The Utility of Mobile Visuomotor Assessment for Neuropsychological Evaluation in Older Adults

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Abstract

Background: The ability to perform visually-guided motor tasks requires the transformation of visual information into programmed motor outputs. When the guiding visual information does not align spatially with the motor output (cognitive motor integration, CMI), the brain processes rules to integrate the information for an appropriate motor response. Performance on such tasks is affected in individuals at risk of or in the early stages of dementia, and may affect their activities of daily living. Using mobile technology with older individuals may provide us with a more sensitive and accessible metric for assessing cognitive and functional motor abilities, when compared to traditional neuropsychological assessments. Here, we investigate the relationship between a traditional neuropsychological test battery and a tablet-based visuomotor skill performance tasks. ***Methods:*** 40 participants, between the ages of 56 and 86, ranging from healthy to early Alzheimer's disease completed the WMS-IV neuropsychological test battery which took about 180 minutes. They also performed three tablet-based tasks that tested the participants' CMI abilities which took about 15 minutes. Specifically, participants performed 1) a standard condition requiring direct interaction with visual targets on a touchscreen, 2) a CMI condition requiring one level of decoupling in which movements on the tablet had reversed visual feedback, and 3) a CMI condition requiring two levels of decoupling in which the finger was moved on the lower half of the screen, while moving the cursor to targets with reversed visual feedback on the upper half of the screen. Thus, there was a spatial dissociation between the gaze and hand movement. Outcome variables included reaction time, movement time, accuracy, precision, path length, and number of direction reversals. ***Results:*** Using a hierarchical linear regression analysis, we observed that 5 of our 6 CMI outcome measures were predictive of four tests from the WMS-IV battery, once variability for sex and age were accounted for ($p<0.05$). These tests include measures related to visuospatial skills, executive function, and memory. ***Conclusions***: Our findings suggest that, to some extent, mobile technology that involves multi-domain cognitive-sensory-motor processing may provide feasible, automated, and remotely deployable assessment alternatives to the current standard methods.

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Glossary of Terms

AE – Absolute error
AD – Alzheimer’s disease
BrDI$^{\text{TM}}$ – Brain Dysfunction Indicator
BVMT – Brief visuospatial memory test
CMI – Cognitive-motor integration
FI – Fluid intelligence
fMRI – Functional magnetic resonance imaging
FR – Feedback reversal
KINARM – Kinesiological instrument for normal and altered reaching movement
MCI – Mild cognitive impairment
MoCA – Montreal cognitive assessment
MT – Movement time (full)
PAL – Paired associated learning
PL – Path length (full)
PC – Plane change
RT – Reaction time
RVGR – Reverse visually guided reaching
SS – Split screen
VE – Variable error
VGR – Visually guided reaching
%DR – Percentage of direction reversals

1. Introduction and Literature Review

1.1 Introduction

Clinical assessment plays a crucial role in all facets of patient care, from diagnosing the specific disease or injury, to management and monitoring of therapeutic or rehabilitation strategies to ameliorate dysfunction. Medicine relies on a breadth of commercial technologies and tests to quantify body function, and this has radically changed accuracy of diagnosis. Alzheimer’s disease pathology typically begins several decades before the onset of clinical dementia and symptoms appear only after there has already been significant damage to the brain (Morris, 2005). Although there is currently no effective treatment for Alzheimer’s disease, early recognition of dementia risk is important for improving patient outcomes both now and in the future when effective therapies become available. Despite this, the ability to assess brain function, particularly sensory, motor, and cognitive functions, is surprisingly limited and continues to be based largely on subjective estimates of performance (e.g. the ability of a patient to touch their nose and a clinician’s finger repeatedly, based on a score of 0, 1, 2 or 3) and traditional paper and pencil tasks. Such simple subjective rating systems are necessarily coarse to ensure reliability and validity, but such coarseness makes it difficult to identify subtle changes in sensorimotor function that accompany focused dysfunction of a discrete pathway or set of pathways or brain areas. Furthermore, subtle impairments such as small delays in reacting or increases in movement variability cannot be identified easily from visual inspection. Many underlying effects of neurological disorders are not fully understood. They may manifest as deficits in motor function, sensory function, cognitive function, or the integration of these different domains (e.g., cognitive-motor integration). Task performance can help us indirectly understand the neural networks associated with eye-hand coordination, something needed for activities of daily living.

1.2 Alzheimer’s Disease

Alzheimer’s disease is an irreversible neurodegenerative brain disease, and is the most common cause of dementia. Unlike popular belief, dementia is not a single disease; rather, it’s an umbrella term that refers to a set of symptoms that arise as a result of damage to brain cells. Dementia is a syndrome characterized by declines in cognitive abilities including memory loss, difficulties with decision making, language problems, and behavioural changes. Korolev (2014) defines mild cognitive impairment (MCI) as “a syndrome characterized by memory and/or other cognitive impairments that exceed the decline in cognition associated with the normal aging process”. MCI is often regarded as a precursor to dementia or the transitional stage between healthy cognitive aging and dementia. A healthy brain consists of neurons that are specialized in transmitting information via chemical and electrical signals to the brain and the rest of the body. Although the brain shrinks with ageing, there is usually minimal loss of neurons associated with this shrinkage. In Alzheimer’s disease, however, a large number of neurons and their connections to parts of the brain are destroyed (NIH.gov). At the cellular level, a progressive loss of cortical neurons (more specifically the pyramidal cells which are the primary excitation units in the cortex) and synaptic dysfunction is seen early in the disease. Degeneration typically begins in the medial temporal lobe, especially in the hippocampus, and spreads throughout the temporal association cortex as well as the parietal areas. Not only does this widespread pattern of neurodegeneration correlate with the cognitive deficits and the behavioural changes exhibited by Alzheimer’s disease patients, it has also been associated with an impaired ability to perform activities of daily living (Korolev, 2014). These are mainly activities that require precise coordination of eyes and hands movement such as cooking and dressing. A well-functioning frontoparietal network interconnected with subcortical areas is required for visuomotor coordination in order to initiate, plan and execute motor actions. One of the most critical structures in the frontoparietal network is the posterior parietal cortex which integrates and transforms visuospatial information into a motor plan. As mentioned earlier, this is one of the areas involved in Alzheimer’s disease pathology. In early stages of Alzheimer’s, significant reduction of connections and loss of white matter can be seen the posterior parietal cortex and since this area is extensively involved in visuomotor integration, visuomotor dysfunction may be directly linked to the presence of Alzheimer’s disease (Verheji et al., 2012). In a study conducted by Verheji and colleges in 2012, AD patients showed impairments in several aspects of eye and hand movements including relative timing of movements at early stages of the disease. These patients demonstrated a slower initiation and execution of goal-directed hand movements and a reduced ability to suppress reflexive saccades compared to controls.

1.3 Visually Guided Reaching

As mentioned earlier, our daily interactions with objects require the simultaneous use of the eyes and hands. There are two types of visually-guided movement. By default, our brains are wired to reach to where we’re looking and therefore, most reaching movements performed in daily life are referred to as standard visuomotor transformations. Standard visually-guided reaching involves a direct interaction with the object we are looking at meaning the eyes are directed towards an object of interest and the hand moves to the same location in space as that acquired by the eyes. Example of this type of movement can be reaching to pick up a cup of coffee. However, many of the reaching tasks that we learn to perform require non-standard visuomotor transformations, in which the motor system must integrate some form of cognitive information (e.g. visual-spatial, memory, rule-based, semantic) into the motor program. These types of visuomotor transformations must be learned or calibrated and entail moving and thinking at the same time. In a non-standard transformation, an indirect interaction with an object is involved in a manner where the end effector must move to a spatial location that is not directly aligned with the location of the visual target. In other words, visual target and movement are dissociated in non-standard transformation. Two types of non-standard transformational mapping have been described in the literature (Wise, di Pellegrino, & Boussaoud, 1996) one of which is referred to as a sensorimotor recalibration (also known as spatial realignment). This form of movement can be seen in situations where the physical location of the visual stimulus is in a different plane relative to the movement required by the limb (e.g. looking at the vertical computer screen to click on an icon while moving a computer mouse on the vertical plane). In this situation both vision and proprioception must be used to remap the visual location of the target and representation of the hand in one plane, onto the true location of the hand and target in the other plane (Bedford, 1993; Clower & Boussaoud, 2000; Lackner & Dizio, 1994).

1.4 Visuomotor Deficits in Alzheimer's Disease

Alzheimer's disease is mainly thought to be associated with memory and other cognitive impairments. Nevertheless, deficits in purposeful movements (i.e. apraxia) have also been identified later as the course of the disease progresses (Parakh, Roy, Koo, & Black, 2004). A number of studies have demonstrated subtle deteriorations in the performance of non-standard sensorimotor transformation tasks in early Alzheimer's disease (Ghilardi et al., 1999; Ghilardi et al., 2000; Tippett & Sergio, 2006; Tippett et al., 2007; Tippett et al., 2012; Verheij et al., 2012). The results from these studies point out to increases in movement time, reaction time, and task performance errors in AD patients compared to age-match controls when they are required to perform reaching tasks that do not allow for continuous visual monitoring of the hand. Interestingly, standard reaches do not show impairment in patient groups (Tippett et al., 2007). These studies suggest that structural degradation of parietal and prefrontal areas, as well as the cortico-cortical connections between them (Braak & Braak, 1991; Ghilardi et al., 2000), may be responsible for the observed impairments in non-standard visuomotor transformations.

1.5 Use of Technology for Assessment

Using multi-modal computer and robotic assessment of older individuals may provide us with a more sensitive, and perhaps more objective and accessible, metric for assessing cognitive and functional motor abilities (when compared to traditional neuropsychological assessments). More generally, multi-domain assessments, in which the examination of an effector system is used to provide insights into brain health, has shown great success in understanding the cognitive impairments observed in aging, dementia, and neuropsychological cases. For example, research from Ryan et al. has demonstrated the utility of oculomotor measures for cognitive assessments in healthy and patient populations (Liu, Shen, Olsen, & Ryan, 2018; Ryan, Shen, Kacollja, et al., 2019; Ryan, Shen, & Liu, 2019; Whitehead et al., 2018). Previous work from Sergio et al. have also shown one of the platforms (BrDI) to be a sensitive assessment of functional rule-based motor ability in early dementia (De Boer, Echlin, Rogojin, Baltaretu, & Sergio, 2018; Tippett & Sergio, 2006; Tippett, Sergio, & Black, 2012), mild cognitive impairment (Salek, Anderson, & Sergio, 2011), and dementia risk (Echlin, Gorbet, & Sergio, 2019; Hawkins, Goyal, & Sergio, 2015; Hawkins & Sergio, 2014, 2016; Rogojin, Gorbet, & Sergio, 2019).

Many groups have examined robotics for stroke rehabilitation, but only recently has their value for neurological assessment been examined (Bourke et al., 2016; Massie et al., 2016). The bilateral Kinarm robotic platforms is the first robotic technologies designed specifically to provide a broad-based approach to neurological assessment. Kinarm has developed the Kinarm Standard Tests (KST) that includes multiple behavioural tasks spanning a range of sensory, motor and cognitive functions with each task generating 10 to 15 parameters to quantify subject performance. By using this suite of standardized protocols, a researcher can conduct a broad-based assessment of brain function in a short period of time (30 to 60 min, depending on the tasks selected and the severity of a subject's impairment).

Although robotic technologies like the Kinarm have been used extensively with older populations recovering from stroke (Coderre et al., 2010), the use of this technology to assess function in individuals affected by dementia has not been studied to date. This study focussed specifically on the use of the Kinarm robotic and Brain Dysfunction Indicator (BrDI) tablet research devices to assess upper limb sensorimotor function and relate it to standard tests of cognitive function.

Current study – purpose and hypothesis

This project was part of an Ontario Research Fund collaborative grant with Queen's University and Baycrest hospital entitled "Translating knowledge on brain function into next-generation technologies for neurological assessment" and examined the use of technology to assess function in older adults affected by neurological disease. Given the impact of age-related neurodegeneration on the voluntary motor actions that reflected cognitive processing, our aim was to find out whether visuomotor deficits seen in early AD could provide a novel behavioral target for dementia risk detection that was both easily accessible and cost-effective, as an alternative to the current expensive and invasive diagnostic tools. In other words, we sought to test if, and to what extent, the data from the tablet technology was consistent with those collected from traditional neuropsychological tests. Our secondary goal was to assess whether the results obtained from the mobile technology can reflect the results obtained through the non-portable technology.

We hypothesized that performance on a given task (i.e., rule-based visually-guided reaching on both BrDI and Kinarm) would correlate across these two platforms, demonstrating the efficacy of the mobile technology. On an exploratory level, to test the feasibility of using simple-to-deploy mobile technology to track brain health, we characterized the relationships between cognitive-motor performance and neuropsychological test battery performance as an exploratory component of our analyses.

2. Materials and Methods

2.1 Participants

A total of 45 individuals; all within the ages of 55-90 years old were recruited. This age group was specifically chosen as this is the age range within which individuals may start showing signs of preclinical AD or dementia. This study included 39 healthy adults and 6 adults with a clinical diagnosis of MCI or older adults with a clinical diagnosis of mild/early AD which were grouped together to have one group of older adults with cognitive states ranging from healthy to early AD. Participants were recruited through the Rotman Research Institute Participant Database and went through a phone screening to ensure eligibility for participation in study. Healthy controls were interviewed about the inclusion and exclusion criteria and assessed through a set of questionnaires (appendix A) and if deemed eligible, were asked to provide the contact information of an informant (someone that can be a good judge of the participant’s ability to perform daily activities) for a secondary interview with them. The MCI/mild AD groups’ electronic medical records (Meditech) were reviewed to further screen for other exclusion criteria (such as disease progression) before they were contacted. The participants in this group were diagnosed with mild cognitive impairment or AD by a physician at Baycrest Hospital's memory clinic. Some exclusion criteria for all participants include history of neurological disorders, active cancer or history of chemotherapy, presence of visual impairment, history of stroke and etc.

2.2 Methods

All participants, regardless of group, took part in the same study design, which consisted of two study visits. Participants were not trained on the experimental tasks prior to beginning, although a verbal description of each condition was given, and the task was demonstrated to them before they began. During their visits, participants took part in a series of KINARM and the tablet Brain Dysfunction Indicator (BrDI) tasks, as well as traditional clinical neuropsychological tasks. Note that this was not an intervention or treatment study; it was a motor-psychophysical behavioral study. Upon completion of the study tasks (i.e., at the final data-collection session), each participant's study participation concluded. Figure 1 illustrates the details of the study sessions' organizations. While the data collection sessions were designed as shown in figure 1, for about 25% of the participants, the order of the sessions were reversed meaning they were assessed on the tasks from 'session 2' on their first collection session (i.e. BrDI was done on the first session instead of the second session).

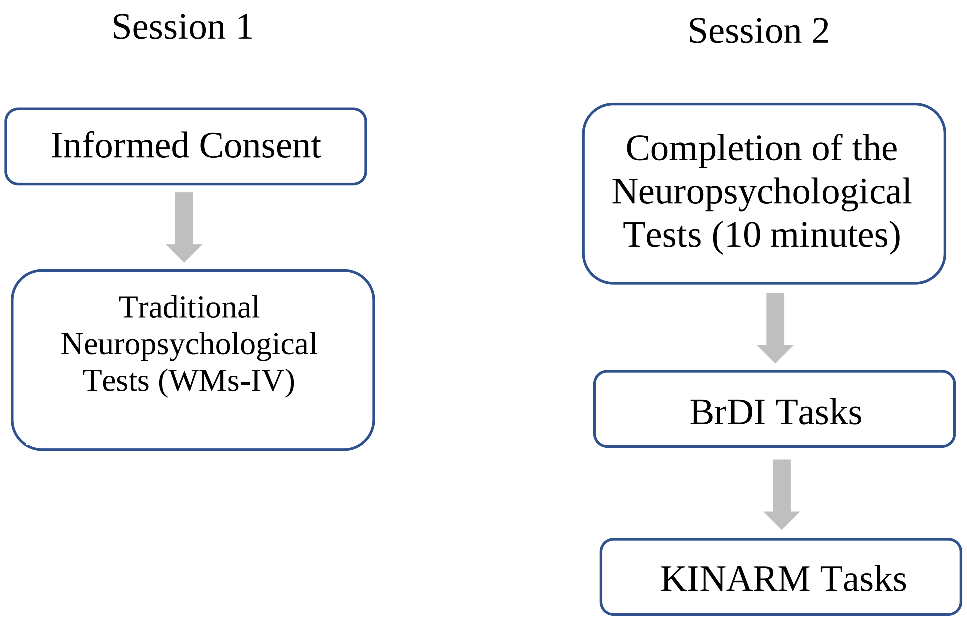


Figure 1. Research procedure flow diagram.

Kinetic and Kinematic limb movement data, as well as cognitive data, were collected from each participant. This project focused on the use of the KINARM robotics and Brain Dysfunction Indicator (BrDI) tablet research devices as visuomotor tasks to assess upper limb sensorimotor function and relate it to cognitive function. Traditional neuropsychological tests were also assessed for comparison purposes.

2.3 Brain Dysfunction Indicator

Brain Dysfunction Indicator (BrDI) is an application available on Android devices. In this study, BrDI was used on a Samsung tablet placed vertically in front of the participant who was asked to sit comfortably at a table. Participants were required to perform visuomotor transformation tasks under three conditions. The task consisted of sliding the index finger of the dominant hand along the touch screen to displace a cursor from a central target to one of four peripheral targets as quickly and accurately as possible (40 mm distance, 5 trials to each target, 20 trials per condition total).

In the first condition, which is the ‘standard condition’, the participant was asked to look directly at the screen and slide their finger directly to the targets that appear on the screen. This condition served as the baseline measure of task performance and was done to assess basic visuomotor brain network function. In this task, a central green target appeared in the center of the screen. Prior to initiation of the trial, the participant was instructed to place their finger on the center of the green target. After a short delay period, a peripheral target was presented 40 mm away from the center (either up, down, left, or right). This served as the ‘go’ signal for the participant to slide their finger along the screen directly to the presented peripheral target. After reaching the peripheral target and remaining there for 500 ms, a registration sound was played, and the peripheral target disappeared. This served as the signal for the end of the trial. Following a delay of 2000 ms, the central target reappeared, signaling the participant to return to the center for the next trial.

In the other two "cognitive-motor integration" conditions (CMI, decoupling of vision and action), the guiding visual information was decoupled from the spatial location of the movement target in two ways: 1) Feedback Reversal and 2) Split screen and feedback reversal simultaneously. In the feedback reversal (non-standard) task, the measurement and timing of the presentation of the targets remained the same. Nonetheless, in this task, participants were instructed to move their fingers in the opposite direction of the presented target to get the cursor to move toward the target. To further illustrate, if the target appeared on the right, the participant needed to slide their finger to the left on the tablet. Lastly, in the feedback reversal + split screen (plane change) condition, the tablet's screen was divided into an upper and a lower half. The cursor and the targets were only shown on the upper half, while the participant could only move their finger in the lower half of the tablet. In addition to the plane change, the feedback for this task was rotated 180° in the same way it was mentioned in the feedback reversal condition, meaning participants should move their finger to the left in the lower half of the screen if they intended to move the cursor to the right on the upper half of the screen. This created a requirement for strategic control. Decoupling vision and action provided a level of dissociation and having two levels of decoupling (due to the incorporation of feedback reversal in the split screen) created a requirement for strategic control. Participants were asked to do all tasks as quickly and accurately as possible.

Altogether, the tasks performed on the BrDI took approximately 20 minutes to complete. Given that BrDI is accessible on all Android (and possibly IOS in the future) devices, it can be a convenient and less expensive mobile method of assessment if proven compatible compared to current methods of assessment for Alzheimer's disease.

2.4 KINARM robotic tasks

The KINARM machine is a sophisticated, yet expensive device connected to two computers and a television. Using the robotic assessment (KINARM), participants were seated in a modified computer chair that did not swivel. They were positioned in front of a workstation while grasping a handle with each hand, allowing movement in the horizontal plane. This machine was calibrated before use in order to minimize errors. Various tasks were performed to assess motor, proprioceptive, and cognitive function. Virtual reality was used to display targets in the horizontal workspace of the arms. The robot could monitor the location of the hands and was able to move each arm independently when required for the behavioral task. Most tasks had visual targets, and instructions for the tasks came either from pre-recorded video immediately before each task or from the KINARM operator.

Out of the 14 tasks done on the KINARM machine, two tasks called ‘Visually Guided Reaching’ and “Reverse Visually Guided Reaching” corresponded to the tasks done on the BrDI tablet and could therefore be utilized as comparison tools. The purpose of the Visually Guided Reaching test was to quantify goal-directed voluntary control (Coderre et al., 2010). This task assessed postural control, visuomotor response time, and arm motor coordination. During this task, a central target was presented, and the subject had to move a cursor (white circle) representing hand position to this target. Once there, a peripheral target appeared, and the subject had to move quickly and accurately to this target. This process was repeated a number of times both to explore the workspace and to measure variability in the subject's responses.

The Reverse Visually Guided Reaching test assessed the ability of subjects to perform goal-directed motor actions when there was a need to inhibit the automatic motor response to move the hand towards the goal and to use a cognitive rule to move in the opposite direction to attain the goal (Tippett & Sergio, 2006). Reverse Visually Guided Reaching was similar to the Visually Guided Reaching task; however, after reaching the initial central target at the beginning of the task, the movement of the cursor (white circle) representing hand position was mirror-reversed relative to the central target (i.e., movement of the hand to the right and away from the subject led to movement of the cursor to the left and towards the subject). The task required subjects to cognitively override and inhibit the natural response to move the hand directly to a target. Corrective responses to reach the goal also had to override the normal coupling between somatosensory and visual feedback. On average, all 14 KINARM tasks took about two hours to complete altogether.

2.5 Standard neuropsychological tasks

Neuropsychological test batteries are commonly used as an aid in diagnosing Alzheimer's disease (Bäckman, Jones, Berger, Laukka, & Small, 2005). These tests are valuable for determining patterns of impairment, assessing changes in impairment over time and after drug treatment or rehabilitation, and are often pencil and paper tasks (McKhann et al., 1984). For the purpose of this study, WMS-IV booklets were used to assess participants' brain function and to look for signs of dementia. This consisted of a total of 14 pencil and paper tests some of which included: Memory functioning questionnaire, MoCA, Functional activities questionnaire, Auditory verbal learning, Visuospatial memory test, etc. Aside from being costly, these tests take about three hours to complete, can only be administered by trained personnel, and are typically done in hospital settings. A short description of each neuropsychological test administered is provided below:

1. Memory Functioning Questionnaire (MFQ): The MFQ is a self-reporting questionnaire for measuring memory complaints among adults and older adults (Gilewski et al., 1990). The outcome assessed is subjective memory and it takes approximately 10 minutes to complete.

2. Functional Activities Questionnaire: The FAQ is a collateral-report measure of difficulties faced in activities of daily living which can help distinguish between healthy individuals and those living with MCI and AD (Pfeffer et al., 1982). It takes about 5 minutes to complete and measures participants' functional status.

3. MoCA: The MoCA (version 8.1) is administered to participants in order to obtain a global cognition measure of the participant samples (Nasreddine et al., 2005). The main outcome of assessment is cognition, and it takes approximately 5 to complete.

4. Rey Auditory Verbal Learning (RAVLT): The RAVLT is a neuropsychological instrument with the goal of evaluating episodic declarative memory. It provides scores for immediate memory, verbal learning, susceptibility to interference, retention of information after a period of time, and memory recognition (Bowler, 2013). It assesses verbal memory and takes 15 minutes to complete.

5. Brief Visuospatial Memory Test Revised (BVMT-R): The BVMT-R is a neuropsychological instrument with the goal of evaluating visuospatial memory. This test entails reproduction of the features and spatial placement of two-dimensional geometric figures. It also requires participants to copy a series of abstract designs on paper, and then recall them from memory immediately after each copy trial. Additionally, there is a delayed recall component, along with delayed recognition trials (Benedict, 1997). Overall, this test takes about 15 minutes to complete.

6. F-A-S verbal fluency subtest: The F-A-S Test is a subtest of the Neurosensory Center Comprehensive Examination for Aphasia; it is a measure of phonemic word fluency, which is a type of verbal fluency (NCCEA; (Patterson, 2011)). It takes 5 minutes to complete and it measures phonemic fluency by requesting an individual to orally produce as many words as possible that begin with the letters F, A, and S within 60 seconds.

7. Camel and Cactus Test: This is a test of semantic association based on the principle of the Pyramids and Palm Trees test (Howard et al., 1992). Subjects are asked to choose the correct one of four response-choice pictures or words that has an associative relationship with the target. For example, in one of the trials, the participant was asked to match the target, camel, to one of four types of vegetation: tree, sunflower, cactus (the correct response), or rose (Bozeat et al., 2000). This test takes 5 minutes to complete.

8. Animal Naming Test: This is a 1-minute test in which participants are asked to name as many four-legged animals as possible within one minute. This activity is associated with the ability to access semantic memory (Rosen,1980).

9. Wechsler Memory Scale (WMS-R) - Logical Memory subtest: This subtest of the WMS-R is a standardized assessment method of narrative episodic memory and takes 10 minutes to complete (Wechsler, 1987). A short story is orally presented to the subject who is then asked to recall the story verbatim (immediate recall). Approximately 30 min later, free recall of the story is again elicited (delayed recall).

10. Shipley Institute of Living - Vocabulary subtest: “The Shipley Institute of Living Scale (SILS) is a measure of intellectual deficit and provides screening measure for intelligence” (Shipley et al., 1941). The SILS consists of two sections: a multiple-choice vocabulary section and a verbal reasoning section. The vocabulary section consists of 40 multiple-choice items which requires the subjects to select the one word out of four choices that is

closest in meaning to a target word. The abstract reasoning section consists of 20 items and asks the subjects to determine solutions for abstract verbal and arithmetic problems. Total test administration time is approximately 25 min, but since this protocol will use only the vocabulary subtest, administration time is approximately 10 minutes.

11. Wechsler Abbreviated Scale of Intelligence (WASI) - specific subtests of: Similarities, Matrix Reasoning, Block Design: The WASI is a general intelligence, or IQ test, designed to assess specific and overall cognitive capabilities of individuals and is administered to children, adolescents and adults (ages 6-89). It is a battery of four subtests: Vocabulary (31-item), Block Design (13-item), Similarities (24-item) and Matrix Reasoning (30-item). This protocol will use the specific subtests of Block Design, Similarities, and Matrix Reasoning and will take approximately 20 minutes to complete.

12. Wechsler Adult Intelligence Scale-IV (WAIS-IV) – subtest of forward and backward digit span: The Digit Span task requires subjects to repeat a series of digits of increasing in length and is a subtest of the WAIS-IV, an IQ test with range of cognitive tests (Dumont et al., 2014). The outcome measure for digit span forward is simple attention, whereas digit span backwards is more dependent on working memory performance. These subsets take approximately 5 minutes to complete.

13. Wechsler Adult Intelligence Scale-III (WAIS-III) – Digit Symbol Substitution: In this 5-minute assessment, the examinee copies symbols that are paired with numbers within a specified time limit using a key. Associative learning (recall of the symbols without reference to the key/legend) is assessed immediately after.

14. Wechsler Memory Scale (WMS-R) – Verbal Paired Associates subtest: This subtest assesses verbal memory for associated word pairs (Wechsler, 1987). The examiner reads 10 or 14 word pairs to the examinee. Then, the examiner reads the first word of each pair, and asks the examinee to provide the corresponding word. There are four trials of the same list in different orders. Approximately 30 minutes later, the examinee is orally presented with the first word of each pair learned in the immediate condition and asked to provide the corresponding word (delayed recall and Recognition). This component takes about 10-15 minutes to complete.

2.6 Data processing

Kinematic measures such as timing, finger position, and error data were recorded for each trial using a custom-written C++ application. Unsuccessful trials were detected by the data collection software and resulted in trial termination if the finger left the home target too early (<4000 ms), reaction time (RT) was too long (>8000 ms) or too short (<150 ms), or movement time was too long (>10000 ms). Trials in which the first ballistic movement exited the boundaries of the center target in the wrong direction (greater than 45° from a straight line to the target) were coded as direction reversal errors and analyzed as separate variables from the correct trials. A custom-written analysis program on Matlab (Mathworks, Inc., USA) software was used to analyze the data. Velocity profiles were computed for each successful trial and displayed alongside a Cartesian plot illustrating finger position data and target locations using a custom analysis program. The movement onsets and ballistic movement offsets (the initial movement prior to path corrections) were scored at 10% peak velocity, while total movement offsets were scored as the final 10% peak velocity point once the finger position plateaued within the peripheral target. In situations where the initial movement successfully brought the finger to the peripheral target, the ballistic and total movement offsets were equivalent. These profiles were then verified by visual inspection, and corrections were performed when necessary. Afterwards, the scored data was processed to compute 6 different movement timing and execution outcome measures. Individual trials that exceeded 2 standard deviations from the participant's mean for each of the outcome measures were eliminated prior to the calculation of outcomes.

2.7 Dependent measures

The kinematic dependent measures in this study were reaction time, constant error, variable error, full path length, total movement time, and direction reversal errors. These measures were computed using the custom analysis software.

Movement timing. Reaction time (RT) describes the time interval between the central target disappearance and movement onset measured in milliseconds (ms). Movement time (MT) is the time between movement onset and offset measured in milliseconds. It is composed of total movement (MTf, full movement offset) as well as ballistic movement (MTb, initial movement offset). If no corrected movements were made, ballistic movements are equivalent to full movement trajectories.

Movement Execution. Path length is the total distance (resultant of the x and y trajectories) travelled between movement onset and offset, measured in millimeters (mm). It is calculated as both the full path length (PLf, start to final offset) as well as the ballistic trajectory (PLb, start to initial movement offset). Absolute error (AE, end-point accuracy) is the average distance from the individual movement endpoints ($\sum x/n$, $\sum y/n$) to the actual target location, in mm. Variable error

(VE, end-point precision) describes the distance between the individual movement endpoints (σ2) from their mean movement, measured in mm. The percent direction reversal errors (%DR) are the percentage of total trials that constituted a deviation of greater than ±45° from the direct line between the center of the central and peripheral targets.

2.8 Statistical analysis

Statistical analysis was done using SPSS statistical software (SPSS 24, IBM). We compared results obtained from using technology to the traditional neuropsychological tests, which are the current gold standard for predicting conversion from impairment to dementia. More importantly, we were interested to see whether the readily deployable mobile BrDI task, which took less time to complete as well, could be a good predictor of dementia symptoms in older adults. Participants were assessed using two-way ANOVA on each dependent variable in order to look for the main effect of age and sex on each visuomotor kinematic measure. Moreover, regression analysis was done between the BrDI and the neuropsychological tasks to examine how well the tablet tasks could reflect the current standards. Lastly, correlation analyses were performed between the BrDI and the KINARM data as a way to evaluate the sensitivity of the mobile technology compared to the more sophisticated but less accessible technology.

3. Results

Overall, we observed a number of relationships between performance on the cognitive-motor integration task and performance on standard neuropsychological tests. Further, we observed a correlation between performance on our mobile device-based software and the non-portable visuomotor testing system. Hence, these data partially support our hypotheses and demonstrate the utility of mobile technology for assessment of brain health in older individuals. Table 1 presents selected demographic characteristics of the participants of this study. Participants whose data were ultimately included in the analyses were 40 older adults (55 years old and above) with their cognitive state ranging from healthy to early Alzheimer's disease. The sample consisted of a somewhat greater number of males (60%). In terms of age, the mean age was 72 years old (±7.486), the median age was 73 years old, and the overall range was from 56 to 86 years old. Data from 4 recruited participants were excluded due to technical issues and drop out. Data from one individual recruited from the healthy database was transferred to the MCI/ early AD group as their performance on the neuropsychological tests indicated signs of mild cognitive impairment after consultation with our team's physician. Table 1 summarizes participants' characteristics.

Participant characteristics (n=40)	
Characteristic	**Sample**
Gender	
Male	24 (60%)
Female	16 (40%)
Age (years)	
Mean	72 (±7.486)
Range	56-86 yrs
Cognitive State	
Healthy	36 (90%)
MCI/ mild AD	4 (10%)

Table 1. Participant Characteristics by Age, Gender, and Cognitive State

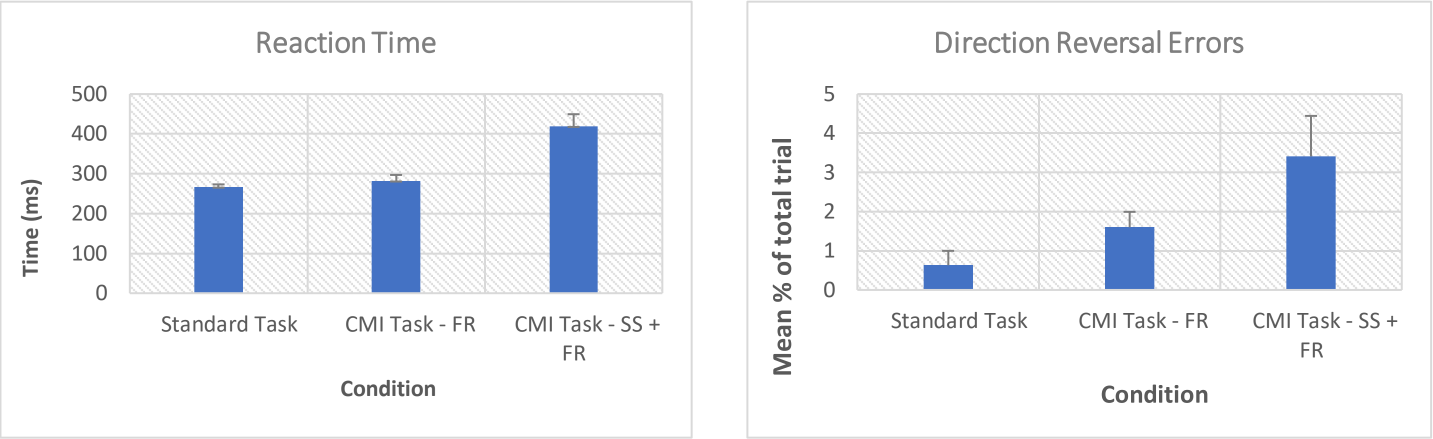
3.1 Performance on Cognitive-Motor Integration task

With respect to basic visuomotor behaviour, we observed reduced performance on the CMI tasks relative to standard tasks, as expected based on previous work; more errors were made as we moved from the standard task to the more dissociated tasks. Descriptive performance data for conditions (standard, CMI- Feedback Reversal, and CMI- Plane Change + Feedback Reversal) are summarized in Table 2.

The two-way ANOVA performed to test for the effect of age and sex on CMI performance demonstrated no main effect for age or sex on any outcome variables in both CMI conditions ($p>0.05$). Similarly, no main effect of age or sex was observed when this ANOVA analysis was done on the healthy participants only ($p>0.05$).

Table 2. Measures of visuomotor performance on the three conditions administered on the BrDI tablet for all participants.

Kinematic Outcome Variables	mean (SD)
Direction reversal errors (mean % of total trials)	
Standard Task	0.63 (2.33)
CMI Task - FR	1.60 (2.49)
CMI Task - SS + FR	3.41 (6.53)
Reaction time (ms)	
Standard Task	266.02 (45.46)
CMI Task - FR	281.40 (98.10)
CMI Task - SS + FR	418.42 (196.45)
Full movement time (s)	
Standard Task	0.95 (0.50)
CMI Task - FR	1.77 (0.64)
CMI Task - SS + FR	2.69 (1.23)
Full path length (mm)	
Standard Task	107.55 (7.04)
CMI Task - FR	111.05 (56.04)
CMI Task - SS + FR	133.85 (32.70)
Absolute error (accuracy) (mm)	
Standard Task	31.29 (20.00)
CMI Task - FR	31.72 (24.70)
CMI Task - SS + FR	25.24 (19.25)
Variable error (precision) (mm)	
Standard Task	3.59 (7.16)
CMI Task - FR	11.74 (10.85)
CMI Task - SS + FR	8.46 (6.78)



Figures 2A and 2B showing participants made more errors and exhibited longer reaction time on the non-standard conditions that required CMI. As the level of task complexity increased, participants performed poorer.

3.1.1 Relationship between performance on mobile device versus KINARM

We observed significant relationships between movement time from the mobile device and the KINARM apparatus. A direct relationship was seen between the standard condition of the BrDI and the visually guided reaching task of the KINARM ($p=0.019$). Moreover, movement time variables derived from the CMI tasks on the BrDI were found to have significant associations with the reverse visually guided tasks on the KINARM ($p<0.001$ for both CMI conditions). This correlation is significant at the 0.05 level (Spearman, 2-tailed). Figures 3,4, and 5 illustrate these relationships.

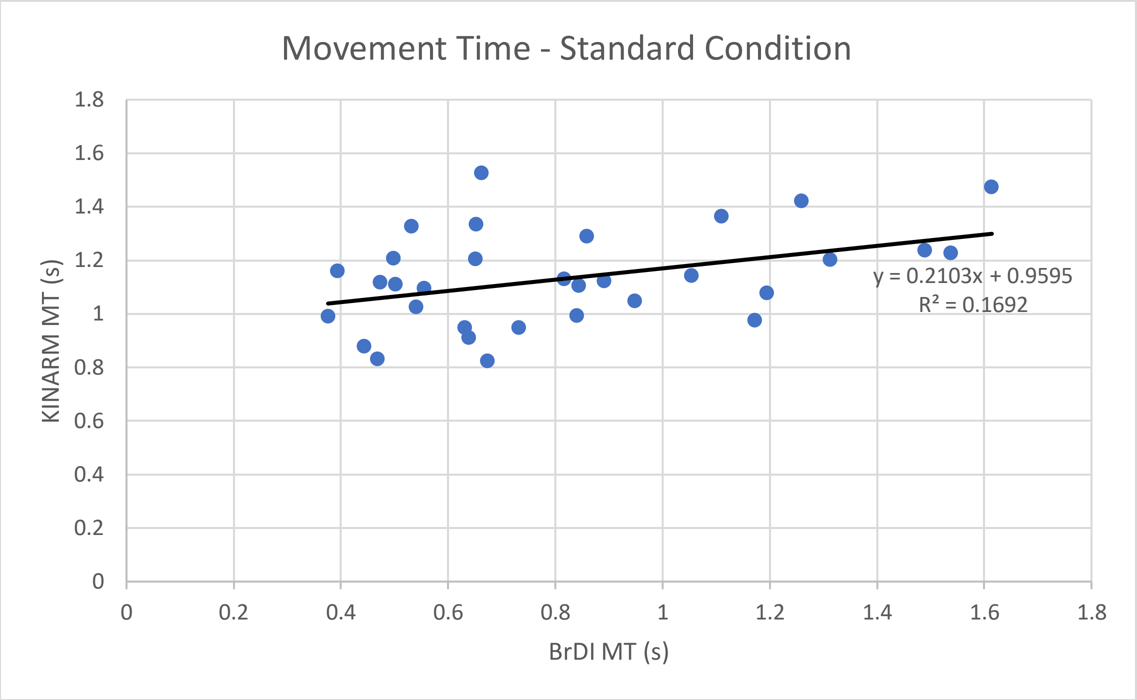


Figure 3. Correlation between the MT variable attained from the standard task on the BrDI tablet (s) and the MT variable attained from the visually guided reaching (VGR) task on the KINARM robot (s). The scatter plot shows a significant direct relationship between the two variables.

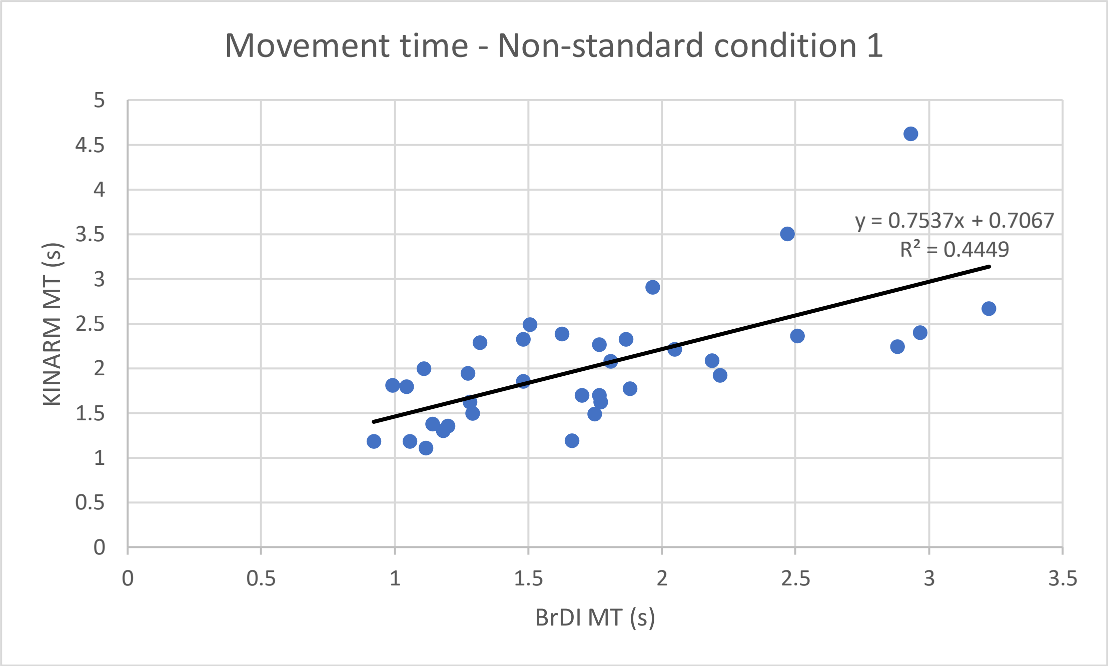


Figure 4. Correlation between the MT variable attained from the FR condition on the BrDI tablet (s) and the MT variable attained from the reverse visually guided reaching (RVGR) task on the KINARM robot (s). The scatter plot shows a significant relationship between the two variables.

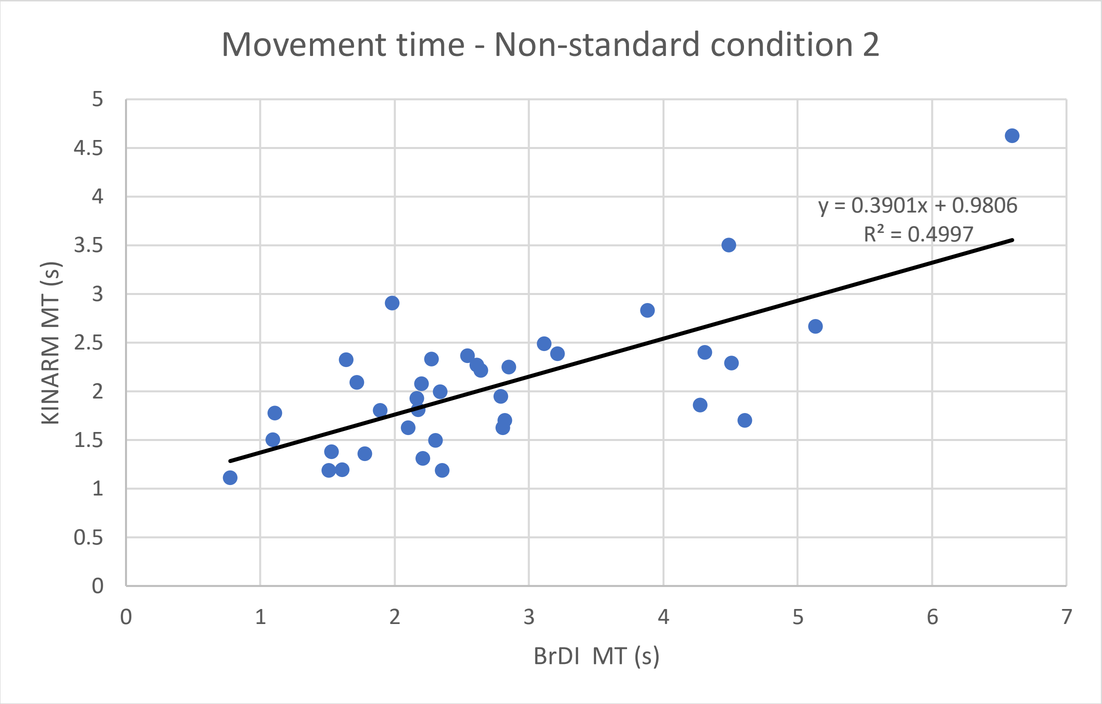


Figure 5. Correlation between the MT variable attained from the FR + SS condition on the BrDI tablet (s) and the MT variable attained from the reverse visually guided reaching (RVGR) task on the KINARM robot (s). The scatter plot shows a significant relationship between the two variables.

3.2 Multivariate regression analyses between the CMI tablet outcome variables and neuropsychological tests

In order to tease apart the relative effects of different factors that may contribute to performance on visuomotor tasks as a function of brain health, a multivariate hierarchical linear regression resulted in a three-variable model of sex, age, and outcome measure as statistically significant predictors of visuomotor performance.

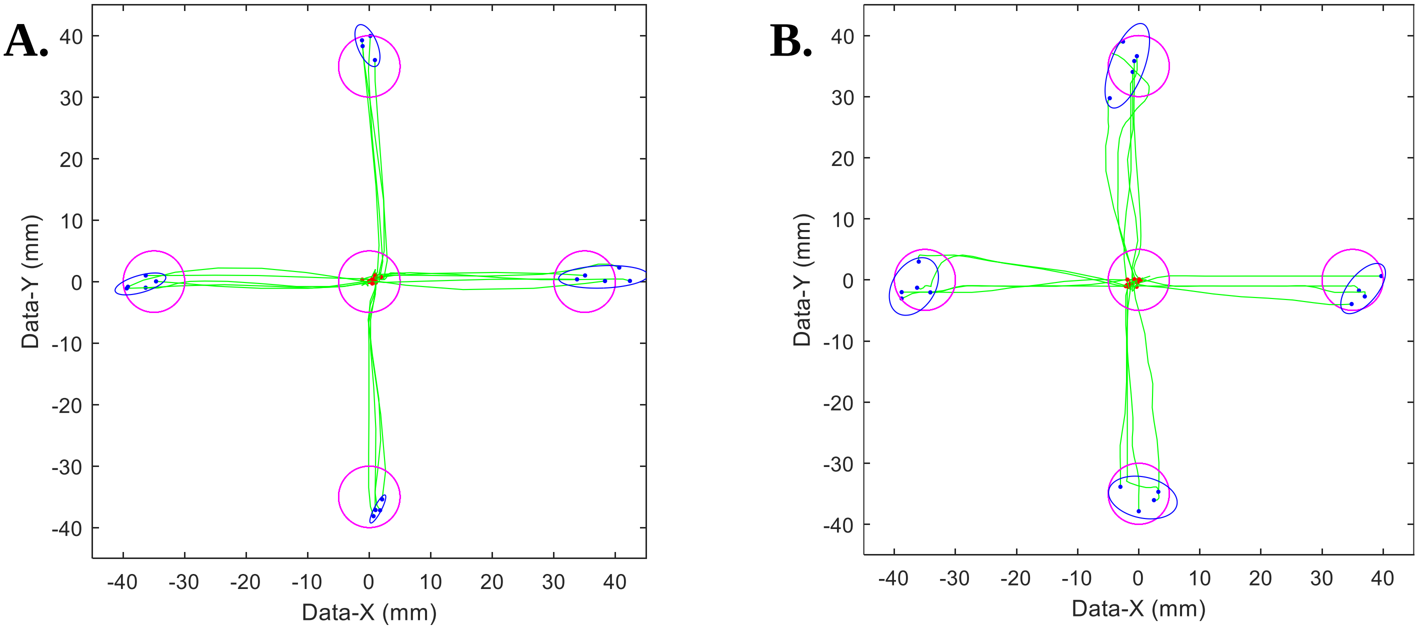
3.2.1 Full movement time.

We found MT in both CMI task conditions to be significantly associated with BVMT delayed recall test of visuospatial memory (ß = -0.179, $p = 0.046$, $R^2 = 0.220$ and ß = -0.106, $p = 0.022$, $R^2 = 0.261$ for FR and FR + SS respectively). Additionally, MT from the most dissociated task (FR

+ SS) was significantly associated with BVMT total recall test (ß = -0.088, p = 0.045, R^2 = 0.281). Lastly, MT from the feedback reversal BrDI condition was found to be associated with Trails time B test (ß = -0.233, p = 0.007, R^2 = 0.305). Notably, all of these findings were calculated while accounting for sex and age.

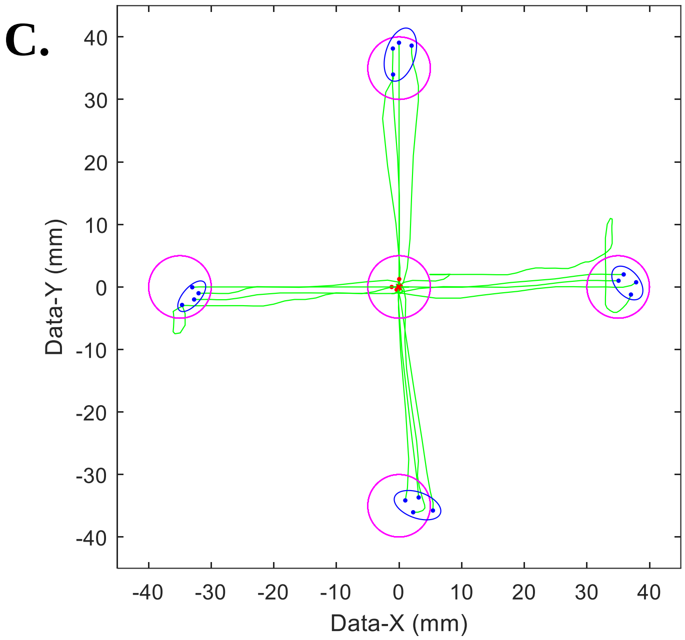
3.2.2 Full path length.

After accounting for sex and age, PL from the CMI task having one level of dissociation (feedback reversal, FR) was significantly associated with the BVMT test series, while the CMI task having two levels of dissociation (feedback reversal plus split-screen, FR + SS) was significantly associated with the WMS verbal PAL test series. To further illustrate, PL from the first CMI condition was affiliated with the delayed recall test (ß = 0.006, p = 0.018, R^2 = 0.244) as well as the BVMT total recall test and (ß = 0.005, p = 0.048, R^2 = 0.248). Moreover, significant relationships were also seen between PL from the second CMI task and the WMS IV verbal PAL VPA I test (ß = -0.057, p = 0.003, R^2 = 0.541) as well as the WMS IV verbal PAL VPA I test (ß = -0.003, p = 0.003, R^2 = 0.541). Figure 6 illustrates the full finger path for movement trajectory across all three tablet tasks.



Finger position (Full Path) – Standard Task

Finger position (Full Path) – FR CMI Task



Finger position (Full Path) – FR + SS CMI Task

Figure 6. Sample hand movement trajectories (full path) from a participant showing declined performance in the visuomotor task conditions requiring cognitive motor integration (tasks in Panels B and C), relative to the standard task (panel A). Hand trajectories begin at the central target (red dots) and move towards one of four peripheral targets, where each green line represents a single movement trajectory. Blue ellipses denote the 95% C.I. for the final endpoint of the finger movements (blue dots).

3.2.3 Absolute error.

We observed that ABSerr from the FR BrDI task was significantly associated with the following neuropsychological tests: 1) BVMT delayed recall test ($ß = -0.19$, $p = 0.042$, $R^2 = 0.209$) as seen in figure 7 and 2) Trails time B ($ß = -0.022$, $p = 0.01$, $R^2 = 0.305$) tests. Our analyses found these relationships to account for this significant amount of ABSerr variance even after accounting for sex and age.

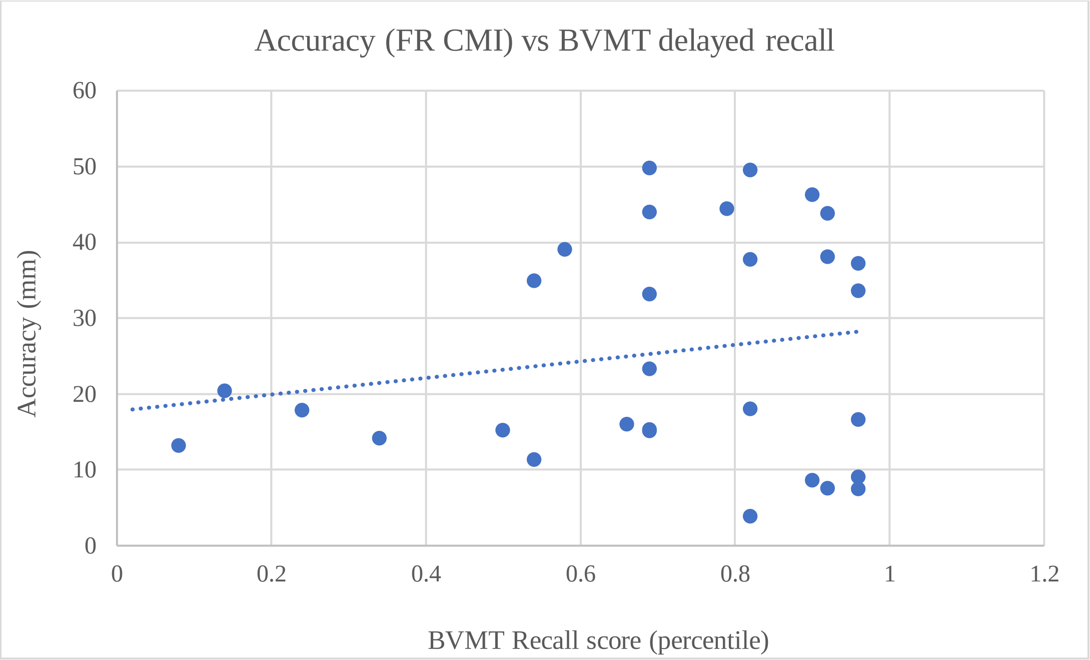


Figure 7. Scatter plot showing linear regression line of absolute error (accuracy) from the feedback reversal (non-standard/CMI) task on the BrDI tablet in mm vs. the score from the Brief Visuospatial Memory (BVMT) delayed recall neuropsychological test as percentile. ($p=0.042$, $\beta=-0.019$, $R^2=0.209$)

3.2.4 Reaction Time.

We found that RT from the FR (less dissociated) BrDI condition was significantly associated with WMS IV verbal PAL VPA I (ß = 0.036, p = 0.023, $R^2 = 0.621$) after accounting for sex and age. In similar conditions, RT from the most dissociated condition (FR + SS) was significantly associated with Trails time B neuropsychological test (ß = 0.001, p = 0.040, $R^2 = 0.301$).

3.2.5 Variable error.

After running the analyses, we noticed significant relationships between the VE variables from both CMI tasks and Trails time B neuropsychological test while accounting for sex and age. VE was indirectly associated with this test (ß = -0.019, p = 0.021, $R^2 = 0.279$ for FR condition (first CMI task) and ß = -0.028, p = 0.010, $R^2 = 0.305$ for FR + SS condition (second CMI task)).

3.2.6 Direction reversals.

No significant relationships were observed between the BrDI outcome variables and the neuropsychological tests.

4. Discussion

The present study sought to determine whether performance on a rule-based visually-guided reaching task, delivered on a tablet, correlated with performance on traditional assessments, demonstrating the efficacy of the mobile technology. A secondary aim of this study was to assess whether the portable tablet technology would adequately reflect the results obtained from the non-portable technology – KINARM - that has been used for the assessment of neurological disorders previously. Our findings indicate that some of the variables from the tablet tasks (CMI conditions) are significantly associated with certain neuropsychological tests (BVMT delayed and total recall, Trails time B, and Verbal PAL I). Additionally, a relationship was observed between one of the BrDI and KINARM performance variables. On a basic level, we observed that performance declined in all participants as the level of dissociation between the visual target and movement increased.

The results of the current study demonstrate that a non-standard visually guided reaching tasks that takes 10 to 20 minutes to complete on a tablet is sufficient for diagnosing only some domains of neuropsychological function assessed by traditional pencil-and-paper collection to measure functional deficits in older adults. Moreover, although some level of association was seen between the BrDI and the KINARM variables, the BrDI tasks were not sensitive enough to reflect the full suite of KINARM tasks. In alignment with previous work, these data confirm that the mobile technology is able to sensitively assess multi-domain integration performance in older adults, as it was designed to do.

4.1 Visually guided reaching

Our findings complement previous studies: visuomotor deficits were evident when there was a dissociation between vision and action, and were observed in the execution and accuracy of movements (Rogojin et al., 2019). Eye-hand coordination plays a crucial role in visually guided reaching tasks; it allows individuals to accurately coordinate their eye movements with hand movements to interact with objects in the environment. While eye-hand coordination tends to decline with age, this decline becomes more pronounced in non-standard visually guided reaching tasks that deviate from familiar or typical patterns.

Age-related declines in cognitive processing can affect the ability to efficiently and accurately extract relevant visual cues and incorporate them with motor actions (Murman, 2015). Therefore, the complexity of the visual stimuli can overwhelm older adults' cognitive systems, resulting in reduced accuracy, slower processing, and impaired eye-hand coordination in non-standard reaching tasks (Verheji et al., 2012). In addition to cognitive decline, with aging, motor control processes involved in reaching movements also undergo changes (Seidler et al., 2010). According to previous studies, older adults demonstrate reduced movement accuracy, slower movement initiation, and increased movement variability compared to younger adults (Ketcham & Stelmach, 2004). These deviations may stem from changes in the neuromuscular system, such as alterations in muscle fiber composition, declines in muscle strength, and reduced proprioceptive feedback (Seidler et al., 2010).

These declines in coordination and motor control associated with advancing age can negatively impact non-standard visually guided reaching performance, in which both vision and proprioception must work hand in hand to remap the visual location of the target and representation of the hand in one plane onto the true location of the hand and target in the other plane.

4.2 Sex differences

Throughout the course of analyses, significant sex differences were continuously observed where females performed better than males. The sex differences observed after adjusting for other factors, is consistent with previous work in which males performed worse in a CMI task (Rogojin et al., 2019). There are a variety of factors that could be the underlying reason for this difference such as biological factors that could affect cognition.

Certain structural and organizational differences in brain can contribute to the differences observed. Females tend to have relatively larger corpus callosum which can enhance interhemispheric connectivity and therefore improve coordination and integration of cognitive and motor processes (Liu et al., 2020). Furthermore, previous studies have observed that both CMI and standard tasks evoke a more bilateral pattern of activity in premotor and parietal regions in women compared to men. This is while men show greater lateral sulcus activity than women do in CMI tasks (Gorbet & Sergio, 2007; Sergio et al., 2020). Additionally, studies have shown that hormonal variations between females and males may play a role in cognitive-motor performance, giving females an advantage in certain tasks. In particular, estrogen and progesterone have been linked to enhanced spatial cognition and fine motor control (Gurvich et al., 2018; Ali et al., 2018). Lastly, research suggests that women may have an advantage in attentional control and multitasking, which can be beneficial in cognitive-motor tasks that require processing of multiple information streams simultaneously (Lui et al., 2021). Our data further supports these differences with our observed sex differences in neuropsychological test performance as a function of sex.

4.3 Fluid Intelligence and Visuomotor Skills

Fluid intelligence (FI) refers to the capacity to solve new problems, think abstractly, and adapt to new situations independently of prior knowledge or experiences. It involves the ability to identify patterns from novel information, make logical connections and judgements, and draw conclusions (Jaeggi et al., 2008). As mentioned, fluid intelligence is not reliant on previously acquired knowledge; rather, it centers on raw cognitive processing power. It has been shown that FI declines steeply during aging (Kievit et al., 2018). Previous studies with fMRI suggest that FI is strongly associated with activation of a frontoparietal brain network, and focal damage to these regions confirms that the integrity of these regions is of importance to the functionality of FI (Mitchell et al., 2023). As a result, it is possible that age or disease related functional differences in frontoparietal activity contribute to the decline in FI.

On the other hand, visuomotor skills (or visuomotor integration) refer to the coordination between visual perception and motor control. They involve the ability to process visual cues from the surrounding and translating them into appropriate motor responses. The main area of the brain involved in visuomotor integration is the parietal lobe followed by the cerebellum, brainstem and frontal lobe (Khatib et al., 2022).

While fluid intelligence and visuomotor skills might seem distinct, they are intertwined in various ways due to the utilization of similar brain regions. In this study, some of the neuropsychological tests, such as Trails B and Verbal paired associated learning, were also indicators of fluid intelligence. While they may not directly measure fluid intelligence, they involve cognitive processes that can be related to fluid intelligence and visuomotor skills. These tests challenge one’s cognitive flexibility, attention, mental processing speed, and visuomotor coordination and therefore, highlight the intricate interplay between these cognitive domains. As mentioned earlier, aging is associated with changes in brain structure and function that can impact both fluid intelligence and visuomotor skills. Changes in the frontoparietal brain regions and prefrontal cortex, reduced neural plasticity, and alterations in neurotransmitter systems can all contribute to the age-related decline seen in fluid intelligence (Mitchell et al., 2023). Through the significant associations observed between the BrDI variables and neuropsychological tests (Trails B and Verbal paired associated learning), we believe that by incorporating the tablet task, we are generalizing from neuropsychological tasks that are usually a cognitive pairing, to a visuo-motor pairing that requires cognition. Instrumental activities of daily living are an important indicator of one’s quality of life and are often assessed by occupational therapists in order to determine the level of an individual's need for assistance and cognitive function. Taking these factors into consideration, we can propose that BrDI would be a simple test to examine one’s instrumental activities of daily living.

4.4 Technology for Health Assessment

Mobile technology has revolutionized various aspects of our daily lives. More specifically, one of its most promising applications is in the field of health assessment through the integration of smartphones and wearable devices. While these have made significant improvements, the progression has been slower for an assessment tool for early dementia symptoms. With a rapidly aging population, comes an increase in the number of older adults living with chronic conditions such as dementia, which has become one of the leading causes of disability and dependency worldwide (WHO, 2023). The current technologies used in this field are single domain and lack the ability to assess one’s cognitive state from a psycho-motor-behavioural aspect (Koo & Vizer, 2019; Shu & Woo, 2021). We have established that while our mobile technology has certain limitations, it is a more well-rounded method of assessment compared to other mobile technologies. In other words, BrDI has some limited utility as a quick and easy first level of assessment which can flag an individual for further assessment and follow up. Considering that BrDI uses a multi-domain approach that is missing from the other mobile technologies, utilizing it can be an improvement over the current available technology.

Strengths and limitations

The current study investigated if, and to what extent, performance on visually guided reaching tasks delivered on a tablet is consistent with performance on standard neuropsychological tests, as well as more expensive and non-portable technology. It is often difficult to find older individuals without a history of or current serious medical condition who are not prescribed to take medication with effects that may alter study results. Therefore, one of the key strengths of this study is the wide age range (~ 30 years) of the healthy older adult participants.

One of the probable limitations of this study can be the physical variability in musculoskeletal health in individuals in this age range. Given that participants were offered breaks as requested and fatigue was never reported in participants' feedback, we believe it did not significantly impact performance. Due to the COVID-19 pandemic, all stages of this study had to be put on hold multiple times. As a result, we were unable to recruit as many MCI/ early AD participants as we were initially aiming for. Having more mild cognitive disorder and/or early Alzheimer's disease participants could have made the comparisons and the results more generalizable and in depth. This could perhaps be a good objective for future studies in this field.

Conclusion

The current study sought to determine whether visuomotor tasks delivered on mobile technology can be utilized as an assessment tool in older adults with neurological conditions, specifically dementia. A secondary goal of this study was to compare our portable mobile technology to the current non-portable and more expensive technology used for assessment of certain conditions. Data was collected from individuals ranging from healthy to early Alzheimer's disease/ mild cognitive impairment. Our analyses showed a few overlaps and significant relationships between the results obtained from the BrDI tasks and those attained from the traditional neuropsychological tests and the KINARM machine. Results showed that our tasks are capable of detecting very small changes in some of the outcome variables. Although our 15-minute test did not fully align with the other assessment methods, considering that it is a multi-domain task with the ability to take factors such as fluid intelligence into considerations, it can be a good first-step assessment tool to flag individuals that may be at risk of dementia. Future work and adjustments to the tasks can possibly turn the BrDI tablet tasks into an even more sensitive assessment platform.

Appendix

A. Health Questionnaire for recruitment

Study Phone Screening Form – Healthy Controls

Completed by: ___________ Date: ___________

Yes	No	Inclusion criteria (one no = ineligible)
☐	☐	No confirmed diagnosis of MCI or AD
☐	☐	Aged 55+

Yes	No	Exclusion criteria (one yes = ineligible)
☐	☐	• History of neurological disorders (e.g., malignant brain tumour, multiple sclerosis, Down's syndrome or other developmental disorders, epilepsy, seizures, Parkinson's, any dementia or neurodegenerative disorder)
☐	☐	• Stroke or history of transient ischemic attack (TIA)
☐	☐	• History of traumatic brain injury (TBI) with loss of consciousness lasting longer than 30 min
☐	☐	• Active cancer, history of chemotherapy, or history of radiation to the head
☐	☐	• History of psychiatric conditions, including: o Diagnosis of major depressive disorder, generalized anxiety disorder, or other psychiatric diagnosis within 90 days of study entry, or o lifetime history of psychosis, bipolar disorder, obsessive

		compulsive disorder, schizophrenia, or post-traumatic stress disorder (PTSD) ○ history of substance use within the past year
		• Serious medical disease that would/could lead to death over the next 2-3 years (e.g. cardiac/renal/liver disease, or cancer) with poor prognosis
☐	☐	• Difficulty with vision, including cataracts or glaucoma
		• Presence of colour blindness
☐ ☐ ☐	☐ ☐ ☐	• Started taking psychotropic medication (anti-anxiety, anti-psychotics) or cognitive enhancers (memantine, acetylcholinesterase inhibitors) less than 3 months prior to enrolment, or has had a change in dosages of any acetylcholinesterase inhibitors or cognitive enhancers within 6 weeks of enrolment, or has had any changes in all types of medications or dosages within 4 weeks of enrolment.
		• Unable to understand, read, and speak English
☐	☐	

If all “yes” for inclusion and all “no” for exclusion, enroll participant with study ID: ___________

Supplementary Tables

Table 3. Results from models 1 (sex only), 2 (age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Brief Visuospatial Memory Test (BVMT)-Delayed Recall (one of the neuropsychological tests administered to the participants) and BrDI variables from FR condition. (N = 40).

BVMT Delayed Recall Percentile Score vs. BrDI FR			
	Unstandardized B	p value	R^2
Sex†	0.153	0.190	0.112
Age	0.002	0.824	0.115
% Direction Reversal	0.013	0.611	0.133
Sex†	0.199	0.066	0.099
Age	0.004	0.519	0.110

Full Movement Time (s)	-0.179	**0.046**	0.220
Sex†	0.187	0.072	0.090
Age	0.004	0.512	0.101
Absolute Error/Accuracy (mm)	-0.019	**0.042**	0.209
Sex†	0.187	0.072	0.090
Age	0.004	0.512	0.101
Variable Error/Precision (mm)	-0.015	0.077	0.184
Sex†	0.187	0.072	0.090
Age	0.004	.512	0.101
Full Path Length (mm)	0.006	**0.018**	0.244
Sex†	0.595	0.230	0.068
Age	0.009	0.328	0.113
Reaction Time (ms)	0.001	0.443	0.140

† Females compared to males

A positive unstandardized B indicates better performance on BVMT and a negative unstandardized B indicates a poorer performance on BVMT. Significant values are shown in bold.

Table 4. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Brief Visuospatial Memory Test (BVMT)-Delayed Recall (one of the neuropsychological tests administered to the participants) and BrDI variables from FR+SS condition. (N = 40).

BVMT Delayed Recall Percentile Score vs. BrDI FR + SS			
	Unstandardized B	p value	R^2
Sex†	0.295	0.069	0.191
Age	-0.006	0.547	0.211
% Direction Reversal	0.013	0.209	0.298
Sex†	0.187	0.072	0.090
Age	0.004	0.512	0.101
Full Movement Time (s)	0.106	**0.022**	0.261
Sex†	0.187	0.080	0.088
Age	0.005	0.494	0.101
Absolute Error/Accuracy (mm)	-0.017	0.170	0.153
Sex†	0.172	0.101	0.077
Age	0.007	0.293	0.108
Variable Error/Precision (mm)	-0.009	0.405	0.128

Sex†	0.176	0.119	0.074
Age	0.005	0.515	0.087
Full Path Length (mm)	-0.002	0.274	0.123
Sex†	0.173	0.116	0.075
Age	0.005	0.448	0.093
Reaction Time (ms)	0.000	0.170	0.149

† Females compared to males

A positive unstandardized B indicates better performance on BVMT and a negative unstandardized B indicates a poorer performance on BVMT. Significant values are shown in bold.

Table 5. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Brief Visuospatial Memory Test (BVMT)-Total Recall (one of the neuropsychological tests administered to the participants) and BrDI variables from FR+SS condition. (N = 40).

BVMT Total Recall Percentile Score vs BrDI FR			
	Unstandardized B	p value	R^2
Sex†	0.299	0.027	0.285
Age	0.001	0.898	0.286
% Direction Reversal	0.016	0.556	0.306
Sex†	0.247	0.017	0.160
Age	0.002	0.747	0.163
Full Movement Time (s)	-0.011	0.190	0.209
Sex†	0.236	0.018	0.149
Age	0.002	0.738	0.152
Absolute Error/Accuracy (mm)	-0.015	0.088	0.224
Sex†	0.236	0.018	0.149
Age	0.002	0.738	0.152
Variable Error/Precision (mm)	-0.012	0.148	0.205
Sex†	0.236	0.018	0.149
Age	0.002	0.738	0.152
Full Path Length (mm)	0.005	**0.048**	0.248
Sex†	0.250	0.050	0.170
Age	0.005	0.606	0.182
Reaction Time (ms)	0.002	0.257	0.236

† Females compared to males

A positive unstandardized B indicates better performance on BVMT and a negative unstandardized B indicates a poorer performance on BVMT. Significant values are shown in bold ($p<0.05$).

Table 6. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Brief Visuospatial Memory Test (BVMT)-Total Recall (one of the neuropsychological tests administered to the participants) and BrDI variables from FR+SS condition. (N = 40).

BVMT Total Recall Percentile Score vs BrDI FR + SS			
	Unstandardized B	p value	R^2
Sex†	0.354	0.022	0.287
Age	-0.008	0.331	0.332
% Direction Reversal	0.003	0.742	0.337
Sex†	0.262	0.010	0.180
Age	0.002	0.730	0.183
Full Movement Time (s)	-0.088	**0.045**	0.281
Sex†	0.240	0.019	0.151
Age	0.003	0.654	0.156
Absolute Error/Accuracy (mm)	-0.010	0.398	0.175
Sex†	0.225	0.026	0.137
Age	0.004	0.533	0.147
Variable Error/Precision (mm)	-0.002	0.849	0.148
Sex†	0.247	0.020	0.158
Age	0.002	0.735	0.161
Full Path Length (mm)	-0.003	0.123	0.226
Sex†	0.209	0.047	0.118
Age	0.002	0.766	0.120
Reaction Time (ms)	4.308E-5	0.884	0.121

† Females compared to males

A positive unstandardized B indicates better performance on BVMT and a negative unstandardized B indicates a poorer performance on BVMT. Significant values are shown in bold.

Table 7. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between MoCA (one of the neuropsychological tests administered to the participants) and BrDI variables from FR condition. (N = 40).

MoCA Total Score vs BrDI FR			
	Unstandardized B	p value	R^2
Sex†	0.121	0.913	0.001
Age	-0.104	0.191	0.120
% Direction Reversal	-0.106	0.644	0.135
Sex†	1.048	0.251	0.040
Age	0.014	0.811	0.042
Full Movement Time (s)	-0.001	0.368	0.067
Sex†	0.994	0.261	0.036
Age	0.015	0.797	0.038
Absolute Error/Accuracy (mm)	0.014	0.869	0.039
Sex†	0.994	0.261	0.036
Age	0.015	0.797	0.038
Variable Error/Precision (mm)	-0.008	0.922	0.038
Sex†	0.994	0.261	0.036
Age	0.015	0.797	0.038
Full Path Length (mm)	0.020	0.388	0.060
Sex†	0.331	0.763	0.004
Age	-0.040	0.622	0.017
Reaction Time (ms)	0.025	0.087	0.161

† Females compared to males

A positive unstandardized B indicates better performance on MoCA and a negative unstandardized B indicates a poorer performance on MoCA.

Table 8. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between MoCA (one of the neuropsychological tests administered to the participants) and BrDI variables from FR+SS condition. (N = 40).

MoCA Total Score vs BrDI FR + SS			
	Unstandardized B	p value	R^2
Sex†	0.643	0.664	0.012
Age	0.074	0399	0.059
% Direction Reversal	-0.004	0.967	0.060
Sex†	0.994	0.261	0.036
Age	0.015	0.797	0.038
Full Movement Time (s)	-0.001	0.071	0.130

Sex[†]	1.125	0.209	0.046
Age	0.039	0.525	0.058
Absolute Error/Accuracy (mm)	0.025	0.809	0.060
Sex[†]	0.925	0.305	0.031
Age	0.028	0.651	0.037
Variable Error/Precision (mm)	0.126	0.208	0.084
Sex[†]	0.964	0.310	0.032
Age	0.041	0.518	0.045
Full Path Length (mm)	-0.018	0.338	0.075
Sex[†]	0.821	0.378	0.024
Age	0.019	0.754	0.027
Reaction Time (ms)	-0.001	0.632	0.035

[†] Females compared to males

A positive unstandardized B indicates better performance on MoCA and a negative unstandardized B indicates a poorer performance on MoCA.

Table 9. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Verbal Fluency F-A-S (one of the neuropsychological tests administered to the participants) and BrDI variables from FR condition. (N = 40).

Verbal Fluency FAS Percentile Score vs BrDI FR			
	Unstandardized B	p value	R^2
Sex[†]	0.130	0.199	0.107
Age	0.007	0.306	0.174
% Direction Reversal	0.006	0.790	0.179
Sex[†]	0.200	0.025	0.144
Age	0.001	0.161	0.145
Full Movement Time (s)	0.000	0.066	0.234
Sex[†]	0.199	0.017	0.152
Age	0.001	0.867	0.152
Absolute Error/Accuracy (mm)	-0.010	0.155	0.203
Sex[†]	0.199	0.017	0.152
Age	0.001	0.867	0.152
Variable Error/Precision (mm)	-0.009	0.215	0.191
Sex[†]	0.199	0.017	-0.152
Age	0.001	0.867	0.152

Full Path Length (mm)	0.002	0.252	0.186
Sex†	0.153	0.129	0.106
Age	0.009	0.236	0.168
Reaction Time (ms)	0.000	0.766	0.172

† Females compared to males

A positive unstandardized B indicates better performance on Verbal Fluency F-A-S and a negative unstandardized B indicates a poorer performance on Verbal Fluency F-A-S.

Table 10. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Verbal Fluency F-A-S (one of the neuropsychological tests administered to the participants) and BrDI variables from FR+SS condition. (N = 40).

Verbal Fluency FAS Percentile Score vs BrDI FR + SS			
	Unstandardized B	p value	R^2
Sex†	0.090	0.452	0.036
Age	-0.001	0.853	0.038
% Direction Reversal	0.008	0.340	0.101
Sex†	0.199	0.017	0.152
Age	0.001	0.867	0.152
Full Movement Time (s)	-5.16E-5	0.156	0.203
Sex†	0.181	0.28	0.134
Age	-0.002	0.707	0.138
Absolute Error/Accuracy (mm)	-0.007	0.460	0.153
Sex†	0.196	0.022	0.145
Age	0.002	0.791	0.147
Variable Error/Precision (mm)	-0.016	0.072	0.230
Sex†	0.167	0.054	0.111
Age	-0.002	0.756	0.114
Full Path Length (mm)	-0.001	0.391	0.136
Sex†	0.202	0.022	0.153
Age	0.002	0.684	0.158
Reaction Time (ms)	0.000	0.182	0.207

† Females compared to males

A positive unstandardized B indicates better performance on Verbal Fluency F-A-S and a negative unstandardized B indicates a poorer performance on Verbal Fluency F-A-S.

Table 11. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Trails Time B (one of the neuropsychological tests administered to the participants) and BrDI variables from FR condition. (N = 40).

Trails Time B Percentile Score vs BrDI FR			
	Unstandardized B	p value	R^2
Sex†	0.231	0.164	0.125
Age	0.006	0.625	0.141
% Direction Reversal	-0.018	0.603	0.159
Sex†	0.221	0.041	0.121
Age	0.001	0.888	0.121
Full Movement Time (s)	-0.233	**0.007**	0.305
Sex†	0.242	0.018	0.149
Age	0.001	0.869	0.149
Absolute Error/Accuracy (mm)	-0.022	**0.010**	0.305
Sex†	0.242	0.018	0.149
Age	0.001	0.869	0.149
Variable Error/Precision (mm)	-0.019	**0.021**	0.279
Sex†	0.242	0.018	0.149
Age	0.001	0.869	0.149
Full Path Length (mm)	0.003	0.177	0.196
Sex†	0.193	0.172	0.087
Age	0.013	0.208	0.158
Reaction Time (ms)	-0.001	0.429	0.186

† Females compared to males

A positive unstandardized B indicates better performance on Trails Time B and a negative unstandardized B indicates a poorer performance on Trails Time B. Significant values are shown in bold ($p<0.05$).

Table 12. Results from models 1(sex only), 2(age, after accounting for sex) and 3(CMI variable after accounting for sex and age) of hierarchical linear regression showing the association between Trails Time B (one of the neuropsychological tests administered to the participants) and BrDI variables from FR+SS condition. (N = 40).

Trails Time B Percentile Score vs FR + SS			
	Unstandardized B	p value	R^2
Sex†	0.292	0.094	0.166
Age	-0.006	0.538	0.187
% Direction Reversal	-0.011	0.324	0.244

Sex[†]	0.242	0.018	0.149
Age	0.001	0.869	0.149
Full Movement Time (s)	0.094	**0.043**	0.244
Sex[†]	0.243	0.021	0.148
Age	0.002	0.830	0.149
Absolute Error/Accuracy (mm)	-0.019	0.115	0.214
Sex[†]	0.238	0.023	0.143
Age	0.002	0.803	0.145
Variable Error/Precision (mm)	-0.028	**0.010**	0.305
Sex[†]	0.215	0.051	0.114
Age	0.002	0.784	0.116
Full Path Length (mm)	0.000	0.961	0.116
Sex[†]	0.272	0.012	0.183
Age	0.004	0.552	0.193
Reaction Time (ms)	0.001	**0.040**	0.301

† Females compared to males

A positive unstandardized B indicates better performance on Trails Time B and a negative unstandardized B indicates a poorer performance on Trails Time B. Significant values are shown in bold ($p<0.05$).

Table 13. Summary of the range of scores attained by participants (either as a scaled score or percentile) on some of the neuropsychological tests.

Neuropsychological test	**Healthy Group**			**MCI/ Early AD Group**		
	Mean Score	**Lowest Score**	**Highest Score**	**Mean Score**	**Lowest Score**	**Highest Score**
MoCA	27.11	21	30	21.6	15	25
Trails Time B (%)	59.61	<10	>90	14.4	<10	30
Verbal Fluency FAS (%)	68	5	95	31	5	70
BVMT Total Recall (%)	60	3	98	14	<1	50
BVMT Delayed Recall (%)	66.66	2	96	10.58	<1	21
Verbal PAL VPA I	12.58	5	19	6.25	4	11
Verbal PAL VPA II	12.39	7	18	6	4	8

WAIS Block Design	12.28	8	18	9.4	6	11
WAIS Similarities	12.89	2	19	9.6	8	12
WAIS Matrix reasoning	13.19	6	19	9.4	4	14
Camel and Cactus	58	53	62	57.4	53	60

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