REVIEW

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Cognitive-motor dual-task training on gait and balance in stroke patients: meta-analytic report and trial sequential analysis of randomized clinical trials



Lu Zhang^{1,3†}, Jiangping Ma^{2,3†}, Xiaoqing Liu⁴, Aiping Jin², Kai Wang⁵ and Xiaobing Yin^{4*}

Abstract

Objective Cognitive-motor dual-tasking training (CMDT) might improve limb function and motor performance in stroke patients. However, is there enough evidence to prove that it is more effective compared with conventional physical single-task training? This meta-analysis and Trial Sequential Analysis of randomized clinical trials (RCTs) aimed to evaluate the effectiveness of CMDT on balance and gait for treating hemiplegic stroke patients.

Methods The databases were searched in PubMed, Web of Science, Ovid Database and The Cochrane Library, SinoMed database, Chinese National Knowledge Infrastructure (CNKI), Wan Fang database, and VIP database up to December 8, 2023. The Cochrane-recommended risk of bias (RoB) 2.0 tool was employed to assess risk of bias in trials. The statistical analysis was employed using R version 4.3.2. In addition, subgroup analyses and meta-regression were performed to explore the possible sources of heterogeneity. The evidence for each outcome was evaluated according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. The Copenhagen Trial Unit's Trial Sequential Analysis (version 0.9.5.10 Beta) was used for sequential analysis.

Results Seventeen randomized clinical trials (RCTs) (n = 751 patients) were included. The results demonstrated that cognitive-motor dual-task training (CMDT) might be beneficial on stroke patients on Berg Balance Scale (BBS) (MD = 4.26, 95% Cl 1.82, 6.69, p < 0.0001) (low-quality evidence). However, CMDT might not affect Time Up and Go test (TUG) (MD = -1.28, 95% Cl -3.63, 1.06, p = 0.284); and single-task walking speed (MD = 1.35, 95% Cl -1.56, 4.27, p = 0.413) in stroke patients (low-quality evidence). The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) results indicated that all findings were very low to low certainty. Trial Sequential Analyses demonstrated larger sample sizes are required for confirming our findings.

Conclusion Cognitive-motor dual-task training (CMDT) compared with conventional physical single-task training might be an effective intervention for improving static balance function in stroke patients (low-quality evidence), which should be interpreted cautiously due to heterogeneity and potential biases. Nevertheless, further research is required to support the abovementioned findings.

Trial Registration This protocol was registered in PROSPERO (CRD42023490530).

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Keywords Stroke, Cognitive-motor, Dual Task training, Gait, Balance, Meta-analysis, Trial Sequential Analysis

Introduction

Stroke is an acute cerebrovascular disease that can cause cognitive, motor, and balance dysfunctions [9, 77]. These dysfunctions can significantly impact the patient's quality of life and are leading causes of disability and death [44]. Motor dysfunction that affects the ability to walk is a significant factor in the reintegration of stroke survivors into social activities. Evidence-based medicine confirms that early post-stroke rehabilitation is an effective method to reduce disability rates and improve patients' limb dysfunction [13]. Stroke patients are typically treated with early rehabilitation under single-task (ST) conditions [69]. This approach improves patients' limb function [69]. However, research has shown that only 60%-80% of stroke patients who have undergone singletask training can walk independently [69]. Additionally, A significant proportion of patients continue to exhibit reduced gait function and an increased risk of falls following their discharge from the hospital.

Cognitive-motor dual-task training (CMDT) involves performing cognitive tasks alongside motor training [70, 85, 87], a novel rehabilitation tool to help stroke patients. Studies of the neural bases of the effects of CMDT have shown that there was an increase in brain activity during dual-task (DT) especially in the pre-frontal cortex (PFC) [5, 36]. A meta-analysis of thirteen studies that utilized fNIRS to investigate cognitive challenges during dynamic balance control found that dual-tasking resulted in increased pre-frontal cortex activation compared with single-tasking [79]. It achieves this by accelerating central neural transduction, activating the higher cortex of the brain, optimizing the allocation of attentional resources, and facilitating neurological remodeling, which simulates a real-life environment for rehabilitation in both motor and cognitive domains [71, 75, 81]. Motor training is thought to promote synaptic plasticity and cell proliferation. In contrast, cognitive training seems to direct these newborn neurons into connection with pre-existing neural networks [6, 18, 25], which can increase the speed of information processing. CMDT can effectively strengthen the functional network connections between cognitive and motor regions, activating the cerebral cortex and facilitating the remodeling of brain functional networks. [56] CMDT enables the reorganization of cognitive task allocation strategies, optimizes the allocation of cognitive resources, increases coordination between tasks, and increases the flexibility of resource allocation [11].

There are three main underlying theories of cognitivemotor dual-task training (CMDT): the bottleneck, the cross-talk, and the capacity-sharing theory. The bottleneck theory indicates that encompassing the process of task training is sequential, not parallel [58]. the crosstalk theory postulates that if two tasks are from the same cognitive domain and neuronal populations in the brain, they will not interfere with each other [52]. the capacitysharing theory postulates that humans have limited cognitive capacity and that doing two tasks simultaneously decreases performance on one or both [27].

Cognitive functions include attention, working memory, and executive ability. The interaction between these two executive functions, working memory and attention, could promote neurological rehabilitation outcomes. Hard cognitive tasks (HC) distracted more attention and reduced attention to conscious postural control in stroke patients [28]. One possible explanation may be that cognitive tasks require more complex mental processes such as working memory, mental tracking, and decision-making [2]. Working memory tasks are designed to retain things in the mind to perform complex tasks such as reasoning, understanding, and learning [3]. It has been found that working memory requires increased presynaptic glutamate release and changes in postsynaptic glutamate receptor activity [65]. The bottleneck theory assumes that all tasks involving stimulus-response associations depend on a central processor, i.e., only one task can be processed at a given moment, while the other waits, i.e., the central processing stages of the two tasks cannot overlap. This means that the central processing stages of the two tasks cannot overlap, thus creating a central processing bottleneck in the secondary task. Although the bottleneck theory emphasizes that the tasks are processed in a strict serial order, and this serial processing model will include some primitive requirements and possibly additional processing demands, it has also been found that these additional mental processes are closely related to working memory [53]. Attention is the ability of an individual to focus and concentrate on perception, thought, and behavior selectively. [66]. Attention is often considered to be the basis of cognitive functioning. The capacity-sharing theory suggests that two tasks can run in parallel but compete for limited processing resources, resulting in reduced performance. The extent to which a single task is affected during dual-tasking ultimately depends on how one allocates attention to the corresponding task, so we must match appropriate attentional resources to each task [68]. During dual-task training, the decline in cognitive or motor performance ability in the cognitive-motor dual-task training (CMDT) group at the beginning, which gradually diminished with the prolongation of the treatment time, may suggest that the patients were progressively able to allocate their attentional resources appropriately during repeated training. So that the speed of synaptic signaling of brain neurons is accelerated, attention and executive function can be significantly improved [42].

After comparing the capacity-sharing theory with the bottleneck theory, it is easy to find that the two theories have different focuses. The former believes that there is sharing in multitasking and that tasks can be processed simultaneously so that attentional resources can be allocated appropriately. The latter, on the other hand, believes that there is no sharing in task processing and that tasks are processed in a strict order of priority, which also requires further research to clarify the mechanism of multitasking.

A previous meta-analysis demonstrated that cognitivemotor dual-task training (CMDT) improves balance, gait, and upper limb function in patients with chronic-phase stroke. However, the sample size was relatively small, and the source of heterogeneity was not explored. Performing dual tasks requires more cognitive aspects including attention and working memory [83], which requires meta-analyses to explore whether different elements of cognitive domains impact neurorehabilitation to meet the mental needs of stroke patients. To further elucidate the benefits of CMDT on balance and gait function in stroke patients, this study evaluated the clinical efficacy of CMDT based on moderator analysis and Trial Sequential Analysis (TSA) [78]. Furthermore, the study aimed to determine the necessary sample size.

A lack of precision characterizes the results of metaanalyses with sparse data. Such meta-analyses are typically updated periodically to obtain additional experimental data, necessitating repeated significance tests. The repetition of tests on accumulating data increases the overall risk of a type 1 error occurring. Applying Trial Sequential Analysis necessitates meticulous consideration of statistical significance thresholds, trial size, heterogeneity, and potential random errors. This approach necessitates the calculation of the requisite information to ascertain the optimal sample size required to determine a specific effect size and achieve a specified level of statistical power. Trial Sequential Analysis (TSA) is a novel tool that can reduce the risk of inflated type one error to verify the robustness of the findings [78]. Therefore, to extend previously available evidence, this study employed meta-analysis to evaluate and analyze the results of randomized controlled clinical trials of cognitive-motor dual-task training (CMDT) applied to poststroke gait and balance disorders published by December 8, 2023. The aim was to provide a basis for the future clinical practice of cognitive-motor dual-task training in gait and balance recovery in stroke patients.

Method

Study design and protocol registration

Our meta-analysis was aligned with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [43] and was registered with PROSPERO (registration number CRD42023490530).

Search strategy

A comprehensive literature search was performed to find studies published up to December 8, 2023. The English databases were done with PubMed, Web of Science, Ovid Database, and The Cochrane Library, while the Chinese databases included the SinoMed database, Chinese National Knowledge Infrastructure (CNKI), Wan Fang database, and VIP database. English search terms included "Stroke", "cerebral infarction", "cerebral hemorrhage", "cerebrovascular disease", "cerebrovascular accident", "apoplexy", "cerebrovascular stroke", "cerebral ischemia", "Cognitive motor dual-task training", "cognitive-motor dual-task", "cognitive-motor dual-task interference", "cognitive and motor dual task", "CMDT", "cognitive dual task gait training", "Cognitive-motor interference", "Dual-task interference", "Multitasking Behavior", "multitasking", "Multi-tasking behavior", "Dual-tasking", "Dual Tasks", "Dual Task", "Dual-Task", "Dual-Tasks", "Dual-Tasking", "Dual-Task paradigm". The equivalent Chinese terms were used to search Chinese databases. A search formula was created by combining subject terms with free words. References to the included literature were supplemented by literature tracing and other methods. The search strategies for each database were presented in Supplementary Table S1.

Inclusion criteria and exclusion criteria

Study screening was conducted according to the PICOS principles [51]: (P: participant,I: intervention; C: control intervention; O: outcome indicator; S: study type). Selected studies were determined by the following criteria:(1) *Participants* the patients (aged 18 and above) were diagnosed with stroke by clinically relevant examinations

(computed tomography, magnetic resonance imaging). (2) *Intervention* The experimental group underwent cognitive-motor dual-task training. (3) *Control intervention* The control group received conventional physical single-task training. (4) *Outcome indicators* Primary outcome indicators included static balance assessed by Berg Balance Scale (BBS), dynamic balance assessed by the Time Up and Go Test (TUG), and gait ability assessed by single-task walking speed. Secondary outcome indicators (DTUGT), dual-task walking speed, the ability to perform activities of daily living (ADL), and lower extremity motor function. (5) *Study design* randomized clinical trials (RCTs).

The studies were excluded based on the following:(1) There were issues with duplicate publications or literature, incomplete research data or test data could not be extracted, and full text not available (0.2) Articles were written in languages other than Chinese and English.(3) Research data cannot be combined quantitatively.

Data extraction

Two researchers conducted independent literature search screening and extracted data if the inclusion criteria were met. Any disagreements were resolved through discussion with a third researcher to reach a consensus.

Extracted data included: (1) Sample characteristics: age, sex ratio, course of disease, sample size, author region, rehabilitation treatment, and publication year. (2) Motor cognitive Dual-task training characteristics: duration of each training session, training frequency, total training time. (3) The primary outcomes: a. balance: static balance measured by the Berg Balance Scale (BBS), dynamic balance measured by the Time Up and Go Test (TUG). b. gait: continuous statistics assessed by the single-task walking speed. (4) The secondary outcomes: a. activities of daily living (ADL): measured by Barthel Index (BI) or Functional Independence Measure (FIM). b. lower extremity motor function: measured by the Fugl-Meyer Assessment (FMA). c. dynamic balance and gait under dual-task conditions: DTUGT and dual-task walking speed.

Quality assessment

Two reviewers independently evaluated the quality of the literature using the latest revised version of the Cochrane-recommended risk of bias (RoB) 2.0 evaluation criteria [34, 88]. The tool is designed to provide a comprehensive assessment of five domains of bias including the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. For randomized clinical trials (RCTs), a low risk of bias was assigned if all domains were rated as "Low". If a domain received a rating of "Some concerns" and no domain was rated as "High risk", the study was considered to have a medium risk of bias. If at least one domain was rated as 'High risk', the study was considered to have a high risk of bias. In cases of disagreement, the third researcher was consulted to reach a consensus.

Statistical analysis

The statistical analysis was conducted using R version 4.3.2. The main process of meta-analysis was performed using the 'meta' package. Continuous variables were expressed as a mean difference (MD) if reported on the same scale, or as a standardized mean difference (SMD) if reported using different continuous scales. The 95% Confidence Intervals (CI)were calculated as well. Heterogeneity was tested using the chi-square test, and both fixed and random-effects models were reported. If the fixed-effect and the random-effects meta-analyses show different results, then the most conservative result (the analysis with the highest P-value) was chosen as the main result. To evaluate the quality and consistency of the combined results, sensitivity analyses were performed by excluding studies one by one to determine whether the changes significantly affected balance and gait ability in stroke patients. Begg test and Egger test were used to test whether publication bias was asymmetric. To detect heterogeneity, we have employed Moderator analysis with subgroup analysis and meta-regression [32]. The quality of the body of evidence for each outcome was evaluated according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADEpro) (https://www.gradepro.org) Working Group criteria[30]. We conducted the Trial Sequential Analysis (TSA) in the present study and the required information size (RIS) was established using a two-sided alpha of 0.025 and a power of 80%, corresponding to a beta of 0.20, utilized software version 0.9.5.10 Beta (http://www.ctu.dk/tsa) for a conclusive finding. We searched for the minimally relevant clinical effects (MRCI) [29, 47, 55, 60] and variances of the outcome measures (BBS, TUG, single-task walking speed, FMA) from previous literature for TSA. We used three random-effects models (DL, SJ & BT) for comparative analyses. Given that this study employed three primary outcome indicators, we conducted multiple corrections for the alpha of meta-analysis and TSA following the guidelines set forth by Jakobsen and colleagues [35].

Results

Literature search

A total of 868 relevant publications were identified in the literature search (PubMed: 185; Cochrane: 201; Web of Science: 280; Ovid: 27; SinoMed: 53; Chinese National Knowledge Infrastructure (CNKI): 60; WanFang Database: 36; VIP Database: 26). There were 576 remaining articles after deduplication using EndNote 20, then reading the titles and abstracts, 537 additional publications were excluded. Upon the completion of a comprehensive review of the remaining 39 studies. 10 studies were excluded due to discrepancies in the intervention. 7 studies were excluded due to outcome indicators not available. 4 studies were excluded due to protocol. Meanwhile, 1 study was supplemented by reading references from the included articles.

Ultimately, only 17 studies met the pre-established inclusion criteria [4, 14–16, 19, 21, 23, 33, 37–39, 45, 57, 62, 74, 82], PEI SHIXIU, 2023). Figure 1 displays the selection algorithm and the numbers of included and excluded studies. All titles, abstracts, and text were reviewed by the authors, blinded to the study authorship,

based on the inclusion and exclusion criteria to minimize bias. The analytical strategy of the experimental group of studies is displayed in Supplementary Fig. S1.

Study characteristics

The study comprised 17 randomized clinical trials (RCTs), with 11 conducted in English and 6 in Chinese. The total number of patients was 751, with 374 in the experimental groups and 377 in the control groups. Table 1 presents the basic features of the included studies.

Study quality

There is only one study [74] where the randomization process was unclear, which used arrival time for randomization, eleven studies [14, 15, 19, 21, 23, 33, 37, 38, 74, 82], PEI SHIXIU, 2023) reported that allocation concealment was unclear, Only one study[62] reported a significant difference at baseline. Seven studies[4, 15, 16, 45, 57, 62, 82] were utilized for blinding, one[16] of which researchers, outcome assessors, and data analysts were blinded to the group assignments, and three[4, 57, 62] of which were blinded to the outcome assessors, and three[15, 45, 82], although blinding was



Fig. 1 Flowchart for identification of studies

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Study-ID	fear Place	Design an sample	dSex ra (M: F)	atio	Mean age, y	ears	Course of Disease		Intervention (Experimenta group)	llntervention (Control group)	Base treatment	Randomized approach	Outcomes(MD/SMD 95%Cl)
		size (EXP: CTL)	EXP	f	EXP	сл	EXP	CTL					
[4]	2021 South Korea	16:15	12:4	8:7	56.94 ± 8.79	56.13±10.25	56.31 ± 21.00months	53.07 ± 25.31 months	Dual-task gait training (cognitive tasks compris- ing mental tracking, verbal fluency, and executive function), 30min/d, 2d/week 6 weeks	The training and the cogni- tive task were conducted sepa- rately, 30min/d, 2d/week, 6weeks	1	Participants were required to randomly select a num- bered paper inside a sealec box	Single-task speed0.00[-2.942.94],stride, cadence Dual-task speed4.00[0.42.7.58], stride, cadence CRR, DTC, FES
[15]	2015 Korea	10:10	6:4	6:4	64.80 ± 10.50	54.60±11.80	22.90 ± 8.90 days	23.20 ± 9.70days	Dual-task trainling using BioRescue(cognitive tasks including memory and attention),30 min/d,5d/ week, 4weeks	Balance training, 30 min/d, 5 d/ week, 4weeks	Traditional reha- bilitation program, 5d/week,4 weeks	I	FMA- LE(H)-0.90[-6.63;4.83], ADL(MBI)0.20[-0.68;1.08] MMSE, DST, TMT, LOS
Choi, W [16]	2014 South Korea	19:18	17:2	14:4	49.11 ± 11.93	49.33±8.27	18.16±6.83months	18.28 ± 4.70months	Cognitive-motor dual-task (CMDT) using an auditory cue (the auditory cue sign by ringing the bell), 15min/ session, 3 times/week4 weeks	Walking on a treadmill only, 15min/ session, 3times/ week, 4weeks	Conven- tional reha- bilitation (CR), 5times/ week, 4 weeks	Random num ber table	TUG047[-3.25,4.19]
Fengshan . Huang [33]	2023 China	44:44	23:21	24:20	58.29±5.33	58.75±5.48	12.53±2.69weeks	13.05 ± 2.78 weeks	Balancing instrument motor-cognitive dual task training (CBT)(cognitive task including the capacity of calculation),30min/d,5d/ week, 6weeks	1	Compre- hensive rehabilita- tion training (CR)	The red and yellow double-color method	BBS3.04(1.56;4.51), FMA TUG-2.32[-3.81;-0.81], DTUGT-3.79[-5.46; -2.12], ADL2.19[1.65;2.72]
(37) [37]	2019 USA	10:10	7:6	6:5	57.50 ± 8.04	61.00±4.60	8.90±5.39years	9.09 ± 6.3 6 years	Cognitive-motor exergame training (CMT) (cognitive tasks including memory, attention, and calculation), 90 min/session,20 sessions in 6 weeks	Progressive balance training (CR), 90 min/ses- sion, 20 sessions in 6 weeks	I	Flipping a coir	IBBS4.2812.15.6.4.2), TUG1.39[-5.19;7.97] 6MWT ABC
[38] [38]	2014 Korea	10:10	I	1	58.40 ± 7.58	58.20±8.07	16.60±11.88months	19.30 ± 14.12months	Dual-task gait training with cognitive tasks (variable priority (VP)conditions were applied), 30min/d, 3 d/week, 4 weeks	Single-task gait training, 30min/d, 3 d/ week, 4 weeks	Traditional reha- bilitation program, 5 d/week, 4 weeks	1	TUG-6.19[-23.41;11.03], DTUGT-7.37[-26.09;11.35] 10MWT Stroop test F8WT
[39]	2018 Korea	13:13	8:5	7:6	52.62 ± 9.84	56.15±10.82	12.62 ± 3.52 months	11.46 ± 3.80months	Progressive treadmill cogni- tive dual-task gait training (PTCDG) (cognitive tasks including memory, reaction, and calculation),5times/ week,4 weeks	Conventional treadmill gait training (CTG), 5 times/week, 4 weeks	I	Choosing one of 30 sealed envelopes	Single-task speed4.03(0.89,7.17), cadence, stride 10MWT

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Study-ID Year Place	Design an sample	dSex ra (M: F)	atio	Mean age, yt	ears	Course of Disease		Intervention (Experimentall group) (ntervention Base Control group) treatment	Randomized approach	Outcomes(MD/SMD 95%Cl)
	SIZE (EAF: CTL)	EXP	Ę	EXP	сЪ	EXP	ц				
Liu, Y. C 2017 China [45]	9:10		8:2	51.00 ± 7.10	50.8±13.5	36.40±14.60months	49.80 ± 59.80 months	cognitive dual-task gait training (CDTT), (cognitive p tasks including memory) 30 (min/session, 3 sessions/weeks for 4 weeks	Conventional – bhysical therapy CPT), 30min/ ession, 3 ses- ions/week for 4 veeks	Electing sealed enve- lopes to assigr participants	Single-task speed,1.6[-4.13;7.33] ncadence, stride; Dual-task speed,8.9[- 0.40;18.20] DTC
Park, M.O. 2019 Korea [57]	15:15	9.11	13:7	56.30 ± 7.14	59.75±7.75	21.67±5.64months	21.45 ± 2.83months	Cognitive-motor dual-task (program (CMDT) (cognitive of tasks including Stroop word t task and memory),30min/ d,3d/week,6weeks	-onventional - occupational herapy (COT), 30min/d, 3d/ veek, 6 weeks	Using a com- puterized randomization calculator	BB53.94(1.66,6.21) MFRT Stroop test TMT DST
Ping Fang 2023 China [23]	34:34	21:13	23:11	62.60±7.20	62.58±7.18	38.24± 6.20days	38.21 ±6.19days	Variable-priority cognitive- motor dual-task training (cognitive tasks includ- ing memory, attention, and calculation).30min/ses- sion, once/d, 30d	- Bobath treatment, once/d, 30	Touch-ball method d	BB53.90[1.47;6.32] NIH5S MoCA
Plummer, 2021 USA P. [62]	17:19	7:10	6:01	54.40 ± 16.40	59.60±14.50 .	4.80-16.70months	3.90–13.40m on ths	Dual-task gait training(DTGT) S (cognitive tasks includ-t ing Calculating time, Backward spelling,Working v memory and so on),3times/ week, 4 weeks	ingle-task gait – raining (STGT), t times/week, 4 weeks	The rand- omization sequence was com- puter- generated by the biostat- istician	Sing-task speed- 7.00[-18.33,4.33], Dual-task, speed- 5.00[-12.66;2,66], TUG1.40[-1.67,4.47], TUG1.40[-0.36;3.36] ABC
Shixiu Pei 2023 China [59]	30:30	16:14	15:15	51.10±5.28	52.50±6.85	15.10±4.17weeks	14.70 ± 3.85 weeks	Balance-cognitive dual-task 5 training (cognitive tasks t including memory,attention, r directive force, and calcula- tion), 30min/d,5d/week, 8 weeks	ingle balance Routine raining (SBT), 30 rehabilita- nin/d, 5 d/week, tion trainin 8 weeks 120 min/d, 5 d/week, 8 weeks	Table of ran- dom numbers g, 3	BB53.59f1 23;596J ADL(MB)2.73[201:3.44] FMA-LE4.77[3.595.95]
Tetik 2018 Turkey. Aydoğdu, Y. [74]	y 25:28	20:5	19:9	69.28±5.03	71.21±4.92	1	1	Dual-task walking training 5 (DTW) (cognitive tasks v including Verbal cognitive (tasks), 30min/d, 5d/week, 5 8 weeks v	ingle task Conven- valking training tional reha. SWT), 30min/d, bilitation d/week, 8 programs veeks (CR), 56/week,8 s6/week,8		BB54.03[1.66;6.41], ADL(FIM)-0.04[-0.58;0.50] FES

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Study-ID Year Place	Design an sample	dSex ra (M: F)	tio	Mean age, yƙ	ears	Course of Disease		Intervention (ExperimentalIntervention Ba group) (Control group) tre	se Randomiz atment approach	ed Outcomes(MD/SMD 95%CI)
	size (EXP: CTL)	EXP	ಕ	EXP	Ъ	EXP	تا	I		
Wenqiong 2023 China Dai [19]	49.49	27:22	26:23	70.38±6.19	70.55±6.23	8.04 ± 2.00 days	8.21 ± 2.03days	Dual-task training in music Routine care, – cognition and movement once/d, 90d (Music cognitive task training),1h/d, 2d/week, 90d	I	FMA-LE7.38[6.06,8.70] MoCA SF-36
Xiaoqiong 2022 China Dong [21]	31:32	21:10	18:14	57.90±11.81	59.94±12.61	55.48 ± 11.66 days	5634±13.21 days	Dual task walking Monotask Rc training(cognitive tasks walking ba including memory training,20min/ fui and calculation),20min/ time2times/d5d/tta time.2times/d, 5d/week,4 week, 4 weeks weeks	utine Table of rar ance dom numb uction ining	 BB53 88[1,45;6.31], ers ADL(MBI)0.37[-0.13;0.87]
Xiuen 2020 China Chen [14]	20:20	13:7	15.5	69.20±12.60	70.10±13.20	90.8±11.20days	89.6 ± 10.30days	"Stroop paradigm + trunk – Rc control" dual task rel training(Stroop paradigm bil task training), 30 40min/d,5d/ 30 week,4weeks 40min/d,5d/ 5d	utine Table of rar. a- dom numb tation, 40min/d, 'week, eeks	 BBS3.61[1.26;5.96] ers MoCA TMT, SOT, LOS
Yeh.T. 2023 China [82]	22:20	19:3	16:4	63.55 ± 7.08	60.88±12.28	63.68±88.83	52.10 ± 46.07	dual-task exercise-cognitive Non-aerobic - training (DUAL)(cognitive physical tasks including visuospatial exercise, 60 processingattention,memory, min per day, etc.)60min per day, spanning spanning 3 days 3 days per week, for 12 weeks per week, for 12 weeks	Utilizing the Researc Randomize web-based tool,	TUG-4.84[-7.96; -1.72] h MoCA 6MWT WMS
M Male. F Female. EXP	experimenta	aroup	CTL co	ntrol group. TL	/G Time Up and	d Go Test, <i>DTUGT</i> TUG	5 time under dual-task	conditions. BBS Berg Balance Scale. ADL activitie	of daily living, MB/I	Aodified Barthel Index. FIM

M Male, *F* Female, *EXP* experimental group, *CTL* control group, *TUG* Time Up and Go Test, *DTUG*TTUG time under dual-task conditions, *BBS* Berg Balance Scale, *ADL* activities of daily living, *MBI* Modified Barthel Index, *FIM* Functional Independence Measure, *FMA-LE* (*H*) lower extremity score on the hemiparetic side in the Fugl-Meyer Assessment, *CRR* correct response rate, *DTC* dual-task cost, *FES* Fall Efficacy Scale, *MMSE* Mini-Mental State Examination, *DST* digit span test, *TMT* Trail Making Test, *6MWT* 6 Meter Walk test, *ABC* Activity-specific Balance confidence, *10MWT* 10 Meter Walk test, *F8WT* Figure-of-8 walk test, *MFRT* Modified Functional Reach Test, *NHSS* National Institutes of Health stroke scale score, *MoCA* Montreal cognitive assessment score, *SF-36* MOS Item Short From Health Survey, *SOT* sensory organization test, *LOS* limit of stability, *WMS* Weehsler Memory Scale



Fig. 2 The risk of bias graph in the single study

As percentage (intention-to-treat)



Fig. 3 The risk of bias graph in the average of all included studies

mentioned, only participants were blinded. BBS assessments are vulnerable to outcome assessors' subjectivity and a fair assessment cannot be obtained without blinding the outcome assessors. One study[37] had an attrition rate of = 12% and no intention-to-treat analysis was performed, therefore it scored a high risk of

attrition bias, eleven studies' risk of reporting bias [14, 15, 19, 21, 23, 33, 38, 39, 57, 74], PEI SHIXIU, 2023) was unclear because there were no available protocols or trial registries. The risk of bias graph reflecting a single study was shown in Fig. 2 and the average of all included studies was showed Fig. 3. Evidence of

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Question: Effect of Dual-Task Training on Gait and Balance in Stroke Patients Patients: Stroke patients

Setting: Intervention: CMDT

Certainty asse	ssment					Nº of patients		Effect		Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	intervention	comparison	Relative (95% Cl)	Absolute (95% CI)	
Static Balance (assessed with BBS	(5								
œ	serious	serious	not serious	not serious	none	210	212	I	MD 4.26 higher (1.82 higher to 6.69 higher)	0000 towah
Dynamic Balan	ce (assessed with	TUG)								
9	serious	serious	not serious	not serious	none	122	120	I	MD 1.28 lower (1.06 Hiaher to 3.63 lower)	
Dual-Task Dyna.	mic Balance (asse	issed with DTUGT)								
2	serious	not serious	not serious	serious	none	54	54	I	MD 3.82 lower (2.15 lower to 5.48 lower)	000 Low ^{a,c}
Gait (assessed v	with single-task sp	seed)								
4	serious	serious	not serious	serious	none	55	57	I	MD 1.57 higher (0.41 lower to 3.55 higher)	DOOO Very low ^{a,b,c}
Dual-task Gait (;	assessed with dué	al-task speed)								~
ſ	serious	serious	not serious	serious	none	42	44	I	MD 2.52 higher (4.61 lower to 9.64 higher)	Herv low ^{a,b,c}
Activities of dail	ly life (assessed w	ith BI/FIM)								
5	serious	serious	not serious	not serious	none	140	144	ı	SMD 1.09 SD higher (0.02 lower to 2.20 higher)	0000 towah
Lower extremit	y motor function	(assessed with FMA	4)							
4	serious	serious	not serious	not serious	none	106	108	ı	MD 3.74 higher (0.47 higher to 7.01 higher)	⊕⊕OO Low ^{a,b}
The Grading of R CMDT cognitive-1	lecommendations / motor dual-task tra	Assessment, Developi ining; TUG Time Up a	ment, and Evaluatio	n (GRADE) Workin UG time under du	g Group grades of evic al-task conditions; <i>BBS</i>	lence Berg Balance Scale;	ADL activities of d	aily living; <i>Bl</i> Baı	rthel Index; <i>FIM</i> Functional Indepe	ndence

Ś 'n

^a Risk of bias: Downgraded by one level for > 30% high risk of bias

 $^{\rm b}$ Inconsistency: Downgraded by one level for $\rm I^2$ value is larger than 40%

^c Imprecision: Downgraded by one level for imprecision (fewer than 150 participants)

High quality Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality We are very uncertain about the estimate

Primary outcomes	CMDT with working memory	CMDT Without working memory	CMDT	MCID
BBS	3.50	4.43	4.26	1.90[29]
TUG(s)	-1.64	0.47	-1.28	1.60[47]
Singe task walking speed(cm/s)	0.97	1.6	1.57	5.00[<mark>60</mark>]

 Table 3
 Comparison of the effect size of CMDT versus Control groups with MCID values

CMDT cognitive-motor dual-task training, TUG Time Up and Go Test, BBS Berg Balance Scale, MCID minimal clinically important difference

different outcomes was qualified using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) in Table 2.

Primary outcomes

In this subsection, we reviewed primary outcomes, including the Berg Balance Scale (BBS), Time Up and Go Test (TUG), and single-task walking speed. The Trial Sequential Analysis (TSA) results were visually depicted in Fig. 11. Comparison of the effect size of cognitive-motor dual-task training (CMDT) versus Control groups with minimal clinically important difference (MCID) values was visually depicted in Table 3.

Balance

Static balance-berg balance scale (BBS) In this study, the Berg Balance Scale (BBS)[8] assessed an individual's ability to perform a range of balance tasks as one of the primary outcome indicators for static balance function. Eight studies involving 422 stroke patients used the Berg Balance Scale (BBS) as an outcome indicator. We conducted a meta-analysis of the change in mean scores in the experimental and control groups by calculating the change in Berg Balance Scale (BBS) scores from baseline to the end of treatment. The findings indicated that cognitive-motor dual-task training (CMDT) significantly improved static balance function in stroke patients compared with conventional rehabilitation training (random-effect model: MD=4.26, 95% CI 1.82 to 6.69, p < 0.0001; fixed-effect model: MD=4.61, 95% CI 3.95 to 5.27, p=0.0006; see Fig. 4) (low-quality evidence).

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was low. (Table 2).

In sensitivity analyses, where we excluded individual studies one by one, the results did not change significantly.

Begg test (z = -0.12, p = 0.902) and Egger test (t = -0.22, p = 0.831) did not indicate publication bias.

Concerning the Berg Balance Scale (BBS), the Trial Sequential Analysis (TSA) showed that the position of the cumulative Z-curve crossed beyond the conventional threshold and did not reach the Trial Sequential Analysis monitoring boundary instead. Furthermore, the sample size did not meet the specified required information size. (Fig. 11A). Therefore, it may be a false-positive result that the CMDT can improve static balance in stroke patients and further trials are required to validate the above result.

In the meta-analysis of CMDT and control groups, BBS reached the minimal clinically important difference (MCID). (TABLE 3.)

Dynamic balance-time up and go test (TUG) In this study, the Time Up and Go Test (TUG) observed the

		Exp	erime	ntal		Cor	ntrol						Weight	Weight
Study	Intervention	Total	Mean	SD T	otal	Mean	SD Me	ean Dif	fference	MD	9	5%-CI	(common)(I	random)
Xiuen Chen 2020	DTBT+CR:CR	20	12.30	4.59	20	6.40	4.93			5.90	[2.95;	8.85]	5.1%	12.4%
Xiaoqiong Dong 2022	DTWT+CBT:CTWT+C	BT 32	18.56	2.81	31	15.16	2.55			3.40	[2.08;	4.72]	25.1%	14.5%
Ping Fang 2023	VPCMDT+BT:BT	34	5.80	2.68	34	2.54	2.59			3.26	[2.01;	4.51]	28.1%	14.5%
Fengshan Huang 2023	DTBT+CR:CR	44	17.29	3.97	44	6.84	3.88			10.45	[8.81;	12.09]	16.4%	14.2%
Shixiu Pei 2023	DTBT+CR:STBT+CR	30	8.27	4.11	30	2.39	4.18		-	5.88	[3.78;	7.98]	10.0%	13.6%
Park, M.O. 2019	CMDT:COT	15	2.85	7.70	15	0.85	11.23 ·		•	2.00	[-4.89;	8.89]	0.9%	6.8%
Kannan, L. 2019	CMT:CR	10	4.23	2.83	10	5.67	6.46-	•		-1.44	[-5.81;	2.93]	2.3%	10.2%
Tetik Aydoğdu, Y. 2018	DTWT+CR:STWT+CF	R 25	3.60	3.20	28	1.50	3.90	ŀ	-	2.10	[0.19;	4.01]	12.0%	13.8%
Common effect mode	el	210)	:	212				•	4.61	[3.95;	5.27]	100.0%	
Random effects mod Heterogeneity: $I^2 = 90\%$	el , τ ² = 10.2120, <i>p</i> < 0.01					Γ	1		-	4.26	[1.82;	6.69]	·	100.0%

-10 -5 0 5 10 CMDT:Cognitive-motor dual-task training; CR:Conventional Rehabilitation; DTWT:Dual-task walking training; STWT:Single-task walking training; STBT:Single-task balance training; VPCDMT:Variable-priority cognitive-motor dual-task training; BT:Bobath Technology; DTBT:Dual-task balance training; COT:Conventional occupational therapy; CMT:Cognitive-motor exergame training

Fig. 4 A forest plot for meta-analysis of Berg Balance Scale (BBS)

		E>	perim	ental		Co	ontrol							Weight	Weight
Study	Intervention	Total	Mean	SD	Total	Mean	SD		Mean	Differ	ence	MD	95%-CI	(common)	(random)
Huang Fengshan 202	3 DTBT+CR:CR	44	-4.50	3.62	44	-2.19	3.56			-		-2.31	[-3.81; -0.81]	59.1%	29.1%
Kannan, L. 2019	CMT:CR	10	-3.42	7.93	10	-4.81	7.06		-		_	1.39	[-5.19; 7.97]	3.1%	9.2%
Choi, W. 2014	DTGT+CR:STGT+C	R 19	-4.14	2.16	18	-4.61	7.77			- <u>i</u> -		0.47	[-3.25; 4.19]	9.6%	18.0%
Kim, G.Y. 2014	DTGT+CR:STGT+C	R 10	-9.68	17.70	10	-3.49	21.42-					-6.19	[-23.41; 11.03]	0.4%	1.8%
Plummer, P. 2021	DTGT:STGT	17	-0.50	3.96	18	-1.90	5.25					1.40	[-1.67; 4.47]	14.1%	21.1%
Ting-Ting, Y. 2023	CMDT:CR	22	-0.30	5.60	20	4.54	4.71					-4.84	[-7.96; -1.72]	13.7%	20.8%
Common effect mod	el	122			120							-1.77	[-2.92; -0.62]	100.0%	
Random effects mod	el									◆		1.28	[-3.63; 1.06]		100.0%
Heterogeneity: $I^2 = 54\%$, $\tau^2 = 4.3423$, $p = 0.05$							1	I	I	I	I			
								-20	-10	0	10	20			

CMDT:Cognitive-motor dual-task training; CR:Conventional Rehabilitation; DTGT: dual-task gait training; STGT: single-task gait training; DTBT:Dual-task balance training; CMT:Cognitive-motor exergame training

Fig. 5 A forest plot for Time Up and Go Test (TUG)

patient completing the complete movement of getting up, walking, and sitting down was only applicable to patients who can walk to reflect their dynamic balance [63]. Therefore, TUG was one of the primary outcome indicators for the dynamic balance function. Six studies involving 242 stroke patients used the Time Up and Go Test (TUG) as an outcome indicator. We conducted a meta-analysis of the change in mean scores in the experimental and control groups by calculating the change in the Time Up and Go Test (TUG) from baseline to the end of treatment. The current findings can not clarify the efficacy of cognitivemotor dual-task training for dynamic balance function (measured by Time Up and Go Test) in stroke patients compared with conventional rehabilitation training (random-effect model: MD = -1.28, 95% CI -3.65 to 1.06, p = 0.284; fixed-effect model: MD = -1.77, 95% CI -2.92 to -0.62, p = 0.003; see Fig. 5). (low-quality evidence).

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was low. (TABLE 2).

In sensitivity analyses, where we excluded individual studies one by one, the results did not change significantly. Begg (z=0.00, p=1.00) and Egger test (t=0.48, p=0.658) did not indicate publication bias.

Concerning the Time Up and Go Test (TUG), the Trial Sequential Analysis (TSA) showed that the cumulative Z value had not crossed the traditional threshold or the Trial Sequential Analysis (TSA) threshold, and the sample size did not meet the specified required information size (Fig. 11B). Therefore, the meta-analysis of TUG is inconclusive and further trials are required to analyze the effects of cognitive-motor dual-task training (CMDT) on dynamic balance (measured by Time Up and Go Test) in stroke patients.

In the meta-analysis of CMDT and control groups, although there was no statistical significance in CMDT including working memory, the minimal clinically important difference (MCID) was reached, which may be of some clinical importance. (Table 3.)

Gait-Single task walking speed

In this study, single-task walking speed was one of the primary outcome indicators for gait functional outcomes. Four studies involving 112 stroke patients used singletask walking speed as an outcome indicator. We conducted a meta-analysis of the change in mean scores in

Study	Intervention	E Tota	xperir al Mea	nental In SD	Tot	C al Me	ontrol an SD	Mean	Difference	MD	95%-CI	Weight (common)	Weight (random)
Baek, C.Y. 2021	DTGT:STGT	16	4.00	4.69	15	4.00	3.61		- 	0.00	[-2.94; 2.94]	45.4%	38.9%
Kim, K.J. 2018	PTCDG:CTG	13	9.11	3.27	13	5.08	4.77] }	4.03	[0.89; 7.17]	39.6%	36.7%
Plummer, P. 2021	DTGT:STGT	17	11.00	17.93	19	18.00	16.59-		_ <u>_</u>	-7.00	[-18.33; 4.33]	3.1%	6.0%
Liu, Y.C. 2017	CDTT:CPT	9	4.30	6.60	10	2.70	6.10	-	-	1.60	[-4.13; 7.33]	11.9%	18.4%
Common effect mo Random effects mo	del	55			57					1.57 1.35	[-0.41; 3.55] [-1.56; 4.27]	100.0%	100.0%
Heterogeneity: $I^2 = 47$	%, τ ² = 3.4472, <i>p</i> =	0.13						1 1 1	1 1 1	I			
								-15 -10 -5	0 5 10) 15			

DTGT: dual-task gait training; STGT: single-task gait training; PTCDG: progressive treadmill cognitive dual-task gait training; CTG: conventional t readmill gait training; CDTT: cognitive dual task gait training; CPT: conventional physical therapy.

Fig. 6 A forest plot for meta-analysis of single-task walking speed

the experimental and control groups by calculating the change in single-task walking speed from baseline to the end of treatment. The current findings can not clarify the efficacy of cognitive-motor dual-task training for single-task walking speed in stroke patients compared with conventional rehabilitation training (random-effect model: MD=1.35, 95% CI -1.56 to 4.27, p=0.413; fixed-effect model: MD=1.57, 95% CI -0.41 to 3.55, p=0.119; see Fig. 6) (very low-quality evidence).

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was very low. (Table 2).

In sensitivity analyses, where we excluded individual studies one by one, the results did not change significantly.

Begg test (z = -0.34, p = 0.734) and Egger test (t = -0.83, p = 0.492) did not indicate publication bias.

Concerning single-task walking speed, the Trial Sequential Analysis (TSA) showed that the cumulative Z value had not cross the traditional threshold or the Trial Sequential Analysis (TSA) threshold, and the sample size did not meet the specified required information size (Fig. 11C). Therefore, the meta-analysis of singletask walking speed is inconclusive and further studies are required to analyze the effects of cognitive-motor dual-task training (CMDT) on gait (measured by singletask walking speed) in stroke patients.

In the meta-analysis of CMDT and control groups, single-task walking speed did not reach the minimal clinically important difference (MCID). (Table 3.)

Secondary outcomes

TUG under dual-task conditions (DTUGT)

In this study, TUG under dual-task conditions (DTUGT) reflected a dynamic balance function under dual-tasking [56] and was one of the primary outcome indicators for balance function outcome. Two studies involving 108 stroke patients used DTUGT as an outcome indicator. We conducted a meta-analysis of the change in mean scores in the experimental and control groups by calculating the change in DTUGT from baseline to the end of treatment. The 2 studies were tested for heterogeneity, and the results showed insignificant heterogeneity among them $(I^2 = 0\% < 50\%, p = 0.71)$. Therefore, a fixed-effect model was used to combine the effect sizes. The findings indicated that cognitive-motor dual-task training (CMDT) significantly improved dynamic balance function under dual-task conditions (measured by DTUGT) in stroke patients compared with conventional rehabilitation training (MD=-3.82, 95% CI -5.48 to

Study	Intervention	Experime Total Mean	ental SD Total	Control Mean SD	Mean Difference	MD	95%-CI	Weight (common)	Weight (random)
Fengshan Huang 2023 Kim, G.Y. 2014 DTG	DTBT+CR:CR T+CR:STGT+C	44 -6.66 R 10 -9.37 1	3.91 44 18.75 10	-2.87 4.09 -2.00 23.68		-3.79 -7.37	[-5.46; -2.12] [-26.09; 11.35]	99.2% 0.8%	99.2% 0.8%
Common effect mode Random effects mode Heterogeneity: $I^2 = 0\%$, τ	el el z ² = 0, <i>p</i> = 0.71	54	54		-20 -10 0 10	-3.82 -3.82	[-5.48; -2.15] [-5.48; -2.15]	100.0%	100.0%

Fig. 7 A forest plot for meta-analysis of DTUGT

Study	Intervention	E Total	xperin Mean	nental SD	Total	Co Mean	ontrol SD	Mean [Difference	e	MD	95%-CI	Weight (common)	Weight (random)
Baek, C.Y. 2021 Plummer, P. 2021 Liu, Y.C. 2017	DTGT:STGT DTGT:STGT CDTT:CPT	16 17 9	9.00 4.00 6.90	5.63 12.26 11.10	15 19 10	5.00 9.00 -2.00	4.51 11.06 9.40		 		4.00 -5.00 8.90	[0.42; 7.58] [-12.66; 2.66] [-0.40; 18.20]	73.2% 16.0% 10.8%	42.8% 30.8% 26.4%
Common effect m Random effects m Heterogeneity: $l^2 = 6$	odel nodel 17%, τ ² = 27.530	42 06, p = 0	0.05		44		-15	-10 -5	0 5	-] 10 15	3.09 2.52	[0.03; 6.16] [-4.61; 9.64]	100.0%	100.0%

DTGT: dual-task gait training; STGT: single-task gait training; PTCDG: progressive treadmill cognitive dual-task gait training; CTG: conventional t readmill gait training; CDTT: cognitive dual task gait training; CPT: conventional physical therapy.

Fig. 8 A forest plot for meta-analysis of dual-task walking speed

-2.15, p < 0.001; see Fig. 7) (low-quality evidence). We did not perform subgroup analyses, meta-regression, or sensitivity analyses because there was no significant heterogeneity between studies. Because of the small number of studies (n=2), we did not perform publication bias testing.

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was low (Table 2).

Dual-task walking speed

Three studies involving 86 stroke patients used dual-task walking speed as an outcome indicator. We conducted a meta-analysis of the change in mean scores in the experimental and control groups by calculating the change in dual-task speed from baseline to the end of treatment. The current findings can not clarify the efficacy of cognitive-motor dual-task training for dual-task walking speed in stroke patients compared with conventional rehabilitation training (random-effect model: MD=2.52, 95% CI -4.61 to 9.64, p=0.489; fixed-effect model: MD=3.09, 95% CI=0.03 to 6.16, p=0.048; see Fig. 8) (very low-quality evidence).

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was very low (Table 2).

In sensitivity analyses, where we excluded individual studies one by one, the results change significantly sometimes.

Begg test (z=0.00, p=1.000) and Egger test (t=-0.21, p=0.869) did not indicate publication bias.

Activities of daily living (ADL)

In this study, Activities of daily living (ADL) [80] was one of the secondary outcome indicators. Five studies involving 284 stroke patients used the Barthel Index (BI) or Functional Independence Measure (FIM) as an outcome indicator. We conducted a meta-analysis of the change in mean scores in the experimental and control groups by calculating the change in Barthel Index (BI)/Functional Independence Measure (FIM) scores from baseline to the end of treatment. The current findings can not clarify the efficacy of cognitive-motor dual-task training for Activities of daily living (BI/FIM) in stroke patients compared with conventional rehabilitation training (random-effect model: SMD=1.09, 95% CI -0.02 to 2.20, p=0.055; fixed-effect model: SMD=1.03, 95% CI 0.764 to 1.294, p=0.0001; see Fig. 9) (low-quality evidence).

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was low (TABLE 2).

In sensitivity analyses, where we excluded individual studies one by one, the results did not change significantly.

Begg test (z=0.24, p=0.810) and Egger test (t=0.29, p=0.789) did not indicate publication bias.

The Trial Sequential Analysis (TSA) does not apply to ADL, as the included studies employed disparate outcome metrics.

lower extremity motor function [Fugl-Meyer Assessment (FMA)]

In this study, the Fugl-Meyer Assessment (FMA) was one of the secondary outcome indicators. Our studies used the Fugl-Meyer Assessment (FMA) as an outcome indicator. We conducted a meta-analysis of the change in mean scores in the experimental and control groups by calculating the change in Fugl-Meyer Assessment (FMA) scores from baseline to the end of treatment. The current findings can not clarify the efficacy of cognitive-motor dual-task training for lower extremity motor function (FMA) in stroke patients compared with conventional rehabilitation training (randomeffect model: MD=3.74, 95% CI 0.47 to 7.01, p=0.025;



CR:Conventional Rehabilitation; DTWT:Dual-task walking training; CBT:Conventional balance training; DTBT:Dual-task balance training; STBT: Single-task balance training; STWT:Single-task walking training

Fig. 9 A forest plot for meta-analysis of Activities of daily living (ADL)

		Ex	perime	ntal	Cor	ntrol					Weight	Weight
Study	Intervention	Total	Mean	SD Tota	l Mean	SD	Mean Di	ifference	MD	95%-CI	(common)	(random)
Shixiu Pei 2023	DTBT+CR:CR	30	12.42	2.31 30	7.65	2.37		—	4.77	[3.59; 5.95]	44.4%	28.7%
Choi, J.H. 2015	DTBT+CR:STBT+	CR 10	2.50 4	4.99 10	3.40	7.79-	•		-0.90	[-6.63; 4.83]	1.9%	15.6%
Plummer P 2021		49	2 00 1	3.40 48 2.83 10	0 5.01	3.20	-		- 7.38	[0.00; 8.70]	35.7%	28.5%
1 101111161, 1 . 2021	0101.0101	17	2.00 /	2.00 13	0.50	2.00			1.50	[-0.00, 0.00]	10.070	21.270
Common effect n	nodel	106		108	3			♦	5.01	[4.22; 5.80]	100.0%	
Random effects r	model								3.74	[0.47; 7.01]		100.0%
Heterogeneity: / 2=	90%, τ^2 = 9.3292, μ	> < 0.01					- ·					
							-5 (0 5				

CMDT:Cognitive-motor dual-task training; CR:Conventional Rehabilitation; DTBT:Dual-task balance; STBT: Single-task balance training; DTGT: dual-task gait training; STGT: single-task gait training

Fig. 10 A forest plot for meta-analysis of Fugl-Meyer Assessment (FMA)

fixed-effect model: MD = 5.01, 95% CI 4.22 to 5.80, p = 0.001; Fig. 10) (low-quality evidence).

The GRADE analysis showed that the overall quality of the evidence supporting this outcome was low (TABLE 2).

Further research is required to analyze the effects of cognitive-motor dual-task training on lower limb motor function in stroke patients as the results of sensitivity analyses were found to be unstable.

Begg test (z = -0.34, p = 0.734) and Egger test (t = -0.99, p = 0.425) did not indicate publication bias.

Concerning Fugl-Meyer Assessment (FMA), the Trial Sequential Analysis (TSA)showed that the cumulative Z value had not crossed the traditional threshold or the Trial Sequential Analysis (TSA) threshold, and the sample size did not meet the specified required information size (Fig. 11D). Therefore, the meta-analysis of FMA is inconclusive and further trials are required to analyze the effects of cognitive-motor dual-task training (CMDT) on lower limb motor function (measured by FMA) in stroke patients.

3.6. Subgroup analyses and meta-regression analysis for primary outcomes [Berg Balance Scale (BBS), Time up and go test (TUG) and single-task walking speed]

Because of the observed heterogeneity among studies in which the Berg Balance Scale (BBS), Time up and go test (TUG), and single-task walking speed were measured, we conducted subgroup analyses and meta-regression analysis to explore potential sources of heterogeneity (Table 4).

These subgroup analyses were (1) whether the cognitive components of cognitive-motor dual-task training (CMDT) were combined with working memory: Yes vs. No; (2) motor components of CMDT: Gait vs. Balance vs. Others; (3) stroke duration: Acute/subacute phase (<6 months) vs. Chronic phase (>=6months); (4) frequency (week) of CMDT: Low (<=4 sessions) vs. High (>4 sessions); (5) duration of each CMDT session: Short(<=30min) vs. Long(>30min); (6) Length of CMDT: Short (<=4 weeks) vs. Long (>4 weeks); (7) publication year: Before 2020 vs. After 2020.

In the meta-regression analysis, potential moderator variables included sex distribution (percentage of male and female participants), average age, and sample size. (A p-value for the moderator variable of < 0.05 was considered statistically significant.)

Regarding the sub-group analysis for Berg Balance Scale (BBS), stroke duration and frequency (week) of CMDT were statistically significant moderator variables (p < 0.05). The results of the meta-regression models revealed that only sample size (B=0.13, p=0.005) was a significant moderator variable.

Regarding the sub-group analysis for Time Up and Go test (TUG), motor components of CMDT, publication year, duration of each CMDT session, and Length of CMDT were statistically significant moderator variables (p < 0.05).

Regarding the sub-group analysis for single-task walking speed, frequency (week) of CMDT was a statistically significant moderator variable (p < 0.05).

Discussion

This meta-analysis included seventeen randomized clinical trials involving 751 patients comparing the effectiveness of cognitive-motor dual-task training (CMDT) with conventional interventions in stroke patients. The results showed that the CMDT might improve static balance function (measured by Berg Balance Scale) in stroke patients (low-quality evidence). Meta-regression analysis showed that sample size might be one of the important sources of heterogeneity and the course of disease and frequency of CMDT might be the potential moderator variables in BBS. On the other hand, the current findings can not clarify the efficacy of cognitive-motor dual-task training for dynamic balance-TUG, gait ability, ADL, and lower extremity motor function in the meta-analysis



Fig. 11 The Trial Sequential Analysis of Berg Balance Scale (A), Time Up and Go Test (B), Single-task walking speed (C), and Fugl-Meyer Assessment (D) D: Cumulative Z-curve (solid blue lines) were constructed using a random-effects model, with the light red line showing the traditional threshold and the dark red line representing the Trial Sequential Analysis (TSA)threshold



(very low to low quality evidence). Trial Sequential Analysis of RCTs demonstrated that further RCTs will be required to reach conclusive evidence on BBS, TUG, single-task walking speed and FMA. Notably, the effectiveness of CMDT on BBS in the meta-analysis reached the minimal clinically important difference (MCID).

Mechanism of the effects of the cognitive-motor dualtask training (CMDT).

CMDT improved balance function, and its neurophysiological mechanism may lie in the fact that CMDT interventions can induce plasma neurotransmitter Brain-derived neurotrophic factor (BDNF) and neurostructural plasticity variability [6, 12, 18, 25, 31]. Specifically, the motor regulates many growth factors, such as Brain-derived neurotrophic factor (BDNF), which plays a crucial role in neuroprotection and synaptic plasticity [1]. The combination of motor and an enriched environment induces more new neurons and has greater benefits for the brain than the motor alone [22] CMDT involves simultaneous cognitive and motor tasks. The combination of multiple stimuli such as cognitive and motor can generate new neuronal networks (synaptogenesis) or cause enhanced synaptic activity, which increases brain plasticity. [26]Furthermore, the motor task-induced increases in BDNF are transient and usually return to baseline levels 10-60 min after cessation of the motor.[41]. If cognitive training is introduced concurrently before returning to baseline levels, these newborn neurons can be guided to establish connections with pre-existing neural networks [6, 18, 25]. Consequently, concurrent cognitive training and motor training are more effective. From this, it can be concluded that the simultaneity of cognitive and motor tasks is critical.

Furthermore, the mechanism by which dual-tasking affects balance is related to neuroplasticity, changes in neurotransmission and brain activity patterns after stroke [73], Animal research found that the addition of further cognitive loads may have resulted in the effective stimulation of common cortical areas in the dorsomedial frontal cortex and prefrontal cortex, particularly the premotor and supplementary motor areas, which were involved in regulating balance and cognitive functions[48]. and dual-tasking training induces neuroplasticity through perceptual arousal activation of brain regions involved in central executive functions such as the dorsolateral prefrontal cortex. This promotes endogenous neural repair mechanisms, increases the number of neuronal synapses in the cerebral cortex, and facilitates axonal and dendritic transmission [54], thereby improving neurological control of the body and the patient's balance function [5, 36, 79].

Cognitive functions include attention, working memory, and executive ability. Working memory is highly correlated with other cognitive domains, particularly attention and executive function [64, 76], and working memory and attention often involve overlapping frontoparietal brain regions [7, 40]. Xiuen Chen's (CHEN [14]) results suggest that the Stroop paradigm and trunkcontrolled dual-task training improve cognitive functioning in patients, particularly attention and executive ability. Attention is often considered to be the basis of cognitive functioning. The Stroop task has been used as the gold standard for attentional measures [49]. Stroop Conflict Inhibition Cognitive Training, which requires the active participation of the subject, decreases activation in the anterior cingulate cortex, which monitors

Variable	BBS				TUG				Single-tas speed	¥		
	∡	MD	95% CI	d	¥	MD	95% CI	٩	¥	MD	95% CI	٩
Meta-regression analysis												
Sample size	9	B=0.13		0.005	4	B=-0.04		0.49	2	B = 0.19		0.854
Mean age	9	B=-0.01		0.929	4	B=-0.39		0.096	2	B=-0.45		0.168
Sex ratio (Male: Female)	9	B=-1.73		0.423	I	I	I	I	2	B = -0.34		0.263
Subgroup analysis												
Cognitive components of CMDT				0.677				0.372				0.863
With working memory	5	3.5	[1.76, 5.24]		5	-1.64	[-4.43, 1.14]		ŝ	0.97	[-3.28, 5.22]	
Without working memory	m	4.43	[0.43, 8.43]		-	0.47	[-3.25, 4.19]		, -	1.6	[-4.13, 7.33]	
Motor components of CMDT				0.355				0.014				I
Balance	5	5.03	[1.03, 9.03]		2	-1.9	[-4.17, 0.36]		I	I	I	
Gait	c	3.1	[2.28, 3.92]		m	0.89	[-1.46, 3.23]		I	I	I	
Other	I	I	I		-	-4.84	[-7.96, -1.72]		I	I	I	
Course of disease				0.013				0.41				I
< 6months	5	5.74	[3.09, 8.39]		-	-2.31	[-3.81, -0.81]		I	I	I	
≥6months	m	1.28	[-1.05, 3.61]		-C	-0.84	[-3.99, 2.31]		I	I	I	
Publication year				0.153				0.012				0.119
≤2020	4	2.42	[-0.68, 5.51]		4	0.95	[-1.26, 3.16]		2	3.47	[0.71, 6.23]	
> 2020	4	5.72	[2.41, 9.03]		2	-3.19	[-5.55, -0.83]		2	-1.27	[-6.57, 4.02]	
Frequency (week) of CMDT				0.014				0.41				0.048
≤ 4sessions	2	-0.45	[-4.14, 3.24]		5	-0.84	[-3.99, 2.31]		e	-0.04	[-2.58, 2.51]	
> 4sessions	9	5.14	[2.67, 7.60]		-	-2.31	[-3.81, -0.81]		<i>—</i>	4.03	[0.89, 7.17]	
Duration of CMDT				0.908				0.025				0.404
≤ 30min	5	4.27	[0.50, 8.03]		5	-0.47	[-2.70, 1.75]		e	2.09	[-1.85, 6.03]	
> 30min	m	4.02	[2.12, 5.92]		-	-4.84	[-7.96, -1.72]		,	0	[-2.94, 2.94]	
Length of CMDT				0.908				0.024				0.404
< 4weeks	2	4.29	[1.94; 6.63]		m	0.89	[-1.46, 3.23]		e	2.09	[-1.85, 6.03]	
> 4weeks	9	4.05	[0.71; 7.39]		ŝ	-2.73	[-4.82, -0.64]		-	0	[-2.94, 2.94]	

conflict signals, and increases activation in the prefrontal cortex, which carries out conflict resolution thereby strengthening top-down cognitive control, which in turn leads to an increase in interference control.

Although single-task training programs can enhance balance function, they require a greater investment of resources, which in turn impairs the patient's ability to utilize cognitive and control abilities during daily walking effectively. In other words, In the traditional rehabilitation process, patients usually passively accept the therapist's 'static' functional training, at this time the patient's attention is more concentrated, and the training effect seems to be good; but in fact, the patient's ability to allocate and manage their attention is reduced. [24, 67] Lord's study [46] illustrated that patients in single-task training who returned to the community might experience falls and gait decline. In the future, CMDT may become a training tool for home rehabilitation to improve patients' balance function, preventing the onset of falls.

The continuous shift of patients' attention from the balance task to the cognitive task during training has been shown to promote the automated regulation of postural control, effectively improving patients' balance and lower limb motor function. Dual-task training requires individuals to perform two tasks simultaneously, allocating attention rationally to the primary and secondary tasks, with different goals. The capacity-limited process movement pattern will tend to be automated with practice, which can reduce the influence of limited attention on postural control, reduce the proportion of postural control components, and improve the efficiency of postural control. Individuals can complete the task when the difficulty of the dual task is within the central processing capacity; if it is beyond the central processing range, the two tasks interfere with each other [72]. In stroke patients, brain damage leads to prolonged dual-task reaction times, increased dual-task consumption, and increased error rates. Training can enhance the functioning and processing efficiency of executive centers, movement patterns tend to be automated, optimize cognitive allocation strategies, improve coordination between cognition and balance, improve dual-tasking skills, reduce unnecessary muscle contractions and muscle tension, and increase the stability of postural control [10].

The mechanism by which CMDT can improve static equilibrium is that the cognitive load theory suggests that when the total cognitive load does not exceed the cognitive load possessed by the organism, there is excess cognitive load available for use. This provides a theoretical basis for the completion of dual-task training in stroke patients. However, when the total cognitive load exceeds the cognitive load possessed by the organism, insufficient cognitive load can result in a reduction in task performance [50]. The walking process is initially based on the ability to maintain balance and subsequently requires a certain level of executive functioning, which entails the simultaneous performance of several tasks [67]. When limited attentional resources are available, the performance of two attentively demanding tasks simultaneously is likely to result in a decline in performance on at least one of them [67, 83].

Effectiveness of cognitive-motor dual-task training (CMDT) in improving gait and balance performance.

The present results demonstrated that CMDT might improve balance function [Static balance-Berg Balance Scale (BBS)] in stroke patients (low-quality evidence). Furthermore, the results of sensitivity analyses confirmed the robustness of the results. This was consistent with the findings of previous meta-analyses of studies on dual-task training to improve balance function in stroke patients [70]. Dual-task training typically consists of a motor or balance task and a secondary task required for distraction and is divided into two main types: motormotor dual tasks and cognitive-motor dual tasks. Motormotor dual-task refers to performing both motor training and postural control training, such as walking while tapping or kicking a ball. In contrast, cognitive-motor dualtask training refers to performing motor training as well as cognitive training tasks, such as counting or reciting poetry while walking. Different dual-task strategies had different intervention effects, with the motor-motor dual task reducing gait changes during walking and cognitivemotor dual-task training reducing dual support time during walking. [17, 86]

However, previous studies have not analyzed cognitivemotor dual-task training separately from motor-motor dual-task training in depth. Furthermore, their inclusion of only English-language literature did not reflect the true representation of intervention effects. Although there was no statistically significant impact on dynamic balance-TUG outcomes in this study, we found that stroke patients benefited from improved static balance-BBS with CMDT. Nevertheless, across the studies, the dose effect of the intervention specifically combining the cognitive tasks and motor tasks concurrently was difficult to perform as the intensity of the CMDT was poorly described in the methods, and the timing of the CMDT was different. Efforts to address the intensity of the prescribed CMDT and provision of detailed CMDT protocol should be considered in future studies.

Subgroup analyses of the effects of CMDT on static balance-BBS showed that a frequency of intervention greater than four times per week, implemented within six months of symptom onset, was more effective in improving BBS. In general, the period of neuroplasticity following a brain injury in a stroke patient lasts between one and three months [84], after which neuroplasticity decreases. Consequently, early cognitive-motor dual-task training is of paramount importance for the functional recovery of stroke patients.

CMDT has shown an impact in terms of clinical outcomes in stroke patients. However, much remains to be explored regarding the potential benefits of this rehabilitation tool in stroke patients with different cognitive needs. For example, it may be valuable to examine the effectiveness of different cognitive-motor dual-task training programmes among stroke patients. However, interpretation of the results remains challenging due to the limited number of available studies and the heterogeneity of intervention programs. Therefore, further studies with larger sample sizes and standardized protocols are necessary to fully elucidate the potential benefits of combining different cognitive training with different motor training.

Subgroup analyses of the effects of CMDT on dynamic balance-TUG demonstrated that sessions greater than 30 min per session and intervention lengths greater than 4 weeks helped to improve TUG. While CMDT combined with regular gait or balance exercise training did not improve TUG, CMDT engaged in simultaneous stationary bike cycling and cognitive training helped to improve TUG (but only this study of T. T. Yeh demonstrated this result). CMDT in the literature published after 2020 helped to improve TUG, considering the possibility that CMDT programmes have progressed and been optimized over time.

The results of this study indicated that cognitive-motor dual-task training did not significantly improve gait (single-task and dual-task walking speed) (very low-quality evidence), Activities of daily living (ADL) (low-quality evidence), and lower extremity motor function (lowquality evidence) in stroke patients compared to conventional rehabilitation. In comparison to the findings of a previous meta-analysis, our results did not indicate a discernible advantage for CMDT to gait speed [61]. Previous studies have demonstrated that dual-task walking speed predicts post-stroke mobility more accurately than single-task walking speed. Additionally, dual-task gait speed more closely resembles real-world walking, suggesting that dual-task walking speed may offer a more accurate representation of post-stroke mobility [20]. Consequently, cognitive-motor dual-task training (CMDT) does not demonstrably enhance dual-task step speed, and thus, it is similarly ineffective in significantly improving Activities of daily living (ADL). Hence, it is vital for rehabilitation physicians and clinicians to meticulously consider the intensity of CMDT. Detailed, comprehensive protocols are required for promoting gait, lower extremity motor function and activities of daily living. However, CMDT is a cost-effective, non-pharmacological treatment that can improve patients' quality of life.

Impact of small trial sizes on the efficacy of CMDT.

An important limitation was the small trial sizes of the included studies, as small trials tend to over- or underestimate the underlying treatment effect. The pooled intervention effect can be dramatically overestimated in combination with publication bias (preferred publication of positive results). However, in the current metaanalysis publication bias seems not to play a role in most of the outcomes. Nevertheless, evidence was limited by the indirectness of effect estimates. As small trials also tend to have limited heterogeneity in their patient population and/or implemented intervention (low withinstudy clinical heterogeneity) the estimated treatment effects of meta-analyses including solely small trials possess lower external validity and generalizability.

Interpretation of random-effect and fixed-effect models.

One of the key reasons for the discrepancy between the findings of the random-effect and fixed-effect models was the presence of inter-study heterogeneity.

The inconsistency between the random-effect model and the fixed-effect model in the meta-analysis of TUG was due to significant heterogeneity across the studies. Firstly, the inconsistency in the design of the intervention programme, namely the motor task of CMDT in Tingting Yeh's study, which comprised cycling resistance aerobic training, differed from the design of the motor task of CMDT in other studies. This resulted in clinical heterogeneity. Secondly, the duration and frequency of the CMDT intervention might be also influential in causing heterogeneity in the results and some clues can also be found in the subgroup analyses results. Finally, the small sample size of the included studies, the varying degree of risk bias, and the variable quality of the studies may also contribute to the above results.

The discrepancies in the outcomes of the fixed-effect and random-effect models in the meta-analyses of ADL and FMA can be attributed to the following factors. The number of participants in the RCT studies included for these two outcome indicators was too small, and the majority of studies were classified as high-risk in ROB, exhibiting significant methodological heterogeneity. Furthermore, concerning the measures of ADL, there are two indicators, namely the MBI and FIM, which might cause clinical heterogeneity. The significant differences in the results of the aforementioned outcome metrics between the two models can be attributed to the severe heterogeneity caused by the aforementioned reasons.

The results of the meta-analysis on dual-task walking speed, as visualized in the forest plot, revealed that the results of Plummer P's study and the results of the other two RCTs exhibited minimal overlap in the confidence intervals. This may be a significant source of heterogeneity. In the risk of bias assessment, the study conducted by Plummer P was identified as having a high risk of bias due to the loss of outcome data. Conversely, the other two RCTs were classified as having a low to medium risk of bias. Furthermore, the inclusion of only three RCTs and the very small sample size in the present results may also contribute to significant heterogeneity in the study results. Accordingly, the aforementioned results should be presented conservatively.

Limitations

It is important to consider the following limitations when interpreting the results of this study. Firstly, it should be noted that this study only included literature from randomized clinical trials (RCTs) in English and Chinese, and did not take into account literature in other languages and relevant studies from non-RCTs. Second, the quality of the study data determines the quality of the findings. Based on our quality assessment of this meta-analysis, it has to be acknowledged that some of the included studies had some concerns or high risk of bias, such as not being explicitly blinded or implementing an allocation concealment process, or high attrition rates without intentionto-treat analysis, or no registration of the protocol. In addition, different assessment tools can have a potential impact on the heterogeneity of results. Therefore, it is crucial for researchers who should firstly have no knowledge about the implementation of the trial and secondly carefully select objective assessment tools, preferably gold standard tools, to ensure the robustness of future findings. Thirdly, the relatively small sample sizes of several studies included in this meta-analysis may affect the precision and robustness of the pooled effect sizes, limiting the internal validity of the findings. Finally, the trial sequential analyses also indicated that the current sample sizes may not be as expected. Therefore, to obtain more comprehensive and reliable evidence, larger sample sizes are needed in the future to determine the effectiveness of the intervention. Given these limitations, it is suggested that future meta-analyses will also need to include some grey literature. It is emphasized that future trials clearly state the randomization, allocation concealment, and blinding procedures, and strictly follow the requirements of randomized controlled trials. To enhance the robustness of future studies, we advocate larger, more homogenous RCTs, including large sample sizes, and extended short- and long-term follow-up periods, and recommend the inclusion of clinically meaningful outcomes such as relapses and readmissions. They can also be applied to different populations and settings or studies focusing on specific subtypes of CMDT to obtain more high-quality information, thereby strengthening evidence-based practice in the field.

Conclusion

In conclusion, the findings of this study suggested that cognitive-motor dual-task training (CMDT) might improve static balance function (measured by Berg Balance Scale) in stroke patients (low-quality evidence). Nevertheless, the effectiveness of CMDT on dynamic balance and gait in stroke patients was inconclusive. Trial Sequential Analysis (TSA) demonstrated that further RCTs would be required to reach conclusive evidence on BBS, TUG, and single-task walking speed. The low-quality evidence observed in Grading of Recommendations Assessment, Development, and Evaluation (GRADE) systematic reviews highlighted the need for more targeted randomized clinical trials (RCTs). Meanwhile, further studies are required to corroborate these findings through large-scale, multicenter, high-quality randomized clinical trials (RCTs). Furthermore, future studies should be conducted to ascertain the differences in the effects of various types of CMDT on the gait and balance of stroke patients.

Others

There are several flaws in the content of this article and some differences from that of PROSPERO, including PROSPERO register times, inclusion and exclusion criteria, subgroup analyses, meta-regression analyses, Grading of Recommendations Assessment, Development, and Evaluation (GRADE) assessments, and Trial Sequential Analysis (TSA).

What is already known

- Conventional physical single-task training can be beneficial in improving gait and balance in stroke patients.
- The efficacy of cognitive-motor dual-task training plus conventional physical single-task training in enhancing gait and balance in stroke patients remains uncertain compared with conventional physical single-task training.

What this paper adds

• Cognitive-motor dual-task training plus conventional physical single-task training may enhance static balance function in stroke patients compared with conventional physical single-task training (low-quality evidence), which did not reach the required information size In the Trial Sequential Analysis.

- The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) analysis revealed low-quality evidence supporting Cognitive-motor dual-task training in improving Static Balance in stroke patients.
- Regarding the effectiveness of cognitive-motor dual-task training on static balance, the disease course and frequency of CMDT might be the potential moderator variable.

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12984-024-01507-6.

Additional file 1.

Author contributions

Lu Zhang: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. Jiangping Ma: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. Xiaobing Yin: Writing – review & editing, Validation, Supervision, Conceptualization. Kai Wang: review & editing, Validation. Xiaoqing Liu: Supervision. Aiping Jin: Validation.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

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Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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