

**A randomised controlled trial of a walking training with simultaneous cognitive demand (dual task) in chronic stroke.**

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## **Abstract**

### **Objective**

To evaluate the tolerability of, adherence to and efficacy of a community walking training programme with simultaneous cognitive demand (dual-task) compared to a control walking training programme without cognitive distraction.

### **Methods**

Adult stroke survivors, at least 6 months after stroke with a visibly obvious gait abnormality or reduced two-minute walk distance were included into a 2-arm parallel randomized controlled trial of complex intervention with blinded assessments. Participants received a 10 week, bi-weekly, 30 minutes treadmill program at an aerobic training intensity (55-85% heart rate maximum), either with, or without simultaneous cognitive demands. Outcome measured at 0, 11 and 22 weeks. Primary: two-minute-walk tests with and without cognitive distraction, dual task effect on walking and cognition; secondary: SF-36, EuroQol-5D-5L, Physical Activity Scale for Elderly (PASE), and step activity.

### **Results**

Fifty stroke patients were included, 43 received allocated training and 45 completed all assessments. The experimental group (n = 26) increased mean (SD) two-minute walking distance from 90.7 (8.2) to 103.5 (8.2) metres, compared with 86.7 (8.5) to 92.8 (8.6) in the control group, and their PASE score from 74.3 (9.1) to 89.9 (9.4), compared with 94.7 (9.4) to 77.3 (9.9) in the control group. Statistically, only the change in the PASE differed between the groups ( $p = 0.029$ ), with the dual-task group improving more. There were no differences in other measures.

### **Conclusions**

Walking with specific additional cognitive distraction (dual-task training) might increase activity more over 12 weeks, but the data are not conclusive.

*Clinical Trial Registration.*

<http://www.isrctn.com/ISRCTN50586966> Unique identifier: ISRCTN50586966

## Introduction

Improvements in community walking ability and engagement in meaningful activities are important goals for stroke survivors during rehabilitation <sup>1,2</sup>. In one survey, 93% of 130 stroke survivors indicated that walking in the community was essential (41%), very important (34%) or important (18%) for their life quality <sup>3</sup>. However, achieving independent walking does not necessarily mean that a stroke survivor can walk independently in the community <sup>4</sup>.

Walking safely in the community requires sufficient cognitive skill to deal with distraction such as advertisements, noise and busy streets with uneven paths and other interferences <sup>4</sup>. Being able to walk safely with other simultaneous cognitive demands, such as considering what to buy, is also important <sup>5</sup>. Dual task ability is often reduced after stroke and the effects of dual task interference on gait and cognition are greater after stroke compared to in healthy older adults <sup>5</sup>. One randomised trial found benefit from simultaneously training cognitive tasks during walking exercise <sup>6</sup>. The research to date has only included small numbers of stroke survivors, short intervention periods (2-6 weeks) and no control group or unmatched control interventions <sup>6-9</sup>. This was again concluded recently by Plummer and Iyigü <sup>10</sup>. The evidence suggests that this combined training may improve community mobility.

This study set out to explore feasibility and effect sizes of 10 weeks of treadmill training with a concurrent cognitive demand (with content relating to daily life situations) in comparison to 10 weeks of treadmill training alone. We hypothesized that training cognitive demand during walking would improve community walking levels, dual task ability and confidence about community walking.

## Methods

The study was approved by the local NHS Research Ethics Committee (REC reference: 12/SC/0403), was registered at isrctn.nl (ISRCTN50586966) and all participants gave informed consent according to the recommendations for physicians involved in research on human participants adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Stroke survivors were recruited from hospitals, GP practices, stroke clubs and via advertisements in local newsletters and magazines in Oxfordshire, UK. Eligibility criteria were: 18 years or older, at least 6 months after any type of stroke, reduced two-minute-walk distance compared to reference data (Bohannon et al. <sup>11,12</sup>) or a visibly abnormal gait, able to walk on a treadmill, no concurrent neurological conditions or psychological disorder, and no contra-indication to safe participation in exercise.

The design was a single blinded two-arm parallel randomized controlled trial of a complex intervention with two equal training groups. The number of patients recruited was based on the number needed for the cerebral imaging aspect of this project, to be reported later. Previous work <sup>13</sup> has shown that stroke survivors who are only able to walk inside their household (i.e. very limited community walking ability), walk at speeds lower than  $0.4\text{ms}^{-1}$ . Therefore, to balance training groups for walking performance the randomization process was stratified through minimisation for baseline

treadmill speeds slower or faster than  $0.4\text{ms}^{-1}$ . The recruiting researcher contacted the principal investigator, giving the gait speed. The principal investigator used a bespoke randomisation programme to allocate the group and informed the recruiting researcher of the patient's allocation into either a treadmill training with simultaneous cognitive demand, so called dual task treadmill training, or a control treadmill training group.

### *Interventions*

In both groups, each participant was trained individually by health or fitness professionals in community leisure facilities in a quiet room for 20 sessions divided over 10 weeks. The walking component of training consisted of: 10 minutes warm-up, 5 minutes cool down and in between 30 minutes of walking at an intensity which required the body to work in the aerobic training zone, between 55% and 85% of the age predicted maximum heart rate ( $220 - \text{age}$ )<sup>14</sup>. Blood pressure was measured in advance and directly after each training session to make sure it was within safe limits (systolic  $\leq 170$ , diastolic  $\leq 100$ ). Heart rate was assessed throughout training sessions to ensure training remained in the aerobic training zone. The aim of training was to increase self-selected walking speed and training intensity over the course of 10 weeks. If participants were not able to walk safely for the full 45 minutes, the session was shortened. If for logistical reasons, the full amount of 20 sessions could not be completed, effort was made to achieve as many sessions as possible and on some occasions the training period was extended by 2 or 3 weeks.

Participants in the dual task treadmill training group were distracted whilst treadmill walking using three types of distraction: cognitive tasks, a listening task or talking about planning daily activities. Ten minutes of training time were devoted for each type of distraction (Table 1). Participants who received CT-TT were trained to walk with a focus on walking and with as little distraction as possible.

### *Measures*

Assessments were conducted at 0 weeks (baseline), 11 weeks (after 10 week training period) and 22 weeks (follow-up). Data were collected by researchers who were unaware of the participant's training group allocation. For primary measures, during each assessment, participants completed a two-minute-walk test<sup>15</sup> twice, once under normal conditions and the other in which the subject was distracted during the walk with questions related to daily life activities (e.g. can you tell me how your day started?). The order of walking tests was alternated between participants and visits to prevent differences in walking distance due to exhaustion from the first to the second walk.

Secondary measures included: cognition measured with the Montreal Cognitive Assessment<sup>16</sup> (MoCA), functional ability measured with the Barthel ADL Index<sup>17</sup>, dual task effect on walking and cognition (i.e. performance on cognitive task when walking, and on walking when doing a cognitive task as compared with doing task alone), step activity for a week measured with a StepWatch Activity Monitor™ (OrthoCare Innovations, Seattle, WA) and the Physical Activity Scale for Elderly (PASE)<sup>18</sup>. Health and Wellbeing were measured with the Short-Form-36<sup>19</sup> and the EuroQol-5D<sup>20</sup>.

In addition, two community walking questions were asked: "Do you get out of the house as much as you like?" and "Do you feel confident when walking in the community?". For both questions participants were asked to answer "yes" or "no".

Demographic measures included: any available or obtainable descriptive about the stroke (type, location, date of stroke), and the Edinburgh handedness questionnaire <sup>21</sup>.

## ➔ Position of Table 1. Overview of tasks used in dual task training

### *Statistical analyses*

Statistics were performed in SPSS version 21. Normality of data was checked using the Shapiro-Wilk test. Independent t-tests were performed to test for significant differences in descriptive data and clinical characteristics between groups at baseline. In case of non-normal distributed data, Mann-Whitney U Test, Chi-square or Fishers exact test were used. A Linear Mixed Models approach was used <sup>22</sup> with fixed factors for time and training group to explore changes over time and between groups. An interaction term for group\*time was only added to the model if this interaction was significant. Generalized linear models were used to explore effects of group and time on binary data. To explore changes in measures in the dual-task treadmill training group compared to the control, treadmill training only group from study start to study end, Cohen's *d* effect sizes with 95% confidence intervals were calculated for change from baseline to follow-up.

### **Results**

Participants were recruited between March 2013 and August 2014. Final data were collected in January 2015. Fifty patients were recruited, and Figure 1 shows the flow of patients. We could not record the number of people screened due to various routes we used: GP surgeries, stroke units and stroke group meetings or newsletters. Apart from a larger mean time since stroke onset for the dual-task treadmill training group ( $p = 0.018$ ), no other significant differences between groups were found for any variables at baseline (table 2). Discontinuation of training occurred in both groups and reasons are specified in figure 1. Two participants who discontinued with the dual-task treadmill training did complete final assessments but not week 11 and week 22 assessments. One person was excluded from analysis as it was discovered that he/she had depression sufficiently severe to confound the follow-up measures. The depression was judged to be unrelated to trial participation. No other adverse events occurred during this study.

### *Linear Mixed Model results between assessments and between groups*

Results of the model for all outcome measures at each assessment point are summarized and presented in table 3 together with generalized mixed model results for confidence to walk in the community and Cohen's *d* effect sizes. Over time, both groups showed significant increases in walking distances for both two-minute walking alone and two-minute walking with dual task ( $p < 0.001$ ), cognitive response during dual-task walking ( $p = 0.007$ ), SF-36 total score ( $p = 0.002$ ), and EQ-5D index ( $p = 0.026$ ). When asked about confidence during community walking, confidence increased in both groups ( $p = 0.008$ ), with a significant group\*time interaction with larger numbers of participants gaining confidence in the control group over time ( $p = 0.027$ ). Physical activity as

measured with the PASE questionnaire showed no significant differences between groups or changes over time ( $p > 0.05$ ), although a significant interaction for group\*time ( $p = 0.029$ ) was found, with greater increases in physical activity over time found in the dual-task treadmill training group. Dual task effect on walking distance during two-minute walking with dual task and mean step activity did not significantly change over all three time points or between groups. In addition, no significant differences between groups and over time were seen in answers to the question: “Do you get out of the house as much as you like?”.

To explore difference in the change from baseline to follow-up between groups, Cohen’s  $d$  effect sizes with 95% confidence intervals are added to results in table 3. Positive Cohen  $d$  values in the dual-task treadmill training compared to the control training reflect a larger effect and negative Cohen  $d$  values reflect vice versa. Two minute walk distance and PASE increased over time in both groups with positive medium effect sizes of 0.50 and 0.59 and a positive small effect size of 0.20 for distance on two-minute walk with dual task. Negative small to medium effect sizes for comparison between groups were seen for increases in cognitive response during dual task walking ( $d = -0.31$ ) and EQ-5D ( $d = -0.20$ ). Dual task effect on walking distance during dual task walking, daily step activity and SF-36 total score showed insignificant effect sizes of  $-0.20 < d < 0.20$  (see table 3).

Data collected throughout training showed that mean relative heart rate for both groups were within the target range of 55-85%HRmax with a mean (SD) relative heart rate of  $61 \pm 1\%$ HRmax for the single-task group and  $62 \pm 1\%$ HRmax for the dual-task group ( $t(41) = -0.04$ ,  $P = 0.97$ ). There were no differences in training parameters between the single-task group and the dual-task group with respect to starting values, end values and change in values ( $P > 0.05$ ) (see table 4 and 5 of supplemental data).

➔ **Position of Figure 1. Flow diagram**

➔ **Position of Table 2. Descriptive data containing population mean and standard deviation values**

➔ **Position of Table 3. Linear mixed model results for walking, dual task walking, physical activity, health & wellbeing and community walking**

## **Discussion**

We did not find any consistent, statistically-significant differences in clinical outcome at 22 weeks between patients given simple treadmill-training and those given treadmill training while also undertaking a cognitive task. Both groups improved significantly on walking distances under normal and dual task situations. There were improvements on the SF-36 total and EQ-5D index scores.

The study was under-powered to find clinical differences, being powered for differences in cerebral blood-flow measured using near infra-red spectroscopy. Nonetheless, the results suggest further research would be warranted. Our linear mixed model found a significant interaction between group and time for the physical activity scale, reflecting greater increases in the dual task group. We also noted that change from baseline to follow-up showed a larger improvement in cognitive functioning during the dual-task two-minute walking test. This could suggest that the cognitively trained group focused on walking during dual task, at the expense of cognitive performance. However great care needs to be taken with the interpretation of cognitive performance during dual task measurements in stroke. In recent years, Yang et al.<sup>23</sup> found that the reliability of dual task effect measurement on gait in community-dwelling stroke survivors was moderate to good, but only poor to fair for the cognitive aspect of a dual task.

Surprisingly, confidence during community walking improved relatively more in the control group, with a statistically significant interaction between group and time in favour of the control group. This was unexpected, but is possibly explained by the larger proportion of “no” responders at baseline in the control group. Increases in self-reported community walking were not reflected by data from the StepWatch Activity Monitors™ suggesting that the training intervention did not result in participants actually engaging in more walking and physical activity, but possibly just changing where they walked.

The main limitation of this trial is the small sample size. The difference between groups in time from stroke onset is unlikely to be relevant, because they were all late after stroke. The linear analysis will have controlled for this if it was having an influence. Both training programs were delivered one-on-one to provide highest quality and an individual training approach. In order to include more study participants at the same time, it would be necessary to increase training facilities, training sites and personnel. Cognitive distraction tasks during dual task training worked well, but in-training analyses of cognitive performance could help to tailor specific distraction tasks for individual’s dual task limitations. This was not possible within the resources available to this study.

To keep the assessments within a certain time limit (2-3 hours), this study used limited measures on community walking. In future work an extra tool such as the activities-specific balance confidence scale<sup>24</sup> could be added to measure (un)confidence in balance, risk of falls and community participation.

Considering that dual-task training used limited resources, was easy to deliver and well tolerated with no adverse events, we think a substantive evaluation of dual-task walking training is warranted.

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## Disclosures

None

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**SUPPLEMENTAL DATA TABLES (ONLINE ONLY)**

**Table 4. Supplementary data: generalized linear model results for Barthel Index and Moca Scores and Mean relative heart rate during training between groups.**

Outcome measure	Visit	DT-TT Group	CT-TT Group	Wald Chi Square Test <sup>a</sup>	
		<i>Quartile</i> (25%; <b>Median</b> ; 75%)	<i>Quartile</i> (25%; <b>Median</b> ; 75%)	<i>Effect</i>	<i>F-value</i> ( <i>p-value</i> )
<b>Barthel Index</b>	Week 0	(19; <b>20</b> ; 20)	(19; <b>20</b> ; 20)	Group	
	Week 11	(19; <b>20</b> ; 20)	(18; <b>20</b> ; 20)	Time	0.121 (0.728)
	Week 22	(19; <b>20</b> ; 20)	(18; <b>20</b> ; 20)		
<b>Moca</b>	Week 0	(22; <b>26</b> ; 28)	(23; <b>26</b> ; 28)	Group	
	Week 11	(24; <b>25</b> ; 28)	(25; <b>27</b> ; 28)	Time	0.190 (0.728)
	Week 22	(25; <b>27</b> ; 28)	(26; <b>27</b> ; 28)		

	Visit	DT-TT Group	CT-TT Group	Independent T-test <sup>b</sup>		
				t	df	p-value
Mean Relative Heart Rate (% HR <sub>max</sub> )	Training week 1	61 ± 10	60 ± 10	0.31	39	0.760
	Final Training week	62 ± 13	66 ± 9	-0.96	39	0.340
	Change week 1 to final week	+4 ± 10	+7 ± 8	-1.35	38	0.180

**DT-TT: Dual Task Treadmill Training, CT-TT: Control Treadmill Training**

**Table 5. Training parameters for the control treadmill training and dual task treadmill training group.**

	CT-TT (Mean ± SD)	DT-TT (Mean ± SD)	t	df	p.value
Mean speed - week 1 (km/h)	2.2 ± 1.6	2.5 ± 1.3	-0.65	41	0.52
End speed (km/h)	2.9 ± 1.5	3.4 ± 1.6	-1.00	41	0.32
Change in speed (km/h)	+0.8 ± 0.6	+1.0 ± 0.7	-1.21	41	0.23
Mean training duration – week 1 (min)	29 ± 11	31 ± 9	-0.76	36	0.46
End training duration (min)	41 ± 7	42 ± 6	-0.41	40	0.68
Change in training duration (min)	+13 ± 11	+12 ± 8	0.40	37	0.69
Mean distance walked - week 1 (km)	1.2 ± 1.2	1.3 ± 0.9	-0.29	36	0.77
End distance walked (km)	2.1 ± 1.2	2.3 ± 1.2	-0.61	39	0.54
Change in distance walked (km)	+0.9 ± 0.6	+1.0 ± 0.6	-0.50	36	0.62
Mean relative heart rate – week 1 (%HR <sub>max</sub> )	60 ± 10	61 ± 10	-0.31	39	0.76
End relative heart rate (%HR <sub>max</sub> )	66 ± 9	62 ± 13	0.96	39	0.34
Change in relative heart rate (%HR <sub>max</sub> )	+7 ± 8	+4 ± 10	1.35	38	0.18

**DT-TT: Dual Task Treadmill Training, CT-TT: Control Treadmill Training**