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Divided attention and manual visuomotor control in stroke: a combined dual-task and eye movement study

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Abstract

Background Daily manual tasks require cognitive-motor interactions. There is limited research on cognitive-motor dual-tasks involving the upper extremity. In this study we used a manual visuomotor dual-task to measure post-stroke cognitive-motor impairments. Given previous evidence of impaired cognitive-motor interaction in stroke we hypothesized that the presence of enhanced dual-task cognitive load will impact motor performance in stroke patients. We also hypothesized that this dual-task effect would be greater in stroke patients compared to healthy controls. We also explored whether cognitive-motor impairments observed in these single- and dual-task conditions would relate to deficits in manual dexterity.

Methods 30 chronic stroke participants (29.77 ± 35.39 months post-stroke) with mild-to-moderate hemiparesis without cognitive impairment (global screening test) and 30 age-matched healthy subjects performed a visuomotor grip force-tracking task in single- and dual-task conditions, requiring divided attention (resisting visual distraction) and working memory (mental addition of transiently displayed numbers). Gaze was simultaneously recorded to probe cognitive performance through saccades. Dexterity impairments were separately quantified using a kinetic device.

Results Stroke patients had increased visuomotor tracking error but did not show significantly increased change in visuomotor tracking error during the dual-task, with no significant difference between single task condition vs. divided attention or vs. working memory dual-task conditions. In contrast, age-matched healthy controls did show the expected difference with significantly higher dual-task force-tracking error. The between-group analysis only revealed a significant group difference (Stroke vs. Control) with stroke patients producing twice as much tracking error in both single and dual-task conditions. Stroke participants showed significantly reduced dual-task saccade modulation, with a reduced difference in saccades to displayed numbers (similar in both groups) vs. to distractors (higher in stroke) (median $\pm$ IQR: stroke $14.6 \pm 18.75\%$; controls: $26.4 \pm 32.41\%$). Non-inhibited saccades to distractors explained certain dexterity group differences (force control and timing of finger movements).

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Conclusion The visuomotor force-tracking error, although increased, did not show enhanced cognitive-motor interaction in stroke. However, the task-related saccade analysis did detect impaired divided attention post-stroke, that may contribute to impaired dexterity, particularly in tasks requiring on-line sensorimotor integration. Upper limb dual-tasking practice may be relevant for engaging attention and enhancing post-stroke activities in daily life.

Trial registration **ClinicalTrials.gov ID NCT05454748.**

Keywords Stroke, Visuomotor dual-task, Force-tracking, Manual dexterity, Attention, Working memory

Introduction

Persisting upper limb motor impairment is present in about 50% of persons with chronic stroke [1]. Upper limb movements, and manual dexterity in particular, require cognitive functions, such as attention, memory and executive function [2]. About 40% of persons with stroke also suffer from cognitive impairments in the chronic phase [3] and these impairments may further impact upper limb movements and activities of daily living (ADL). For example, motor and cognitive impairments can lead to reduced dual-task capacity, i.e., performing a cognitive and a motor task simultaneously, reflecting a limitation in divided attention [4]. Upper limb movements are considered more cognitively demanding and less automated than gross motor activities such as walking, which may lead to more distinct cognitive motor interference [5, 6]. Many ADL require divided attention during manual dexterity tasks (e.g., eating while watching TV, or talking while dressing), and there is a growing interest in using upper limb dual-tasks in post-stroke rehabilitation [7]. However, this phenomenon has been most extensively studied after stroke during walking [8], or for proximal upper limb movements [5] and for gross dexterity with rapid arm transport (reach) tasks [7], but few studies incorporated distal, graded manual control tasks [9]. Therefore, dual-task assessment involving the hand after stroke could aid detection of impaired divided attention during upper limb movements, and dual-task training post-stroke may have potential for enhancing effectiveness of therapy [10].

Dual-task conditions require two tasks to be carried out simultaneously, which typically results in lower performance when compared to the single-task condition. Most commonly post-stroke dual-tasking is studied by combining a motor and a cognitive task, which often results in reduced performance (in one or both tasks), even in healthy subjects [11, 12]. Reduced motor/cognitive task performance during dual-tasking is considered to arise from less automatized tasks being performed with limited cognitive resources [13] affecting (divided) attention, executive function, working memory and potentially other cognitive functions used during motor tasks. During movement execution, the attentional demands of the motor system increase in relation to task complexity, as goal-directed actions require sophisticated planning and

motor processing. It has been shown that stroke survivors need to allocate greater attentional resources to perform specific tasks compared to healthy individuals [14]. Increased attentional demands, even for a well-learned manual skill, can impair performance by requiring step-by-step monitoring thus disrupting automatic execution [15]. If the motor task requires a disproportional amount of attention, dual-task interference will be observed, resulting in decreased performance of either the motor task, the cognitive task, or both, which is evidenced by slower performance and increased errors compared to single-task performance [15]. Reduced capacity to perform dual-tasks can be detrimental for independence in daily life [16]. Dual-task approaches in stroke may help elucidate the relative role and interaction of cognitive and motor dysfunction and guide elaboration of novel therapeutic strategies [16].

Previous dual-task studies in stroke found a detrimental effect on proximal motor control (arm reaching) when combined with cognitive tasks [17, 18]. Moreover, stroke can also be associated with decreased dual-task cognitive performance when making upper limb movements [12], indicating that stroke can conjointly affect cognitive and motor (upper limb) performance. However, most previous upper limb dual-task studies in stroke used arm reaching tasks [4, 6, 17, 19]: few have investigated more distal motor tasks (hand movements, grasp, pinch, finger individuation subserving manual dexterity), which might enhance knowledge on what cognitive functions contribute to dexterous post-stroke motor performance. Furthermore, previous studies have shown that after stroke, voluntary eye movement impairment can play a role in the loss of functional activities and that excessive number of saccades can be predictive of diminished task performance during a reaching task with a robotic arm [20]. Since eye and proximal limb movements are highly coupled during visuomotor dual-tasking after stroke, could it be the same for distal limb movements?

In this study, we used a visuomotor dual-task paradigm to measure motor performance via grip force-tracking. The precise control of grip force is a pre-requisite for dexterous object manipulation and force-control capacity relates to daily activity limitations in stroke [37]. Performance on the grip force-tracking task informs on force generation, modulation and release and previous

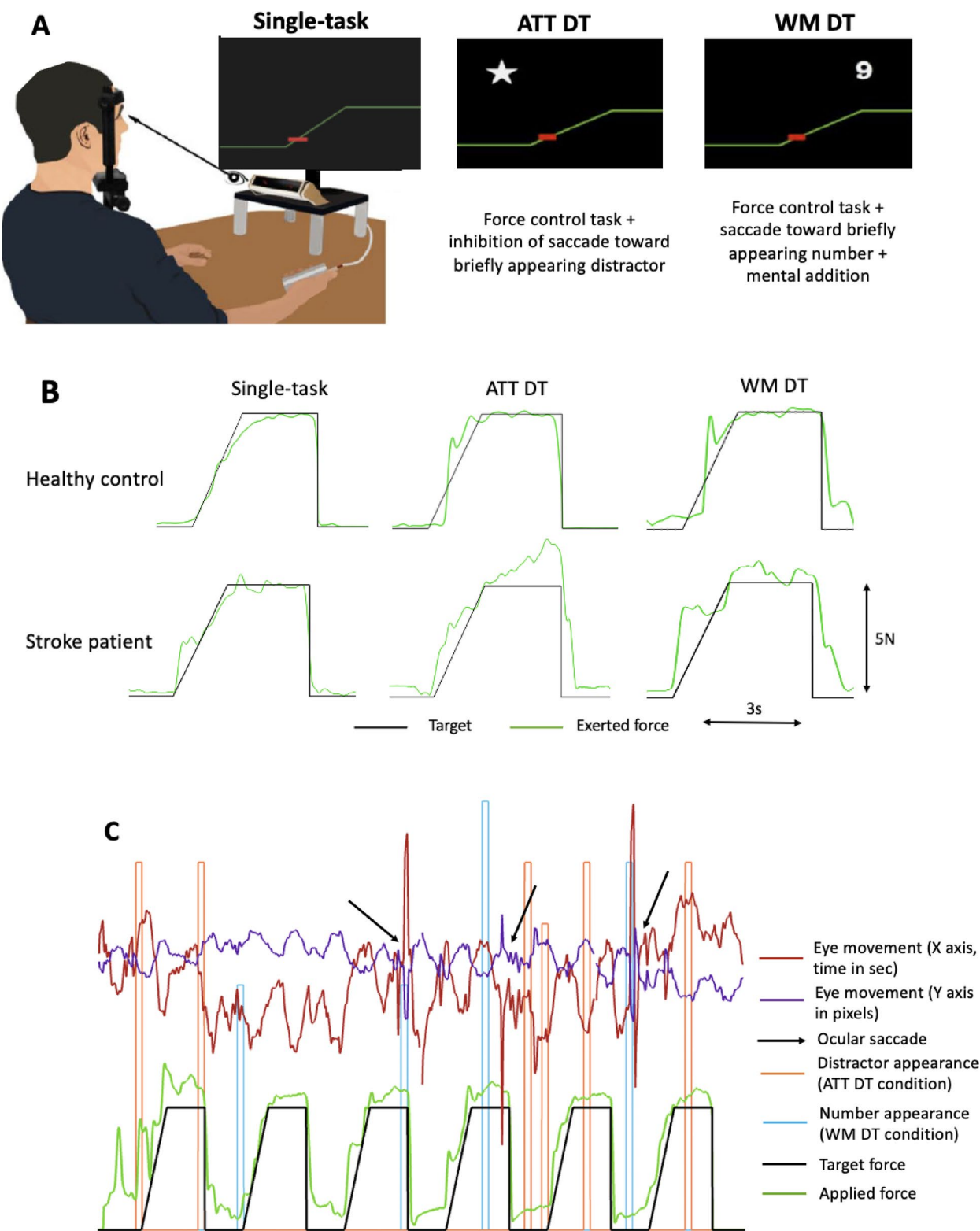


Fig. 1 (See legend on next page.)

(See figure on previous page.)

Fig. 1 Visuomotor grip force-tracking task and eye movements. **A** Set up and conditions of the visuomotor force-tracking task. The subject sat in front of a screen that displayed the task (modified from [11]). **B** Single trial examples in a healthy control subject (BBT score = 65) and in a stroke participant (BBT score = 22). Both subjects show increased tracking error (distance between target and exerted force) in ATT DT and WM DT conditions. **C** Raw signals obtained during the tracking task. Brief appearance of distractors (ATT DT) indicated in orange, appearance of numbers (WM DT) in light blue. The amplitude of traces indicating distractor and number appearance in ATT DT and WM DT reflects their height on the screen, both appearing always above the force-tracking trace. Eye movements are represented along the X-axis (dark red) and Y-axis (purple). Arrows indicate detected saccades. Note: eye position (x-axis, dark red) showed positive increases (indicating rightward eye movement) during each ramp and before the end of each hold phase. This gaze shift corresponds to anticipation of dynamic force generation and force release, found in healthy controls and stroke patients. ATT DT: Attentional dual-task condition, WM DT: Working Memory dual-task condition.

results have shown that force-release explains additional variance in predicting recovery of dexterous hand use post-stroke [21]. Under single-task conditions, subjects integrated visual information in real-time to modulate grip force. Two dual-task conditions were introduced to assess the impact of cognitive functions on motor performance, i.e., working memory and divided attention. Task-related oculomotor (saccade) recordings [11] provided indicators for quantifying divided attention and saccadic control, i.e. saccade execution and saccade inhibition. The first aim was to quantify post-stroke cognitive-motor interaction impairments during a manual visuomotor task. We hypothesized that stroke patients would show reduced grip-force control during dual-tasking, reflecting an involvement of attention and memory functions in manual visuomotor tracking [11, 12, 22]. The second aim was to compare motor dual-task performance between stroke patients and age and gender matched healthy controls. We hypothesized that motor performance in single- and dual-task conditions would be reduced in persons with chronic stroke compared to age- and gender-matched healthy controls, since stroke is associated with impaired manual visuomotor control [23] and reduced allocation of attention during dual-tasking [19]. Finally, since the visuomotor task involved isometric power grip force control, but no key components of manual dexterity (such as single finger force control, timing of finger movements or finger individuation), we explored how cognitive performance during dual-task (probed by saccadic control and mental addition) was associated with manual dexterity impairments measured separately with the Dextrin Manipulandum™. We expected that cognitive dysfunction measured during the visuomotor dual-task would explain some manual dexterity impairments in stroke since studies showed that dexterity is less automatized than proximal upper limb movements [24], that mild cognitive decline negatively impacts dexterity [22], and that cognitive impairment post-stroke explains unique variance in recovery of hand function [25].

Methods

Study design and participants

This cross-sectional observational study (NCT05454748) was undertaken at the GHU Psychiatry and Neuroscience hospital, Paris (France), between February 2022 and

June 2023. The flow diagram describing patient inclusion and exclusion is shown in Supplementary Materials SM1. The study design followed STROBE Guidelines (Supplementary Materials SM2). Medical records were screened according to following inclusion criteria: >18 years old, first ischemic or haemorrhagic symptomatic stroke >3 months ago, mild-to-moderate manual dexterity impairment (i.e. Box and Blocks Test score >0 and <52, ability to actively extend metacarpophalangeal joints by $\geq 10^\circ$), ability to understand study protocol, and no major cognitive dysfunction (Mini Mental State Examination score >25/30). Exclusion criteria: psychiatric disorder, pre-stroke deficits that could interfere with study assessments (e.g., neurologic or orthopaedic disorders affecting manual dexterity), and pregnancy/breastfeeding. Age- and gender-matched healthy subjects without neurological or orthopaedic disorders were recruited as control group thanks to the local GHU research database for healthy controls and the RISC website (CNRS, risc.cnrs.fr). The study was approved by the regional ethics committee (19.12.2057753 (2020/08) CPP Ouest II). All subjects provided written informed consent.

Clinical assessments

We assessed the following hand motor functions: maximal voluntary grip force (MVC, kg) using the Jamar dynamometer (JAMAR®, dominant hand in healthy controls, paretic hand in stroke patients). MVC was repeated 3 times and the highest was retained [26]. Gross manual dexterity was assessed with the Box and Blocks test (BBT) [27] and fine manual dexterity with the Moberg Pick Up Test (MPUT) [28]. Patients also underwent the Action Research Arm Test (ARAT) to assess functional limitations of the upper limb, including grasp, grip, pinch and global movements of the paretic hand [29]. The Motor Activity Log [30] (MAL) was used to assess restrictions in ADL [30]. Clinical cognitive assessments included: the Mini-Mental State Examination (MMSE) to globally screen memory capacity and cognitive state of the participants [31], the Stroop test to assess selective attention and inhibition [32], and the Test of Attentional Performance (TAP) [33], i.e. Incompatibility subtest assessing inhibition during cognitive interference, and Divided attention subtest measuring focused attention.

Visuomotor grip force tracking: single- and dual-task conditions

The Power Grip Manipulandum (www.sensix.fr), running with Spike2V6 software, was used to study grip force-tracking. Recorded data were analyzed with Matlab R2022b (MathWorks, Inc. Natick, MA, USA). Subjects were instructed to reproduce as precisely as possible and in real time the force trajectory displayed on the screen by modulating the (power) isometric grip force applied on the sensor (Fig. 1A, task adapted from [11]). Healthy subjects used their dominant hand, stroke patients their paretic hand (Fig. 1B) and they performed 3 runs (two dual-task and one single-task runs), pseudo-randomized between subjects. One run was dedicated to the motor task only (single-task condition) and the two other runs represented dual-task conditions (Attentional dual-task ATT DT, and Working Memory dual-task WM DT, respectively). A run was separated into 6 blocks and each block consisted of 6 ramp-and-hold trials. Each block had trials with a target (hold) force of either 5 N (to assess similar absolute force levels among the participants) or 10% MVC (to assess similar force levels according to required effort) [23]. They were randomized within a run (consisting of 6 blocks) and within each force-block (consisting of 6 trials). ATT DT entailed the appearance of 6 unpredictable distractors per block (36 distractors per run; stars, squares, circles displayed during 500ms each). Subjects were instructed to avoid (inhibit) eye movements (saccades) toward distractors. In WM DT, in addition to the force control task, 4 numbers per block (between 1 and 9) appeared unpredictably on the screen during 500ms (24 numbers per run). Subjects had to look at the number (perform a saccade), add the 4 numbers of the block mentally, and give the result of the running sum throughout the block orally to the examiner. Distractors and numbers appeared on the screen always well above the motor tracking trace in order to avoid visual superposition. The quantity of distractors and of numbers appearing on the screen was equally distributed across each phase of the trial (rest, ramp, hold, release).

To quantify accuracy of force control (tracking error) we calculated the Root Mean Square Error (RMSE in N) between target force and exerted force. 5 N RMSE and 10% MVC RMSE were separately calculated during the ramp and hold period in each respective trial [23, 34]. Total RMSE corresponded to the median of average 5 N RMSE and 10% MVC RMSE of each condition per subject and is the key variable for force-tracking accuracy.

Recording of eye movements and task-related cognitive measures

Eye movements were recorded with the Mobile EBT Tracker (www.suricog.com) during single- and dual-task conditions in a darkened room. The head was stabilized

and eyes were aligned with the camera. Calibration was performed with eye tracker software. It was verified that the subject could direct the gaze to all parts of the screen (suggesting absence of hemianopsia or spatial neglect). Horizontal (X-axis) and vertical (Y-axis) eye movement coordinates (Fig. 1C) were sampled at 300 Hz and analysed at 1 kHz after linear interpolation using MatlabR2022b. Saccade amplitude was calculated as the difference of eye position (distance) between appearance and disappearance of the stimulus. Since ocular movements in elderly and patients are less rapid, saccadic and more irregular than in young healthy control subjects, we had to adjust the original Matlab script for saccade detection in our cohort. The number of saccades detected with the script was confirmed by visual analysis. Saccade onset was defined as the first point with a velocity $> 30^\circ/\text{s}$, in the interval of 150 to 600 ms post-stimulus.

We measured several variables representing cognitive performance. The Saccade count in the two dual task conditions was separated into (unwanted, non-inhibited) saccades toward distractors, and (wanted, executed) saccades to numbers. (i) ATT DT-saccade count = 100% represented saccades to all appearing distractors, reflecting absence of saccadic inhibition. (ii) WM DT-saccade count = 100% represented a saccade toward each appearing number, reflecting perfect saccade execution. (iii) Relative Saccade Count (RSC) represented the difference between the saccade count in the two conditions (WM DT – ATT DT) and reflected the ability to modulate gaze (attention) across the two types of dual-task trials. Perfect saccadic control, i.e. no saccades to any distractor in ATT DT (accurate inhibition), and a saccade to each number in WM DT (correct execution), would result in a RSC = 100%. (iv) Saccade latency is the time between stimulus onset and saccade onset and (v) saccade duration is the time between saccade onset and arrival at target (i.e. when gaze was fixed on the number or shape). (vi) The mental addition error, observed during the WM condition, expressed the absolute error between the result given by the subject and the expected mathematical result after a running sum throughout the block.

Key components of manual dexterity

We measured key components of manual dexterity [35, 36], including finger force control, timing of finger movements and finger individuation [37] using the Dextrain Manipulandum™ (www.dextrain.com). This was done before or after the visuomotor task in the same session (task order was randomized between subjects to avoid task-specific fatigue). Manual dexterity components have been shown to explain greater variance in upper limb post-stroke activity limitations compared to conventional clinical upper limb assessments [38], but the relation between key components of manual dexterity and

dual-task cognitive control remains to be explored (additional information in Supplementary Materials SM3).

Statistical analysis

Sample size was based on a previous study which compared force tracking in 24 stroke patients and 24 age-comparable healthy control subjects, showing a significant ($p < 0.001$) group effect with effect size of 0.8 for the main variable force-tracking RMSE with power > 0.85 [23]. In order to reach similar statistical power, we aimed for inclusion of 30 subjects in each group. Analysis was carried out with R (version 2023.09.0+463) and IBM SPSS Statistics (version 29.0.0.0+241). Data distribution of the variables was tested using Shapiro-Wilk tests. Non-parametric data are reported as median with inter quartile range (IQR), parametric data as mean $\pm$ SD. Group differences in clinical data were tested using Student t-test or Mann Whitney U-test.

Force tracking analysis:

Table 1 Demographic and clinical data in stroke participants and healthy control subjects

Demographic/clinical status	Stroke (n = 30)	Healthy controls (n = 30)	Group comparison, p-value
Age (y)	62.93 $\pm$ 14.13	63.03 $\pm$ 8.30	0.866
Gender (M/F)	16/14	16/14	1
Assessed hand (R/L)	14/16	26/4	0.002**
Stroke type (ischemic/haemorrhagic)	20/10	–	–
Time since stroke (months)	29.77 $\pm$ 35.39	–	–
Inclusion between 3- and 6-months post-stroke (number (%))	6 (20)	–	–
Clinical sensorimotor assessments			
Max force (kg)	22 $\pm$ 9.81	32.63 $\pm$ 9.81	< 0.001 ***
Box & Blocks Test (#blocks/min)	33.77 $\pm$ 11.13	62.87 $\pm$ 6.2	< 0.001 ***
Moberg Pick Up Test (sec)	23 (23.11)	12 (4.49)	< 0.001 ***
Motor Activity Log (0–5)	3.23 $\pm$ 1.36	–	–
Action Research Arm Test (0–57)	57 (2)	–	–
Clinical cognitive assessments			
MMSE (max = 30)	28.77 $\pm$ 1.14	29.23 $\pm$ 1.01	0.073
STROOP Interference (sec)	145 (64)	115 (34)	< 0.001 ***
TAP Incompatibility (ms)	673.66 $\pm$ 171.94	555.11 $\pm$ 93.75	0.003**
TAP auditory divided attention (ms)	680 (93)	579 (70)	0.02*
TAP visual divided attention (ms)	937 (240)	856 (146)	0.026*

Normally distributed data given as mean $\pm$ SD; Non-normally distributed data as median (IQR). Statistical significance of tests (p-value): * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. MMSE: Mini Mental State Examination; TAP: Test of Attentional Performance

Due to non-analyzable data, we excluded data from 1 control subject and 2 stroke patients. We performed a PERMANOVA on tracking error with 1000 permutations of the variable group [39] using the R “Vegan” package (given the assumption that observations are interchangeable under the null hypothesis). This test uses the same principles as the Repeated Measures ANOVA, assessing sum of squared differences between points and their mean, but without any assumptions about normality or homogeneity of variances. First we performed a PERMANOVA within the stroke group to assess whether the dual-task impacts motor performance. Then a similar analysis was applied to healthy controls to verify presence of the expected dual-task effect. Finally, we performed a PERMANOVA including a factor of condition (Single-task, WM DT, ATT DT) and a group factor (Controls vs. Stroke) to assess between-group differences in the visuomotor task. Post-Hoc tests were performed with Wilcoxon Signed-Rank Tests. Supplementary Methods SM4 describes outliers and data imputation.

Eye tracking analysis:

Saccade count data were non normally distributed and analysed with a PERMANOVA with 1000 permutations. Relative Saccade Count (RSC) and mental addition error were analysed with Mann Whitney U-tests.

Cognitive-motor interaction and association with manual dexterity:

Components of dexterity were compared between groups using parametric or non-parametric statistics, as above. For the timing of finger movements, data were non normally distributed in all conditions and frequencies. A PERMANOVA was performed with a level of condition (Auditory vs. No auditory cue) and a level of Frequency (1 Hz vs. 2 Hz vs. 3 Hz). As an exploratory analysis, we applied quantile regression to test whether cognitive dual-task performance could explain group differences in dexterity outcomes. The models were estimated at the median ($q = 0.5$) to reduce the influence of skewness and outliers. Two dependent variables were considered (Release Duration during the Finger force-tracking task and timing of finger movement accuracy) because they were significantly different between groups and represented some impaired key components of manual dexterity in stroke [35]. In the initial model for each outcome, Group was entered as the sole predictor. In a second step, cognitive performance measures (Addition error, Relative Saccade Count, ATT DT–Saccade Count) were included as covariates to assess whether they accounted for the observed group effect.

Results

Clinical data

Clinical assessments of stroke patients and healthy controls are shown in Table 1. Hand motor and cognitive

assessments differed significantly between groups, but not global cognitive status according to MMSE.

Visuomotor grip force tracking: single- and dual-task conditions

Data from 28 persons with stroke (mean age 62.93 ± 14.13 years old) and 29 healthy participants (mean age 63.03 ± 8.30 years old) were analysed.

In stroke participants the within-group PERMANOVA showed no effect of condition [$F(2,165) = 0.15$, $R^2 = 0.002$, $p = 0.96$] on tracking error (Table 2). In contrast, healthy controls did show the expected effect of condition [$F(2,168) = 2.82$, $R^2 = 0.03$, $p = 0.04$] on tracking error. Post hoc Wilcoxon Signed-Rank Tests performed in healthy controls showed significant differences between Single-task and WM DT (0.24 (0.18) vs. 0.32 (0.23), $p = 0.019$), between Single-task and ATT DT (0.24 (0.18) vs. 0.28 (0.12), $p = 0.028$) but not between ATT DT and WM DT ($p = 0.137$) (Table 2).

The between-group PERMANOVA showed that stroke patients had higher total tracking error (RMSE) in all conditions compared to healthy controls (effect of group [$F(1,330) = 96.51$, $R^2 = 0.22$, $p = 0.04$]. In both groups, the tracking error was also highest in WM DT (Table 3; Fig. 2). However, there was no effect of condition [$F(2,330) = 1.57$, $R^2 = 0.007$, $p = 0.16$] and no condition $\times$ group interaction [$F(2,330) = 0.84$, $R^2 = 0.004$, $p = 0.47$].

In order to test whether degree of gross dexterity motor impairment (measured with the BBT) or time since stroke would explain the group differences in visuomotor tracking, we computed separate between-group PERMANOVAs with either BBT or time since stroke as covariates. Although adding time since stroke did not change the outcome effects of the analysis, adding BBT scores to the model explained the PERMANOVA group effect ($p = 0.15$, no longer significant), suggesting that

Table 2 Visuomotor measures compared within groups

	Single-Task (ST)	ATT DT	WM DT	p value
Stroke patients ($n = 28$)				
Force control				
Total RMSE (N)	0.63 (0.56)	0.59 (0.60)	0.71 (0.60)	N.S.
Eye tracking				
Saccade count (%)	/	51.40 (40.20)	72.90 (41.60)	ATT DT vs. WM DT: $p < 0.001$
Healthy controls ($n = 29$)				
Force control				
Total RMSE (N)	0.24 (0.18)	0.28 (0.12)	0.32 (0.23)	ST vs. WM DT: $p = 0.019$ ST vs. ATT DT: $p = 0.028$ ATT DT vs. WM DT: N.S.
Eye tracking				
Saccade count (%)	–	37.50 (30.55)	70.83 (22.95)	ATT DT vs. WM DT: $p < 0.001$

Most of the variables (especially in the patient group) were non-normally distributed. To be homogeneous, data are given as median (IQR). Post hoc with a Wilcoxon Signed-Rank test and a Mann Whitney U Test. Note: RSC was based on the individual difference, not on the difference between ATT DT and WM DT group values. ATT DT: Attentional dual-task condition with distractors to avoid, WM DT: Working Memory dual-task condition with numbers to look at and to successively add, RMSE: Root Mean Square Error, N.S: not significant.

BBT scores might explain group differences in visuomotor tracking error.

Dual-task-related eye-movements (saccades)

Within-group analysis showed that saccade count differed significantly between the dual-task conditions in stroke participants (ATT DT: 51.40 (40.20) vs. WM DT: 72.90 (41.60), $p < 0.001$) and in healthy controls (ATT DT: 37.50 (30.55) vs. WM DT: 70.83 (22.95), $p < 0.001$) (Table 2).

Table 3 Visuomotor measures compared between groups

	Stroke patients ($n = 28$)			Healthy controls ($n = 29$)		
	Single-task	ATT DT	WM DT	Single-task	ATT DT	WM DT
Force control						
Total RMSE (N)	0.63 (0.56) $p < 0.001^{***}$	0.59 (0.60) $p < 0.001^{***}$	0.71 (0.60) $p < 0.001^{***}$	0.24 (0.18)	0.28 (0.12)	0.32 (0.23)
Eye tracking						
Saccade count (%)	–	51.40 (40.20) $p = 0.173$	72.90 (41.60) $p = 0.664$	–	37.50 (30.55)	70.83 (22.95)
Relative Saccade count (RSC: WM DT – ATT DT, %)	14.60 (18.75) $p = 0.008^{**}$			26.40 (32.41)		
Mental addition error			2.38 (2.43) $p = 0.003^{**}$			0.50 (1.71)

Between-group comparison in the 3 conditions. Most of the variables (especially in the patient group) were non-normally distributed. To be homogeneous, data are given as median (IQR). Effects of group and post-hoc comparisons (Mann-Whitney U Tests) between specific conditions are shown with: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. Note: RSC was based on the individual difference, not on the difference between ATT DT and WM DT group values. ATT DT: Attentional dual-task condition with distractors to avoid, WM DT: Working Memory dual-task condition with numbers to look at and to successively add, RMSE: Root Mean Square Error

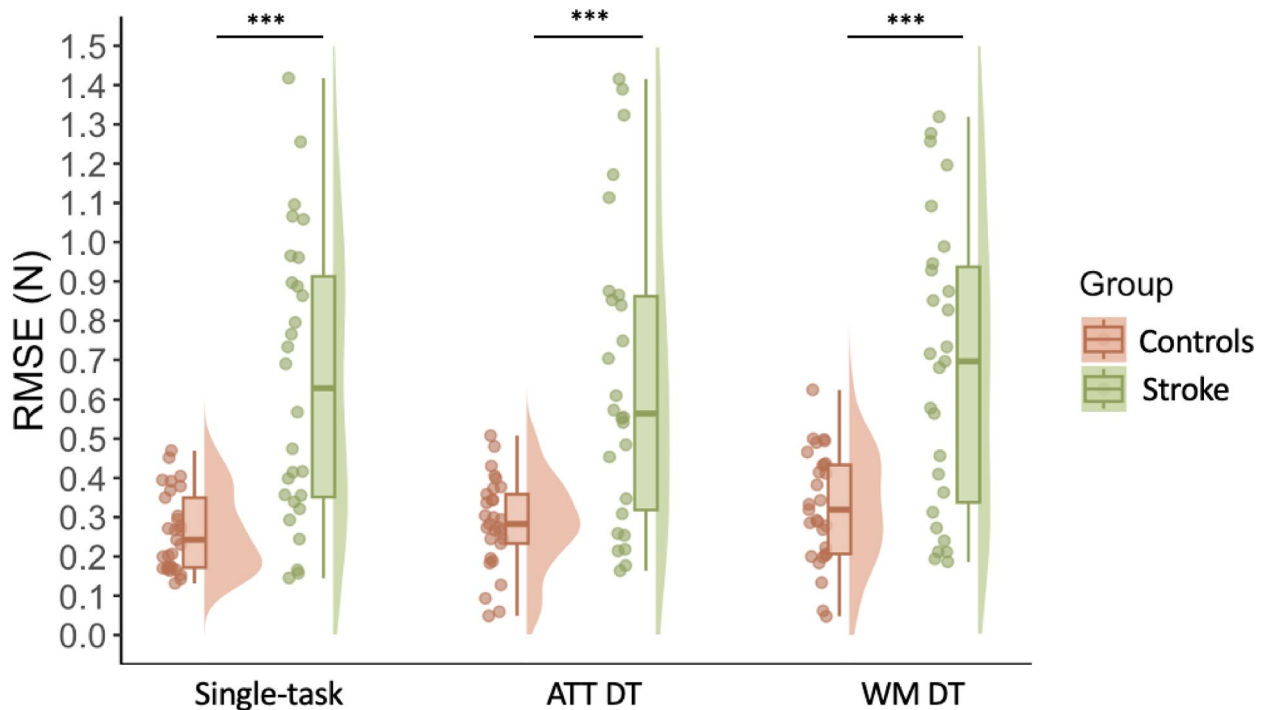


Fig. 2 Force-tracking error as a function of group and condition. Violin plots showing total RMSE according to groups and conditions (Single-task, ATT DT, WM DT) with bold horizontal lines indicating group medians, boxes showing 50% quartile range, and whiskers showing min/max values within 1.5 times the interquartile range. RMSE was calculated as the mean across 5 N and 10%MVC blocks. Significant between-group differences: black horizontal lines on top (Mann Whitney U-test) with $***p < 0.001$. RMSE: Root Mean Square Error; ATT DT: Attentional dual-task condition, WM DT: Working Memory dual-task condition.

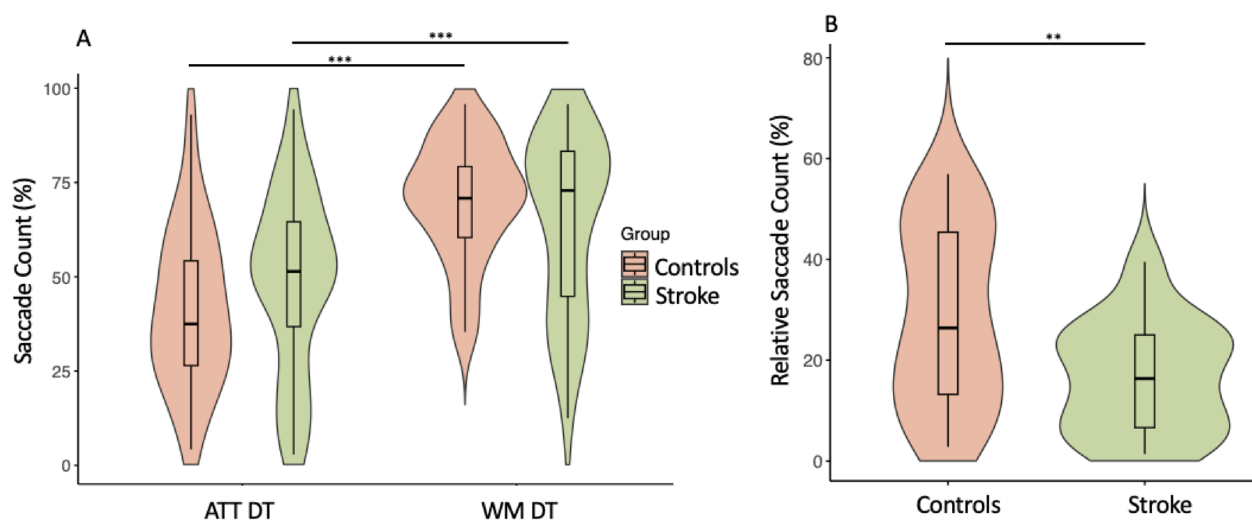


Fig. 3 Saccade count. **A** Violin plot of Saccade count according to groups and dual-task conditions. Significant within-group differences: horizontal black lines (Wilcoxon matched paired test) with $***p < 0.001$. **B** Violin plot of Relative Saccade Count (RSC) according to groups, measured by the difference between the Saccade Count in the two dual-task conditions (WM DT – ATT DT). Significant between-group difference: black horizontal line (Mann Whitney U-test) with $**p < 0.01$. ATT DT: Attentional dual-task condition, WM DT: Working memory dual-task condition. Bold horizontal lines indicate group medians, boxes show 50% quartile range, and whiskers show min/max values within 1.5 times the interquartile range

The between-group PERMANOVA of saccade count showed a significant effect of group [$F(1,108) = 0.21$, $R^2 = 0.002$, $p < 0.001$] and of condition [$F(1,108) = 18.14$, $R^2 = 0.14$, $p < 0.001$]. There was no interaction condition x

group [$F(1,108) = 2.48$, $R^2 = 0.02$, $p = 0.074$] (Fig. 3A). Post hoc testing revealed that WM DT-saccade count was 64% higher than ATT DT-saccade count across both groups (WM DT: 72.53 (26.46) % vs. ATT DT: 46.51 (30.17) %,

Table 4 Key components of manual dexterity between groups

Dexterity as- essments using Dextrain™	Stroke (n = 30)	Healthy con- trols (n = 30)	Group com- parison p-value
Force control of the index finger			
Tracking error (RMSE, N)	0.30 ± 0.15	0.26 ± 0.12	0.261
Release duration (ms)	566.39 ± 366.32	240.96 ± 132.37	< 0.001***
Finger individuation			
Success rate (%)	40.28 ± 31.7	67.3 ± 18.57	< 0.001***
Reaction time (ms)	1476.80 ± 385.46	1152.80 ± 173.68	0.003**
Finger individuation	0.89 ± 0.09	0.94 ± 0.04	0.013*
Max. Finger Tapping capacity			
Mean frequency (Hz)	3.12 ± 1.21	5.35 ± 0.58	< 0.001***
Timing of finger movement			
Rhythm: with audi- tory cues (%)			
1 Hz	95.47 (5.21)	96.28 (3.30)	0.536
2 Hz	93.87 (19.5)	97.77 (3.30)	0.004**
3 Hz	83.46 (17.97)	96.93 (4.51)	0.006**
Rhythm: no auditory cues (%)			
1 Hz	82.74 (45.73)	93.90 (11.40)	0.172
2 Hz	95.91 (16.16)	97.23 (3.45)	0.024*
3 Hz	90.39 (22.42)	96.09 (6.07)	0.002**

Normally distributed data given as mean ± SD; Non-normally distributed data as median (IQR). Statistical significance of tests (p-value): * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

$p < 0.001$). In the ATT DT condition, stroke patients performed more saccades to distractors but this was not significant between groups (stroke patients: 51.4 (40.2) % vs. healthy controls: 37.5 (30.55) %, $p = 0.173$). In the WM DT condition, patients generated similar amounts of saccades (72.9 (41.6) %) as did healthy controls (70.83 (22.95) %) ($p = 0.664$) (Table 3). In contrast, the Relative Saccade Count (RSC), quantifying how each participant modified saccades to dual-task demands, was significantly lower in the stroke group (14.6 (18.75) % vs. controls (26.4 (32.41) %, $p = 0.008$) (Fig. 3B).

Saccade latency and fixation duration were similar across groups, with a higher latency in the WM DT condition for both groups (supplementary results SR1).

Cognitive performance during dual-task: mental addition

In the WM DT stroke participants failed significantly more often than controls in the mental addition (stroke median addition error: 2.38 (2.43) vs. controls 0.50 (1.71), $p = 0.003$). The addition error in stroke patients correlated with total RMSE in WM DT (Spearman Rho = 0.390, $p = 0.040$) and with total RMSE in ATT DT (Spearman Rho = 0.449, $p = 0.017$). No such correlation was found

in healthy controls (Spearman Rho = 0.051, $p = 0.827$ and Spearman Rho = 0.197, $p = 0.392$, respectively).

Manual dexterity impairments in stroke

Force control of the index finger

Although stroke participants made 15% more motor errors than healthy controls (Table 4), finger force tracking error was not statistically different between groups (0.30 ± 0.15 N vs. 0.26 ± 0.12 N, $t(56) = -1.26$, $p = 0.261$, Cohen's $d = -0.04$). The release duration was significantly higher in patients (566.39 ± 366.32 ms vs. 240.96 ± 132.37 ms, $t(34) = -4.41$, $p < 0.001$, Cohen's $d = -325.4$).

Finger individuation (independence)

Stroke patients had significantly reduced success rate (% of correct trials) compared to healthy controls ($40.28 \pm 31.75\%$ vs. $67.3 \pm 18.57\%$, $t(41) = 3.83$, $p < 0.001$, Cohen's $d = 7.05$). They also had reduced capacity to individuate fingers compared to controls (0.89 ± 0.09 vs. 0.94 ± 0.04 , $t(36) = 2.6$, $p = 0.013$, Cohen's $d = 0.05$) and had higher reaction times (1476.80 ± 385.46 ms vs. 1152.80 ± 173.68 ms, $t(25) = -3.34$, $p = 0.003$, Cohen's $d = -323.9$; Table 4).

Maximal finger tapping capacity

Patients were significantly slower than healthy controls (3.12 ± 1.21 Hz vs. 5.35 ± 0.58 Hz, $t(38) = 8.86$, $p < 0.001$, Cohen's $d = 2.23$), on average by 43% (Table 4).

Timing of finger movement

The capacity to follow a rhythm was similar across groups. The PERMANOVA showed a main effect of condition (Auditory vs. No auditory cue) ($F(1,352) = 3.98$, $p = 0.044$), no effect of group ($F(1,352) = 22.37$, $p = 0.229$), no effect of frequency (1 Hz, 2 Hz, 3 Hz) ($F(1,352) = 0.73$, $p = 0.47$) no group $\times$ condition interaction ($F(1,352) = 0.009$, $p = 0.741$) and no group $\times$ frequency interaction ($F(1,352) = 1.82$, $p = 0.226$) (Table 4). Post hoc test showed a significant difference between conditions (Auditory vs. No auditory cue: 94.27 (9.17) vs. 92.55 (17.75), $p < 0.001$).

Relation between cognitive-motor interaction and manual dexterity

We used quantile regression to investigate group differences in two motor measures: Release Duration during the Finger Force-Tracking task and timing of finger movement accuracy in the Rhythm Tapping task since those two measurements were different between groups and since they represent highly impaired key components of manual dexterity in stroke [35]. In the initial models including only Group as a predictor, significant group effects were observed for both outcomes ($p < 0.001$ and $p = 0.002$, respectively). However, when Addition

error or Relative Saccade Count were included as covariates in the model predicting Release Duration, the group effect was no longer significant (Group $p=0.20$ and $p=0.053$, respectively), suggesting that these variables may account for the observed group difference. Similarly, in the model predicting timing of finger movement accuracy, the inclusion of ATT DT–Saccade Count or Addition error reduced the group effect to non-significance (Group $p=0.16$ and $p=0.09$, respectively), indicating that these covariates also explained part of the group difference in this measure.

Discussion

In this study we assessed manual dual-task capacity post-stroke by combining a visuomotor grip force task with cognitive tasks, i.e. avoidance of visual distractors and mental addition of numbers. Oculomotor recordings of saccades during the motor task allowed fine-grained investigation of cognitive dysfunction and its impact on motor control of the hand. Under dual-task conditions in stroke patients, adding a cognitive task (attentional or working memory) did not negatively impact grip force precision, contrary to controls, who showed decreased precision, as predicted. However, patients did show reduced cognitive performance compared to controls as expected, specifically reduced inhibition of saccades to distractors, i.e. more frequent unwanted saccades. Furthermore, decreased performance in the cognitive components (saccade inhibition and mental load) of the dual-task explained impairments in manual dexterity in patients.

Stroke patients did not show a dual-task effect of motor performance

In stroke patients, tracking error did not vary across task conditions. Within-group analyses revealed a dual-task effect on motor performance only in healthy controls, who showed greater motor error in the dual-task than in the single-task condition—consistent with previous findings in younger healthy adults (mean age 30 years) using the same task [11]. This dual-task motor effect was also accompanied by reduced inhibition of (unwanted) saccades, confirming the presence of a dual-task oculomotor effect with our tracking task in an older healthy control group. Nonetheless, notable age-related differences emerged when comparing the two healthy control samples: both the tracking error and the frequency of unwanted saccades toward distractors were almost three times higher in the present older controls than in the younger group. These differences may reflect common age-related changes in manual [22] and saccadic control [40]. However, these age differences do not explain the lack of a dual-task effect in stroke patients. Other possible factors are discussed below.

Task difficulty may be one factor explaining the lack of dual-task costs on motor performance in stroke patients. Force-tracking difficulty was probably higher for stroke patients since they showed twice the error in single-task tracking compared to control subjects. Force-tracking difficulty has been shown to be related to severity of the motor impairment after stroke [15]. To accommodate for this we adapted the force-level in one of the conditions to the maximal grip force strength (10%MVC). However, we did not adapt the speed constraints of the task, which may be another age-relevant factor. Nonetheless, lower motor performance in single-task tracking is in line with simple motor tasks engaging cognitive brain areas to a greater extent post-stroke [41] and it is consistent with our results showing that adding unilateral gross dexterity assessment (BBT) as a covariate explained the PERMANOVA group difference in force-tracking performance. This association with BBT is consistent with visuomotor force-tracking performance reflecting functionally important distal upper limb motor abilities [21]. McIsaac et al. (2015) proposed a dual-task taxonomy describing how performance (motor or cognitive) and attentional resources in dual-task contexts may be influenced by the novelty and difficulty of the component tasks. These factors can affect the degree of task automatization and the attentional demands required. According to this framework, resource allocation during dual-tasking can prioritize one task, or distribute attention equally, or else shift between tasks [42]. In our study, although the tasks were novel for all participants, stroke patients already exhibited motor error levels approximately twice as high as controls in the single-task condition, indicating greater baseline motor task difficulty. This higher initial impairment could have masked any potential changes in motor performance under dual-task conditions.

Another possibility is that psychomotor slowing, partly reflecting general slowing of processing speed [43], may have affected force-tracking results in the stroke patients. Slowed processing speed may have created a time-constraint not present in healthy subjects, implying that stroke patients engage more cognitive resources to achieve a similar performance as controls (who have higher processing speed). Stroke patients were also 43% slower in the maximal finger tapping task indicating significant psychomotor slowing [43]. In terms of motor performance, attentional slowness in integrating visual cues for movement, may partly explain group differences in single-task performance [44]. However, since stroke patients did show similar saccade latencies and similar number of saccades to numbers in the WM DT condition, the slowness may reside more in sensorimotor integration and movement execution than in visual perception and gaze.

Also, we cannot rule out that the tracking error measured during our grip force task may saturate. Patients may have reached a maximal level of error detectable by the method, potentially indicating a ceiling effect in the tracking error measure. However, against this explanation we noted error distributions in patients that were far from maximal values recorded (Fig. 2). Splitting stroke patients into high/low motor impairment did not change results, arguing against a ceiling effect in tracking error. Given these factors, we consider it most likely that task difficulty in the single-task was already engaging attentional resources significantly so that the expected dual-task effect in motor performance did not occur in stroke patients.

Attentional impairment after stroke

After stroke, patients may suffer from cognitive impairments, undetected by conventional screening tests (e.g. MMSE [45]), but which affect ADL and particularly eye-hand coordination [19]. Here, patients typically executed more saccades to distractors than control subjects and this despite performing similar number of saccades to relevant (working memory-related) stimuli. This led to a significantly lower Relative Saccade Count, which was related to lower accuracy in grip force control. This indicates that stroke patients had deficient inhibitory oculomotor control during the tracking task. These results are consistent with observed impairments in divided attention and inhibitory control (STROOP, TAP) and extend previous findings providing evidence of diminished dual-task saccade control in a distal manual visuomotor task [19]. Thus, reduced inhibitory control in stroke [21, 23] is most likely a common mechanism that affects oculomotor and motor control in distal [36] and proximal upper limb tasks [20].

The working memory task (mental addition) performed concomitant with the force-tracking task showed more addition errors in stroke patients compared to controls and the mental addition error correlated with deficient inhibitory saccadic control. This is indicative of conjoined impaired working memory function [46] and deficient divided attention, consistent with recent models based on task-dependent interactions between attention and working memory [46].

Relation to manual dexterity

Despite elevated ARAT scores, indicating mild hand function impairments, more detailed dexterity testing did show impaired finger force control, timing of finger movements and independent finger movements, in line with previous studies [35, 38]. We expected to find a relation between measures of cognitive-motor interaction and manual dexterity performance since manual dexterity is considered to rely on attention and memory

functions [24]. The cognitive parameters assessed during the visuomotor task (e.g. saccade count, saccade rate, or addition error) explained certain group differences in dexterity components, such as release duration (finger force-tracking) and timing of finger movements. The inhibition of saccades to distractors may serve as a proxy of divided attention capacity. The inclusion of the saccade measures in the analysis eliminated the group differences in two manual dexterity tasks requiring on-line sensorimotor integration, i.e., visuomotor control of finger force-tracking and audiomotor control in rhythmic tapping. This result suggests that stroke patients who had impaired divided attention also suffered from manual dexterity impairments, particularly in dexterous tasks requiring visuomotor and audiomotor control. This further suggests that cognitive deficits revealed in one motor task may indicate broader cognitive-motor impairments, affecting performance in other motor tasks, even in the absence of added cognitive load.

This supports that cognitive functions are involved in manual dexterity tasks requiring sensorimotor integration [22]. Our findings are in line with previous reports linking deficits in gross dexterity to impairments in motor inhibition [21], or alternatively to psychomotor slowing after stroke [44]. Thus, cognitive impairments, in particular altered inhibition and divided attention, may also affect manual dexterity, which is largely coherent but more specific than a previous meta-analysis showing a moderate association between post-stroke cognitive impairment and proximal upper limb motor improvement [3]. Our findings support cognitive-motor relation of importance for hand motor control with potential consequences for activity limitations. Use of manual dual-task exercises during rehabilitation may represent a potential untapped avenue to increase patient participation in activities of daily living and warrants further study.

Our findings also suggest several considerations for future study designs. First, including not just a single-task motor condition but also a single-task cognitive condition would help isolating and quantifying dual-task costs in the motor as well as in the cognitive domain. Second, incorporating fine finger movements into the motor component would more directly capture deficits in manual dexterity under dual-task conditions. Finally, adjusting task difficulty to each patient's capacity may allow for dual-task interference analysis while controlling for baseline performance.

Limitations

Several limitations need to be considered. Our patient sample included patients with mild-to-moderate hemiparesis and no or mild cognitive impairment (according to MMSE), leaving generalization of results to more

severe cases open. The task methodology did not include a cognitive task under single task condition, i.e., mental addition without force tracking, preventing us from calculating the direct cognitive dual-task cost and from concluding on dual-task interference in cognitive performance. Moreover, even in patients with a low level of impairment, as in our cohort, the visuomotor tracking task already seemed difficult to perform (almost 3 times more motor errors in the patients under single-task conditions), requiring a great deal of attentional resources, which points to a limitation in the design of the task. The majority of patients was in the chronic phase, although a few were 3–6 months post-stroke [47], but controlling for time since stroke in PERMANOVA did not change results. Whether the observed results are similar in the acute phase remains unclear. We only checked absence of neglect indirectly (non-clinically) during calibration of the eye-tracker: all patients and controls performed similar eye movements to all sides and corners of the computer screen. We explored cognitive-dexterity association using cognitive performance measures obtained during power-grip force tracking, thus assessing if the cognitive performance in a different task would generalize to other finger control (dexterous) tasks. A more direct approach would have been to study dual-tasking during visuomotor control of dynamic finger movements. It is likely that such task-specificity would provide stronger evidence of cognitive-dexterity relations, although this needs to be tested in future studies.

Presence, amount and type of patient rehabilitation was not documented and may have influenced results. Patient MRI was not available, ruling out study of lesion location/size relations with dual-tasking results. Further study is needed to pinpoint brain networks involved in post-stroke dual-task control [48]. Finally, the experiment was quite long (up to 3 h including pauses) and some patients reported fatigue. However, pseudo-randomized data collection should have controlled for this.

Conclusion

Sub-acute to chronic hemiparetic stroke patients did not show an increased motor performance deficit (higher tracking error) in visuomotor grip force control under dual-task conditions compared to healthy, age-matched control subjects, probably due to task difficulty (almost three-fold increase in tracking error in single-task conditions). However, patients showed cognitive performance deficits compared to controls in the dual-task, expressed as deficient oculomotor control (reduced saccade control) and poorer mental addition. The results indicate impaired divided attention (probed by saccade execution/inhibition) and reduced working memory (probed by mental addition) during distal upper limb movements in stroke. Manual dexterity performance, separately

quantified, was affected in stroke. Group differences in these dexterity tasks requiring on-line sensorimotor integration were partially explained by alterations in dual-task divided attention (increased saccades to distractors and increased addition error). These findings highlight the importance of cognitive-motor interaction in impaired manual dexterity and its consequences for activity capacity post-stroke. The impact of diminished cognitive-motor interaction on recovery of upper limb function, including manual dexterity, needs to be considered and explored to optimize efficacy and ADL-relevance of post-stroke therapy.

Abbreviations

MVC	Maximal voluntary contraction
BBT	Box and blocks test
MPUT	Moberg pick up test
ARAT	Action research arm test
MAL	Motor activity log
MMSE	Mini mental state examination
TAP	Test of attentional performance
ATT DT	Attentional dual-task
WM DT	Working memory dual-task
RMSE	Root mean square error
RSC	Relative saccade count

Supplementary Information

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Additional file 1.

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Author contributions

PGL and JLM designed the study, GT, CR, LD, DC, SH helped find stroke patients to include, QB developed task and analyzed the data, LC created the visuomotor task, ED, CVR and SM ran experiments and acquired data, ED, PGL and MAM wrote the manuscript. All authors read and approved the final manuscript.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was performed according to the declaration of Helsinki. This study received approval of regional ethics committee (19.12.2057753 (2020/08) CPP QUEST III).

Consent for publication

Not applicable.

Competing interests

MAM and PGL have patented the method for multidimensional measurement of manual dexterity (WO2016184935A3). PGL is founding member of start-up company Dextrain (started in 2021) and reports no financial gain in advising the company. CR is a member of the scientific board of the company but receives no financial benefits. The other authors report no financial interests or potential conflicts of interest.

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