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Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review

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Objective: To critically review studies evaluating the effects of external rhythmical cueing on gait in patients with Parkinson's disease.
Methods: Articles published from 1966 to January 2005 were searched by two physiotherapists in MEDLINE, PiCarta, PEDRo, Cochrane, DocOnline, CINAHL and SUMSEARCH. To be included, articles had to investigate the effects of external rhythmical cueing (i.e., auditory, visual or tactile cueing) on gait parameters in patients with idiopathic Parkinson's disease. Both controlled and noncontrolled studies were included. Based on the type of design and methodological quality a meta-analysis or best-evidence synthesis was applied.
Results: Twenty-four studies (total number of patients = 626) out of the 159 screened studies were evaluated in this systematic review. Two out of 24 were randomized controlled trails (RCT), both of high methodological quality. One RCT did not focus specifically on external rhythmical cueing of individual patients with Parkinson's disease, but on group exercises in general, including walking with cues. All other studies were pre-experimental studies. Best-evidence synthesis showed strong evidence for improving walking speed with the help of auditory cues. Insufficient evidence was found for the effectiveness of visual and somatosensory cueing.
Conclusion: Only one high-quality study, specifically focused on the effects of auditory rhythmical cueing, suggesting that the walking speed of patients with Parkinson's disease can be positively influenced. However, it is unclear whether positive effects identified in the laboratory can be generalized to improved activities of daily living (ADLs) and reduced frequency of falls in the community. In addition, the sustainability of a cueing training programme remains uncertain.

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Introduction

Parkinson's disease is a progressive neurological disorder, with a prevalence increasing with advancing age. In Europe, 1.8 per 100 inhabitants over the age of 65 are diagnosed with Parkinson's disease, whereas in the age category of 65–69 years 2.4 per 100 inhabitants are affected. For the age group of 85–89 years, the prevalence increases up to 2.6 per 100 inhabitants.[1]

The idiopathic form of Parkinson's disease results from a degeneration of dopamine-producing cells in the substantia nigra which leads to clinical symptoms such as hypokinesia, bradykinesia, postural instability, rigidity and tremor.[2–4] These symptoms are accompanied by difficulties in motor performance such as gait problems and falls.[4–7]

Despite optimal medication therapy, gait problems associated with Parkinson's disease are often characterized by a decreased stride length[8] and walking speed, an increased cadence and double limb support,[2,6] shuffling gait, gait festination and freezing.[9–11] Physiotherapy is reported to be a low-cost[12–14] treatment and an useful addition to standard medication.[15–19] De Goede *et al.*[16] demonstrated small but significant improvements in activities of daily living (ADLs), walking speed and stride length in a meta-analysis on the effects of physiotherapy on Parkinson's disease using a fixed effects model. Deane *et al.* conducted a Cochrane review[15] on the effects of physiotherapy on Parkinson's disease. They were not able to draw firm conclusions regarding the efficacy of physiotherapy, because of methodological weaknesses and due to the small number of trials at the time of their review. Recently, Gage *et al.*[18] reported positive effects of physiotherapy on motor performance, gait, ADLs and cardiovascular fitness in their narrative review of the effects of multidisciplinary rehabilitation on Parkinson's disease. All reviews included studies in which intervention was offered with the help of external rhythmic stimulation or external rhythmic cueing. Facilitation of gait of patients with Parkinson's disease with the help of cueing has been reported since 1942.[20] The first detailed analysis of external cueing on gait was performed by Martin in 1967.[21] Two non-systematic reviews by Rubinstein *et al.*[17] and Darmon *et al.*[22] evaluated the effects of external cueing on gait in Parkinson's disease. They concluded that external cueing can significantly improve gait and gait-related activities in patients with Parkinson's disease.

The precise definition of a cue is problematic and intervention based on external rhythmical cueing has not been clearly described. According to Cools,[23] cues are 'contextual or spatial stimuli which are associated with behaviour to be executed, through past experience'. Horstink *et al.*[24] distinguish between cues and stimuli, stating that 'cues give information on how an action should be carried out and are hence more specific than simple stimuli'. Based on the observations of Cools[23] and Horstink *et al.*,[24] and given the fact that parkinsonian symptoms particularly affect complex and sequential movements, for the purposes of this review external rhythmical cueing is operationally defined as 'applying temporal (rhythmical) or spatial stimuli associated with the initiation and ongoing facilitation of motor activity (gait)'.[25]

The aim of the present systematic review is to add to the literature a systematic review based on (1) a qualitative synthesis method and (2) the above-mentioned, prestated definition of cueing.

Methods and materials

Literature search

Articles were compiled for this study from a number of sources. Two physiotherapists (SB/OD) independently performed a search in the databases of MEDLINE (1966–2004), PiCarta, PEDro, Cochrane, DocOnline, CINAHL and SUMSEARCH using the following keywords and their combinations: Parkinson, Parkinson's disease, Parkinson disease, cue, cueing, physical therapy, physiotherapy, exercise, locomotion, gait, optical flow field, visual, auditory, sensory, tactile, behavioural, external, rhythmic, stimulus, stimuli and walking.

Studies were accepted when: (1) they investigated the effects of external rhythmical cueing on gait in patients with idiopathic Parkinson's disease; (2) the intervention was applied to improve gait performance; (3) they were published in a peer-reviewed journal and (4) they were written in

English, German, French or Dutch. Single-case studies were excluded.

Intervention types

For the present review, the external rhythmical intervention was classified into four types of cueing: (1) auditory cueing; (2) visual cueing; (3) tactile cueing; and (4) a combination of above-mentioned types of cueing.

Data analysis

If appropriate, quantative analysis of the results was performed separately for each intervention and restricted to RCTs. When these RCTs were comparable in terms of intervention, patient characteristics and outcome measures, statistical pooling was considered. In case of heterogeneity, with respect to intervention and measurements of outcome, or lack of RCTs, a best-evidence synthesis was applied. The method for applying a best-evidence synthesis was based on the list proposed by van Tulder *et al.*[26] and modified by Steultjens *et al.*[27] (see Appendix 1). The design of the studies and the methodological quality was taken into account when rating the levels of evidence. The methodological quality of all studies was evaluated by two independent reviewers (IL, MD). Disagreements were resolved by discussion. If no consensus was met a third reviewer (GK) made the final decision. A kappa statistic for inter-rater agreement was calculated.

A list of methodological criteria recommended by Van Tulder *et al.*[26] was used to rate the methodological quality of RCTs. This list, containing all the criteria proposed by Jadad *et al.*[28] and Verhagen *et al.*,[29] consists of 11 criteria for internal validity, six for descriptive criteria and two for statistical criteria (see Appendix 2). One modification was made regarding the specification of the eligibility criterion: this involved the addition of the Hoehn and Yahr stage.[30] Studies were considered to be of high quality if at least six criteria for internal validity, three descriptive criteria, and one statistical criterion were met.[26]

To rate the methodological quality of the studies with another design than controlled trials (i.e., pre-experimental studies[31]) the same methodological scorings list was used, with an adaptation made by Steultjens *et al.*[27] This adapted scorings list includes seven criteria for internal validity, five descriptive and two statistical criteria. A study with a noncontrolled design was considered to be of sufficient quality if at least four internal validity criteria, two descriptive criteria and one statistical criterion were rated positively (see Appendix 2). RCTs and noncontrolled studies who did not meet the above-stated criteria were considered to be of low quality.

Results

Overview of literature and rating of the studies

Based on abstracts and titles, a total of 159 articles was identified and 40 of these candidate studies investigated the effects of external rhythmical cueing. Twenty-four studies, with a total number of 626 patients included, matched all inclusion criteria and were selected for qualitative analysis.[3,32–53]

General characteristics of the different studies concerning design of the study, type of cueing, number of subjects, characteristics of the subjects, type and dose of intervention, outcome measurements and ratings of results are presented in Table 1.

The methodological quality was assessed for two RCTs and 22 pre-experimental studies. None of these studies were controlled clinical trials (CCTs). One publication[3] presented three independent studies. These studies are separately rated on methodological quality. In two publications[48,53] more than one study was presented. As the effects of cueing were investigated in only one study per publication, only those studies were taken into account for analysis.

The two RCTs[32,33] were of high methodological quality, five pre-experimental studies were of sufficient methodological quality,[36,41,42,47,52] and all other studies were of low methodological quality (Appendix 2). A kappa statistic of 0.84 was calculated for inter-rater agreement on scoring the list for methodological quality.[27] Applying a quantitative analysis was not possible due to the lack of RCTs, therefore a best-evidence synthesis has been applied on all intervention types.

Auditory cueing

Fourteen studies, two RCTs[32,33] and 13 studies with a pre-experimental design[37,39–42,45–48,50,51,53]

Table 1 Overview

Reference	Study design	Cue type	Characteristics of subjects				Intervention	Results		
			Subjects (*N*)	Age (years) mean ± SD (range)	H-Y (score) mean ± SD (range)	Disease duration (score) mean ± SD (range)	Protocol	Measurement outcomes	Results	
Ellis[33]	RCT (cross-over design)	A	E = 68, divided into: Early intervention = 35 Late intervention = 33	64 ± 8.4 63 ± 8.8	2.5 ± 0.5 2.4 ± 0.5	nr nr	Therapy sessions for 6 weeks, twice a week 1.5 h, consisting of strength-, stretch-, balance- and relaxation exercises and walking exercises with auditory cueing for 15 min	Walking speed (therapy vs. no therapy)	+	
Thaut[32]	RCT	A	E = 15 C1 = 11 C2 = 11	69 ± 8 74 ± 3 71 ± 8	2.4 2.5 2.6	7.2 ± 4 5.4 ± 3 8.5 ± 4	E = 30 min walk training with music, with a rhythm embedded of 1 2 Hz, every day for 3 weeks C1 = same programme as the E-group without an auditory cue C2 = no intervention	Walking speed Stride length Cadence	+ + +	
Azulay[34]	Pre-experimental	VRS	E = 13 hC = 7	68.5 (45 78) 70.3 (57 -82)	2.3 ± 0.7	6.9 (1 - 10)	Walking without cues, in on- and off-phase vs. walking with floor markers	Walking speed Stride length Phase oscillation Angles hip/ knee/ ankle	on-phase 0 0 – – / – / –	off-phase 0 0 0 0/0/0
Azulay[35]	Pre-experimental	VRS	E = 16 hC = 16	68.8 ± 4 65.7 ± 5	2.3 ± 05	6.3	Walking without cues vs. Walking with floor markers (fm) and normal light With floor markers and stroboscopic light (fm + sl) to suppress the dynamic visual cues while walking	Walking speed Stride length Cadence	fm + + 0	fm + sl – – 0

Bagley[36]	Pre-experimental	VRS	10	77.8 (69 88)	nr	nr	Walking without cues vs. walking with floor markers	Walking speed (relative) Stride length Cadence Stride time Single support time Double support time Step length	– + – + + + +			
Cubo *et al.*[37]	Pre-experimental	A	12	65.8±11.2	Median 2 (2 4)	12.4±7.3	Subjects walked a complex track with a metronome (M) and without metronome (nc) at the start of the trial. After practising at home for a week, subjects walked the track again. The track was a 60-ft track, in which the subject arose from a chair, walked through 2 doorways, made 4 turns and sat down	Time needed to complete track Walking time Freeze time Number of freezing episodes Average duration of a freezing episode	Pretest Nc vs. M 0 – 0 0 0	Pretest vs. posttest (with metronome) 0 + 0 0 0		
Del Olmo[54]	Pre-experimental	A	E = 15 hC = 15	61.7±.22 63.1±4.28	2±0.54	7.3±4.3	Pretest: Subjects walked (1) at preferred speed without cues, (2) at preferred speed with a manual task, (3) at fast speed, (4) after listening to different auditory rhythms and (5) with an auditory cue	Walking speed Step length Cadence Step to step variability	Pretest vs. posttest Preferred gait 0 0 0 +	With manual task 0 0 0 0	Fast gait 0 0 0 0	

Table 1 (*Continued*)

Reference	Study design	Cue type	Characteristics of subjects				Intervention	Results				
			Subjects (*N*)	Age (years) mean ± SD (range)	H-Y (score) mean ± SD (range)	Disease duration (score) mean ± SD (range)	Protocol	Measurement outcomes	Results			
							A rehabilitation programme was offered to the PD patients, 5 times a week, for 4 weeks, with sessions of one hour. This programme consisted of walking exercises with cueing After the rehabilitation programme the subjects with PD were tested again following the same protocol as the pretest					
Dietz[38]	Pre-experimental	VRS	8	70.5 ± 8.2 (56–83)	3.5 ± 0.76 (2–4)	8.2 ± 5.4 (2.4–18)	Pre-test: subjects walked a 60-ft track, consisting of 15 ft hallway, with a chair on one end and a doorway on the other end: unassisted and without cues vs. – with a straight walking stick (sws) – with a visual cue-stick (vcs) floor markers (fm) Subjects practised at home with vcs until they felt that they obtained maximum profit of it, after that they were tested again unassisted vs. vcs (posttest)		Pretest sws Time needed to complete track – Number of freezing episodes 0	vcs – 0	fm + 0	Posttest vcs 0 0

Ebers-bach[39]	Pre-experi-mental	A	E1 = 22 hC = 22	61.8±8.7 61.9±9	< 2	< 2	Walking without cues vs. walking with a metronome, set at 80% of baseline frequency	Stride length Step to step variability	+ +						
Enzens-berger[40]	Pre-experi-mental	A, T	E = 23	nr	3 4	nr	Walking without cues vs. different cuetypes: - music: Hohenen-friedberger march (Mhf) - music: march from Prokofiev (Mp) - a metronome set at 95 bpm (M) tactile cueing (T) applied by shoulder taps Subjects walked on a track existing of 4 x 10 meters, with 3 curves, inside and outside	Time needed to complete track: inside outside Steps needed to complete track inside outside		Mhf 0 0 + +		Mp 0 0 0 0	M + + + +	T – – – +		
Freed-land[41]	Pre-experi-mental	A	E = 16	74±7.2 (60 84)	nr	nr	Walking without cues (nc) as a pretest (pr) vs. 1) walking with a metronome set at baseline frequency (M) 2) 10% above baseline frequency (110) 3) without a cue as posttest (po)	Walking speed Cadence Cycle time Double support Step length Step extremity-ratio (step length/leg length) Base of support	M-nc 0 + + 0 0 0 0	pr-M 0 + 0 0 0 0 0	M-110 0 0 0 0 0 + 0	M-po 0 0 + – + 0 0	110-po 0 – – – – 0 0	pr-po + + + + + + 0	

Table 1 (*Continued*)

Reference	Study design	Cue type	Characteristics of subjects				Intervention	Results				
			Subjects (*N*)	Age (years) mean ± SD (range)	H-Y (score) mean ± SD (range)	Disease duration (score) mean ± SD (range)	Protocol	Measurement outcomes	Results			
Howe[42]	Pre-experimental	A	E = 11	54 (30–67)	1–2	nr	Walking with a metronome set at baseline frequency vs. walking with a metronome set at - 15% under baseline frequency (85) - 7,5% under baseline freq. (92.5) 7,5% above baseline freq. (107.5) 15% above baseline freq. (115)		85	92.5	107.5	115
								Walking speed	+	0	+	+
								Stride length	0	0	0	0
								Cadence	+	0	+	+
Kompoliti[43]	Pre-experimental	VRS	E = 28	67.8 ± 7.54	nr	13.0 ± 7.5	Walking unassisted and without cues vs. - walking with a modified inverted walking stick (mis) - walking with a laser beam stick (lbs) Subjects walked a track consisting of a 30 ft hallway with a chair at one end and a doorway at the other end		mis			lbs
								Time to complete track	0			0
								Freezing episodes	0			0
Lewis[44]	Pre-experimental	VRS	E = 14 hC = 14	71.3 ± 7.6 (58–84) 70.5 ± 6.5 (57–80)	2.8 ± 0.8	9.1 ± 5.7	Walking without cues vs. - walking with floor markers (fm) - walking with a subject mounted light device (smld) projecting 2 laser beams on the floor continuously		fm			smld
								Walking speed	+			+
								Stride length	+			+
								Cadence	+			+

McCoy[45]	Pre-experimental	A	E = 7	72.2 ± 8.0	1–3	nr	Walking without cues vs. walking with a metronome set at: – baseline frequency (M) – 15% above baseline freq. (115%) in on-phase (on) and in off-phase (off)	Walking speed, right side Walking speed, left side Stride length, right side Stride length, left side Cadence	M-on + + 0 +	M-off + + 0 +	115-on + + 0 +	115-off + + 0 +
McIntosh[46]	Pre-experimental	A	E = 6	71	3.2 ± 1 (2–4)	7.5	Walking without cues vs. walking with a metronome set at – baseline frequency (M) 10% above baseline frequency (110)	Walking speed Stride length Cadence	M ? ? ?		110 + + +	
McIntosh[47]	Pre-experimental	A	E on = 21 E off = 10 hC = 10	71 ± 4 73 ± 4 72 ± 5	2.8 ± 0.7 (2–4) 2.6 ± 0.5 (2–3)	7.5 7.8	Walking without cueing (nc) vs. walking with music with a click tone embedded, set at: 1) baseline frequency 2) with a click tone 15% above baseline 3) without cueing to check immediate carry-over effect. In on- and off- phase	Walking speed on Walking speed off Cadence on Cadence off Stride length on Stride length off	cue vs nc + + + + + +		cue vs post test 0 0 0 0 0 0	

Table 1 (*Continued*)

Reference	Study design	Cue type	Characteristics of subjects				Intervention	Results				
			Subjects (*N*)	Age (years) mean ± SD (range)	H-Y (score) mean ± SD (range)	Disease duration (score) mean ± SD (range)	Protocol	Measurement outcomes	Results			
Morris[48] *study 3*	Pre-experimental	A VRS	E = 32 hC = 12	75 ± 7.5 (65 87 nr	2.6 ± 0.5	nr	Walking without cues vs. - walking with a metronome (M) at comfortable walking speed (c) walking with a metronome and instructed to walk fast (f) walking with floor markers (fm) at comfortable walking speed walking with floor markers and instructed to walk fast		M-c	M-f	fm-c	fm-f
								Walking speed	0	+	0	0
								Stride length	0	0	+	+
								Cadence	0	+	+	+
Morris[49]	Pre-experimental	VRS	E = 15 hC = 15	72.2 ± 6.2 72.5 ± 6.46	2.7 ± 0.7	nr	Walking without cues (nc) vs. walking with floor markers (fm) at - comfortable walking speed (c) - fast speed (f) Outcomes parameters are compared with healthy matched subjects and rated positive if they are comparable or better.		nc-c	nc-f	fm-c	fm-f
								Walking speed	0	0	0	+
								Stride length	0	0	+	+
								Cadence	+	+	0	+
Morris[3] *Study 1*	Pre-experimental	VRS	E = 16 hC = 16	65.8 ± 4.2 (67 81) 72.7 (63 68)	nr	nr	Walking without cues vs. 1) walking with floor markers (fm) 2) without cues to measure the retain effects (ret)		fm vs baseline		ret vs fm	
								Walking speed	+		0	
								Stride length	+		0	
								Cadence	+		0	
								Double support	+		0	

Study 2	Pre-experimental	VRS	E = 16 hC = 16	74.1 ± 5.6 (64 - 82) 73.1 (63 - 81)	nr	nr	Walking without cues vs. walking with floor markers (fm) walking with fm and cognitive task (T). Cognitive tasks were graded from T1 (easy) to T5 (difficult) Outcomes parameters are compared with healthy matched subjects and rated positive if they are comparable or better.		baseline vs fm			fm vs fm +T
								Walking speed	+			- (> T2)
								Stride length	+			- (> T2)
								Cadence	+			- (T4)
								Double support	+			nr
Study 3	Pre-experimental	VRS	E = 8 hC = 8	71.0 ± 4.1 (64 75) 70.1 (59 77)	nr	nr	Walking without cues vs. 1) walking with floor markers (fm) 2) walking without cues after the cued condition to measure retention effects (ret). Subjects were aware of recording data half of the trials (o) and unaware the other half (c). The effects of the open trials (fm-o, ret-o) are compared with data of control subjects, data of the covered trials (fm-c, ret-c) with data of the open trials		fmo	fmc	ret-o	ret-c
								Walking speed	+	–	+	–
								Stride length	+	–	+	–
								Cadence	+	–	+	0
								Double support	+	–	+	0

Table 1 (*Continued*)

Reference	Study design	Cue type	Characteristics of subjects				Intervention	Results					
			Subjects (*N*)	Age (years) mean ± SD (range)	H-Y (score) mean ± SD (range)	Disease duration (score) mean ± SD (range)	Protocol	Measurement outcomes	Results				
Nieuwboer[50]	Pre-experimental	A	E freezers = 10 E nonfreezers = 10	68.4 (58.5–80) 60.6 (48–67)	1.5–4	68.4 (58.5–80) 60.6 (48–67)	Walking without cues (nc) vs. walking with a metronome set at baseline frequency (M). 20% above baseline (120) 10% above baseline (110) 10% below baseline frequency (90) 20% below baseline frequency (80) Cueing conditions are compared with the condition that was one step lower in frequency	Walking speed, freezers Walking speed, nonfreezers Stride length, freezers Stride length, nonfreezers Cadence, freezers Cadence, nonfreezers	M vs.nc ? ? ? ? 0 +	90 vs 80 + + + + + +	M vs 90 + + – – + +	110 vs M 0 + – 0 + +	120 vs 110 + + 0 0 + +
Suteerawattananan[51]	Pre-experimental	A VRS A+ VRS	E = 24	68.9±10.4	2.75	6.9±4.46	Walking without cues (nc) vs. walking with a metronome set at 25% (M) above baseline frequency, walking on stripes with floor markers (fm) or a combination of visual and auditory cueing (M+ fm)	Walking speed Stride length Cadence	M + 0 +	fm 0 + 0			M + fm + 0 0
Van Wegen[52]	Pre-experimental	VRS + VRT	E medicated = 16 E non medicated = 8 hC = 7	62.3±9.8 56.1±9.9 59.2±10.2	2.3±0.5 2.2±0.6	4.9±3.5 2.3±2.3	Walking on a treadmill without cue and with a screen in front without projection vs. a screen: on which a hallway is projected (sc)	Stride length Cadence	sc 0 0		fm + +	vrt + +	vrt+sc 0 +

							– on which a hall way with stripes on the floor is projected (fm) – without projection, but with a flashing LED mounted on the spectacles of the subject(vrt) – on which a hall way is projected and a flashing LED mounted on the spectacles of the subject (vrt +sc)				
Zijlstra[53] *Study 1*	Pre-experimental	A, VRS	E = 10 hC young = 5 hC old = 5	44–74 25–30 55–60	1.5–4	nr	Walking without cue vs. – walking with a metronome set at a self selected frequency (M), increasing to 100 walking with floor markers (fm)	Walking speed Cadence Stride length	M 0 1 0	fm 0 0 0

RCT, randomized controlled trial; *N*, number of subjects; SD, standard deviation; H-Y, Hoehn and Yahr[30]; E, Experimental group; hC, healthy control; A, auditory cue; VRS, visual rhythmic spatial cue (e.g., floormarkers); VRT, visual rhythmic temporal cue (e.g., a flashing light); T, tactile cue; nr, not reported.
For intervention: All interventions are applied in the on-phase unless mentioned otherwise. When conditions are numbered they are applied in this order, when they are not numbered, they were applied in random order. Floor markers are light coloured stripes on the floor, perpendicular to the walking direction.
For the results: +, results are statistically significant ($p < 0.05$) better than control group or baseline assessment; −, results are statistically significant worse than control group or baseline assessment ($p < 0.05$). 0, results are statistically not significant better or worse than control group or baseline assessment ($p > 0.05$).

investigated the effects of auditory cueing (music, metronome) on gait (Table 1). Both RCTs were of high methodological quality and three studies with a pre-experimental design were of sufficient methodological quality,[41,42,47] all other studies were of low methodological quality.[37,39,40,45,46,48,50,51,53]

Measurement outcomes

Walking speed was measured in two RCTs[32,33] and in 10 studies with a pre-experimental design.[39,41,42,45–47,50,51,53] Both RCTs found significant improvement on walking speed as an outcome measurement and therefore strong evidence was shown in a best-evidence synthesis. Stride length and cadence were measured in one RCT[32] and 11 pre-experimental studies.[39,41,42,45–48,50,51,53] As significant improvements were found for stride length and cadence as outcome measurements in one RCT, limited evidence was available for these parameters. Step length, step–extremity ratio, double support, cycle time and base of support[41] were assessed in one pre-experimental study of sufficient quality. Step to step variability was assessed in one pre-experimental study of sufficient quality and in one pre-experimental study of low quality.[47,54] Time[37,40] and number of steps[40] needed to complete a complex track with freezing-inducing elements (e.g., turns and doorways) were assessed in studies of low quality. Therefore, insufficient evidence was found for these gait parameters after applying a best-evidence synthesis.

Visual cueing

Fourteen studies[3,34–36,38,43,44,48,49,51–53] measured the effect of visual cueing on gait in Parkinson's disease (Table 1), however no RCTs were found investigating the effects of visual cueing on gait. Two studies showed sufficient methodological quality,[36,52] whereas 12 studies[3,34,35,38,43,44,48,49,51,53] were of low methodological quality.

Measurement outcomes

Ten studies[3,34,35,44,48,49,51,53] investigated the effect of floor markers on walking, by using stripes on the floor, perpendicular to the walking direction. All but one[36] of these studies were of low methodological quality. Therefore, insufficient evidence was found, when applying a best-evidence synthesis. Stride length was measured in two studies of sufficient methodological quality[36,52] and 10 studies of low quality.[3,34,35,44,48,49,51,53] One of the 2 studies with sufficient quality[52] reported positive effects of floor markers on stride length. In the other studies,[36] no changes were found and therefore insufficient evidence was shown. Insufficient evidence was found for the effect of floor markers on cadence,[3,34,35,44,48,49,51,53] step length, stride time, single support[36] and double support,[3,36,38] due to the low quality of the studies measuring these parameters.

Several studies investigated the effect of other visual cues than floor markers (e.g., (modified) walking sticks,[38,43] a rhythmic flashing light, mounted on the spectacles of the subjects[52] or a subject-mounted light device.[44] Insufficient evidence was found for all of these visual cues, applying best-evidence synthesis.

Tactile cueing

One pre-experimental study of low quality[40] studied the effects of tactile cueing (shoulder taps) (Table 1). Best-evidence synthesis showed insufficient evidence for rhythmical shoulder taps on the time and number of steps needed to complete a complex track.

Combination of auditory and visual cueing

One pre-experimental study of low quality[51] investigated the effects of a combination of auditory cueing and floor markers (Table 1). Insufficient evidence was found for this on walking speed, stride length and cadence, applying a best-evidence synthesis.

Discussion

This is the first systematic review of the literature using an explicit analysis method that explored the effects of external cueing on the gait of patients with Parkinson's disease. Two RCTs and 24 studies with a noncontrolled design were identified investigating four different types of cueing and 13 different measurements of outcome. Unfortunately, only one study investigated the effects of tactile cueing on parkinsonian gait. Strong

Clinical messages

- There is strong evidence that rhythmical auditory cueing enhances walking speed in patients with Parkinson's disease.
- However, generalization of reported effects measured in a gait laboratory to gait-related ADLs and patients' own home situations remains unclear.

evidence was found for effects with the use of auditory cueing on walking speed in Parkinson's disease. Limited evidence was available for improving stride length and cadence with the use of auditory cueing, applying best-evidence synthesis. Insufficient evidence was found for improving gait of patients with Parkinson's disease with the help of visual cueing (i.e., floor markers, walking sticks, subject-mounted laser beams or a flashing light mounted on the spectacles of the subject), tactile cueing (shoulder taps) or a combination of auditory and visual cueing (an auditory rhythm and floor markers). Although external rhythmical cueing is often used in rehabilitation of patients with Parkinson's disease, only two RCTs investigated the effects of auditory cueing on gait. However, in the RCT of Ellis *et al.*,[33] auditory cueing was only a third part of an exercise programme given to patients with Parkinson's disease (Table 1). It is therefore not clear whether the improved walking speed was a result of external rhythmical cueing or due to other elements in this group exercise programme. Leaving this study out, the evidence for improving gait in Parkinson's disease with the help of auditory cueing was reduced to limited evidence for walking speed, stride length and cadence.

Although many studies have found significant improvements of gait, evidence for this can not be established, due to the low methodological quality of these studies, therefore pooling of the studies for quantitative meta-analysis was not possible. Steultjens *et al.*[27] compared effect-sizes with the levels of evidence found for the different interventions in their study and concluded that the levels of evidence confirmed the findings found with a meta-analysis, underpinning the reliability of the method used in the current study.

Although strong evidence was found in favour of auditory cueing, the interpretation of reported effects on walking speed needs further consideration. First most studies were executed in a laboratory setting and focused on instantaneous effects only, whereas four intervention studies were reported in which patients were taught to take advantage of auditory rhythms by systematic training.[32,33,37,54] In three studies an exercise programme was applied[32,33] and in two studies the subjects were able to practise using the cues in their own home situation.[32,37] Although these studies showed positive results for auditory cueing,[32,33] the impact of reported effects measured in a laboratory setting is difficult to generalize to the home. It is known that patients with Parkinson's disease have severe problems apply the learned skills in a clinical setting to their home situation.[55] For this reason it is preferable for intervention and assessments to be carried out in the patient's own home environment.

Secondly, the impact of walking speed on ADLs and extended ADLs remains unclear. In particular the carry-over effects of external cues on symptoms such as freezing and falling needs further investigation.

Thirdly, it is not clear how the external cues need to be presented to the patient with Parkinson's disease to obtain maximum effect. Both instantaneous effects and training effects were found in the current review. Future studies should focus on the best way to use the cues in the clinical setting.

A possible explanation for the uncertainty about the best way to present cues and to assess the effects on gait is the lack of an uniform definition for external cueing. For this review, a definition was formulated based on the descriptions of cues by Cools[23] and Horstink.[24] In addition the mechanism behind external cueing remains unclear.

The present study has some limitations. The review based itself on a restricted number of languages within a limited number of electronic databases. Some relevant studies may therefore have been missed. In addition, the precise way of cueing as well as appended instruction to the cued patient was not always clear in found studies. This might have resulted in misclassification of the intervention type. Further studies should evaluate the effects of different types of cueing on gait-related activities in the patient's own home situa-

tion and community, in a well-conducted RCT, including measurements related to ADLs, falling, freezing and perceived quality of life in general.

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Appendix 1 – Best-evidence synthesis

Strong evidence	Provided by consistent, statistically significant findings in *outcome* measures in at least two high-quality RCTs[a]
Moderate evidence	Provided by consistent, statistically significant findings in *outcome* measures in at least one high-quality RCT and at least one low-quality RCT or high-quality CCT[a]
Limited evidence	Provided by consistent, statistically significant findings in *outcome* measures in at least one high-quality RCT
or	
	Provided by consistent, statistically significant findings in *outcome* measures in at least two high-quality RCTs (in absence of high-quality RCTs)
Indicative findings	Provided by consistent, statistically significant findings in outcome and/or process measures in at least one high-quality CCT or low-quality RCT[a](in the absence of high-quality RCTs)
or	
	Provided by consistent, statistically significant findings in outcome and/or process measures in at least two noncontrolled studies with sufficient quality (in absence of RCTs and CCTs)
No or insufficient evidence	In the case that results of eligible studies do not meet the criteria for the above stated levels of evidence In the case of conflicting results (statistically significant positive and statistically significant negative) results among RCTs and CCTs In the case of no eligible studies

RCT, randomized controlled trial; CCT, controlled clinical trial.
[a]If the number of studies that show evidence is $< 50\%$ of the total number of studies found within the same category of methodological quality and study design (RCTs, CCTs or noncontrolled studies), no evidence will be stated.

Appendix 2 – Fulfilled items of methodological quality plus quality criteria for randomized controlled trials (RCT) and noncontrolled studies

First author	Design	Items positively scored on criteria for 'Internal Validity'	Items positively scored on 'Descriptive criteria'	Items positively score d on 'Statistical criteria'	MQ
Ellis[33]	RCT	b_1, b_2, f, g, i, j, l, n	a, c, d, c m_2	o, q	HQ
Thaut[32]	RCT	b_1, g, j, l, n, p	c, d, m_1	o, q	HQ
Azulay[34]	Pre-experimental	f, j, l, n, p	d	o, q	LQ
Azulay[35]	Pre-experimental	f, j, l, n, p	d	o, q	LQ
Bagley[36]	Pre-experimental	f, j, n, p	d, m_1	q	SQ
Cubo[37]	Pre-experimental	i, j, n	m_1	o, q	LQ
Del Olmo[54]	Pre-experimental	j	a, d, m_1	q	LQ
Dietz[38]	Pre-experimental	j, l, p	d, m_1	o, q	LQ
Ebersbach[39]	Pre-experimental	j, n	a	o, q	LQ
Enzensberger[40]	Pre-experimental	j, l, n	a	o	LQ
Freedland[41]	Pre-experimental	j, l, n, p	d, m_1	o, q	SQ
Howe[42]	Pre-experimental	f, j, l, n, p	a, d	o, q	SQ
Kompoliti[43]	Pre-experimental	f, j, l, n, p	d	o	LQ
Lewis[44]	Pre-experimental	f, j, l, n, p	d	o, q	LQ
McCoy[45]	Pre-experimental	f, j, n	d	q	LQ
McIntosh[46]	Pre-experimental	f, j, n, p	m_1	–	LQ
McIntosh[47]	Pre-experimental	f, j, l, n, p	d, m_1	o	SQ
Morris[a 48]	Pre-experimental	f, j, n	d	–	LQ
Morris[49]	Pre-experimental	f, j, n	d	q	LQ
Morris, study 1[3]	Pre-experimental	f, j, n	d, m_1	q	LQ
Morris, study 2[3]	Pre-experimental	f, j, n	d, m_1	q	LQ
Morris, study 3[3]	Pre-experimental	f, j, n	d, m_1	q	LQ
Nieuwboer[50]	Pre-experimental	f, j, n	–	q	LQ
Suteerawattananon[51]	Pre-experimental	f, j, n	a, d	–	LQ
Van Wegen[52]	Pre-experimental	f, j, l, n, p	a, d	o	SQ
Zijlstra[53]	Pre-experimental	j, l, n	–	o	LQ

MQ, methodological quality; HQ, high methodological quality; SQ, sufficient methodological quality, LQ, low methodological quality.
All studies were scored on items concerning 'internal validity', 'descriptive criteria' and 'statistical criteria'. An 'a' indicates a positive score on a description of the eligibility criteria; 'b_1' means that a randomization procedure has been applied, whereas 'b_2,' means that the treatment allocation was concealed; 'c' indicates that groups were similar at baseline; 'd' means that index and control interventions were adequately described; 'e' indicates that the care provider was blinded for allocation of the patients; 'f' indicates that co-interventions were avoid of comparable between the index and the control groups; 'g' means that compliance was acceptable; 'h' means that the patient was blinded for allocation; 'i' means that the assessor of the outcomes measurements was blinded for allocation; 'j' means that the outcome measures were relevant; 'k' indicates that adverse effects were described; 'l' means that withdrawal/ dropout rate was described; 'm_1' means that a short-term follow-up measurement was applied (at the end of the intervention), whereas 'm_2' means that a long-term follow-up measurement was applied (after three months or later); 'n' indicates that the timing of outcome assessments was comparable for all groups; 'o' means that the sample size for each group was presented at randomization and for most important outcomes assessments; 'p' means that an intention-to-treat analysis was applied; 'q' means that all point estimates and measures of variability were presented. Criteria 'b_1', 'b_2', 'c', 'e' and 'h' were not scored for noncontrolled studies.