and % standing, and (*b*) % dynamic activity, further specified as % walking, % walking periods exceeding 5 seconds (W>5s) and 10 seconds (W> 1 0s). Random coefficient analysis was applied. *Results*. A total of 153 patients participated in this trial. Significant improvements were found for dynamic activity (b = 4.46; $P < .01$), static activity (b = -3.34; $P < .01$), walking (b = 4.23; $P < .01$), W>5s (b = 2.63; $P < .05$), and W> 1 0s (b = 2.90; $P < .01$). All intervention effects declined significantly at 6 weeks follow- up. *Conclusion*. Cueing training in PD patients' own home significantly improves the amount of walking as recorded by AM. Treatment effects reduced after the intervention period, pointing to the need for permanent cueing devices and follow-up cueing training.

Keywords

Parkinson's disease, rehabilitation, physical activity, gait, cueing, activity monitoring

Introduction

Parkinson's disease (PD) is one of the most common neurological disorders in elderly people.[1] Between the age of 55 and 85 years, 4.2% of all women and 6.1% of all men develop PD.[2] The major motor symptoms in PD are tremor, rigidity, bradykinesia, and postural instability, resulting in problems with gait, balance, transfers, and posture.[3] These problems can lead to reduced mobility and decreased levels of physical activity, which in turn can cause increased dependency and social isolation and thereby reduce quality of life.[4] It is therefore important to encourage patients to maintain their mobility and to stay active, for example, by referring them to physical training programs.[5-7]

These physical exercise programs include use of rhythmic cues. Cueing can be defined as using external temporal or spatial stimuli to facilitate movement (gait) initiation and continuation.[8] Unfortunately, evidence-based knowledge about effects of cueing in PD is limited. Best-evidence synthesis of 24 studies, up to 2002, showed only 1 high- quality study specifically focused on the effects of auditory rhythmical cueing.[9] Studies claim positive effects of cueing on gait speed of patients with PD; however, it was unclear whether positive effects identified can be generalized to

improved activities of daily living in patients' own home setting and reduced frequency of falls in the community.[10] In addition, the sustainability of a cueing training program remains uncertain.[10] A recent review on cueing suggests that cueing can have an immediate and powerful effect on gait in PD.[10] The studies included in this review, however, suffered from lack of methodological quality and were mostly executed in laboratory situations. The need for studies with high methodological quality stimulated the initiation of a randomized controlled trial with the acronym RESCUE (REhabilitation in Parkinson's disease Strategies for CUEing). It was shown that a cueing program using auditory, visual, and tactile cues improved posture and gait scores, gait speed, step length, and timed balance tests in patients with PD.[8] In addition, secure mobility during functional activities was improved, and freezers showed a reduction in the severity of freezing. These RESCUE trial results are single, cross-sectional snapshots of the capacity of the PD patients and were

obtained in the on-phase of medication. Results from such clinical testing are assumed to reflect patients' "real-world" activities related to gait. However, test performance achieved in optimally medicated situations, often when patients are not fatigued, combined with patients' desire to perform optimally, may overestimate their actual performance.

In contrast, ambulatory activity monitoring (AM) provides an objective way to determine type and amount of gait-related activities for up to 72 hours.[11] Recent advances in technology have resulted in the development of AMs capable of assessing a number of functional abilities, such as (*a*) the length of time spent in body positions (including static positions such as supine, side lying, prone, sitting, and standing), (*b*) the number of transitions between these positions, (*c*) the length of time spent in dynamic activities such as walking and cycling, (*d*) the number of walking periods, and (*e*) stride frequency.[12] Therefore, AM could provide more "real-world" information about patients' behavior during a day, irrespective of daily fluctuations in on-phase and off-phase. AM is a reliable and valid method for determining walking activity in PD patients.[12,13] In a recent reliability study, high intraclass correlation coefficients (ICCs) ranging from .81 to .96 were found for monitoring walking in patients with PD.[12] However, the test–retest reliability coefficients between 3 consecutive measurements were relatively lower for the categories transfers (ICC = .56), sitting (ICC = .65), and standing (ICC = .75) when compared with walking (ICC = .92).[12] In addition, the RESCUE trial is a collaboration between 3 European countries in which day-time AM is used. Both findings legitimate reliability testing between the 3 observers in terms of absolute agreement in the RESCUE project.

The objective of the present study is to investigate the effect of cueing training on the amount of physical activity, specifically walking, in patients with PD, when monitored in their own home environment. We hypothesized that cueing therapy for 3 weeks would specifically increase the dynamic activities such as walking and accordingly decrease the static activities such as sitting and lying, when compared with no cueing training. A second aim of this study was to investigate the reliability of AM over a 3-week interval.

Methods

For the RESCUE trial, 153 patients were recruited in 3 different countries: 48 patients were recruited at Northumbria University, Newcastle upon Tyne (UK); 51 patients were recruited at the Katholieke Universiteit Leuven (Belgium); and 54 patients were recruited at the VU University Medical Center, Amsterdam (The Netherlands). Main eligibility criteria were (*a*) idiopathic PD, (*b*) Hoehn and Yahr[15] stage II to IV, (*c*) showing mild to severe gait disturbances, (*d*) stable medication usage, (*e*) age 18 to 80 years, and (*f*) absence of cognitive impairment and disorders interfering with participation in cueing therapy. A more detailed description of all eligibility criteria can be found in Nieuwboer et al.[8] All patients gave written informed consent. The study was approved by all medical ethics committees of the participating centers.

Design and Procedures

The RESCUE trial was a single-blind, randomized clinical trial with a crossover design (Figure 1). Patients were randomly allocated using permuted blocks of 6 to an early or late intervention group by an independent person who was otherwise not involved in the study. Allocation was concealed, using opaque sealed envelopes. The early intervention group received cueing training for a period of 3 weeks immediately after randomization. The training program consisted of 9 sessions of 30 minutes over 3 weeks and was immediately followed by a control period of 3 weeks. Patients were encouraged to practice on their own after each training session. At each visit the therapist checked the use of the cueing device outside training time. The late intervention group was put on a waiting list for the first 3 weeks and subsequently received the same cueing program in the second 3 weeks. The choice of 9 treatment sessions of 30 minutes each given in 3 weeks was pragmatically chosen based on the existing policies for reimbursement of physical therapy sessions at home at the time of the study. The early intervention group had a follow-up period of 9 weeks, and the late training group had a follow-up period of 6 weeks. Medication treatment stayed stable throughout the study. Prior to the trial all RESCUE therapists and assessors participated in joint training sessions to standardize their treatment and assessment procedures. Each country had 1 therapist and 1 assessor.

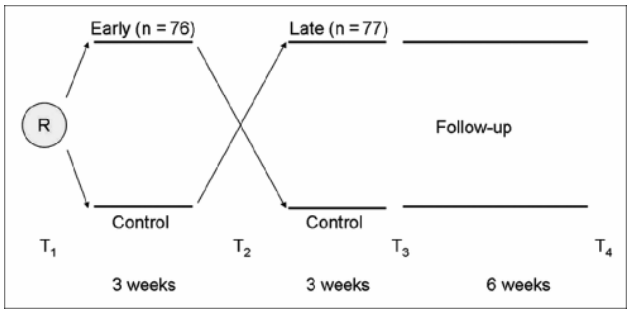


Figure 1. Cross-over design of the RESCUE trial. R, time of randomisation; Early, early intervention group; Late, late intervention group; T1-T4, times 1-4 of assessments with monitoring at 0, 3, 6 and 12 weeks.

Intervention

Each participant received cueing training in the home situation with the help of a prototype cueing device. This cueing device was specifically developed for this project and provided 3 rhythmical cueing modalities: (*a*) an auditory modality (a beep), (*b*) a visual modality (a flashing light at the side of the spectacles), and (*c*) a somatosensory modality (a miniature vibrating cylinder on the wrist).[8] Patients tried out every modality during the first week and practiced with their preferred cueing modality in the second 2 weeks. In addition to the cueing device, parallel lines on the floor or pavement were used in the training as visual cues. Cueing training was aimed at improving gait and gait-related activities (such as step length, walking speed, and management of freezing).

Based on previous experiments undertaken by the RESCUE consortium[14,16-18] and the literature,[9,10] evidence-based guidelines were drawn up, specifying the cueing parameters and instructions for different profiles of patients (available on CD-ROM, http://www.rescueproject.org). Patients were instructed to use the cues and encouraged to practice without the assistance of the therapist outside the regular training time.

Outcome Measures

In addition to recording time, the following outcomes were analyzed:

1. The percentage of time spent in walking, transfer, turning, stair climbing, and cycling activities ("dynamic activities"), with percentage of time spent on walking alone (% walking), further specified as (*a*) average number of walking periods registered per hour exceeding 5 seconds (W_5s)

   and (*b*) average number of walking periods registered per hour exceeding 10 seconds (W_10s).
2. The percentage of time spent in standing, sitting, and lying postures ("static activities").

The primary outcome measure was percentage of time spent on walking activity assuming 10% change in favor of cueing therapy.

Assessment Protocol

All patients were tested by an assessor in their home environment prior to randomization (t_1) and at 3 (t_2), 6 (t_3), and 12 weeks (t_4). Time points for follow-up (t_3 and t_4) were kept identical between early and late intervention for practical reasons. The assessor was blind to group allocation. Each patient was visited at approximately the same time of the day in the on-phase, about 1 hour after medication intake, to control for variations due to the medication cycle. A test battery was used to assess gait and gait-related activities of the patient (for results, see Nieuwboer et al[8]). In addition, an AM (Yitaport3, TEMEC Instruments BY, Kerkrade, The Netherlands) was applied by the assessor to record the body movements of the subject during the day. To measure the effects of practice with cueing and not the immediate effects during cueing, the cueing device was not used during monitoring. Moreover, training was not received on testing days.

The activity monitor consisted of a montage of 5 accelerometers connected to a portable data recorder worn on a belt around the waist. The accelerometers were attached to the body as follows: one on each leg positioned on the lateral aspect of the thigh midway between the greater trochanter of the femur and the midpoint of the patella, orientated in the

sagittal plane; 3 accelerometers were placed on the lower third of the sternum, with the sensors on a specially designed block positioned so that they were orientated in the sagittal, longitudinal, and transverse planes. The skin was prepared by cleaning the area with an alcohol swab and shaving when necessary. The accelerometers were mounted on a piece of thin foam and attached to the skin using Hypafix® tape (BSN Medical, Charlotte, NC). Each accelerometer was connected to a portable battery-powered activity monitor (Yitaport 3, TEMEC Instruments) by cables that ran under the clothes.

Data were sampled at a frequency of 256 Hz and stored at 32 Hz on a removable flash memory card for off-line analysis. The accelerometers recorded gravitational force and accelerations of the moving lower limbs and trunk. The data were analyzed using a specifically designed software program (Yitagraph; TEMEC Instruments Inc), which classified activity into static activity (ie, sitting and standing) and dynamic activity (amount of walking and walking

Table 1. Comparison Between Early and Late Intervention Groups for Demography, Characteristics of Parkinson's Disease, Clinical Data, and Data Derived From Activity Monitoring at Baseline

	Early Intervention Group (n = 76), Median (Q 1 -Q3)	Late Intervention Group (n = 77), Median (Q 1 -Q3)	*P* Value
Demography			
Gender (male/female)[a]	48/28	40/37	.16
Age (years)	67.5 (61.5-72)	69 (62.5-73)	.70
PD characteristics			
Disease duration (years)	7 (4-11)	8 (4-12)	.59
H&Y (on)	2.5 (2.5-3)	3 (2.5-3)	.56
Freezers/nonfreezers[a]	3 1/45	32/45	.92
Clinical data			
UPDRS total	54 (46-65.5)	56 (49-63)	.62
UPDRS motor scale	31 (25-37)	34 (28-41)	.32
Levodopa (mg)	500 (300-700)	350 (200-550)	.07
Data derived from AM			
Registration time (hours)	4.9 (3.5-5.8)	4.56 (3.7-5.5)	.17
Percentage of time spent on dynamic activity	9.4 (5.2-16.7)	10.6 (4.8-16.3)	.74
Percentage of time spent on static activity	90.6 (81.8-94.8)	89.1 (83.7-95.2)	.55
Percentage of time spent on sitting	50.3 (38.6-65.6)	49.2 (35.5-63.6)	.49
Percentage of time spent on standing	25.0 (15.5-36.0)	25.8 (16.0-32.6)	.69
Percentage of time spent on walking	7.3 (4.0-10.9)	7.9 (4.2-13.6)	.55
N walking period ≥5 seconds per hour	13.7 (7.9-21.5)	13.5 (8.6-18.9)	.65
N walking periods ≥10 seconds per hour	8.6 (4.4-13.0)	8.0 (5.2-12.0)	.93

Abbreviations: Q 1 -Q3, interquartile range; PD, Parkinson's disease; M/F, male and female; H&Y (on), Hoehn and Yahr during on; UPDRS, Unified Parkinson's Disease Rating Scale; AM, activity monitoring; N, number.
Source: Adapted from Nieuwboer et al.[8]
[a]Expressed as number of patients, and *P* values based on Mann–Whitney *U* tests.

periods exceeding 5 seconds and 10 seconds). The patient was not told about the specific function of the apparatus until after the study and was specifically instructed to maintain their usual daily activities.

Analysis

AM data were initially processed using Vitagraph (TEMEC Instruments Inc). Data were analyzed using SPSS (SPSS Inc, Chicago, IL). For ordinal scaled outcomes, nonparametric tests were used for data comparison between the early intervention group and the late intervention group (ie, Mann–Whitney *U* test) at baseline. For dichotomous and normally distributed data, Fisher exact tests and unpaired *t* tests were used, respectively. The level of significance was set 2 sided at $P = .05$.

Intervention effects were estimated using the first 3 assessments (t_1, t_2, and t_3). Random coefficient analysis was used assuming a normal distribution to evaluate the effects of intervention on % static activity, % dynamic activity, % standing, % sitting, % walking, W≥5s, and W≥10s (MLWinN version 2.02).[19] When the outcome variable failed to show a normal distribution on visual inspection, a logarithmic or square root transformation was applied. In this multilevel model, effects of intervention were corrected for differences of the outcome variable at baseline, time effects, and carryover effects. In addition, possible interaction effects between intervention and time were investigated for significance.[19] Change at follow-up was assessed by comparing the change between t_3 and t_4 using a model with 2 factors (time and group) fitted onto outcomes of t_1, t_2, t_3, and t_4 for distribution, for early and late intervention groups. Two-tailed analysis was performed on all tests with a significance level of 5%. Intervention effects

are reported as b estimates. Effect sizes were computed, using Cohen's *d*, for t_1-t_2. The difference in length of follow-up was addressed by separate testing of the decrements for late (t_3-t_4) and early intervention (t_2-t_4) using a paired *t* test.

Data from t_1 and t_2 of the late intervention group were used to investigate the reliability of AM. ICCs, using a 2-way mixed model with an absolute agreement definition, were employed to calculate reliability of % static and % dynamic activity.[20] According to the recommendations of Fleiss,[21] ICC values less than .40 represent poor reliability, values between .40 and .75 moderate to good reliability, and values more than .70 represent excellent reliability. Agreement was further analyzed using the Bland and Altman[22] method; the "limits of agreement," defined as ±1.96 × standard deviation of the difference scores, were computed.

Results

Out of 289 potential candidates, 153 patients participated in the present study. A trial flow chart is presented in Nieuwboer

Table 2. Medians and Interquartile Ranges of the Outcomes in the Early and Late Intervention Groups at Tests 1 to 4

	Test 1, Median (Q1-Q3)	Test 2, Median (Q1-Q3)	Test 3, Median (Q1-Q3)	Test 4, Median (Q1-Q3)
Registration time (hours)				
Early	4.9 (3.5-5.8)	4.6 (3.6-5.6)	4.8 (3.6-5.5)	4.5 (3.4-5.7)
Late	4.6 (3.7-5.5)	4.7 (3.7-5.8)	4.8 (3.6-5.5)	4.9 (3.5-5.5)
Percentage of time spent on dynamic activity[a]				
Early	9.4 (5.2-16.7)	13.7 (7.3-22.7)	11.7 (6.4-21.3)	9.6 (5.5-15.4)
Late	10.6 (4.8-16.3)	9.6 (5.8-18.9)	15.1 (7.4-22.8)	11.3 (6.6-20.5)
Percentage of time spent on static activity[a]				
Early	90.6 (81.8-94.8)	86.3 (76.9-92.7)	88.3 (77.9-93.6)	90.3 (83.5-94.5)
Late	89.1 (83.7-95.2)	89.8 (80.6-94.2)	84.0 (73.9-92.4)	88.7 (79.4-93.4)
Percentage of time spent on sitting[a]				
Early	50.3 (38.6-65.6)	40.8 (32.2-59.3)	46.8 (33.7-60.7)	49.6 (34.2-59.5)
Late	49.2 (35.5-63.6)	48.7 (34.5-59.4)	45.9 (35.5-57.4)	48.8 (34.2-65.3)
Percentage of time spent on standing[a]				
Early	25.0 (15.5-36.0)	25.8 (19.1-37.8)	24.3 (17.6-35.7)	25.3 (16.0-38.7)
Late	25.8 (16.0-32.6)	28.7 (17.4-39.2)	23.5 (16.2-32.1)	25.6 (19.0-38.0)
Percentage of time spent on walking[a]				
Early	7.3 (4.0-10.9)	10.4 (6.0-18.7)	8.5 (4.8-13.0)	6.6 (4.1-11.7)
Late	7.9 (4.2-13.6)	7.6 (3.4-12.9)	11.8 (5.9-18.5)	7.9 (4.5-15.0)
N walking periods ≥5 seconds per hour				
Early	13.7 (7.9-21.5)	15.1 (11.1-24.2)	15.3 (9.4-23.7)	14.1 (10.0-20.3)
Late	13.5 (8.6-18.9)	14.9 (8.3-20.3)	15.7 (9.6-26.1)	14.8 (10.1-22.6)
N walking periods ≥10 seconds per hour				
Early	8.6 (4.3-13.0)	9.6 (5.9-14.5)	8.8 (5.5-14.7)	7.8 (5.4-12.0)
Late	8.0 (5.2-12.0)	8. 5 (4.2-12.2)	9.8 (6.2-17.1)	8.1 (5.6-14.9)

Abbreviations: Q 1-Q3, interquartile range; N, number. [a]Percentage of time spent of total registration time.

et al.[8] Participants were randomly allocated to the early intervention group (n = 76) or late intervention group (n = 77). Both groups showed comparable baseline characteristics (see Table 1, adapted from Nieuwboer et al[8]) confirming the success of the randomization procedure.

As all patients received training, with only 1 dropout occurring 3 weeks after randomization because of a necessary change of medication, an "intention-to-treat" analysis was not necessary. Patients did not report any falls or other problems while wearing the activity monitors. In total, 556 of all 612 AM datasets, representing collected data of actual intended 4 repeated measurements within 153 included patients, were available for random coefficient modeling. All AM data showed a normal distribution on visual inspection.

Table 2 shows the median and interquartile ranges of all outcomes at tests 1 to 4. Average recording time was 4.6 hours (median 4.8 hours) and did not differ between testing days (*P* > .9). The mean amount of therapy received in the early intervention

group (271.8 minutes) was not significantly different from the late intervention group (270.4 minutes; $t = .27$; $P = .79$). Most patients (n = 95, 67%) chose auditory cueing as their preferred cueing modality, whereas the other patients (n = 58, 33%) favored somatosensory cueing.

Treatment Effects

Tables 2 and 3 show the results for each assessment and the estimated intervention effects corrected for time and carryover; correction for interaction effects was not necessary. The % dynamic activity improved from 9.4 to 13.7 (median) in the early intervention group and from 9.6 to 15.1 in the late intervention group ($b = 4.25$; $P < .01$); an equal decrement in static activity was shown. No significant effect was shown for % sitting and % standing. The % walking increased from 7.3 to 10.4 in the early intervention group and from 7.6 to 11.8 in the late intervention group ($b = 4.2$; $P < .01$). Periods of W = 5s increased from 13.7 to 15.1 times per hour (median) in the early intervention group and from 14.9 to 15.7 times per hour in the late intervention group ($b = 2.6$; $P = .01$) after cueing training, and periods of W = 10s increased from 8.6 to 9.6 times per hour in the early intervention group and from 8.5 to 9.8 times per hour in the late intervention group ($b = 2.9$; $P = .00\ 1$) after the intervention phase. Effect sizes ranged from small for % sitting (0.14) and % standing (0.14) to medium for % static activity (0.25), W = 5s (0.26), % dynamic (0.33), and W = 10s (0.35) to large for % walking (0.43; Table 3).

Table 3. Intervention Effects for t_{1}-t_{2} (Early Intervention Group) and t_{2}-t_{3} (Late Intervention Group) Combined, Effect Size for t_1-t_2, and Percentage of Change at Follow-up (Difference t_{3}-t_{4} Intervention Groups Separately)

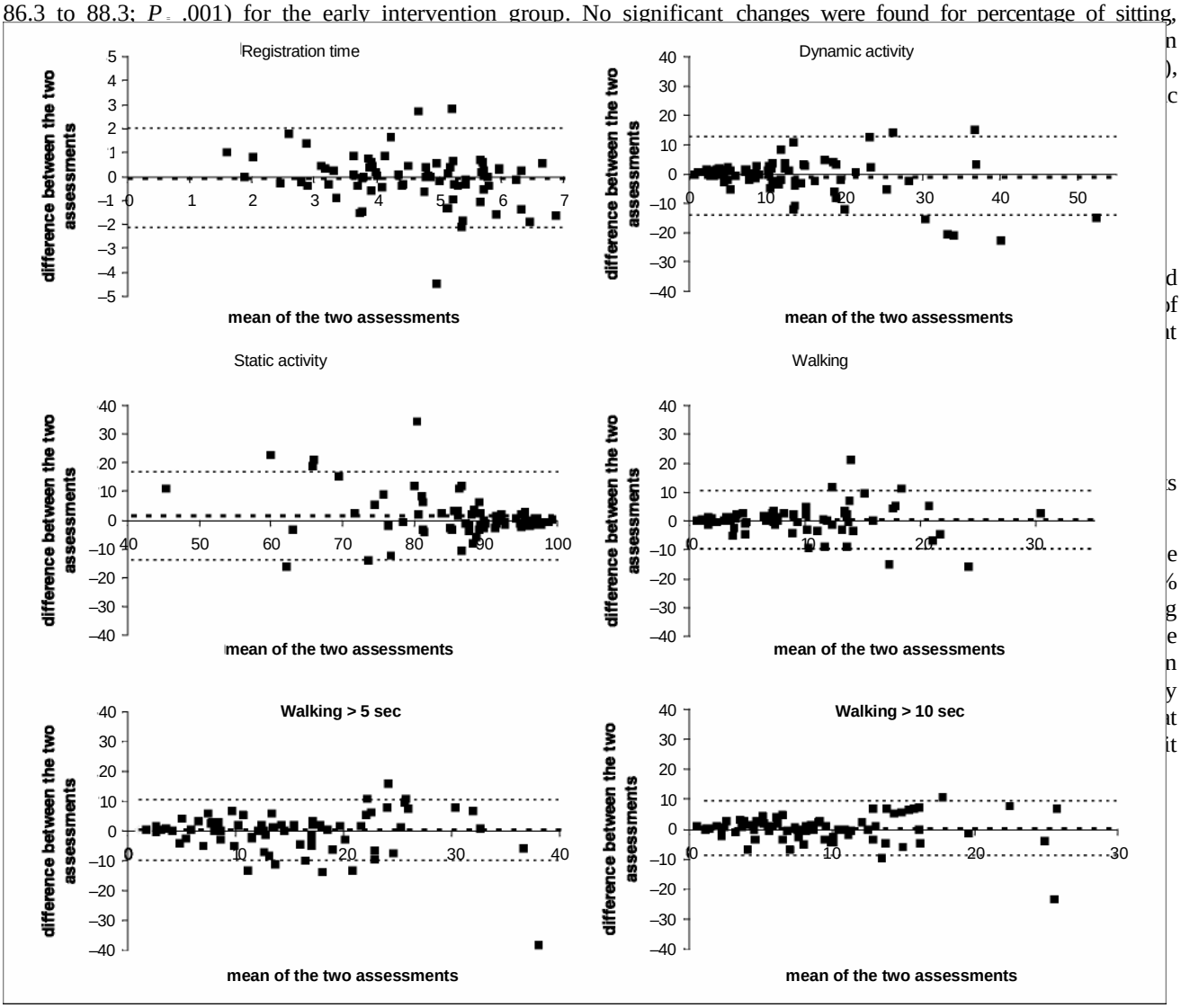
	Intervention Estimate (SE)	Effect Size (Cohen's *d*), for t_1-t_2	Change in Minutes	Follow-up Estimate (SE)	Percentage of Change t_2-t_4, Early Intervention Group	Percentage of Change t_3-t_4, Late Intervention Group
Percentage of time spent on dynamic activity[a]	4.46[b]	.33	12.6	4.17[b]	12.5[c]	17.3[b]
Percentage of time spent on static activity[a]	3.34[b]	.25	9.4	4.69[b]	1.8	5.0[b]
Percentage of time spent on sitting[a]	3.48	.14	9.8	4.20[c]	3.2	7.9[c]
Percentage of time spent on standing[a]	1.41	.14	4.0	0.98	5.5	1.7
Percentage of time spent on walking[a]	4.23[b]	.43	11.9	3.57[b]	9.9	27[b]
N walking periods = 5 seconds per hour	2.63[c]	.26	2.6 N	3.32[b]	6.4	6.3[b]
N walking periods = 10 seconds per hour	2.90[b]	.35	2.9 N	2.68[b]	6.9	20[b]

Abbreviations: SE, standard error; N, number.
[a]Percentage of time spent of total registration time.
[b]$P < .01$.
[c]$P < .05$.

Follow-up (Early t_2-t_4, Late t_3-t_4)

Tables 2 and 3 also show the changes at follow-up. All intervention effects declined between 6 and 9 weeks. The % dynamic activity was significantly reduced (from 13.7 to 11.7 in the early intervention group (t_2-t_4) and from 15.1 to 11.3 in the late intervention group (t_3-t_4; $b = 4.2$; $P < .001$), and the % static activity increased from 86.3 to 90.3 in the early intervention group and from 84.0 to 88.7 in the late intervention group ($b = 4.7$; $P < .001$). The % sitting increased significantly ($b = 4.2$; $P = .02$) from 40.8 to 49.6 in the early intervention group and from 45.9 to 48.8 in the late intervention group; the % standing did not change significantly. The % walking ($b = 3.6$; $P < .001$), W = 5s ($b = 3.3$; $P < .001$), and W = 10s ($b = 2.7$; $P < .001$) decreased as well. When separating the early and late intervention groups, significant decrements between t_2 and t_4 were shown for percentage of dynamic activity (from 13.7 to 11.7; $P = .001$), walking (from 10.4 to

8.5; $P < .001$), and W10s (from 9.6 to 8.8; $P = .02$), and an increment was shown for percentage of static activity (from 86.3 to 88.3; $P = .001$) for the early intervention group. No significant changes were found for percentage of sitting,



with PD.[25] Indeed, the present findings are in line with the results from clinical assessments in the RESCUE trial.[8] Briefly, clinical assessments showed a 4.2% increase on the posture and gait score, a 5.0 cm/s increase in walking speed, a 4.0 cm increase in step length, and a 5.5% reduction in severity of freezing symptoms according to the Freezing of Gait Questionnaire when analyzed in freezers only.[8] The agreement in effects between AM and clinical gait assessments suggests that improvements in clinically used outcomes such as posture and gait score, step length, and gait speed reflect a general enhancement in patients' actual walking performance. A major advantage of AM is that patients do not have to undergo a fatiguing test battery, and

more detailed information about the actual activity profile is achieved.[26] The relatively small effects in favor of rhythmic cueing are comparable with found effects in gait-related outcomes after meta-analysis of studies on exercise therapy in PD.[27] These effects are also in line with found effects of exercise therapy in stroke rehabilitation showing favorable effects of exercise therapy ranging from 5% to 1 0%.[28] Improvements in activity were reduced at follow-up, assessed 9 weeks after the end of cueing training for the early intervention group and 6 weeks for the late intervention group. The reductions were approximately the same for both groups, suggesting that the effect of intervention largely wears off in the first 6 weeks. Continuous training

Table 4. Intraclass Correlation Coefficients, 2-Way Mixed Model With Absolute Agreement Definition

Variable	ICC (95% CI)
Registration time	.68 (.53-.78)
Dynamic activity	.81 (.71-.87)
Static activity	.76 (.65-84)
Sitting	.59 (.42-.72)
Standing	.50 (.31-65)
Walking	.72 (.58-.81)
Walking periods exceeding 5 seconds	.68 (.53-.78)
Walking periods exceeding 10 seconds	.73 (.60-.82)

Abbreviations: ICC, intraclass correlation coefficients; CI, confidence interval.

with use of a permanent cueing device may therefore be indicated for people with PD. The optimal dose–response relationship needs to be investigated in future studies. The pragmatic selected dose of 9 treatments of physical therapy may be an insufficient dose of therapy to have introduced longterm effects. Thus, further studies are needed to investigate the optimal dose–response relationship in patients with PD. The impact of placebo effects as a result of increased attention during therapy was not controlled for, which is a limitation of this study.

In line with a previous study,[11] AM proved to be a reliable method for monitoring gait performance with fair to good reliability (ICC = .50-.72) for registration time, static activities, sitting and standing and excellent reliability (ICC = .76-.81) for dynamic activity, W5s and W10s. In addition, Bland Altman plots[22] showed good to excellent agreement between 2 consecutive AM measurements with respect to the different static and dynamic activities of AM.

AM may cause so-called reactivity effects: subjects may, consciously or subconsciously, limit their movements due to the presence of the recorder, its weight, and the wiring or because they are afraid to break or damage the monitoring equipment. On the other hand, subjects may be more active to "make the measurement better" and meet the expectations of the research goal. Therefore, it is important to prevent AM-induced behavioral adaptations by keeping the participants naive about the purpose of the AM device and giving appropriate instructions about maintaining usual daily routines.

A limitation of the AM device used in the present study is that the accelerometers do not produce valid information about spatial parameters of gait such as step length and walking distance and with that speed. In particular, it is difficult to quantify parameters such as step length in patients with PD where the variability in step-to-step length is large.[29,30] Lack of insight into patients' on–off status is another limitation in this study. It is, for example, not known whether patients walked more during their off periods after receiving cueing training. This may be addressed by asking patients to record their on–off status in a diary while undertaking AM to provide complementary data. Future studies should focus on gait parameters including walking speed, step length, and interlimb coordination of parkinsonian gait during "on" and "off" periods. In addition, efforts should be made to develop smaller and cheaper AM devices that are wireless enabled and better able to monitor continuously for more than 48 hours.

The application of AM in patients with neurological disorders such as PD to evaluate the effects of a rehabilitation program is new in the field of neurology. However, it should be noted that AM can also be used for evaluating other interventions such as medication[31] and deep brain stimulation on motor performance. Moreover, AM proved to be a harmless, noninvasive way of collecting "real-world" information about postures and activity undertaken in patients' own environment for extended

periods of time.

Data from the current study further support the positive effects of cueing in PD as found in earlier studies[8,10]; however, the neurological mechanisms underpinning these effects are still unclear. Studies suggest that cueing may stimulate alternative cortical pathways (eg, visual motor pathways)[32] to bypass the basal ganglia, whereas other studies suggest that cueing synchronizes the simultaneous timing of interlimb coordination in the cerebellum needed for normal gait.[33,34] Further studies are needed to investigate the neurophysiological mechanisms underpinning the effectiveness of rhythmic cueing in patients with PD.

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References

1. Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders? *Neurology*. 2007;68:326-337.
2. De Lau LM, Giesbergen PC, De Rijk MC, Hofman A, Koudstaal PJ, Breteler MMB. Incidence of parkinsonism and Parkinson disease in a general population: the Rotterdam Study. *Neurology*. 2004;63: 1240-1244.
3. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. *Arch Neurol*. 1999;56:33-39.
4. Herman T, Giladi N, Gruendlinger L, Hausdorff JM. Six weeks of intensive treadmill training improves gait and quality of life in patients with Parkinson's disease: a pilot study. *Arch Phys Med Rehabil*. 2007;88:1154-1158.
5. Stankovic I. The effect of physical therapy on balance of patients with Parkinson's disease. *Int Rehabil Res*. 2004; 27:53-57.
6. Brichetto G, Pelosin E, Marchese R, Abbruzzese G. Evaluation of physical therapy in parkinsonian patients with freezing of gait: a pilot study. *Clin Rehabil*. 2006;20:3 1-35.
7. Morris ME. Locomotor training in people with Parkinson disease. *Phys Ther*. 2006;86: 1426-1435.
8. Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *J Neurol Neurosurg Psychiatry*. 2007;78: 134-140.
9. Rubinstein TC, Giladi N, Hausdorff JM. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. *Mov Disord*. 2002;17:1 148-1160.
10. Lim I, Van Wegen E, De Goede C, et al. Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review. *Clin Rehabil*. 2005;19:695-713.
11. Salarian A, Russmann H, Vingerhoets FJ, Burkhard PR, Aminian K. Ambulatory monitoring of physical activities in patients with Parkinson's disease. *IEEE Trans Biomed Eng*. 2007;54:2296-2299.
12. White DK, Wagenaar RC, Del Olmo ME, Ellis TD. Test-retest reliability of 24 hours of activity monitoring in individuals with Parkinson's disease in home and community. *Neurorehabil Neural Repair*. 2007;21 :327-340.
13. White DK, Wagenaar RC, Ellis TD. Monitoring activity in individuals with Parkinson disease: a validity study. *J Neurol Phys Ther*. 2006;30:12-21.
14. Van Wegen E, De Goede C, Lim I, et al. The effect of rhythmic somatosensory cueing on gait in patients with Parkinson's disease. *J Neurol Sci*. 2006;248:210-214.
15. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology*. 1967;17:427-442.
16. Rochester L, Hetherington V, Jones D, et al. The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease. *Arch Phys Med Rehabil*. 2005;86:999-1006.
17. Van Wegen E, Lim I, De Goede C, et al. The effects of visual rhythms and optic flow on stride patterns of patients with Parkinson's disease. *Parkinsonism Relat Disord*. 2006; 12:21-27.
18. Willems AM, Nieuwboer A, Chavret F, et al. The use of rhythmic auditory cues to influence gait in patients with Parkinson's disease, the differential effect for freezers and non-freezers, an explorative study. *Disab Rehabil*. 2006;28:721-728.
19. Goldstein H, Browne W, Rasbash J. Multilevel modelling of medical data. *Stat Med*. 2002;21 :3291-3315.
20. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull*. 1979;86:420-428.
21. Fleiss JL. *The Design and Analysis of Clinical Experiments*. New York, NY: Wiley; 1986.
22. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurements. *Lancet*. 1986;1 :307-310.
23. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA*. 1995;273:402-407.

24. Giladi N, Balash Y. The clinical approach to gait disturbances in Parkinson's disease; maintaining independent mobility. *J Neural Transm Suppl*. 2006;70:327-332.
25. Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL. The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis. *Mov Disord*. 2008;23:63 1-640.
26. Bussmann JB, Martens WL, Tulen JH, Schasfoort FC, Van den Berg-Emons HJG, Stam HJ. Measuring daily behavior using ambulatory accelerometry: the Activity Monitor. *Behav Res Methods Instrum Comput*. 200 1;33:349-356.
27. De Goede CJ, Keus SH, Kwakkel G, Wagenaar RC. The effects of physical therapy in Parkinson's disease: a research synthesis. *Arch Phys Med Rehabil*. 2001;82:509-515.
28. Van Peppen RP, Kwakkel G, Wood-Dauphinee S, Hendriks HJ, Van der Wees PJ, Dekker J. The impact of physical therapy on functional outcomes after stroke: what's the evidence? *Clin Rehabil*. 2004;18:833-862.
29. Willems AM, Nieuwboer A, Chavret F, et al. Turning in Parkinson's disease patients and controls: the effect of auditory cues. *Mov Disord*. 2007;22:1871-1878.
30. Almeida QJ, Frank JS, Roy EA, Patla AE, Jog MS. Dopaminergic modulation of timing control and variability in the gait of Parkinson's disease. *Mov Disord*. 2007;22: 1735-1742.
31. Moore ST, MacDougall HG, Gracies JM, Ondo WG. Loco- motor response to levodopa in fluctuating Parkinson's disease. *Exp Brain Res*. 2008;184:469-478.
32. Azulay JP, Mesure S, Amblard B, Blin O, Sangla I, Pouget J. Visual control of locomotion in Parkinson's disease. *Brain*. 1999;122:11 1-120.
33. Cerasa A, Hagberg GE, Peppe A, et al. Functional changes in the activity of cerebellum and frontostriatal regions during externally and internally timed movement in Parkinson's disease. *Brain Res Bull*. 2006;71:259-269.
34. Chuma T, Faruque Reza M, Ikoma K, Mano Y. Motor learning of hands with auditory cue in patients with Parkinson's disease. *J Neural Transm*. 2006;113:175-185.