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Using virtual reality-based neurocognitive testing and eye tracking to study naturalistic cognitive-motor performance

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ABSTRACT

Natural human behavior arises from continuous interactions between the cognitive and motor domains. However, assessments of cognitive abilities are typically conducted using pen and paper tests, i.e., in isolation from "real life" cognitive-motor behavior and in artificial contexts. In the current study, we aimed to assess cognitive-motor task performance in a more naturalistic setting while recording multiple motor and eye tracking signals. Specifically, we aimed to (i) delineate the contribution of cognitive and motor components to overall task performance and (ii) probe for a link between cognitive-motor performance and pupil size. To that end, we used a virtual reality (VR) adaptation of a well-established neurocognitive test for executive functions, the 'Color Trails Test' (CTT). The VR-CTT involves performing 3D reaching movements to follow a trail of numbered targets. To tease apart the cognitive and motor components of task performance, we included two additional conditions: a condition where participants only used their eyes to perform the CTT task (using an eye tracking device), incurring reduced motor demands, and a condition where participants manually tracked visually-cued targets without numbers on them, incurring reduced cognitive demands. Our results from a group of 30 older adults (>65) showed that reducing cognitive demands shortened completion times more extensively than reducing motor demands. Conditions with higher cognitive demands had longer target search time, as well as decreased movement execution velocity and head-hand coordination. We found larger pupil sizes in the more cognitively demanding conditions, and an inverse correlation between pupil size and completion times across individuals in all task conditions. Lastly, we found a possible link between VR-CTT performance measures and clinical signatures of participants (fallers versus non-fallers). In summary, performance and pupil parameters were mainly dependent on task cognitive load, while maintaining systematic interindividual differences. We suggest that this paradigm opens the possibility for more detailed profiling of individual cognitive-motor performance capabilities in older adults and other at-risk populations.

1. Introduction

Neurocognitive testing is a general term for clinical tests aimed at assessing specific cognitive abilities in different domains, e.g., attention, memory, language, and perception (Kolb and Whishaw, 2009; Strauss et al., 2006). These tests are mostly used in the clinic for detecting potential cognitive decline in populations at risk, such as older adults (Craik and Bialystok, 2006). The method of administration is usually through pen and paper tests (P&P), or by simple digital translations (e.g., tablets or PCs; Bauer et al., 2012). However, cognitive functioning in "real life" is not done in isolation, but typically operates synergistically with other functional components - namely motor execution, sensory

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perception, and affective state. Consequently, assessing cognition in isolation from "real life" multifactorial behaviors and in artificial contexts might hinder the ecological validity of the outcomes (Chaytor and Schmitter-Edgecombe, 2003). This drawback is especially evident when attempting to assess executive functions (EFs), which are higher-order cognitive abilities that involve cognitive processing for action regulation (Chan et al., 2008). Therefore, EFs are an example of a function that inherently employs cognitive-motor interactions.

Virtual reality (VR) has recently been proposed as an emerging tool for enhancing ecological validity of assessment tools while preserving controlled settings and online behavior tracking (Parsons, 2015). Within this framework, VR cognitive assessment tools, particularly for the evaluation of EFs, have been developed based on standard neurocognitive tests (Borgnis et al., 2022; Sokolov et al., 2020). One such test is the 'Color Trails Test' (CTT), a common trail-making test for the assessment of visual attention abilities, specifically endogenous, sustained visual attention, working memory and low-level semantic processing (D'Elia et al., 1996). The test consists of two parts – Trail A in which participants need to follow a trail of numbered targets in ascending order (measures sustained visual attention), and Trail B in which participants perform the same sequencing while also alternating between two colors (measures divided attention and task switching). We have recently developed a VR version of the CTT (VR-CTT), in which examinees are immersed in a 3D environment and need to perform full reaching movements in order to follow the trail of targets, while the kinematics of their reaching arm and head are recorded (Ben Gal et al., 2019; Galor et al., 2022; Lustig et al., 2023; Plotnik et al., 2017, 2021; Wilf et al., 2022). As a validation step, completion times of the VR-CTT were compared to those of the standard pen and paper CTT (P&P-CTT), and were found to be significantly correlated, but overall longer (Plotnik et al., 2021).

The main advantage of the VR-CTT setup is that it enables a richer evaluation of cognitive abilities, in a more naturalistic context, while employing and measuring simultaneous motor execution (Wenk et al., 2019). This, in turn, can lead to more accurate profiling of individual performance in the cognitive domain, motor domain, and in cognitive-motor interactions. Such profiling can be especially advantageous in older adults, since both these functions and their interactions have been shown to decline with age (Ren et al., 2013), with the rate and extent of decline varying across individuals (Christensen, 2001; Wollesen and Voelcker-Rehage, 2019). Correspondingly, older adults show longer and more variable CTT completion times than young or middle-aged adults, in both P&P and VR platforms (D'Elia et al., 1996; Plotnik et al., 2021). However, drawing clinical conclusions from the VR-CTT scores can be challenging, since changes in the participants' performance might be due to alterations in either cognitive abilities, motor abilities, or both. In order to characterize cognitive-motor interactions during VR-CTT execution in older adults, and to understand the contribution of motor execution and cognitive processing to overall VR-CTT performance, there is a need for a paradigm that can dissociate these two components.

Therefore, in the current study, we developed a novel paradigm based on the VR-CTT that attempts to tease apart the cognitive and motor components of task execution through the following conditions: (i) full VR-CTT performed with the hand ('HandCTT') (ii) a condition where VR-CTT is performed with the eyes only, requiring less motor activity ('EyesOnlyCTT') (iii) a condition where similar manual actions are made without the number sequencing task, thus requiring lower cognitive processing ('NoNumbersCTT').

While the motor and cognitive aspects of a task are often considered separately, they often overlap and cannot be fully dissociated. Rather, during various tasks there is interplay between what are typically called cognitive and motor features. For example, while the selection of where to look and how long to look in visual search would typically be termed "cognitive", and the speed of the eye movements would be considered more "motor", both aspects appear to be controlled by a single mechanism (Yoon et al., 2018) that maximizes reward. Similarly, kinematic features of goal-directed arm movements vary as a function of executive control, as can be observed when looking at people with different working memory capacities (Erb et al., 2021). Studies of sustained attention have also shown that motor aspects (i.e., the selection of speed) interact with measures of sustained attention (Dang et al., 2018). The separation to 'cognitive' and 'motor' conditions is not entirely mutually exclusive also in our current paradigm: the more 'cognitive' condition, i.e., and EyesOnlyCTT, requires head rotations and eye movements, and the 'motor' condition, NoNumbersCTT, is not completely devoid of cognitive processing, and still requires exogenous spatial attention.

In terms of neural substrates underlying task execution – the cognitive aspect relies on dorsal (goal-directed) and ventral (stimulus-driven) attention networks (with the addition of working memory systems and semantic processing pathways for the more cognitively demanding tasks) which are updated based on visual sensory inputs and task demands (Corbetta and Shulman, 2002). These cognitive mechanisms in turn direct motor regions for executing the task-appropriate eye movement (through area frontal eye field; 'FEF') and/or hand reaching (through motor regions and parietal reach regions in the inferior parietal sulcus; 'IPS') areas via top-down interactions (Culham et al., 2003). These factors (i.e., visual search, executive function, and sustained attention) are all integrated during our task, but specific abilities of information processing and task performance might vary between participants more prominently in the motor domain, the cognitive domain, or in the effectiveness of executive control of both these domains and their interaction.

Furthermore, to fully elucidate the factors contributing to cognitive-motor performance, one needs to take into account also physiological signals indicating the autonomic nervous system (ANS) reactivity, which might infer the state of the individual in terms of vigilance and concentration (Oken et al., 2006). One prominent physiological signal that has been associated with cognitive performance is pupil dilation: It has been shown that increases in cognitive task demands lead to increased pupil dilation (Krejtz et al., 2018), and that individuals with larger pupil dilations show better performance than those with smaller pupil dilations (Tsukahara et al., 2016). However, like many cognitive assessment paradigms, most tasks that measured pupil dilation were lab-designed and non-naturalistic (for review see van der Wel and van Steenbergen, 2018). It is still largely unknown how pupil dilation reflects cognitive load and cognitive-motor performance during a naturalistic task. Here, we recorded pupil dilation during all conditions of VR-CTT performance to probe for task-induced modulations and inter-individual differences accounting for performance.

Lastly, we aimed to test the potential usability of the VR-CTT paradigm for clinical profiling of individuals in terms of cognitive and motor abilities. One potential use is for fall-risk assessment in older adults. Falls are the foremost cause of death and disability in adults over 65 (www.cdc.gov). Since both cognitive and motor impairments have been implicated in fall-risk and gait impairments (Demanze Laurence and Michel, 2017; Montero-Odasso et al., 2019), and since declines in both cognitive (Bettio et al., 2017; Ren et al., 2013) and sensorimotor (Seidler et al., 2010) functions are well-established in the aging population, we aimed to test as a proof-of-concept whether VR-CTT on older adults can be related to fall-risk.

In summary, our novel VR-CTT paradigm aims to dissociate and characterize cognitive and motor components of naturalistic cognitive-motor task performance in older adults, while accounting for the underlying physiological state. Specifically, we test how cognitive load and motor demands affect behavior in the cognitive (processing time, visual search time, completion times, errors), motor (hand kinematics, head-hand coordination), and physiological (pupil dilation) domains. We hypothesize that the amount of cognitive load will influence all these domains, with a milder contribution of motor demands. Lastly, we test the potential clinical relevance of these parameters, with the working hypothesis that the participants' clinical profiles will be reflected in their VR-CTT performance measures.

2. Materials and methods

2.1. Participants

Data was collected from 30 healthy older adults [age: 73.5 ± 6.0 (mean ± SD), education years: 15.9 ± 3.2 (mean ± SD), 13 females and 17 males]. Exclusion criteria were using a walking aid, severe sight loss, neurodegenerative or acute orthopedic disease and psychiatric or cognitive conditions that may interfere with understanding the instructions or completing the required tasks (determined by screening interviews). The protocols were approved by the Sheba Medical Center institutional review board (IRB), and all participants signed informed consent before enrolling in the study. Sample size was determined based on our previous work by Plotnik et al. (2021).

2.2. Apparatus and procedure

All 30 participants underwent fall-risk questionnaires, Montreal Cognitive Assessment (MoCA), and P&P CTT at the beginning of the experimental session. Then the participants underwent VR-CTT under three different conditions (see below) and functional fall-risk assessment tests. To minimize learning effects, the three VR-CTT tests were not performed consecutively but instead were interleaved with functional fall-risk assessment tests. To eliminate session order bias, a randomized table was created prior to participant recruitment, which included a randomized order of the VR-CTT versions and the functional fall-risk assessment tests (see below).

2.2.1. Clinical assessments

The fall risk questionnaires consisted of the Activities-specific Balance Confidence (ABC) Scale and the primary fall risk assessment questionnaire. The Montreal Cognitive Assessment (MoCA) was conducted at the beginning of the experimental session by the same examiner (A.K.) in all 30 participants. Then, all participants performed the standard P&P version of the CTT (Trails A and B; see Fig. 1A). The P&P-CTT includes two parts: Trails A and Trails B. In Trails A, the participant draws a line to connect one set of 25 circles numbered 1–25, colored intermittently yellow or pink (these colors are perceptible as different colors also by colorblind individuals; D'Elia et al., 1996). In Trails B the participant performs the same task while alternating between colors, each number appears on both a yellow and a pink circle (for a total of 50 colored circles), and the participant needs to move from 1-pink to 2-yellow to 3-pink, etc. In the P&P-CTT, the colored circles appeared on an A4 page. Participants used a pen to connect the circles and were instructed not to lift the pen from the paper. Participants

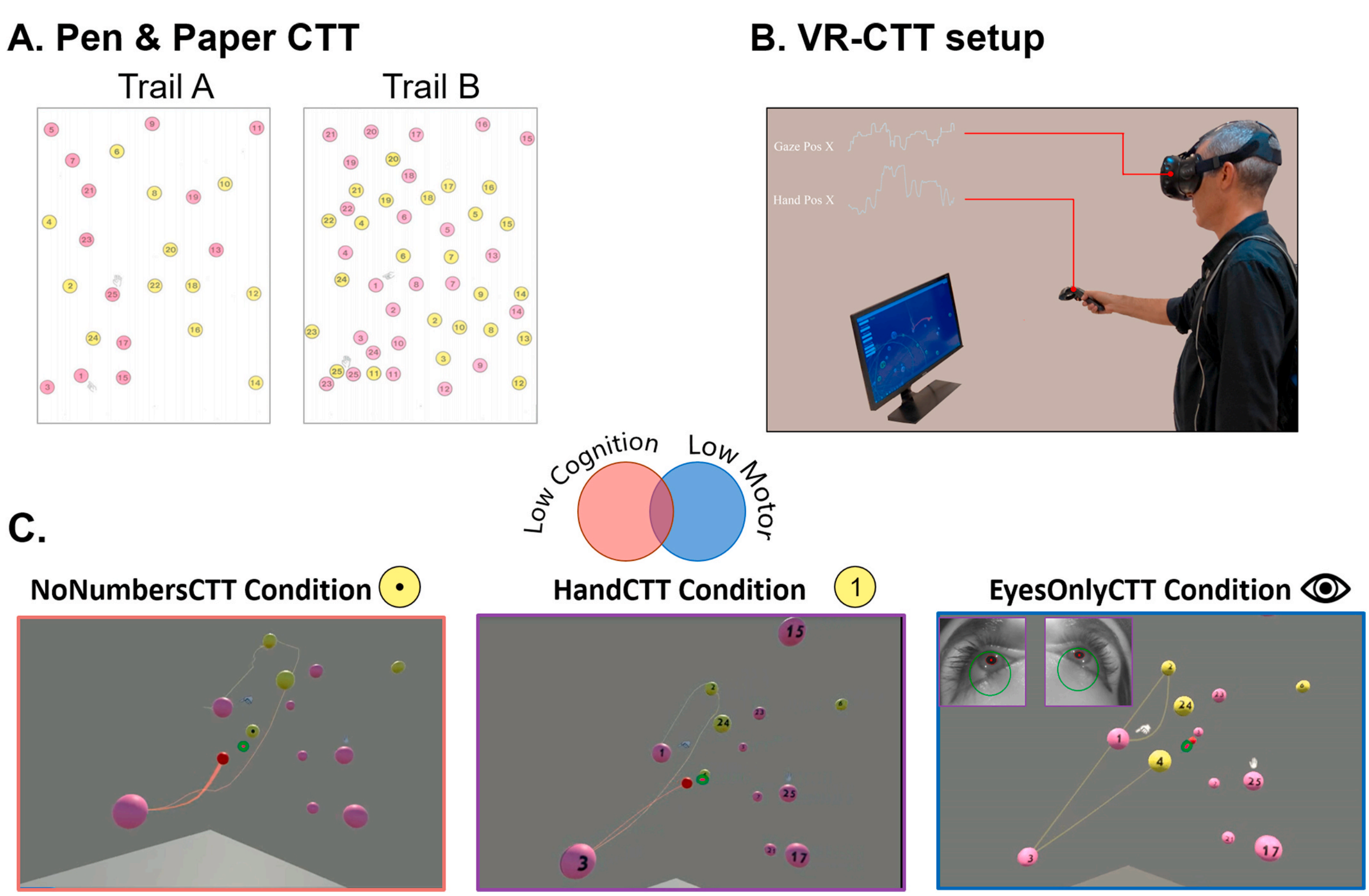

Fig. 1. Experimental paradigm. A group of 30 older adults (age>65) performed Trail A (sustained visual attention) and Trail B (divided attention) of the Color Trails Test (CTT). (A) Standard pen and paper (P&P) CTT. In Trails A participants connect the numbered circles in ascending order, and in Trails B participants perform the same sequencing while also alternating between colors (D'Elia et al., 1996). (B) Experimental setup for VR-CTT. Participants were immersed in VR via a head-mounted device (HTC-VIVE) integrated with eye tracking (Pupil Labs) and performed reaching movements to follow the trail of targets in a 3D space, while motor (hand, head) and eye (gaze direction, pupil dilation) signals were recorded. (C) The VR-CTT was performed under three conditions: (middle) full CTT execution performed manually ('HandCTT'); (Right) CTT performed only with the eyes ('EyesOnlyCTT'); (Left) A low cognition condition in which no numbers appeared on the balls and participants had to hit each time the target cued with a black dot, following the same spatial sequence as the CTT conditions ('NoNumbersCTT'). The red ball represents the participants' hand position throughout the test, and the green circle represents the participants' gaze position (this gaze position was not visible to participants during the experiment, except in the EyesOnlyCTT condition where the red ball corresponded to gaze position).

always performed Trails A first and then Trails B, with a practice session comprising eight targets preceding each part to acclimatize them to the task (D'Elia et al., 1996). The examiner used a stopwatch to record the total completion times of Trails A and Trails B and manually logged the number of errors.

Functional fall risk assessment tests included Timed Up and Go (TUG), Four Square Step Test (FSST), three different measurements were collected for gait speed: 10 m walking at a comfortable speed, 10 m walking at a fast speed, and 10 m walking while performing a dual task (counting backwards from a random number while subtracting 3).

2.2.2. Main VR-CTT experiment

VR-CTT data was collected using immersive 3D virtual reality via a head-mounted device (HMD) with an integrated eye tracking system (Pupil Labs; Germany). Participants used their dominant arm to move a motion capture pointer freely in the 3D space (Fig. 1B; HTC-Vive; New Taipei City, Taiwan). A 3D VR translation of the P&P-CTT was created using UnityVR software (version 2018.3.12f1), where the spatial configuration of the targets followed similar principles to those of the P&P-CTT, except that the targets were dispersed in a larger range of 4.2/5.9 virtual meters horizontally (corresponding to 122/119° visual angle) and 2.0/1.5 virtual meters vertically (corresponding to 62/52° visual angle) in Trails A and Trails B, respectively, and had an additional depth dimension (see Video 1; Plotnik et al., 2021). Eye movements and pupil size tracking were obtained throughout the VR-CTT session.

At the beginning of each VR-CTT condition, participants performed eye tracking calibration via the Pupil Labs plugin for Unity. To ensure well-calibrated tracking, this was followed by a tracking quality check where participants had to gaze sequentially at a grid of five balls evenly scattered in space. Only once calibration was successful, the VR-CTT was launched. Participants performed VR-CTT under three different conditions: HandCTT, EyesOnlyCTT, and NoNumbersCTT (see details below). The spatial configuration of the targets was identical between conditions, to control for target distances and relative positions.

2.2.2.1. HandCTT condition (Fig. 1C; middle). In the HandCTT condition, participants had to hit the targets with their dominant hand by executing 3D hand movements that moved a small red virtual ball representing their 3D hand position. Complete hand, head, and eye kinematics were recorded throughout each session (see Video 1). When a correct target was hit, the target ball inflated. An audible error signal (i.e., a buzz) was heard if the participant touched the wrong target. A continuous trace of the path the red ball effector made was visible throughout the test. As in the P&P test, participants performed first Trails A and then Trails B. Before each part, participants performed two practice sessions: an 8-target practice, as with the P&P, to get acclimatized to the task procedure and the media, and an additional 8-target practice session with a wider spatial range of the targets to practice a larger search range and larger hand movements.

2.2.2.2. EyesOnlyCTT condition (Fig. 1C; right). In the EyesOnlyCTT condition, participants had to perform the cognitive CTT task, but hit the targets by using their eye movements only (without using the hand), which controlled a small red virtual ball representing their gaze in the 3D space (see Video 1). This was implemented by transmitting the 3D coordinates of the gaze from the eye tracking system into a Unity-based game object. Since in order to detect the correct target, the gaze had to pass through many other target balls (sometimes even during saccades), a threshold was set for determining a true 'intentional fixation' on a ball object. An 'intentional gaze fixation' was thresholded to 100ms for correct targets and 500ms for incorrect targets. This was done to optimize the feedback provided to participants on correct and erroneous hits and enable the smooth flow of the test performance. When the participant hit the correct target, in order to maintain the impression that a trace is performed between targets, a curved path was drawn between the previous target to the current target (similar to the trace drawn in the full VR-CTT condition). At each time point, only traces connecting the previous 4 target balls were visible.

Both Trails A and Trails B were performed with an additional two practice sessions prior to each Trail. Eye-tracking data of three participants were removed from the final analysis due to noisy signal. Although all subjects went through a calibration process in the pupil lab software, these subjects' eye movements tracking quality was low, leading to an unstable signal. This made completing the EyesOnlyCTT task more difficult and cumbersome, which in turn increased unproportionally the completion time of the task.

2.2.2.3. NoNumbersCTT condition (Fig. 1C; left). In the NoNumbersCTT condition, participants had to hit targets using the controller with their dominant hand, but without performing the cognitive CTT task. Instead, in this version, the colored ball objects (same locations and colors as in the HandCTT condition) had no numbers on them (empty balls), with only a black dot appearing on the desired target. After hitting the target, the black dot would move to the next target indicating the new target location, and so on (see Video 1). Participants performed Trails A and B of the NoNumbersCTT condition, with two practice sessions before Trails A. Both trails had essentially identical tasks, with the only difference being that Trails A had 25 balls and Trails B had 50 balls.

2.3. Data analysis & statistical tests

All analyses were performed using MATLAB (version R2020b, MathWorks, Natick, MA, USA) and Microsoft Excel, with complementary statistical analysis in JASP software (version 0.16.3.0).

2.3.1. Task completion times

Task Completion time (the time between hitting target #1 to hitting target #25) for each CTT version, including Trails A and B, was measured by the UnityVR software and was extracted for statistical analysis using MATLAB. Then, a 2-way Repeated Measures ANOVA was used to compare the mean completion time values, with factors Condition (HandCTT/EyesOnlyCTT/NoNumbersCTT) and Trail (A/B). Spearman's rank correlation coefficient was used for comparing all VR-CTT versions including the P&P-CTT.

2.3.2. Hand kinematics signal segmentation into search and execution periods

The 3D arm movements trace of each full test condition was segmented into two main periods: search time and execution time (see also Ben Yair et al., 2023). During the search periods, the participant scans the VR environment until target detection. The execution period starts after target detection when the arm starts moving towards the target and ends right after the participant hits the target.

We opted for an algorithm that can detect movement execution onset during VR-CTT based on hand kinematics alone (to be used also when no eye tracking is available). Therefore, we used kinematic parameters (i.e., 3D hand velocity and the Euclidean distance from the relevant target) for detecting 'towards the target movement onset' and validated it against manual scoring using the eye tracking videos of the VR-CTT experiment (i.e., 'gold standard', verifying that indeed reaching movement towards the target starts only after visual detection of the target). See full description of this validation procedure in the supplementary material.

The execution onset was defined as the initiation time of the reaching movement towards the target. This was detected using the 3D hand velocity and the Euclidean distance from the relevant target. Specifically, in order to determine the execution onset of the relevant reaching movement, the following steps were performed for every trial (a trial is defined as the period between two consecutive ball hits, i.e., 24 trials per test):

(a) Identification of all the peaks in velocity profile during the period relevant for movement onset – i.e., where the hand was moving towards the target (Euclidean distance was decreasing; see Fig. 2; bottom) up until the hand reached a distance of 0.4 m from the target (to avoid including jittering movement around the target).
(b) Removal of velocity peaks that are smaller than 1 virtual meter per second (to remove small jittering movements).
(c) Once all the peak velocities above criteria were identified, we tested whether these peaks were part of the same reaching movement or part of two or more different movements (in which case only the last movement will be selected as the one leading to target hit). This was done by testing whether there was a period between each pair of consecutive peaks in which the distance from the target increased by 0.01 or more virtual meters (i.e., moving away from the target). In such cases, the peaks were classified as part of two distinct reaching movement, and the later peak between the two was determined as the peak of the execution. In case the hand was not moving away from the target between either of the peaks in the trial, they were all considered as part of the same execution movement and the first peak was defined as the relevant execution peak.
(d) Once the relevant execution peak velocity was detected, the execution onset was determined as the closest local minimum (velocity trough) before it (i.e., the start of the relevant movement; see Fig. 2; top).

These parameters for detecting movement onset were validated against the gaze data (i.e., 'gold standard'). See full description of this validation procedure in the supplementary material.

The execution offset was determined as the first local minimum of the hand velocity after the target was hit (see Fig. 2; top).

As outcome measures, the total search duration and the total execution duration of the entire trial were each calculated by summing all search durations of all target hits and separately the execution durations.

Finally, the mean execution velocity was calculated by averaging all the hand velocities during execution of all target hits.

For statistical analysis, a 2-way Repeated Measures ANOVA was used to compare the mean values, with factors Condition (HandCTT/NoNumbersCTT) and Trail (A/B). The EyesOnlyCTT condition was not included in these analyses since it contained no hand movements.

2.3.3. Head-hand coordination

Head-hand coordination was quantified by applying cross-correlation analysis on head yaw rotations and hand left-right translation (x coordinates) using MATLAB (Lustig et al., 2023). This analysis was performed on each test condition (the full test period was taken for analysis) and yielded two values: (1) The maximal correlation coefficient between the signals, representing head-hand spatial coherence (2) The temporal lag between the head and hand movements when the maximal correlation was obtained (the optimal lag), representing the temporal synchrony between the head and the hand (see Fig. 3 for demonstration). Both the correlation coefficient and the lag values were taken for further statistical analysis - Repeated Measure ANOVA with factors Condition (HandCTT/NoNumbersCTT) and Trail (A/B). Again, the EyesOnlyCTT condition was not included in these analyses since it contains no hand movements.

2.3.4. Pupil dilation

Raw pupil data was extracted from 'Pupil Labs Player' software for each test condition separately and was preprocessed using MATLAB. Preprocessing included median filter, identification of non-valid samples, which were replaced with interpolation of valid samples, calculation of the mean pupil diameter signal from the valid raw samples of both left and right pupils, and applying a 4th order low-pass Butterworth filter with a cutoff of 2Hz (Kret and Sjak-Shie, 2019), based on the analysis toolkit from https://github.com/ElioS-S/pupil-size.

The algorithm calculated the confidence level for each pupil signal based on the percentage of removed samples during acquisition and signal preprocessing. The confidence value was then used as an exclusion criterion, whereby tests in which the signal confidence was below 70% were excluded from the statistical analysis. This procedure resulted in the exclusion of all task conditions of one participant from the pupil analysis, exclusion of HandCTT and NoNumbersCTT pupil data from another participant, and NoNumbersCTT Trials A from another participant, resulting in 27/28 participants taken into account in the pupil dilation analyses (depending on the condition). There was no significant difference between the experimental conditions in the overall signal

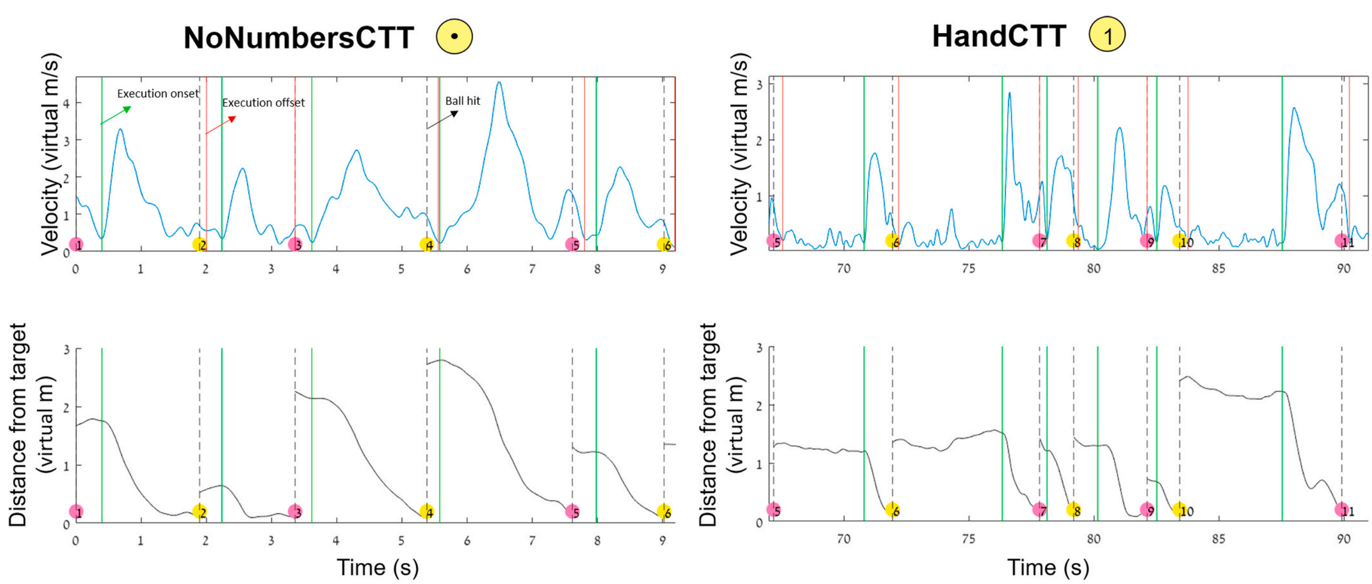

Fig. 2. Segmentation of hand kinematic signals to search and execution periods. An example of segmentation from a NoNumbersCTT and a HandCTT trial. Blue trace denotes the 3D velocity of the hand (in virtual meters/sec). The black trace denotes the hand's Euclidean distance from the next target (in virtual meters). The green vertical lines denote the execution onset, the red vertical lines denote its offset, and the dashed line denotes target hit time. Note that the search time is longer in the HandCTT condition (right side) than in the NoNumbersCTT condition (left side). This segmentation process was applied to HandCTT and NoNumbersCTT Trails A and B of all participants.

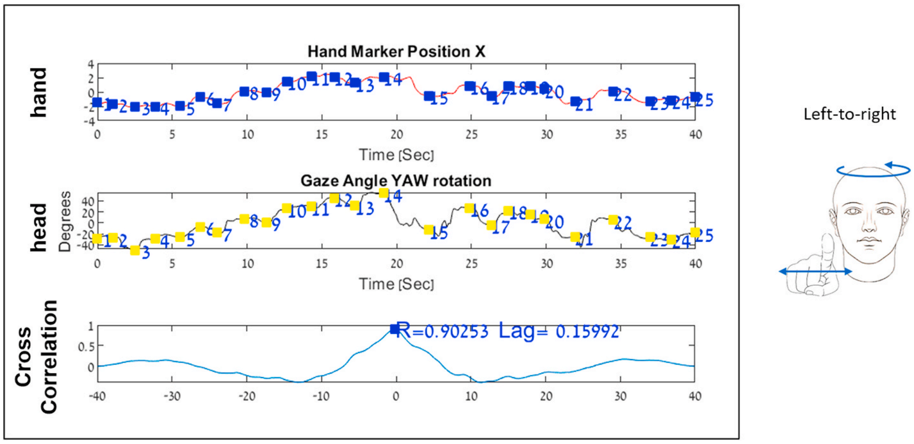

Fig. 3. Head-hand coordination during VR-CTT. Example traces of hand movements (top) and head rotations (middle) along the right-left direction during a VR-CTT task. Colored squares represent the times when the hand hit the target. (bottom) an example of quantifying head-hand coordination using a cross-correlation analysis between head and hand, yielding outputs on both the spatial and the temporal coupling between these two effectors (Lustig et al., 2023). R value represents the maximal correlation value indicating spatial coherence, and Lag value represents the temporal lag between the signals in which the maximal correlation appears, indicating temporal synchrony of these two effectors (head always leads and the hand follows). This analysis was applied to HandCTT and NoNumbersCTT Trails A and B of all participants.

confidence (mean ± SD HandCTT 82 ± 11%, NoNumbersCTT 83 ± 11%, EyesOnlyCTT 84 ± 10%; $p > 0.65$ for rmANOVA across conditions).

Notably, while the occasional signal loss during the experimental runs was handled post-hoc by the interpolation process, it presented a more significant problem during the EyesOnlyCTT runs. The reason for this was that the participants had a continuous visible representation of the gaze position, as a red ball effector. The occasionally unstable representation of the red ball effector, together with the rapid and fidgety nature of free eye movements, caused it to be an unstable, flickery visual stimulus (unlike the red ball representing the hand in the other conditions). This rapid change in physical light conditions might have contaminated the pupil signal and might have caused unreliable pupil dilation values (Drew et al., 2001). Therefore, the data from the EyesOnlyCTT condition was completely excluded from the pupil dilation analysis.

For statistical analyses, to assess the total pupil dilation while not considering transient fluctuations of pupil size, the median pupil dilation value was extracted for each condition (CTT/NoNumbersCTT – Trails A and B). Then a paired *t*-test was performed to compare HandCTT and NoNumbersCTT conditions within each Trail. A direct comparison between trails was not possible, since Trails B had double the number of Target balls compared to Trails A, which caused a substantial difference in luminosity, in turn possibly masking and confounding any pupil dilation results.

Then, the pupil dilation index was generated for each participant by averaging their median pupil dilation values for all tests. This pupil Index was taken for further Spearman correlations with task completion times.

Finally, to quantify the additional pupil dilation response in the more cognitively demanding condition as compared to the less cognitively demanding condition, we computed for each participant the normalized delta pupil size by using the following formula, separately for Trails A and Trails B: $\frac{PupilHandCTT - PupilNoNumbersCTT}{PupilNoNumbersCTT}$.

2.3.5. *Relation to fall-risk analysis*

The participant cohort was divided into two subgroups – fallers and non-fallers. A participant was classified as a 'faller' if they reported having a fall during the year prior to the experiment in the Primary fall risk questionnaire. This division resulted in 7 'fallers' and 23 'non-fallers'.

Then, only for qualitative assessments (since the Fallers group had a very small number of participants), mixed-design ANOVA tests were performed, with between-subject factor of group (Faller/Non-Faller), and within subject factors of Trail (A/B) and Condition (CTT/NoNumbersCTT/EyesOnlyCTT). This was applied for the task completion times, Head-Hand lag, mean execution velocities, and pupil sizes. The p-value for the main effect of group (Fallers/Non-Fallers) was extracted.

3. Results

3.1. *Participants demographics*

Data was collected from 30 healthy older adults (age >65), which were screened to eliminate neurological/psychiatric disorders and physical disability (see methods). All the participants went through a battery of fall-risk functional tests, answered two fall-risk questionnaires and performed a MoCA. Table 1 shows the demographics and the outcome of the clinical measurements for our group of participants. In all the functional tests, questionnaires and MoCA there was no

Table 1
Participants demographic and clinical measurements.

	Mean	Std. Deviation	Range
Demographics			
Age	73.4	6.0	28.0
Education years	15.8	3.1	15.0
Questionnaires	Mean	Std. Deviation	Range
MoCA	24.5	3.9	19
Primary Fall Risk Quest.	21.1	10.4	44
ABC's Fall Risk Quest.	21.4	6.7	25
Fall-risk functional tests	Mean	Std. Deviation	Range
TUG	9.5s	1.6s	6.0s
FSST	10.9s	2.4s	10.0s
10 M walk	8.6s	1.6s	6.5s
10 M walk – fastest	6.0s	1.1s	4.0s
10 M walk + Dual task	11.0s	3.1s	11.0s

MoCA - Montreal Cognitive Assessment
ABC - Activities-specific Balance Confidence Scale
TUG - Timed Up and Go
FSST - Four Square Step Test

significant difference between male and female participants (smallest p = 0.116).

3.2. Task completion times

A total of 30 older adults (age >65) performed trails A and B of the three different VR-CTT conditions ('HandCTT', 'EyesOnlyCTT', and 'NoNumbersCTT'; see Fig. 1). The data of the 'EyesOnlyCTT' condition for three of the participants were excluded due to noisy eye tracking (see methods), leading to a total of 27 participants who completed the full set of tasks. Fig. 4A presents task completion times of Trails A and B in the three different VR-CTT conditions (see also Table 2 for details). We found a significant main effect of Condition ($F(2,26) = 98.8$; $p < 0.001$; $\eta^2 = 0.52$), a main effect of Trail ($F(2,26) = 182.8$; $p < 0.001$; $\eta^2 = 0.17$), and an interaction between them ($F(2,26) = 48.6$; $p < 0.001$; $\eta^2 = 0.098$). The HandCTT condition, in which participants completed the cognitive task using their hand, yielded the longest completion times, with significantly longer completion times in Trails B compared to Trails A ($p_{bonf} < 0.001$; Cohen's $d = 1.92$). Reduced motor demands, as expressed in the 'EyesOnlyCTT' condition where participants performed the cognitive task using their gaze only, showed slightly decreased completion times ($p = 0.016$; Cohen's $d = 0.47$; post-hoc comparison between HandCTT and 'EyesOnlyCTT'), while maintaining differentiation between Trails A and B ($p_{bonf} < 0.001$; Cohen's $d = 1.84$). Reduced cognitive demands, as expressed in the NoNumbersCTT condition where participants used their hand to trace a series of cued targets without a cognitive task, yielded a more significant reduction in completion times ($p_{bonf} < 0.001$; Cohen's $d = 2.48$; post-hoc comparison between HandCTT and NoNumbersCTT), with no differentiation between Trails A and B ($p > 0.5$; the lack of cognitive task also meant similar task demands in Trails A and B, but with Trails B having more empty ball distractors). We then assessed the number of errors in each task (i.e., the number of times the participant hit the wrong target) and found almost no errors in NoNumbersCTT A, NoNumbersCTT B and HandCTT A (median = 0 errors), and a slightly higher number of errors in HandCTT B (median = 2). The errors in the EyesOnlyCTT condition could not be appreciated due to technical reasons, i.e., when participants' gaze was passing through other targets while scanning the field of view.

In summary, we found that completion times increased mainly in correspondence with the amount of cognitive load (Trails B > Trails A > NoNumbersCTT) and were more mildly influenced by motor demands (CTT > EyesOnlyCTT).

Next, to assess similarities in performance level of each participant across the different conditions, we correlated between completion times of Trails A and B in the different tasks (CTT, NoNumbersCTT, EyesOnlyCTT, P&P-CTT). Fig. 4B shows pairwise Spearman correlations between the different CTT trails and conditions. We found medium-high correlations between Trails A and B of the same task condition (except for the EyesOnlyCTT condition), suggesting that the relative performance of participants remained similar between Trails A and B of each task (e.g., participants who had relatively short completion times in Trails A also had relatively short completion times in Trails B). Additionally, we found significant correlations between the different conditions – first, the P&P-CTT was significantly correlated to almost all VR-CTT tasks. Even though the spatial configuration and the motor execution patterns were very different between the P&P and the VR tasks, the relative performance level was comparable - i.e., participants who performed better in the P&P-CTT were also better in the VR-CTT tasks (in agreement with previous findings presented in (Plotnik et al., 2021)). Within the VR tasks, all the tasks and trails were largely correlated, except for the relation between NoNumbersCTT and EyesOnlyCTT condition, which showed the lowest correlations ($0.24 \leq r_s \leq 0.41$). This result is in line with the study assumptions: since these two conditions were designed to capture different components of the VR-CTT task, they each correlated with the full VR-CTT, but not directly with each other (for instance, an individual who has good motor capabilities, but lower cognitive capabilities might perform relatively well in the NoNumbersCTT condition, but poorly in the EyesOnlyCTT condition).

Taken together, these results suggest that within each individual, the amount of cognitive task load and motor demands each contribute to some extent to the overall CTT completion time, and at the interindividual level, performance under the different task conditions was comparable to some extent, reflecting the overall performance level of each individual in cognitive-motor (or visuospatial) tasks.

3.3. Hand kinematics

Our setup enabled us to deepen our investigation into the kinematics

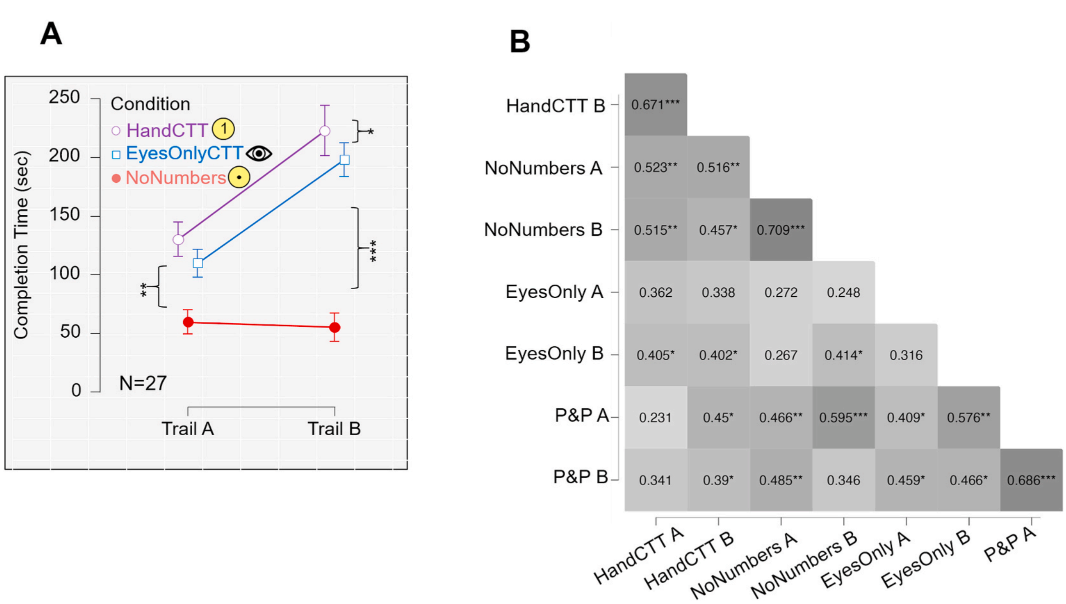

Fig. 4. Test completion times across the different VR-CTT conditions. (A) Average completion times in Trails A and B of the different VR-CTT tasks. Error bars denote standard error of the mean (SEM). (B) Spearman correlation matrix between Trails A and B of the different task conditions. Darker colors denote stronger correlations and brighter colors denote weaker correlations. Cells marked with an asterisk represent significant correlations. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. NoNumbersCTT = low cognition; P&P = Pen & Paper.

Table 2
Calculated outcome measures for all test conditions (mean ± SEM).

		HandCTT		NoNumbersCTT		EyesOnlyCTT	
		Trails A	Trails B	Trails A	Trails B	Trails A	Trails B
Completion time	t (s)	130.0 ± 11[a]	227.4 ± 16[a]	60.3 ± 3.4[a]	56.2 ± 2.1[a]	109.8 ± 7.6 [a]	198.0 ± 9.0[a]
Total Search Duration	t (s)	80.7 ± 9.3	173.7 ± 14	18.1 ± 2.2	15.8 ± 1.4	–	–
Total Execution Duration	t (s)	49.2 ± 2.4	53.6 ± 3.4	42.2 ± 1.6	40.4 ± 1.1	–	–
Mean Execution Velocity	v (virtual m/s)	2.5 ± 0.09	2.6 ± 0.11	3.0 ± 0.10	2.9 ± 0.09	–	–
Head-Hand Spatial Coherence	R_{max}	0.77 ± 0.018	0.73 ± 0.016	0.88 ± 0.007	0.90 ± 0.008	–	–
Head-Hand Temporal Synchrony	LAG (s)	0.79 ± 0.07	1.14 ± 0.10	0.40 ± 0.04	0.34 ± 0.02	–	–
Median Pupil Diameter	DiaP (mm)	3.88±0.15[b]	3.80±0.14[b]	3.73±0.15[b]	3.68±0.15[b]	–	–

Data in this table is corroborated by Supplementary Fig. S1-S2.
[a] See Fig. 4 for additional description of data.
[b] See Fig. 5 for additional description of data.

underlying the test completion times (note that the kinematic analyses were possible only for the HandCTT and the NoNumbersCTT conditions). As a preliminary step, we segmented the test completion times into two periods: (i) periods in which the participant was executing a hand movement towards the target (either towards the numbered ball in the HandCTT condition, or towards the ball cued with a black dot in the NoNumbersCTT condition), and (ii) periods of searching in which the participant was not making goal-directed movements towards the target (see Fig. 2 and *Methods*). Table 2 presents the total time, on average, participants spent in target searching throughout the test under each of the conditions (HandCTT and NoNumbersCTT; see also Supplementary Fig. 1A). We found relatively short search times in the NoNumbersCTT conditions, with no difference between Trails A and B ($p_{bonf} = 0.76$; search time accounted for 27 ± 1.6% of total completion time). When comparing between NoNumbersCTT and HandCTT condition, we found that the total search duration significantly increased with increasing cognitive load: namely HandCTT Trails A had significantly longer search time than NoNumbersCTT ($p_{bonf} < 0.001$; Cohen's d=1.3; 58 ± 2% of total completion time), and HandCTT Trails B had an even more significant increase in search time than Trail A ($p_{bonf} < 0.001$; Cohen's d = 1.9; 74 ± 1.6% of total completion time).

However, the differences between conditions were not confined to the search periods but were also evident during motor execution periods. The total execution duration throughout the test in each condition was assessed (see Table 2 and Supplementary Fig. 1B; note that all participants and all conditions had the same number of targets with a similar spatial layout and roughly the same total required distance to travel between targets). The overall duration of movement execution was longer in the HandCTT condition compared to the NoNumbersCTT condition ($F(1,29) = 28.16$; $p < 0.001$; $\eta^2 = 0.29$), with no overall difference between Trails A and B. Finally, to find out whether the longer execution periods stem from differences in movement properties, we compared the mean execution velocity between conditions (See Table 2 and Supplementary Fig. 1C). Indeed, we found that the mean velocity during execution was higher in the NoNumbersCTT condition compared to the CTT condition ($F(1,29) = 25.9$; $p < 0.001$; $\eta^2 = 0.33$), indicating that the type of task also affected the motor execution itself and not only the searching process that preceded it.

Although these results are likely not completely orthogonal to the results of completion time analysis, they allow a more in-depth insight regarding the mechanisms contributing to differences in total completion times. Together, these results suggest that the cognitive load and task demands directly affect the time it takes for cognitive processing and visual search before movement execution, but also have a more subtle effect on the speed of execution – with the more difficult cognitive task incurring slower hand movements. We suggest that the increase in search time contributes to a large extent to the increases in total completion time when cognitive load increases, with a milder contribution of increased execution times.

As a control, we tested also a small group of young participants (N = 5; aged 30 ± 4; education years 16.8 ± 1.6), who performed a similar paradigm. We performed a Mixed-effects ANOVA to compare between the young and older group results. For test completion times, we found a main effect of group ($F = 8.11$; $p = 0.008$; $\eta^2 = 0.078$), with the young participants presenting shorter completion time. Additionally, we found an interaction between group and condition ($F = 6.04$; $p = 0.008$; $\eta^2 = 0.035$), and an interaction between group and Trail ($F = 5.9$; $p = 0.02$; $\eta^2 = 0.006$; see Supplementary Table 1 for descriptive statistics). We examined this interaction more closely and found that young and older groups did not differ in the NoNumbersCTT condition ($p_{bonf} = 1$; namely, their performance in the more motor condition was comparable), but that the older group had longer completion times in the more cognitively demanding HandCTT condition ($p_{bonf} = 0.002$; Cohen's d = 1.83), with Trail B showing greater difference between the groups ($p_{bonf} = 0.009$; Cohen's d = 1.27). This supported the notion that the cognitive aspect of task execution is more affected by age than the motor aspect.

To further test this hypothesis, we compared between the search and execution durations of the young and older groups. We found that execution duration and execution velocity were not affected by age ($p > 0.13$ for group effect), but that search duration significantly increased in the older group as compared to the young group ($p = 0.01$; $\eta^2 = 0.066$ for group; see Supplementary Table 2 for descriptive statistics). Together, these results suggest a differential effect of aging on the cognitive, but not on the motor component of VR-CTT task performance.

3.4. Head-hand coordination

One prominent feature that is required for visuomotor task performance in a large-scale spatial configuration is head-hand coordination - namely spatial and temporal coordination between hand movements and head rotation directions (which is a proxy for gaze positions; Hardiess et al., 2008). These two effectors have been shown to work together rhythmically during naturalistic visuomotor cognitive tasks (Pelz et al., 2001). It has recently been reported that the amount of cognitive load required in the VR-CTT task, as expressed in Trails A versus B, can affect this coordination (Lustig et al., 2023). To discover potential effects of cognitive load on head-hand coordination, we employed a cross-correlation analysis on the hand horizontal position and head left-right rotations during the VR-CTT and NoNumbersCTT conditions (cf., Fig. 3). First, we examined the spatial coherence between the head and hand movements (represented by the maximal correlation coefficient extracted from the cross correlation). We found a main effect of Condition ($F(1,29) = 96.3$; $p < 0.001$; $\eta^2 = 0.6$), no main effect of Trail ($p = 0.4$), and a significant interaction ($F(1,29) = 7.6$; $p = 0.01$; $\eta^2 = 0.02$), with higher head-hand spatial coherence in the NoNumbersCTT condition as compared to HandCTT (See Table 2 and Supplementary Fig. 2A). The very high spatial coupling in the NoNumbersCTT condition largely means that the hand and head go together in space throughout the test, with minimum need for visual search (expressed by head rotations, but not necessarily by hand movements). Next, we examined the temporal synchrony between the head and the hand – namely the time lag in which the correlation between these signals was the highest. We found a main effect of Condition ($F(1,29) = 80.8$; $p < 0.001$; $\eta^2 = 0.5$), effect of Trail ($F(1,29) = 8.5$; $p = 0.007$; $\eta^2 = 0.03$) and an interaction ($F(1,29) = 15$; $p < 0.001$; $\eta^2 = 0.06$). Table 2 shows the average lags across Trails A and B in HandCTT and NoNumbersCTT conditions (See also Supplementary Fig. 2B). The shortest lags between head rotations and hand movements (head leads hand) were in the NoNumbersCTT condition. Then, HandCTT Trails A had significantly longer lags than NoNumbersCTT ($p_{bonf} < 0.001$; Cohen's d = 1.1) and HandCTT Trails B had even longer lags than Trails A ($p_{bonf} < 0.001$; Cohen's d = 0.94). To summarize, we found that the time lag between hand and head increased with increasing cognitive load (HandCTT B > HandCTT A > NoNumbersCTT), and that during the NoNumbersCTT condition participants had higher spatial coupling between the head and the hand than during the HandCTT condition. While these results somewhat echo the differences in completion times and in search/execution duration, they offer an additional perspective on the effect of cognitive load on task coordinated movement.

3.5. Pupil dilation

To reach beyond cognitive-motor aspects of task performance, we probed for a link between task performance and physiological signals, by analyzing pupil dilation measures. To avoid the potential confound of transient pupil reactivity, we focused on the median pupil diameter value throughout each task and compared between HandCTT and NoNumbersCTT conditions, separately for Trail A and Trail B conditions (other comparisons were not possible due to risk of confounds; see Methods). We found that participants had significantly higher pupil dilation in the HandCTT compared to the NoNumbersCTT conditions, in

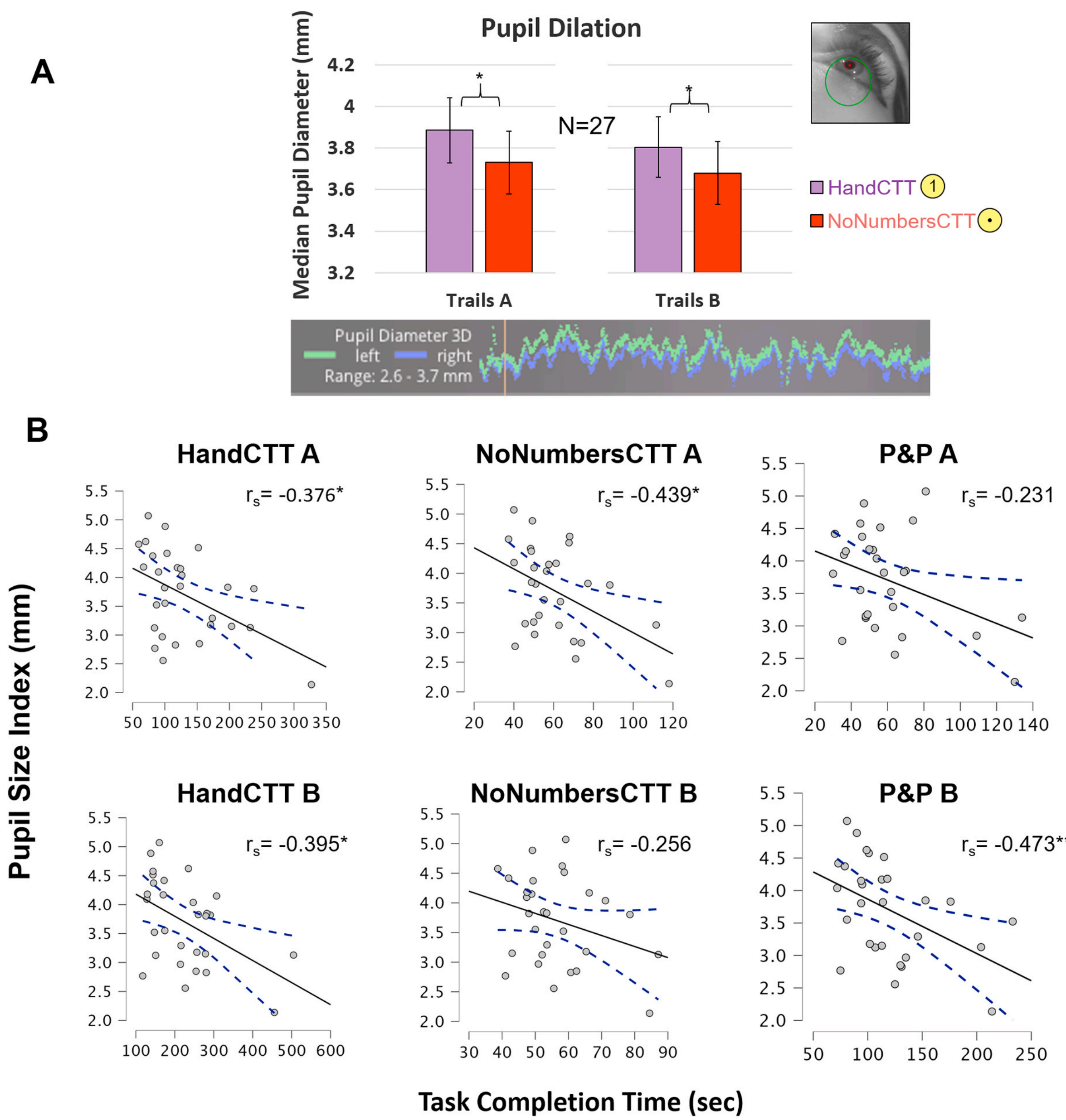

Fig. 5. Pupil dilation and its relation to cognitive load and cognitive task performance. (A) Average median pupil diameter values for NoNumbersCTT and HandCTT conditions. The pupil dilation information (pupil diameter in mm) was extracted from both eyes throughout the tests via Pupil Labs software. Data were preprocessed and both pupils were integrated into a single signal. The median value of the pupil for each condition was taken for further analyses. (B) Scatter plots and Spearman Correlations between pupil index values (calculated by averaging for each participant all their median pupil dilation values), and task completion times (including P&P-CTT conditions). The correlation was negative in all conditions, and significant in most. *$p < 0.05$; **$p < 0.01$.

both Trails A ($p = 0.04$) and Trails B ($p = 0.04$; see Fig. 5A). Next, we probed for a relation between individual pupil size values and interindividual differences in task performance. To that end, we tested to what extent each participant had a characteristic pupil size relative to other participants across tasks. Indeed, a correlation of pupil size values across tasks revealed extremely high interindividual consistency (Supplementary Fig. 3). Therefore, to capture the characteristic pupil size for each individual, we next created for each participant a mean pupil size index and compared this index to task performance levels across participants (as expressed in task completion times). Fig. 5B shows the Spearman correlation values between the pupil size index and task completion times. We found consistent negative correlations between pupil size index and task completion times, applying both for the VR-CTT and the P&P-CTT – meaning that participants with characteristically larger pupil sizes tended to have shorter completion times (i.e., better task performance) and vice versa. We repeated this analysis while correlating completion times with the median pupil size within each test (instead of the pupil size index) and found comparable results (Supplementary Fig. 4). Notably, the pupil sizes during the VR conditions were also inversely correlated to P&P CTT Trails B completion times ($p < 0.05$ for all conditions), implying that the effect is not reliant on pupillary reaction within the specific task, but rather a more general characteristic of the individual throughout the session. To further elucidate whether the effect might be related to pupil dilation response in the more cognitively demanding conditions, we calculated the normalized delta between pupil diameter during HandCTT and that during NoNumbersCTT condition (separately for Trails A and B). We found no correlation between this normalized delta and any of the task completion times (smallest $p = 0.16$; $r_s = -0.27$). In summary, we found that pupil dilation was higher in more cognitively demanding tasks within participants, and that interindividual characteristic pupil size was correlated with cognitive performance scores whereby higher pupil sizes were associated with better performance.

3.6. Clinical relevance of VR-CTT measures

Lastly, as a proof-of-concept, we assessed whether naturalistic cognitive-motor performance during VR-CTT tasks can be related to clinical outcome measures. For this, we focused on a clinical condition associated with cognitive-motor impairments in the elderly – namely, fall-risk. Our participants were divided into two subgroups: Fallers (had fallen during the year prior to the experiment), and Non-Fallers. Following this division, 7 participants were categorized as 'Fallers' (mean age 78.6 ± 8), and 23 as 'Non-Fallers' (mean age 72.3 ± 5; no significant age difference was found between groups $p = 0.11$; *U* Test). We then qualitatively compared some of the outcome measures that were used in the study between the two groups. Fig. 6 shows the mean values of several of these parameters separated into the two groups. As can be seen, fallers had, on average across all conditions, overall longer completions times (Fig. 6A) and longer head-hand lags (Fig. 6B; $p = 0.026$, between-subject effect of Mixed-effects ANOVA). Correspondingly, Fallers showed on average slower hand execution velocities and had relatively smaller pupil sizes (Fig. 6C and D). Other parameters did not show any differences between groups. Please note that these results are mostly qualitative due to the unequal group sizes (this analysis was done post-hoc, therefore participant recruitment did not focus on equalizing the sizes of these groups). These results present a first step towards utilizing the VR-CTT paradigm for individual profiling for

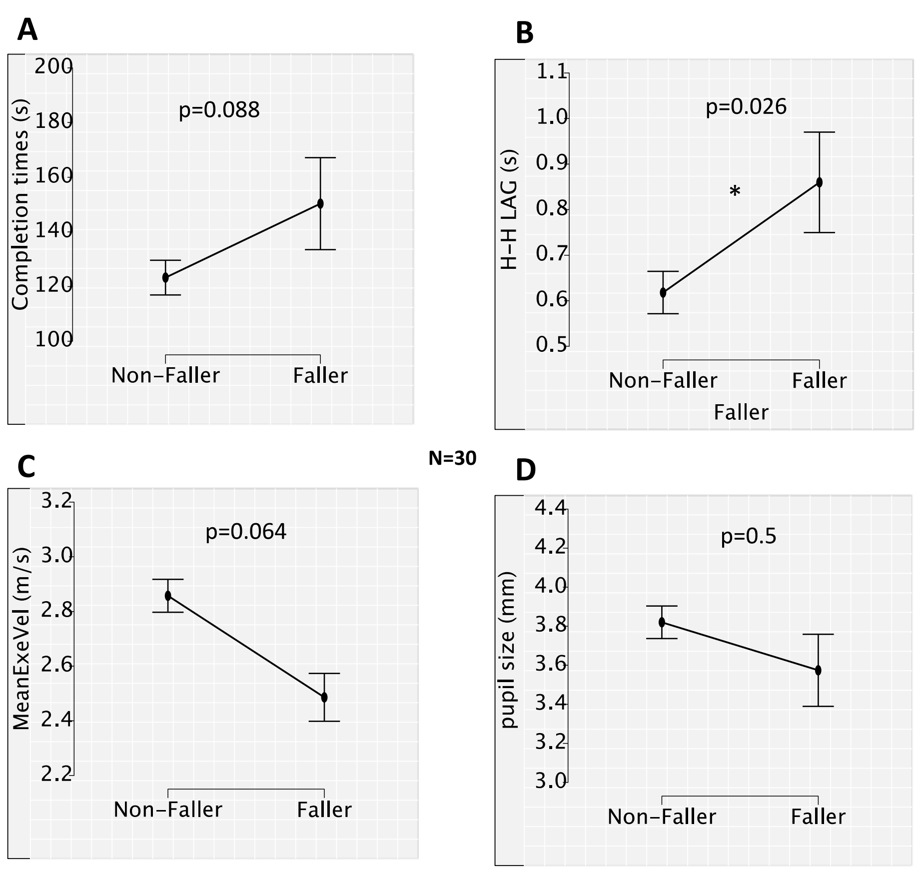

Fig. 6. Qualitative comparison between groups of Fallers versus Non-Fallers. Our group of participants was divided into two subgroups: Fallers (N = 7), i.e., participants who had fallen in the year prior to the experiment, and Non-Fallers (N = 23). (A) Average completion times across all conditions and trails in the Non-Fallers and Fallers) groups. Error bars denote SEMs. (B) Average Head-Hand temporal synchrony (Lag values of cross-correlation) in each group. (C) Average mean hand execution velocities in each group. (D) Average pupil diameter in each group.

detecting clinical indications of cognitive-motor decline.

4. Discussion

In the current study, we examined cognitive-motor performance during VR-CTT in a group of older adults. We found that the time needed for participants to complete the task was mostly dependent on the amount of cognitive load required (task difficulty), with only a mild contribution of the amount of motor requirements (the use of hand movements/gaze only). Likewise, we found that the duration of visual search increased with higher cognitive demands, as reflected in longer lags between head and hand coordinated movements with increasing task cognitive load. Nonetheless, cognitive load also affected the motor aspects of task execution, with slower hand movements in the more difficult tasks. Higher task difficulty, requiring more cognitive effort, was also reflected in larger pupil dilations. At the interindividual level, we found that participants with larger pupil sizes showed overall better task performance. Lastly, we found that participants with a history of falling (indicating poorer cognitive-motor functioning; Demanze Laurence and Michel, 2017) had overall poorer task performance, larger head-hand lags, slower execution speeds, and smaller pupil sizes. Together, these results demonstrate the possibility of using more naturalistic cognitive assessment paradigms, which might be informative both for a general understanding of cognitive-motor behavior, and for characterizing individual performance profiles.

4.1. Dissociating cognitive and motor components of task execution

Our paradigm enabled us to look closely into the cognitive and motor components of task execution as well as their interaction. We found that task cognitive load, more so than motor demands, contributed most to overall task completion time.

Although, as specified in the introduction, we could not completely isolate the cognitive and motor components, we were still able to reduce the relative contribution of these components in our more 'motor' and more 'cognitive' conditions. At face value, removing the number sequencing in the NoNumbersCTT condition does reduce the cognitive load of the task, making it much less reliant on cognitive processing abilities (and completely devoid of semantic processing), and the 'EyesOnlyCTT' condition eliminates the need for arm movements, making this task less motorically demanding. For healthy individuals, the execution of arm movements might not incur a big 'cost' on the completion times, but for individuals with motor disorders, such as Parkinson's Disease, the addition/exclusion of arm movements might have considerable consequences on the overall completion times. A previous study also attempted to create a 'motor-only' control condition for the TMT (Crowe, 1998). In that study the motor condition was the P&P TMT, but empty circles connected by a dotted line. The participants had to follow the trace of the dotted line to complete the test. Although this control condition is less reliant on spatial attention, it does miss out on the motor kinematics of a spontaneous voluntary reaching movement. In our study, we had the possibility to mark the series of targets sequentially, and thus minimize the attention demands (requiring only exogenous attention) while keeping the motor kinematics.

By monitoring motor behavior, we could differentiate between search periods (during which cognitive processing is more dominant) and movement execution periods (during which motor action is more dominant). A segmentation between search/execution was recently performed by our group for a digital tablet-based version of the CTT (Ben Yair et al., 2023). We previously found that increases in search time mostly contributed to differences in total completion times between Trails A and B, and that increased cognitive load caused a decrease in execution speed (Ben Yair et al., 2023). Another recent study utilized a hidden Markov model to segment the cognitive and motor periods in the performance of a similar digital trail-making test (TMT; similar to CTT but with alternation between letters/numbers instead of between colors in Trails B; Du et al., 2022). The researchers found that the duration of motor execution in Trails A was linked to scores on other cognitive tests and physical outcome measures (e.g., gait speed), while in Trails B, both execution time and search ("thinking") time were associated with cognitive scores (Du et al., 2022). Relatedly, in the seminal study by Crowe (1998) the link between performance of a standard P&P-TMT and specific cognitive and motor capabilities in young adults was investigated. He found that Trail A performance was significantly predicted by motor speed and visual search tasks while Trail B performance was predicted by visual search and verbal number/letter alternation tasks (but not by motor speed).

In addition to changes in cognitive processing time, we found that cognitive load affected motor properties of hand reaching movements. Why do the participants move slower when the cognitive load is higher? Presumedly by the time they start the execution phase, they have already found the target and could move at a similar speed as in the less cognitively demanding conditions. The reduced speed selected may be a result of reduced vigor in these movements (Shadmehr et al., 2019). Vigor has been defined as the movement speed as a function of distance (Summerside et al., 2018) and varies as a function of the utility of the movement, i.e., how much a particular action is valued. In conditions with increased cognitive load, the mental effort involved in performing the task is greater, and thus the hand movement component may be valued less (i.e., have a lower utility), which incurs slower movement. A similar finding has been shown for movements that require more physical effort, where participants make slower movements when making longer rather than shorter movements (Reppert et al., 2018) and walk slower when carrying a greater load (Bastien et al., 2005), i.e., they have lower vigor. The findings in this study are comparable to results showing similar devaluation of reward between physical and cognitive effort (Lim et al., 2023).

Relatedly, a recent study measured hand kinematics and eye-hand coordination during P&P TMT performance in older adults and stroke survivors and found that cognitive load causes slower limb movements and reduced eye-hand coordination (Singh et al., 2023). Our results are in line with these studies, while extending them to a 3D ecological setup, suggesting that the amount of cognitive processing needed to complete the tasks is reflected in the duration of search times (Trails B > Trails A > NoNumbersCTT), and in a mild reduction of motor execution speed.

Correspondingly, increased cognitive load has been found to cause temporal decoupling of head-hand coordination. Lustig et al. (2023) found that during VR-CTT execution (only HandCTT condition) there is an increase in hand-head lags in Trails B compared to Trails A in young, middle-aged, and older adults. We found similar temporal decoupling dependent on cognitive load. This was demonstrated even more pronouncedly in the NoNumbersCTT condition, which had extremely short head-hand lags and high head-hand spatial coherence.

In summary, we suggest that the additional search time accounts for the time of cognitive processing required for the task and is therefore dependent on task requirements. In our case – three levels of cognitive processing were required for detecting the correct target: (i) visually process a low-level visual cue and spatially orient to it in 'NoNumbersCTT', (ii) process a slightly more complex visual input (number) + match visual inputs with the desired number in 'CTT A', and (iii) perform similar processes as before and add also the intersection of the desired number and color in 'CTT B'. Presumably, this additional processing time also underlies longer head-hand lags (i.e., decreased temporal coupling), and eventually overall longer completion times with increasing cognitive load. As disscussed above, a milder, but significant effect of slower hand movements was found during the more difficult tasks, possibly as a result of less certainty in decision making and an increase in cognitive-motor interference when the task became more complex (Friedman et al., 2013; Singh et al., 2023).

4.2. Link between cognitive task performance and pupil size

In the current work, we found not only that motor functions interact with cognitive task load, but also that task load is reflected in pupil dilation signals. Specifically, the HandCTT condition yielded higher pupil dilations than the NoNumbersCTT condition in both trails A and B, despite their highly similar visual properties (same number of balls in the same locations with the same colors). This might indicate that higher cognitive task load/cognitive effort caused increases in pupil dilations. This result corresponds to the already well-established connection between cognitive effort and pupil dilation, with tasks that require higher effort associated with increases in pupil size (van der Wel and van Steenbergen, 2018), as mediated by specific brain structures in the locus coeruleus (Joshi and Gold, 2020). For instance, it has been shown that for mental arithmetic tasks, digit span and memory tasks, higher task load causes pupil dilations, up until the point where task demands exceed the available cognitive resources (van der Wel and van Steenbergen, 2018). Nonetheless, previous tasks mostly contained lab-designed artificial stimuli and setup, with no motor involvement. Here, we extend this finding to a cognitive-motor task in ecological settings in older adults. A potential confound of our findings could be that participants experienced more fatigue during VR-CTT compared to NoNumbersCTT due to longer test durations and more cognitive effect. However, although fatigue was not measured directly, this is probably not the case, since fatigue was shown to decrease, rather than increase, pupil size (Morad et al., 2000), while we see the opposite result.

In addition to task-induced effects on pupil size within individuals, we found that interindividual differences in pupil size index were inversely associated with task completion times. These results are in line with previous studies showing relations between baseline pupil size (without a task) and cognitive capabilities. For example, Tsukahara et al. (2016) found a positive correlation between individuals' baseline pupil sizes and their measures of working memory capacity, that were not dependent on demographic variables (e.g., age). A recent study that targeted both young and older adult participants from a large cohort, found associations between pupil size during fixation and processing speed and response generation, which were stable across age groups (Coors et al., 2022). Specifically, and in line with our current results, they found a correlation between TMT (Trails A and B) performance and pupil sizes in a group of older adults. The correlation we found between pupil sizes and completion times (cf., Fig. 5B and Supplementary Fig. 4) might be due either to interindividual differences in baseline pupil sizes, or to differences in pupil dilation responses, as compared to baseline pupil size, during cognitive task performance. The fact that we found that absolute pupil sizes within one condition were correlated also to completion times in other conditions, and that delta pupil sizes were not correlated with completion times, suggest that our effect might be more reliant on baseline differences between participants, and less on differences in pupil dilation responses. However, since we did not have a baseline pupil measurement during resting condition, we could not directly assess the pupil dilation response in each condition, and therefore cannot completely exclude the possibility that the effect we found is partly due to differences in pupillary reactivity during the cognitive tasks. Our findings extend previous results to a more naturalistic cognitive-motor setup.

4.3. Limitations, future directions and implications

We suggest that the VR-CTT can serve as a platform for clinical profiling of at-risk populations, as seen in our preliminary proof-of-concept results where fallers presented overall lower performance values than non-fallers. However, we were limited by the small sample size and unequal group sizes. Furthermore, we did not have good quantification of the clinical measures, or a wide range of functional scores (we tested only healthy older adults). Future studies with larger cohorts of fallers and non-fallers will be needed to further substantiate these findings.

The pathophysiology of falling is not fully understood, mainly due to its multifactorial nature. Motor deficits (e.g., gait impairments, postural instability), mental conditions (e.g., anxiety or depression), and cognitive impairments (e.g., executive functions) were implicated with higher risk of falls (Fasano et al., 2012). Our paradigm enables teasing out, to some extent, motor and cognitive components of task performance, thus potentially enabling individual profiling of capacities in these domains, and their interaction. However, since the more cognitive and more motor conditions in our paradigm each contain also some cognitive-motor interactions, we cannot completely isolate the measurement of scores in each of these domains. Purposefully, the VR-CTT does not address postural and locomotor motor competencies, but rather gross manual movements emphasizing interactions between cognitive abilities (e.g., divided attention) and motor skills (planning, execution). Measuring this interaction is highly relevant for older adults. It has been reported that cognitive-motor interference (e.g., usually measured using dual tasking while walking) increases with aging (Ren et al., 2013; Verrel et al., 2009). This increase is likely due to the numerous changes in the brain with aging, including a reduction in brain volume, lower neurotransmitter levels, and a change in vasculature (Peters, 2006). These consequences of an aging brain in turn cause changes in neural activity, although there is no consensus on which particular brain areas are responsible for the changes in behavior (Leone et al., 2017; Reinhardt et al., 2020). This aging effect is also reflected in the finding that performance scores of TMT are correlated with fall-risk in older adults (Chen et al., 2012), which may be related to the reduced connectivity in brain areas related to information integration observed in fallers (Maidan et al., 2020). The profiling of cognitive-motor performance could be beneficial also in the context of other clinical pathologies that involve cognitive-motor interactions, such as stroke, Parkinson's disease or dementia (e.g., Hausdorff et al., 2010; Plummer et al., 2013; Poletti et al., 2012). However, we acknowledge that in the current paradigm, the cognitive aspect of the task was more parametrically modulated between conditions than the motor aspect, and that generally the cognitive demands were more complex than the motor demands, allowing a more in-depth investigation of the cognitive, rather than the motor, aspect of task performance.

An additional potential application could be to use the EyesOnlyCTT clinically on participants with upper limb deficits (e.g., hemiplegia, hemiparesis, ALS, Rett syndrome), thus enabling the measuring of cognitive abilities without confounding the performance score to upper limb functional limitations (Poletti et al., 2017). Indeed, gaze-operated TMT has been developed in the past, where the researchers created and validated a TMT performed with eye tracking only (Hicks et al., 2013). They found that the scores of gaze-only TMT were correlated with standard manual TMT only for Trails B. However, the previous version was based on a 2D computer screen and was implemented using very simplified visual feedback from the system. Our EyesOnlyCTT version presents a more ecologically valid way of administration, with richer and more straightforward feedback that encourages more naturalistic behavior.

In the current work, we analyzed the coordination between two major motor effectors involved in the task – the head and the hand. It might be argued that eye-hand coordination would be more informative for evaluating task performance. However, it has been shown that for a large spatial span of targets, eye-head coordination is high, with head movement integrating on multiple saccades (Fang et al., 2015), therefore head rotations can serve as a good proxy for gaze positions. Moreover, head rotations and reaching movements work in a well-coordinated manner during naturalistic task execution, giving indication of efficacy of task-coordinated motion (Arora et al., 2019; Pelz et al., 2001). Analysis of detailed gaze behavior can tap more closely into the cognitive processes underlying task performance, thus detecting cognitive deficits stemming from neurodegeneration (Bueno et al., 2019). Measuring eye tracking patterns during VR-CTT tasks might help in detecting working memory deficits, spatial attention deficits, and deficits in planning and strategy. Though eye tracking analysis is not in the scope of the current study, future research might reveal the benefits of this unique setup both for understanding naturalistic 3D visual search and for profiling individual patterns for clinical diagnostics.

5. Conclusions

Using a comprehensive VR-based neurocognitive testing paradigm with motor and eye tracking measurements, we found that cognitive task load is the most dominant factor determining completion time scores. The increase in cognitive load was expressed as additional cognitive processing time, and also influenced motor behavior, as evidenced by reduced hand execution speed and reduced head-hand synchronization, as well as in physiological signals, as evidenced by increased pupil dilation. We posit that these interactions between cognitive, motor, and physiological functions might better represent real-life function and therefore capture multifaceted behavior and be more sensitive in detecting potential deficits. At the interindividual level, we found a link between pupil size and task performance and slowed performance for fallers versus non-fallers within our group of participants. We suggest that this novel paradigm opens the possibility for more detailed profiling of cognitive-motor performance in older adults and other clinical populations while encouraging naturalistic behavior.

Credit author statement

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Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuropsychologia.2023.108744.

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