Walking-adaptability therapy after stroke: results of a randomized controlled trial

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Abstract

Background

The ability to adapt walking to environmental properties and hazards, a prerequisite for safe ambulation, is often impaired in persons after stroke.

Research question

The aim of this study was to compare the efficacy of two walking-adaptability interventions: treadmill-based C-Mill therapy (using gait-dependent augmented reality) and the overground FALLS program (using physical context). We hypothesized better outcomes for C-Mill therapy than the FALLS program due to its expected greater amount of walking practice.

Methods

In this randomized controlled trial, forty persons after stroke (≥3 months ago) with walking and/or balance deficits were randomly allocated to either 5 weeks of C-Mill therapy or the FALLS program. The primary outcome measure was the standard walking speed as determined with the 10 Meter Walking Test (10MWT). Additionally, context-specific walking speed was assessed in environments enriched with either stationary physical context (10MWT context) or suddenly appearing visual images (Interactive Walkway). The walking-adaptability scores of those enriched walking tests served as secondary outcome measures. Furthermore, a cognitive task was added to all three assessments to evaluate dual-task performance. Finally, the participants' experience and amount of walking practice were scored.

Results

While both interventions did not show significant improvements in the standard walking speed, they did show significant improvements in context-specific walking speed, walking adaptability and cognitive dual-task performance. C-Mill therapy led to a greater improvement in context-specific walking speed with stationary physical context compared to the FALLS program; however, this improvement was no longer significant at retention. Both interventions were well received, but C-Mill therapy scored better on perceived increased fitness than the FALLS program. Moreover, C-Mill therapy resulted in twice as many steps per session of equal duration than the FALLS program.

Significance

Both interventions led to long term context-specific improvements in walking speed, walking adaptability and dual-tasking.

Trial registration: The Netherlands Trial Register (NTR4030). Registered 11-June 2013, https://www.trialregister.nl/trial/3842

Background

Walking in everyday life requires the ability to adapt walking to environmental circumstances and hazards [1]. This adaptability is often impaired in people after stroke [2–3], which might contribute to the high risk of falling in this population [4–5]. Moreover, attentional demands of walking are often elevated in people after stroke [6–7], especially when step adjustments or step adjustments under time pressure are required [3, 8]. To improve safe community ambulation in people after stroke, practicing walking adaptability seems essential.

Several training programs have been developed to practice walking adaptability. For instance, the FALLS program [9] is an overground walking-adaptability training that involves practicing complex situations of community walking, such as walking over an obstacle course. The FALLS program is based on the Nijmegen Falls Prevention Program, which was designed for community-dwelling older adults with a history of falling and has been proven effective in reducing the number of falls in this population [10–11]. The FALLS program (or a similar obstacle-course training) is often the walking-adaptability intervention of choice at Dutch rehabilitation centers. Treadmill-based therapy with augmented reality (C-Mill) is a novel and promising form of walking-adaptability training [8, 12–15]. The C-Mill is an instrumented treadmill equipped with a projector (Motek, Amsterdam, the Netherlands) to project visual images representing stepping targets or obstacles onto the walking surface. It has an embedded force platform that allows for gait-event detection and the provision of real-time feedback on performance [16–17]. The instrumented C-Mill further supports projection of interactive context in a gait-dependent manner, facilitating practicing step adjustments under high time-pressure demands, which is especially difficult for people after stroke [3, 8].

Both FALLS and C-Mill interventions (Fig. 1) comprise key ingredients for effective walking rehabilitation and motor learning (task- and context-specificity, variability in practice and feedback of performance) [18–21]. However, the interventions differ in the way in which these ingredients are implemented. The FALLS program uses stationary physical context (e.g., real obstacles) to enrich the environment, whereas C-Mill therapy uses gait-dependent augmented reality (e.g., suddenly appearing projected obstacles attuned to the participant's future foot placement). Moreover, the FALLS program entails overground gait training while C-Mill therapy offers treadmill-based gait training. Treadmill gait training has been suggested to elicit more steps per session of equal duration compared to overground gait training [13, 20]. Therefore, C-Mill therapy is likely to result in a higher amount of walking practice than the overground FALLS program (operationalized as the number of steps taken per unit session time).

The aim of the study was to compare the efficacy of treadmill-based C-Mill therapy (CT) with the overground FALLS program (FP) in persons after stroke. It was hypothesized that CT results in better outcomes than the FP due to its expected higher amount of walking practice per session of equal duration. To test this hypothesis, we compared the total number of steps as well as the number of adaptive steps (i.e. when context was provided) taken per training session and evaluated (differences in) immediate and long-term training effects of the interventions.

Methods

Study design

This was a pre-registered single-centre parallel group randomized controlled trial with pre-intervention (T0), post-intervention (T1), 5-weeks post-intervention retention (T2) and 1-year post-intervention follow-up (T3) tests. Participants were randomly assigned to either five weeks of CT or FP.

Randomization

After giving informed consent, participants were randomly assigned to one of the two interventions using an automated, custom-made minimization algorithm written in MATLAB. This minimization of group differences used time after stroke, age and FAC score as stratifying factors, which together determined 80% of group allocation. Due to the nature of the intervention the assessors, physical therapists and participants were not blinded to group allocation.

Participants

Participants were recruited from the outpatient population of rehabilitation center Reade (Amsterdam, the Netherlands). A sample size calculation was carried out that resulted in a sample size of 14 participants in each group to achieve 80% power with a two-tailed α of 0.05. Considering a drop out of 10–25%, we decided to recruit 20 participants in each group, resulting in a total of 40 participants [24]. All participants had suffered a first-ever ischemic stroke ≥ 3 months before study entrance, had a Functional Ambulation Categories (FAC) score ≥ 4, were clinically diagnosed with hemiparesis and suffered from walking and/or balance deficits established by a physician. Exclusion criteria were orthopedic and other neurological disorders that affect walking (e.g., Parkinson's disease), other treatments that could influence the effects of the interventions (e.g., recent Botulin toxin treatment of the lower extremity), contra-indication to physical activity (e.g., heart failure, severe osteoporosis), moderate or severe cognitive impairments as indicated by a Mini-Mental State Examination score below 21, severe uncorrected visual deficits, or inability to understand and execute simple instructions [24]. All participants provided written informed consent before the start of the trial. The protocol for the study was approved by the Medical Ethical Reviewing Committee of the VU University Medical Centre (Amsterdam, the Netherlands; protocol number 2013/53 and the Central Committee on Research Involving Human Subjects, CCMO, protocol number NL 42461.029.13).

Interventions: treadmill-based C-Mill therapy (CT) and overground FALLS program (FP)

CT is a treadmill-based training with a specific emphasis on practicing walking adaptability, using gait-dependent projector-generated context on the instrumented treadmill surface to elicit step adjustments. CT encompasses various exercises to practice avoidance of projected visual obstacles, foot positioning on a step-to-step basis to regular or irregular sequences of visual stepping targets (goal-directed stepping) with or without obstacles, gait acceleration and deceleration by maintaining position within a projected walking area that moves along the treadmill, walking with tandem steps, and an interactive walking-adaptability game [8, 12]. C-Mill therapy is a patient-tailored type of training in that the therapist can adjust the difficulty of the different exercises by manipulating content parameters as the obstacle size or available response time for obstacle negotiation. Therapists were encouraged to increase the level of difficulty as tolerated by the participant by either changing content parameters or increasing the belt speed.

FP is an overground walking therapy program aimed at reducing the number of falls in people after stroke by including walking-adaptability exercises. The program incorporates an obstacle course consisting of exercises to practice obstacle avoidance, foot positioning while walking over uneven terrain, tandem walking, and slalom walking. Therapists in this program are encouraged to increase the level of difficulty by adding cognitive and motor dual-tasks or to use visual constraints, as described in the pre-defined training protocol [9]. The program also incorporates exercises to simulate walking in a crowded environment and to practice falling techniques (one session per week).

Both interventions were matched in therapy session duration (90 min), frequency (twice per week). CT group trained in groups of two participants and the FP group trained in groups of 4–6 participants. Participants in both groups alternately trained and rested and had similar therapist attention (mean participant-to-therapist ratio, 2:1). Further details of the interventions can be found in the study protocol [24].

Procedure & set-ups

At T0, T1, T2 and T3, participants performed three different walking tasks (see [24, 27] for more details): the standard 10MWT [25], and two context-specific assessments: 1) 10MWT with stationary physical context (10MWT context) and 2) Interactive Walkway assessments with suddenly appearing projected obstacles in a gait-dependent manner (IWW obstacles) [23, 26], all with and without the simultaneous performance of a cognitive task. This resulted in six walking conditions, which were performed in a randomized order. The standard 10MWT and 10MWT context were performed three times at a self-selected comfortable walking speed (Fig. 2A-2B). The 10MWT context comprised three physical obstacles, a tandem-walking path and three stepping targets. Participants were instructed to step over the obstacles, step onto the targets and in-between the tandem-path lines. To assess walking adaptability under time pressure, the IWW obstacles comprised two suddenly appearing visual obstacles in the form of a projected red rectangle, presented in both a gait-dependent (at a predicted foot-placement position) and a position-dependent (at an unpredictable but predefined position) manner. Ten runs were performed, including three dummy trials without obstacles (to retain unpredictability), at a self-selected comfortable walking speed (Fig. 2C). Participants were instructed to step over the suddenly appearing projected obstacle images.

The cognitive dual-task was a serial-3 subtraction task, which had to be performed by counting backwards out loud. The number to start with was varied to avoid task-familiarization. Participants practiced this subtraction task for 30s while sitting. During all dual-task conditions, participants were instructed to simultaneously perform both tasks as effectively as possible at a self-selected walking speed. Additionally, a 60s subtraction task was performed while sitting to determine the degree of cognitive motor-interference (i.e., using sitting as the single-task reference for cognitive-task performance, see below). This 60s seated subtraction task was randomized with the six walking conditions.

Outcome measures

The primary outcome measure was walking speed (m/s) as determined with the standard 10MWT, 10MWT context and IWW obstacles trials (m/s), averaged over repetitions. Secondary outcome measures were walking adaptability, cognitive dual-task performance (the number of correct subtractions per second; sub/s) and cognitive-motor interference (dual-task effects), averaged over repetitions (Fig. 2). For the 10MWT context, walking adaptability was the sum of sub-scores obtained for obstacle avoidance, tandem walking and targeted stepping, averaged over the three repetitions (range 0–10, 1 point per obstacle, 1 point per target and max 4 points for tandem walking). Details regarding the walking-adaptability score can be found in [27]. The walking-adaptability score of the IWW obstacles was the sum of the points received for the first 10 obstacles to obtain the same scoring range as for the 10MWT context assessment (range 0–10). Walking speed and cognitive dual-task performance of this assessment was also averaged over the trials involving the first 10 projected obstacles (i.e., excluding dummy trials). Walking adaptability was scored manually by two observers through visual inspection of sagittal video recordings and averaged in case of discrepancies. Cognitive-motor interference during dual-task walking was quantified using the average of the respective dual-task effects of walking speed, the walking-adaptability score and the cognitive-task performance (with sitting as single-task reference), that is, motor (walking speed, walking adaptability) and cognitive scores were combined to reflect overall task performance. Following [28], dual-task effects were defined as 100% * (dual-task performance – single-task performance)/single-task performance, with a negative cognitive-motor interference score indicating overall poorer dual-task than single-task performance.

Furthermore, participants' experience and attitude towards the interventions were assessed with a purpose-designed evaluation questionnaire consisting of 1–10 rating scales and multiple-choice questions assessing participants' experience, attitude towards the interventions, improvements, and discomforts during and after training (see Appendix 1).

Finally, to test the expectation of different amounts of walking practice per session between CT and FP, we compared the total number of steps and the number of adaptive steps taken per session for two subgroups (CT n = 10 and FP n = 10). This process measure was obtained using the treadmill's inbuilt step counter (CT) and by counting the number of steps (FP) using video recordings of a random selection of training sessions by two observers (averaged in case of discrepancies).

Statistical analysis

Participant characteristics and baseline performance were compared between the two groups using independent *t*-tests for normally distributed interval variables, Mann-Whitney *U*-tests for ordinal and non-normal interval variables and Fisher's exact tests for nominal variables. To analyze the change over time in walking speed (standard and context-specific), walking adaptability, cognitive dual-task performance and cognitive-motor interference (for all participants, compared to baseline), we performed paired samples *t*-tests or Wilcoxon signed rank tests for ordinal or non-normally distributed variables at each time point (T1, T2 and T3). For comparing the effects of the interventions on the outcome measures, we calculated changes in outcome measures by subtracting baseline values from the values at each time point (T1, T2 and T3). These change scores of the outcome measures were analyzed using ANCOVA with correction for baseline values. We used a different statistical analysis (with correction for baseline values) compared to the one described in the study protocol [15], because of the large variation in the baseline (pre-intervention) outcome measures within the groups. We analyzed ordinal and non-normally distributed variables, notably the participants' experience and attitude towards the interventions, using Mann-Whitney *U*-tests. The amount of walking practice was compared using independent *t*-tests for the total number of steps and the number of adaptive steps taken per training session. The level of significance was set at $p < 0.05$, while $0.05 < p < 0.075$ was seen as a tendency towards significance. Effect sizes are presented as partial η^2 for ANCOVA or r for the other tests. This trial was not an intention-to-treat analysis because dropouts were excluded from the analysis and only complete case data were used.

Results

Forty participants were recruited for this trial. Thirty participants after stroke completed the intervention and post-intervention assessments (T1), out of which 29 completed post-intervention retention (T2) and 28 post-intervention follow-up (T3). Figure 3 shows the distribution over groups and reasons for dropout. Table 1 provides the characteristics of the participants who completed the intervention (performed at least seven out of the ten sessions). Participants' characteristics did not differ significantly between intervention groups, except for age: CT participants were significantly younger than FP participants.

Table 1
Participants' characteristics

	C-Mill therapy (n = 14)	FALLS program (n = 16)	*p*-value
Gender (female/male)	8/6	5/11	0.16^C
Age at intake (years)	52 ± 13	61 ± 9	**0.02^A**
Height (cm)	172 ± 10	175 ± 7	0.40^A
Body mass (kg)	78 ± 14	81 ± 15	0.57^A
Time since stroke at intake (months, median)	36 (5-360)	15 (7-136)	0.21^C
Side of lesion (left/right)	8/6	7/9	0.70^C
Functional Ambulation Category (FAC) at intake (1–5, median)	5(4–5)	5(4–5)	0.92^C
Berg Balance Scale (BBS) (0–56, median)	55 (39–56)	54 (46–56)	0.50^C
Mini-Mental State Examination MMSE (0–30, median)	29(26–30)	29 (22–30)	0.73^C
Assistive device (none/(k)evo/walking cane)	5/3/6	9/3/4	0.25^C
Level of activity (1–5 days a week at least 30 min moderate active)	1(0–5)	2(0–5)	0.53^C
Falls past year (n, %)	7, 50%	12, 75%	0.26^B
Fear of falling (1 (no fear of falling) – 10 (extreme fear of falling))	4(1–8)	3(1–10)	0.37^C
Living situation (independently/independently with help)	3/11	6/10	0.35^C
Comorbidities (n, %)	8, 57%	9, 56%	0.63^B

p-values were obtained using ^AIndependent *t*-test, ^BFisher's exact test or ^CMann-Whitney *U*-test. Significant differences are presented in bold ($p < 0.05$).

Primary outcome measure:

Walking speed (standard and context-specific)

Whereas walking speed of the standard 10MWT did not differ over time, significant (or tendencies to it) improvements in context-specific walking speed were observed post-intervention, at retention and follow-up (penultimate column in Table 2, combined over groups). The CT group showed a significantly greater improvement in walking speed for the 10MWT with physical context than the FP group immediately post-intervention ($p < 0.05$, η^2=0.17); however, this between-group difference was no longer significant at retention and follow-up (final column in Table 2).

Table 2
Standard and context-specific walking speed results

Outcome (n: CT, FP)		CT	FP	Change over time, both groups (*p*-value, effect size)	Difference between groups (*p*-value, effect size)
10MWT (m/s)	T0 (14,16)	0.85 ± 0.33	0.91 ± 0.28	-	0.59, 0.10[A]
	T1-T0 (14,16)	0.04 ± 0.14	0.05 ± 0.14	0.10, 0.30[D]	0.81, 0.00[B]
	T2-T0 (13,16)	0.02 ± 0.09	0.03 ± 0.11	0.12, 0.30[D]	0.72, 0.01[B]
	T3-T0 (13,15)	0.02 ± 0.13	0.06 ± 0.14	0.13, 0.29[D]	0.31, 0.04[B]
10MWT cognitive (m/s)	T0 (14,16)	0.67 ± 0.25	0.79 ± 0.25	-	0.21, 0.24[A]
	T1-T0 (14,16)	0.09 ± 0.14	0.01 ± 0.08	**0.04, 0.38[D]**	0.12, 0.09[B]
	T2-T0 (13,16)	0.06 ± 0.11	0.05 ± 0.10	**0.01, 0.50[D]**	0.96, 0.00[B]
	T3-T0 (13,15)	0.07 ± 0.18	0.03 ± 0.12	0.13, 0.29[D]	0.75, 0.00[B]
10MWT context (m/s)	T0 (14,16)	0.56 ± 0.25	0.59 ± 0.17	-	0.74, 0.06[A]
	T1-T0 (12,16)*	0.12 ± 0.11	0.03 ± 0.11	**0.00, 0.53[D]**	**0.03, 0.17[B]**
	T2-T0 (13,16)	0.14 ± 0.13	0.07 ± 0.13	**0.00, 0.61[D]**	0.10, 0.10[B]
	T3-T0 (13,15)	0.09 ± 0.10	0.08 ± 0.13	**0.00, 0.64[D]**	0.84, 0.00[B]
10MWT context and cognitive (m/s)	T0 (14,16)	0.46 ± 0.24	0.55 ± 0.22	-	0.30, 0.19[A]
	T1-T0 (14,16)	0.14 ± 0.13	0.06 ± 0.13	**0.00, 0.59[D]**	0.14, 0.08[B]

p-values were obtained using [A]Independent *t*-test, [B]ANCOVA with baseline performance as covariate, [C]Mann-Whitney *U*-test, [D]Paired samples *t*-test or [E]Wilcoxon signed rank test. Significant differences are presented in bold ($p < 0.05$). *Some participants were excluded (see degrees of freedom) due to technical problems with the IWW and/or video footage.

Outcome (n: CT, FP)		CT	FP	Change over time, both groups (*p*-value, effect size)	Difference between groups (*p*-value, effect size)
	T2-T0 (13,16)	0.17 ± 0.16	0.07 ± 0.12	**0.00, 0.64^{D}**	0.14, 0.08^{B}
	T3-T0 (13,15)	0.09 ± 0.19	0.07 ± 0.17	**0.03, 0.40^{D}**	0.62, 0.01^{B}
IWW obstacles (m/s)	T0 (14,14)*	0.69 ± 0.30	0.85 ± 0.18	-	0.09, 0.36^{A}
	T1-T0 (11,14)*	0.07 ± 0.10	0.03 ± 0.13	**0.04, 0.41^{D}**	0.65, 0.01^{B}
	T2-T0 (8,13)*	0.08 ± 0.06	0.04 ± 0.13	**0.03, 0.46^{D}**	0.64, 0.01^{B}
	T3-T0 (5,11)*	0.06 ± 0.05	0.05 ± 0.17	0.14, 0.14^{D}	0.59, 0.02^{B}
IWW obstacles and cognitive (m/s)	T0 (14,14)*	0.61 ± 0.28	0.74 ± 0.15	-	0.13, 0.33^{A}
	T1-T0 (11,14)*	0.07 ± 0.14	0.05 ± 0.17	**0.02, 0.45^{D}**	0.74, 0.01^{B}
	T2-T0 (8,13)*	0.09 ± 0.07	0.08 ± 0.12	**0.00, 0.64^{D}**	0.96, 0.00^{B}
	T3-T0 (5,11)*	0.03 ± 0.03	0.09 ± 0.12	**0.02, 0.33^{D}**	0.17, 0.14^{B}

p-values were obtained using ^{A}Independent *t*-test, ^{B}ANCOVA with baseline performance as covariate, ^{C}Mann-Whitney *U*-test, ^{D}Paired samples *t*-test or ^{E}Wilcoxon signed rank test. Significant differences are presented in bold ($p < 0.05$). *Some participants were excluded (see degrees of freedom) due to technical problems with the IWW and/or video footage.

Secondary outcome measures:

Walking adaptability

Walking adaptability improved over time, albeit only for walking-adaptability outcomes assessed with IWW obstacles and IWW obstacles with the cognitive task post-intervention, at retention and follow-up (penultimate column in Table 3, combined over groups). However, no significant between-group differences were found (final column in Table 3).

Table 3
Walking adaptability results

Outcome (n: CT, FP)		CT	FP	Change over time, both groups (*p*-value, effect size)	Difference between groups (*p*-value, effect size)
10MWT context (1–10)	T0 (14,16)	5.59 ± 2.43	4.97 ± 2.21	-	0.47, 0.09[A]
	T1-T0 (12,16)*	0.49 ± 1.03	0.27 ± 1.79	0.20, 0.24[D]	0.58, 0.01[B]
	T2-T0 (10,16)*	0.26 ± 1.53	0.23 ± 1.94	0.91, 0.02[D]	0.48, 0.02[B]
	T3-T0 (7,15)*	0.37 ± 1.68	0.07 ± 2.70	0.76, 0.00[D]	0.69, 0.00[B]
10MWT context with cognitive task (1–10)	T0 (14,16)	5.31 ± 2.29	4.36 ± 2.03	-	0.24, 0.22[A]
	T1-T0 (13,16)*	0.42 ± 1.19	0.16 ± 1.33	0.24, 0.22[D]	0.45, 0.02[B]
	T2-T0 (10,16)*	-0.38 ± 1.15	0.34 ± 1.93	0.81, 0.05[D]	0.20, 0.07[B]
	T3-T0 (7,15)*	0.17 ± 1.91	0.28 ± 2.53	0.62, 0.01[D]	0.81, 0.00[B]
IWW obstacles (1–10)	T0 (14,14)*	5.96 ± 3.52	6.25 ± 3.51	-	0.83, 0.04[A]
	T1-T0 (11,14)*	3.09 ± 2.56	2.11 ± 2.31	**0.00, 0.73[D]**	0.59, 0.01[B]
	T2-T0 (8,13)*	2.81 ± 2.55	1.58 ± 2.24	**0.00, 0.66[D]**	0.79, 0.00[B]
	T3-T0 (6,10)*	3.42 ± 3.68	0.9 ± 3.06	*0.05, 0.66[D]*	0.93, 0.00[B]
IWW obstacles with cognitive task (1–10)	T0 (14,14)*	4.75 ± 3.71	5.21 ± 2.96	-	0.72, 0.07[A]
	T1-T0 (11,14)*	1.95 ± 1.67	0.82 ± 2.25	**0.00, 0.55[D]**	0.25, 0.06[B]

p-values were obtained using [A]Independent *t*-test, [B]ANCOVA with baseline performance as covariate or [C]Mann-Whitney *U*-test, [D]Paired samples *t*-test or [E]Wilcoxon signed rank test. Significant differences are presented in bold ($p < 0.05$) and tendencies are presented in italic ($0.05 < p < 0.075$). *Some participants were excluded (see degrees of freedom) due to technical problems with the IWW and/or video footage.

Outcome (n: CT, FP)		CT	FP	Change over time, both groups (*p*-value, effect size)	Difference between groups (*p*-value, effect size)
	T2-T0 (8,13)*	3.5 ± 2.33	1.58 ± 1.30	**0.00, 0.24D**	0.11, 0.14B
	T3-T0 (6,10)*	1.42 ± 2.71	1.05 ± 3.55	0.16, 0.13D	0.28, 0.09B

p-values were obtained using AIndependent *t*-test, BANCOVA with baseline performance as covariate or CMann-Whitney *U*-test, DPaired samples *t*-test or EWilcoxon signed rank test. Significant differences are presented in bold ($p < 0.05$) and tendencies are presented in italic ($0.05 < p < 0.075$). *Some participants were excluded (see degrees of freedom) due to technical problems with the IWW and/or video footage.

Cognitive dual-task performance and cognitive-motor interference

Cognitive dual-task performance significantly improved over time, with significant change scores post-intervention, at retention and follow-up (penultimate column in Table 4, combined over groups). Additionally, immediately post-intervention (T1), the CT group showed a tendency to a greater improvement in cognitive performance during the standard 10MWT with cognitive dual-task compared to the FP group ($p = 0.06$, η^2=0.13), which disappeared at retention and follow-up (final column in Table 4). Cognitive-motor interference outcomes did not differ significantly over time, nor between groups (Table 4).

Table 4
Cognitive dual-task performance and cognitive-motor interference results

Outcome (n: CT, FP)		CT	FP	Change over time, both groups (*p*-value, effect size)	Difference between groups (*p*-value, effect size)
10MWT cognitive (sub/s)	T0 (14,16)	0.43 ± 0.12	0.51 ± 0.31	-	0.36, 0.21 A
	T1-T0 (14,16)	0.09 ± 0.10	0.02 ± 0.09	**0.01, 0.49 D**	*0.06, 0.13 B*
	T2-T0 (12,16)*	0.09 ± 0.07	0.05 ± 0.14	**0.00, 0.52 D**	0.59, 0.01 B
	T3-T0 (8,14)*	0.10 ± 0.08	0.04 ± 0.19	0.10, 0.12 D	0.88, 0.00 B
10MWT context and cognitive (sub/s)	T0 (14,16)	0.31 ± 0.15	0.37 ± 0.25	-	0.36, 0.18 A
	T1-T0 (14,16)	0.11 ± 0.11	0.06 ± 0.12	**0.00, 0.56 D**	0.28, 0.04 B
	T2-T0 (12,16)*	0.08 ± 0.08	0.05 ± 0.08	**0.00, 0.61 D**	0.33, 0.04 B
	T3-T0 (8,15)*	0.06 ± 0.07	0.03 ± 0.18	0.21, 0.07 D	0.59, 0.01 B
IWW obstacles and cognitive (sub/s)	T0 (14,14)*	0.33 ± 0.12	0.51 ± 0.31	-	**0.05, 0.46 A**
	T1-T0 (11,14)*	0.15 ± 0.14	0.12 ± 0.15	**0.00, 0.69 D**	0.40, 0.03 B
	T2-T0 (8,13)*	0.02 ± 0.08	0.04 ± 0.14	0.47, 0.16 D	0.58, 0.02 B
	T3-T0 (5,11)*	0.05 ± 0.14	-0.22 ± 0.30	0.09, 0.18 D	0.16, 0.13 B
Cognitive-motor interference 10MWT (%)	T0 (14,16)	-6 (-28- -1)	-1(-40- 52)	-	**0.03, 0.39 C**
	T1-T0 (14,16)	3 ± 22	-5 ± 20	0.72, 0.07 D	0.83, 0.00 B

p-values were obtained using A Independent *t*-test, B ANCOVA with baseline performance as covariate, C Mann-Whitney *U*-test, D Paired samples *t*-test or E Wilcoxon signed rank test Significant differences are presented in bold ($p < 0.05$) and tendencies are presented in italic ($0.05 < p < 0.075$). *Some participants were excluded (see degrees of freedom) due to technical problems with the IWW and/or video footage.

Outcome (n: CT, FP)		CT	FP	Change over time, both groups (*p*-value, effect size)	Difference between groups (*p*-value, effect size)
	T2-T0 (12,16)*	3 ± 14	2 ± 22	0.55, 0.12^{D}	0.58, 0.01^{B}
	T3-T0 (8,14)*	34 ± 84	13 ± 26	0.08, 0.14^{D}	0.55, 0.02^{B}
Cognitive-motor interference 10MWT context (%)	T0 (14,16)	-15 (-45-23)	-9 (-36-5)	-	0.48, 0.13^{C}
	T1-T0 (12,16)*	-1 ± 15	2 ± 18	0.81, 0.05^{D}	0.46, 0.02^{B}
	T2-T0 (10,16)*	2 ± 24	7 ± 21	0.25, 0.23^{D}	0.50, 0.02^{B}
	T3-T0 (7,15)*	-9 ± 17	8 ± 19	0.51, 0.02^{D}	0.11, 0.13^{B}
Cognitive-motor interference IWW obstacles (%)	T0 (14,14)*	-17 (-39-20)	8 (-32-223)	-	**0.04, 0.38^{C}**
	T1-T0 (11,14)*	0 ± 21	-22 ± 69	0.26, 0.23 ^{D}	0.76, 0.00
	T2-T0 (8,13)*	6 ± 27	-20 ± 68	0.44, 0.17^{D}	0.62, 0.01^{B}
	T3-T0 (5,10)*	-14 ± 22	-33 ± 78	0.13, 0.15^{D}	0.98, 0.00^{B}

p-values were obtained using ^{A}Independent *t*-test, ^{B}ANCOVA with baseline performance as covariate, ^{C}Mann-Whitney *U*-test, ^{D}Paired samples *t*-test or ^{E}Wilcoxon signed rank test Significant differences are presented in bold ($p < 0.05$) and tendencies are presented in italic ($0.05 < p < 0.075$). *Some participants were excluded (see degrees of freedom) due to technical problems with the IWW and/or video footage.

Participants’ experience and attitude towards the interventions

Participants scored the interventions as useful, motivating, fun, challenging, enjoyable and suitable; they were initially somewhat reserved but would recommend it to peers after the interventions (Appendix 2.1). Participants of the CT group showed a tendency to higher ratings on “recommend it to peers” and “perceived fun” compared to participants of the FP group ($U = 69.5$, $p = 0.07$, $r = 0.34$, $U = 70.0$, $p = 0.07$, $r = 0.33$, respectively). After both interventions, participants described an increase in physical fitness, safety of walking, walking speed and confidence during walking (Appendix 2.2). In the CT group, significantly more participants reported an increase in physical fitness compared to the FP group ($U = 65.0$, $p < 0.05$, $r = 0.43$). The CT group also perceived significantly more discomforts during the training than the FP group ($U = 62.5$, $p < 0.05$, $r = 0.42$). However, these were only mild, and no significant difference was found in the perceived discomforts after training (Appendix 3.2).

Amount of walking practice

About twice as many steps and adaptive steps were taken with CT training (2779 ± 582, 2405 ± 505 steps, respectively) than with FP training (1464 ± 196, 1130 ± 175 steps, respectively). Both the total number of steps per session of equal duration ($t(18)=-6.88$, $p < 0.01$, $r = 0.85$) and the number of adaptive steps per session of equal duration ($t(18)=-7.54$, $p < 0.01$, $r = 0.87$) were significantly higher in the CT group.

Discussion

This study compared the efficacy of treadmill-based C-Mill therapy with that of the overground FALLS program in persons after stroke. Although no significant effects were found for the standard walking speed, both groups showed significant improvements in context-specific walking speed, walking adaptability (but only when assessed with the IWW) and cognitive dual-task performance during (adaptive) walking immediately post-intervention, at retention and follow-up. Moreover, C-Mill therapy showed a greater improvement in walking speed as determined with the 10MWT context than the FALLS program. However, this result was no longer significant at retention and 1-year follow-up. Both interventions were well received, but C-Mill therapy scored significantly better on perceived increased fitness, which may be attributed to the higher amount of walking practice (twice as many steps during CT than FP training sessions of equal duration).

In contrast to the proof-of-concept study on C-Mill therapy [12], the participants did not show improvements in walking speed as determined with the standard 10MWT. This finding underscores the importance of including context-specific walking speed assessments, for which significant improvements were observed, and even between-group differences in the change scores (Table 2). The standard 10MWT might not be sensitive or specific enough to evaluate the effect of walking-adaptability training. Furthermore, the results showed that the walking-adaptability improvements over time were only significant for the IWW assessment with suddenly appearing projected obstacles and not for the assessments with stationary physical context (Table 3). This finding underscores the importance of assessing step adjustments under high time-pressure demands, as this is especially difficult for people after stroke [3, 8].

Both walking-adaptability interventions indeed yielded a very high proportion of adaptive steps. As expected, C-Mill therapy showed a greater amount of walking practice. About twice as many steps (total number of steps and number of adaptive steps) were taken during a CT training session compared to a FP training session of equal duration. This may have positively influenced perceived fitness and possibly context-specific walking speed but does not readily explain other between-group differences (or the absence thereof). Other differences between the interventions could have played a role, such as the type of context (stationary physical context vs. suddenly appearing projector-generated context). Whereas training with physical context more closely mimics walking in daily life with physical obstacles, projector-generated context reduces the actual physical risk of falling during the training. As a result, the consequence of failure in walking-adaptability performance was greater in the FALLS program than in C-Mill therapy. Future training interventions should therefore take the type of context into account, as this could potentially result in a difference in task prioritization [27].

Differences in amount of walking practice and context notwithstanding, both interventions showed almost similar significant long-term effects (1-year follow up), which have not yet been demonstrated before. In that regard, the sustained effects of both walking-adaptability interventions in this negative between-groups trial may allow clinicians to opt for both forms of training when considering walking-adaptability training for their patients. They may choose C-Mill therapy because of the higher amount of walking practice inherent to treadmill walking. They may opt for the FALLS program because of the more realistic overground practice environment with e.g. physical obstacles. However, they should keep in mind that C-Mill therapy might require a familiarization period of walking on a treadmill, while the FALLS program is lacking adaptability tasks under high time-pressure demands as well as feedback on performance.

Limitations and recommendations

Even though the number of participants was established with a power analysis and still sufficient after dropouts, the main limitation of this study was the high dropout rate after intake (Fig. 3). A larger (multicenter) trial should be performed to underpin the efficacy of the walking-adaptability interventions, which could benefit from the recently validated development of an automatized, progressive patient-tailored C-Mill training program [29]. In addition, despite the randomization with minimization, the intervention groups did show a significant difference in age. However, the impact of this difference is expected to be low as the participants in both groups are still within the same age category (between 40–60 years old). Another limitation of this study was that due to the nature of the intervention the assessors, neither physical therapists nor participants, were blind to group allocation.

Limitations And Recommendations

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Conclusion

This study showed that both treadmill-based C-Mill therapy and the overground FALLS program did not lead to an improvement in the standard walking speed; however context-specific walking speed and walking adaptability did improve and sustain after both interventions, with little between-group differences. Both walking-adaptability interventions are therefore of clinical value. Moreover, the analyses suggested that the greater amount of walking practice observed for the C-Mill group, an essential aspect of effective intervention programs after stroke, may be linked to the reported increased perceived fitness and observed increased context-specific walking speed for the C-Mill group.

Declarations

Ethics approval and consent to participate

The protocol for the study was approved by the Medical Ethical Reviewing Committee of VU University Medical Centre (Amsterdam, The Netherlands; protocol number 2013/53 and the Central Committee on Research Involving Human Subjects, CCMO, protocol number NL 42461.029.13). All participants provided written informed consent before the start of the trial.

Consent for publication

Informed consent was obtained from the persons who appear in Figure 1.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

No conflict of interest. MR and PJB are inventors of rehabilitation treadmills that include visual context for foot placement. Vrije Universiteit Amsterdam granted this invention exclusively to ForceLink (Culemborg, The Netherlands), an industrial partner of Vrije Universiteit Amsterdam. ForceLink merged with Motek (Amsterdam), who is currently the manufacturer of the C-Mill treadmill and assignee of a patent for rehabilitation treadmills with visual context for foot placement, with MR and PJB listed as inventors. MR and PJB did not receive any reimbursements, fees, funding, or salary from ForceLink or Motek, nor did they benefit personally from patent revenues.

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Not applicable.

Authors' contributions

CT is the executive investigator and drafted this paper. MR, CGM, PJB, and TWJ critically revised the manuscript. All authors read and approved the manuscript and consider themselves accountable for all aspects of the work.

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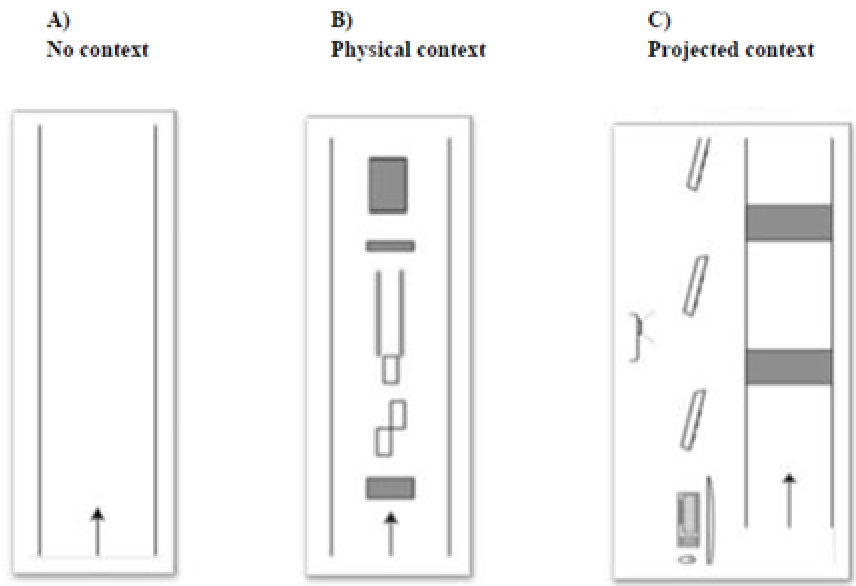
Figures

Figure 1

Snapshots of the two interventions aimed at improving walking adaptability. Left) walking-adaptability exercises of treadmill-based C-Mill therapy (CT); A) obstacle avoidance, B) goal-directed stepping, C) gait acceleration and deceleration, and D) a functional and interactive walking-adaptability game. Right) obstacle course of the overground FALLS program (FP); A) obstacle avoidance, B) walking over uneven terrain, C) tandem walking, and D) slalom walking.



Assessment	10MWT	10MWT +cognitive task	10MWT with context	10MWT with context +cognitive task	IWW obstacles	IWW obstacles +cognitive task
Outcome measures	Standard walking speed	Standard walking speed	Context-specific walking speed	Context-specific walking speed	Context-specific walking speed	Context-specific walking speed
			Walking adaptability	Walking adaptability	Walking adaptability	Walking adaptability
		Cognitive performance & Cognitive motor interference		Cognitive performance & Cognitive-motor interference		Cognitive performance & Cognitive-motor interference

Figure 2

Schematic representations of the three walking assessments and the related outcome measures; A) standard 10MWT B) 10MWT with physical context, comprising three obstacles (at 2.0m, 7.5m and 9.0m, of length×width×height 9.0×20.0×4.5cm, 4.5×20.0×9.0cm and 33.0×21.0×11.5cm, respectively), a 2-m tandem-walking path (with a width of 20cm) and three stepping targets (participants' shoe length + 4cm by shoe width + 4cm), C) IWW obstacles, a 6.6×0.9m walkway instrumented with multiple Microsoft Kinect for Windows sensors and a projector to present two suddenly appearing obstacles (projected red rectangles of 0.4×0.9m) in a gait-dependent (i.e., one obstacle at a predicted foot-placement position appearing two steps ahead) and a position-dependent (i.e., one obstacle at an unpredictable but predefined position appearing when a participant's ankle was within 2m from that obstacle) manner. Participants performed those assessments with and without a cognitive dual task.

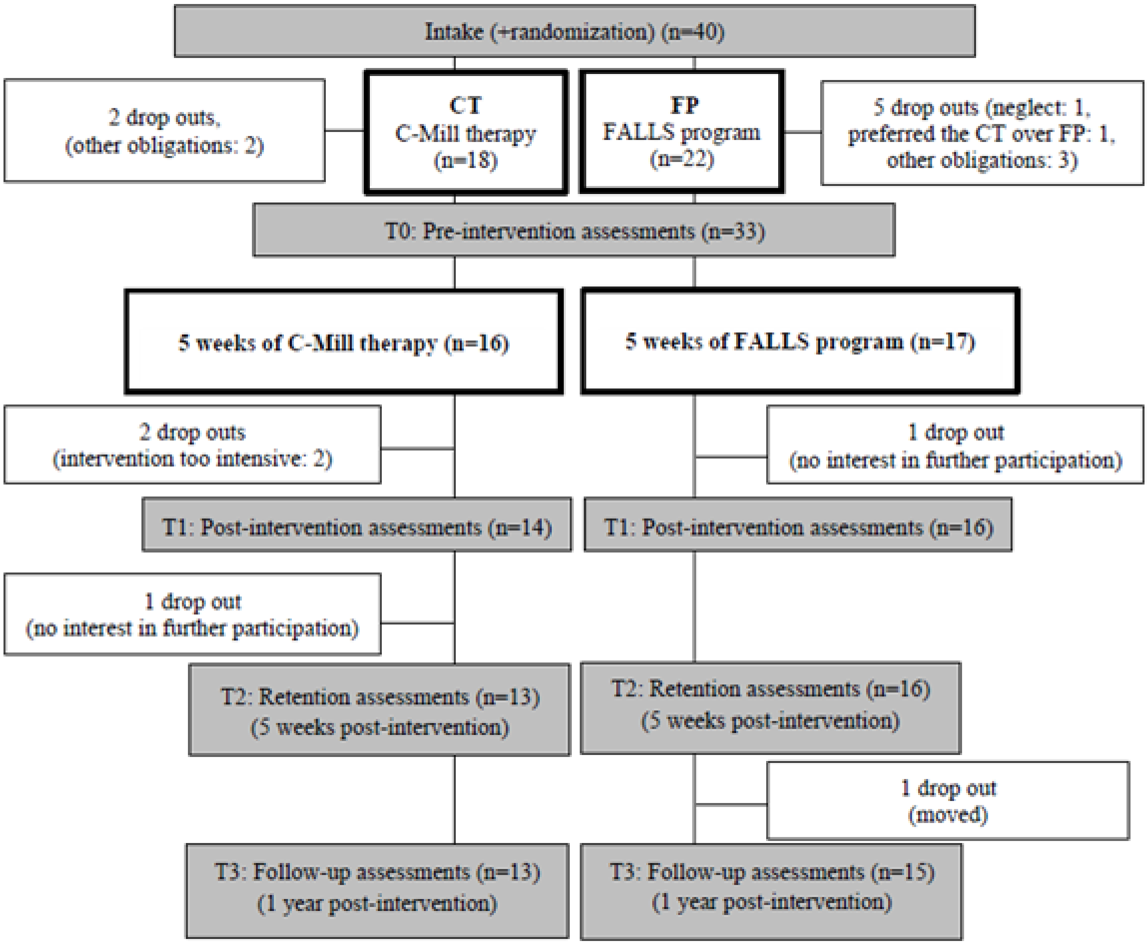


Figure 3

Flow chart with an overview of the procedures and group distribution.

Supplementary Files

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- CelineTimmermansmanuscript2020Appendix1.docx
- Appendix2.docx