2024

USING A REVERSE VISUALLY GUIDED REACHING TASK TO DISTINGUISH BETWEEN HEALTHY AGING AND EARLY ALZHEIMER'S DISEASE

Brandon Woolman
Michigan Technological University, brwoolma@mtu.edu

USING A REVERSE VISUALLY GUIDED REACHING TASK TO DISTINGUISH BETWEEN HEALTHY AGING AND EARLY ALZHEIMER'S DISEASE

By

Brandon Woolman

A THESIS

Submitted in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

In Applied Cognitive Science and Human Factors

MICHIGAN TECHNOLOGICAL UNIVERSITY

2024

This thesis has been approved in partial fulfillment of the requirements for the Degree of MASTER OF SCIENCE in Applied Cognitive Science and Human Factors.

Department of Cognitive and Learning Sciences

Thesis Advisor:	*Kevin M. Trewartha*
Committee Member:	*Shane T. Mueller*
Committee Member:	*Florian Kagerer*
Department Chair:	*Kelly S. Steelman*

Table of Contents

Acknowledgements

Thank you to the National Institute of Health and Michigan Tech Graduate School for providing funding to support this research.

Thank you to my former lab mate, Dr. Alexandra Watral and my advisor, Dr. Kevin Trewartha for their guidance throughout my time as a graduate student.

Abstract

Changes in motor behavior may function as a proxy for cognitive decline. While Alzheimer's disease (AD) is associated with impairments in learning and memory, recent studies suggest that subtle changes in motor task performance may reflect early cognitive changes. For example, the visuomotor rotation task that manipulates visual feedback about hand position during reaching movements, can be used to examine cognitive changes in aging populations. The current study used the reverse visually guided reaching task (rVGR) which rotates visual feedback of participant's hand position 180º relative to the actual hand position. We sought to expand on previous literature by recruiting cognitively impaired individuals to characterize changes in rVGR performance in early AD. We also examined learning curves to assess the impact of cognitive impairment on learning in the rVGR task and probed the cognitive correlates of rVGR performance with a neuropsychological battery. We recruited young adults, and older adults (55 – 85 years old) with and without cognitive impairment to complete a VGR task with veridical mapping, and then the rVGR task. Overall, cognitively impaired adults exhibited longer reaction times and performed more corrective movements. Age differences were observed for nearly all overall measures of performance. The largest differences between healthy older adults and cognitively impaired adults were identified in the earliest stages of the learning curve. In the first few movements, the cognitively impaired group made more angular errors. Both overall- and early- measures of performance were correlated with measures of cognitive control. These findings add to the growing literature suggesting that sensorimotor adaptation tasks may be sensitive to early cognitive changes in AD.

1 Introduction

Alzheimer's Disease (AD) is the most common form of dementia. Dementia is an umbrella term for a variety of age-related diseases that impact cognitive functions, including memory. While late stages of cognitive impairment tend to be detrimental to daily functioning, the early signs of impairment can be difficult to diagnose (Porsteinsson et al., 2021). Since there is no cure for this disease, it is imperative to diagnose patients as early as possible to maximize the benefits of early interventions that might slow the progression of the disease. Alzheimer's Disease is typically diagnosed using cognitive screening tools like the Montreal Cognitive Assessment and full neuropsychological cognitive test batteries like the CERAD battery (Fillenbaum et al., 2008). These assessments measure resources like memory, attention, and executive control. While these tests effectively distinguish between significant cognitive impairment and healthy aging, they lack sensitivity to the pre-clinical stages of AD. Neuropsychological test batteries that are used to diagnose AD have only modest reliability when distinguishing between pre-clinical stages, mild cognitive impairment (MCI), mild AD, and normal aging (Albert et al., 2011; McKhann et al., 2011; Sperling et al., 2011). Until recently, Alzheimer's Disease was only diagnosed definitively in a postmortem exam but improvements in neuroimaging and genetic testing have increased in reliability (Caselli et al., 2017). However, neuroimaging and other biomarker tests are often not accessible to many older adults experiencing cognitive impairment because they are expensive and require access to specialized health professionals. Improving clinical behavioral assessments so that they can identify pre-clinical stages of AD would allow more families to better prepare for the disease's progression. Recent developments in clinical psychology have pushed for investigations into motor behavior as a source for sensitive signs of preclinical stages of dementia.

Motor tasks have been critical diagnostic tools in clinical settings. Popular tests such as the perdue pegboard task can screen for brain damage (Vega, 1969). Movements that include a cognitive component can illuminate changes in behavior during planned movements. Using motor behavior as an indicator for changes in cognition can be beneficial in diagnosing stroke patients. Complex movements like mirror drawing tasks historically have been used to analyze memory in clinical settings, for example H.M. who had significant brain damage (Squire, 2009). Tracking motor behavior over time helps clinicians study changes in memory and learning. For a long time, Alzheimer's patients were thought to have preserved motor behavior during the earlier stages of the disease (Eslinger & Damasio, 1985). Preclinical dementia patients can complete the Perdue pegboard and mirror drawing tasks just as well as healthy older adults, which led clinicians to believe that motor behavior in this population remained unaffected by the disease. These tests while helpful with other diagnoses may not demand enough cognitive resources to illicit changes in behavior of people living with mild cognitive impairment.

Sensorimotor adaptation is one type of motor behavior thought to rely in part on higher cognitive processes like working memory. Research on sensorimotor adaptation in preclinical stages of AD has increased over the last decade. While motor dysfunction in later stages of AD have been previously documented, changes in motor function in the

earlier stages are still poorly understood (Suzumura, Osawa, Naghama, Kondo, Sano & Kandori, 2016). Recent work has highlighted changes in gait patterns, movement speed, and movement consistency in early AD (Mitchell, Rossit, Hornberger, Warman, Kenning, Williamson, Shapland & McIntosh, 2022; Tippett & Sergio, 2006). More generally, slowing and decreased coordination of movements are potential indications of cognitive decline (Camicioli et al., 1998; Yan et al., 2008). There is evidence that performance deficits in more complex motor tasks are more sensitive to differences between prodromal AD and healthy aging individuals (Kluger et al., 1997; Tippet & Sergio, 2006). Complexity includes alterations to normal reaching such as applying loads to the participant's hand or disruption of the visuomotor connection such as rotations in the VMR tasks.

Historically, sensorimotor adaptation was studied using throwing movements while participants wore prism goggles that shift visual feedback about target location. More recent work tends to measure motor behavior using motion tracking methods and high-fidelity robotic devices like the Kinarm endpoint lab (B-Kin technologies, Kingston, ON, Canada) that can track movements while also manipulating the mechanical and sensory environment in which upper limb movements are executed. Many complex motor tasks including sensorimotor adaptation tasks and rapid motor coordination tasks are sensitive to cognitive decline in aging (Seidler, 2007; Watral & Trewartha, 2021). Tasks that tend to utilize planning, learning and/or higher cognitive function tend to better illustrate differences in performance between healthy adults and cognitively impaired adults.

One of the motor tasks that has shown some promise in distinguishing between healthy aging and dementia is a variation of a visually guided reaching (VGR) task. Most of these investigations involve using the upper extremities to make reaching movements to targets while experiencing a physical or visual perturbation. VGR tasks are commonly used to measure movement fluency in patients with movement disorders (e.g., motor impairments due to stroke) and involve a veridical mapping between visual feedback and hand position. Put simply, participants see a target and freely reach to interact with it. Other methods include visuomotor rotation (VMR) tasks, which require participants to adapt their movements to an unexpected and novel mapping between visual feedback and hand position. The cursor displayed to the participant may move tangential to the predicted pathway that would be coordinated with the hand position.

VMR tasks are becoming more popular for assessing cognition (Buch, Young & Contreras-Vidal, 2003) with some work on clinical populations (Aggarwal, Wilson, Beck, Bienias & Bennett, 2006). Sensorimotor tasks like the VMR task require participants to recalibrate the mapping between their movements and visual or proprioceptive feedback about those movements. Such remapping allows the participant to reduce the effort required to reach the target (Wang, Rand & Müsseler, 2013). It has been argued that visuomotor adaptation relies on the development of explicit strategies which build the foundation for task-specific motor remapping (Shabbott & Sainburg, 2010; Schmitz, Dierking & Guenther, 2018). Other studies have suggested that sensorimotor adaptation relies on working memory resources (Angeura et al., 2010; Rajeshkumar & Trewartha, 2019; Trewartha et al., 2014; Wolpe et al., 2020) and other

cognitive control mechanisms associated with planning a movement using recent information about performance errors (see McDougle, Ivry, & Taylor, 2016). AD-related changes in cognitive control as outlined above may thus impact the ability to properly remap visuomotor behavior to effectively respond to the perturbation in VMR tasks. By designing motor tasks that effectively distinguish between levels of cognitive impairment (e.g., MCI or AD), neuropsychological test batteries could be supplemented by measurements of motor behavior.

Consistent with this proposal, previous work has shown that adaptation to a 180-degree rotation of visual feedback in a VMR task, a so-called reverse visually guided reaching task (rVGR) may help distinguish individuals with preclinical AD from healthy older adults (Tippet & Sergio, 2006). A visually guided reaching task with veridical mapping has fewer cognitive demands than the rVGR task since the cursor moves congruently with the participant's hand. Prior work with the rVGR task highlighted subtle differences between high- and low- risk for AD populations (Hawkins & Sergio, 2014; 2016). Both papers suggest changes in movement speed, times and errors while performing reaching movements during the task. However, performance on the reverse visually guided reaching task has yet to be fully characterized in clinical dementia populations.

Learning on sensorimotor tasks can be separated into two processes: a fast process that relies on declarative memory and, a slow process which relies on procedural memory. During the early-declarative stage of learning the participant relies on executive control to learn how to adjust to perturbations in the sensorimotor task (McDougle, Bond & Taylor, 2015). The slow process involves implicit processes that correct errors over time. Changes in the earlier stages of learning during motor adaptation tasks suggest an impairment in explicit memory resources (Wolpe et al., 2015); McDougle, Bond & Taylor, 2015). More specifically, changes in people living with Alzheimer's disease exhibit impairment in explicit memory processes during motor tasks (Gabrieli et al., 1993). These findings suggest that in the rVGR task changes in the early stages of learning might reflect deficits in cognitive control.

The current work seeks to quantify differences in performance in a rVGR task between younger adults, healthy older adults, and individuals with early AD (diagnosed with MCI or mild AD). Previous work has highlighted significant differences in at-risk populations but not with Alzheimer's patients directly. By characterizing differences between healthy populations and AD patients, this investigation can provide a framework for using the rVGR task to supplement contemporary methods of diagnosing Alzheimer's Disease. Additionally, no prior work has examined learning curves nor early stages of learning during the rVGR task. We will test the hypothesis that younger adults perform better on both tasks than both older groups, showing that the atsks is sensitive to aging. We expect that the CI group will exhibit diminished rVGR task performance compared to the healthy older adults overall. We hypothesize that group differences between healthy older adults and the cognitively impaired group will be most evident during the early trials (i.e., initial learning). Lastly, we hypothesize rVGR performance in the older adult participants (healthy and impaired) is correlated with independent cognitive measures of memory and cognitive control.

2 Methods

2.1 Participants

A total of 130 participants were recruited for three groups as follows: 65 healthy younger adults (M = 19.9, SD = 2.6 years old; 31 females), 49 healthy older adults (M = 67.9, SD = 6.2 years old; 30 females) and 16 individuals living with cognitive impairment (M = 72.2, SD = 9.4 years old; 6 females). A priori power analysis showed that for a 2 (task) x 3 (group) ANOVA with power = 0.95 and alpha = 0.05, each group should contain at least 12 participants for a total sample size of 36 to reach an effect size of $\eta p^2 = .325$ that was observed previously with this task (Hawkins & Sergio, 2014). Participants were recruited through the SONA system, word-of-mouth and ads posted virtually and physically. AD patients were recruited through the UP Health System – Portage and the Michigan State University Clinical Center. Older adults were eligible for this study if they met the following inclusion criteria: age 55-90 years old, no significant injuries to hands/arms that would impact movement and no medical conditions that would impact movement. Healthy older adults also could not have any diagnosis that impact cognition. Older participants were screened for Parkinsonian symptoms using the Unified Parkinson's Disease Rating Scale (UPDRS). Participants showing Parkinson's-like symptoms were removed from analyses. All older participants also performed a standard neuropsychological battery including the Montreal Cognitive Assessment (MoCA) to assess cognitive status. If reportedly healthy participants scored below a cutoff score of 24 on the MoCA, they were re-classified into the early AD group. This score was adjusted for rural populations from the typical clinical cutoff of 26 for all participants sampled from Houghton County (Nasreddine et al., 2005). Participant scores were adjusted by adding one point to an individual's score if they have fewer than 13 years of education (Milani et al., 2018).

Outliers were determined for each of the rVGR measures and were categorized by 2.5 standard deviations from the group mean. Participants in the healthy older adults group were removed from analysis if they were outliers on over ¼ of the rVGR measures. Three were removed from the overall analysis. Three were removed from Bin 1 analysis. Since the investigation seeks to characterize cognitive impairment, no outliers were removed from the cognitively impaired group.

2.2 Procedures

2.2.1 Motor Tasks

Participants performed two visually guided reaching tasks in succession: one with a veridical visuomotor mapping, and one with a reversed mapping between the arm movements and the visual feedback about their hand position (as described below). These were performed on a robotic manipulandum (Kinarm endpoint lab) where the participant holds a specialized handle to make reaching movements. They gazed down at a screen where visual targets were displayed, along with a white dot (cursor) that represented the position of their hand. They first moved to a start position centered between the four possible targets. Targets were positioned 90 degrees from one another (Fig. 1).

Participants were told to make a fast and accurate reaching movement to the target. Once they reached the target, the target disappeared, the starting position reappeared, and the participant returned to the starting position before the next trial began. Catch trials were included at various points in the VGR and rVGR task. During these trials the participants remained at the central start position for a 2 second period during which no other target was illuminated. These catch trials allowed for the assessment of postural control of the arm. During the reaching trials, every four trials included one movement to each of the four targets paired with a movement back to the start position, in a random order. For the veridical visuomotor mapping, participants made a total of 20 aimed movements toward the four targets paired with 20 movements back to the start position and 4 catch trials. The reverse visually guided reaching (rVGR) task operated the same way, except after the starting point was reached for the first time, the white cursor moved 180 degrees opposite of the participant's hand movements. The rVGR task was the more cognitively demanding of the two tasks. With the reversed mapping task, participants made a total of 48 aimed movements including 24 reaches to peripheral targets paired with 24 reaches to the central target, plus 5 catch trials.

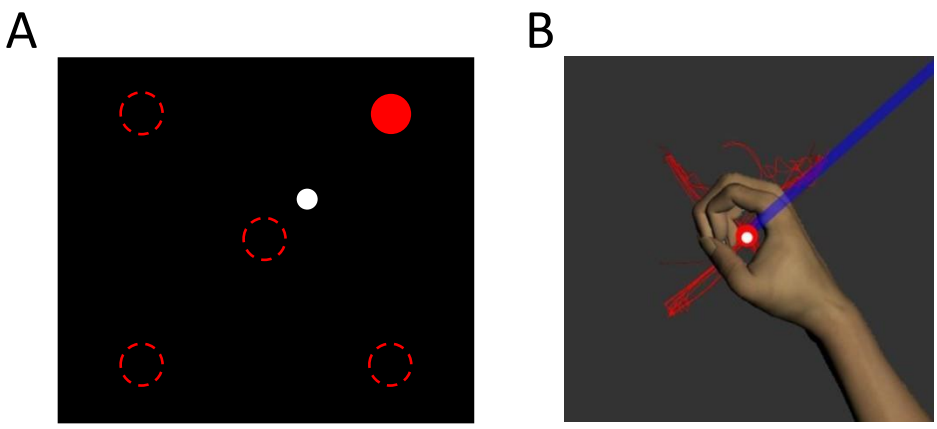

Figure 1. Representation of VGR task.

Panel A: Diagram showing the participant's view of the VGR task. Note: the dashed circles are not visible on the screen while the participant is moving towards the solid red target circle. These are included for display purposes to show the positions of the other targets. Participants make center-out reaching movements to one of the peripheral targets on each trial from the central home target.

Panel B: Diagram showing paths taken by a participant during the VGR task. Each red line shows the participant's hand path toward the target on a single trial and each trial over the course of the entire task is overlayed. Participant does not see these lines while

doing the task. Nor does the participant see their hand or the blue line representing the Kinarm robot's arm.

2.2.2 Neuropsychological Test Battery

All older participants were also screened using a neuropsychological test battery that includes 14 tests: the Montreal Cognitive Assessment (MoCA) and the CERAD battery which includes a test of Verbal Fluency, the Benton Line Judgement, the Trail Making Test Parts A & B, the color-word Stroop test, and a test of Constructional Praxis. The CERAD battery (Rossetti et al., 2010) was developed at Duke University and is a standard battery for assessing cognitive impairment in AD. This battery provided a way to screen the healthy older adult (HOA) sample to ensure that they are cognitively healthy; and was used as a measure of overall cognitive status in supplemental data analyses to identify the relationship between levels of cognitive impairment and visually guided reaching performance.

2.3 Data Analysis

The Kinarm software automatically calculates several dependent measures for this task, categorized into five different groups: posture control (posture speed), visual reaction time (RT), first movement characteristics (initial direction angle, initial distance ratio, initial speed ratio), corrective movements (speed maxima count, min-max speed), and total movement characteristics (movement time, path length ratio, max speed). The rVGR task has two additional first movement measures: direction errors and correction time. These measures are provided as averages across all trials in each task (i.e., VGR and rVGR) and provide overall measures of task performance (akin to Hawkins & Sergio, 2014; 2016).

The Kinarm software also provides trial-by-trial data which included seventeen different measures. These are as follows: full movement (direction, direction error, direction incorrect time, distance, distance error, distance ratio, max speed, max speed ratio, hitch count), min/max speed difference), movement time (max speed, speed maxima count), path length, path length ratio, reaction time, total movement time, and wrong direction time. The rVGR trials were grouped into 12 separate bins with each having an average of 4 consecutive trials (2 reaches to peripheral targets, 2 reaches to central target). This allowed us to examine learning curves and specifically assess performance during early exposure to the task.

2.4 Statistical Analysis

Statistical analyses were performed using R Studio. We tested for group differences in RT, first movement, and total movement performance measures using separate 2 (task) x 3 (group) mixed ANOVAs for the VGR and rVGR tasks. The dependent measures specific to the rVGR task (direction errors and correction time) were each compared with a 3-group one-way ANOVA. Visual inspection of the learning curves and slope analysis of the first half of the rVGR task revealed that performance differed between healthy older adults and individuals living with cognitive impairment specifically in the first bin.

We focused our analysis of early learning on this first bin data by comparing the two older groups performance in the 17 measures using independent-samples *t*-tests. We supplemented these findings by performing an additional 4 independent-samples *t*-tests on the variables of interest with Bin 1 performance removed.

To test the prediction that rVGR performance is correlated with independent measures of memory and cognitive control, we calculated bivariate correlation matrices to assess individual correlations between cognitive measures (MoCA, Word List Recall, Word List Recognition, Verbal Fluency Animals, Verbal Fluency Letter, Stroop Interference, Trails Difference Score) and measures of rVGR performance. Correlations between all cognitive measures and all motor performance measures are provided in Appendix A. We calculated two correlation matrices, one for the overall rVGR scores, and one for the bin 1 measures.

Table 1. Performance Measures from the VGR and rVGR Tasks

Measure	Definition	Task
Reaction Time	Time between illumination of target and onset of movement	VGR & rVGR
Initial Direction Angle	The angular deviation between a) a straight line from the hand position at movement onset and the peripheral target b) a vector from the hand position at movement onset to the hand position after the initial phase of movement	VGR & rVGR
Initial Distance Ratio	The ratio between a) the distance the hand traveled during the initial movement and b) the distance the hand traveled between movement onset and offset	VGR & rVGR
Initial Speed Ratio	The ratio between a) the maximum hand speed during the initial movement and the hand speed maximum of the trial	VGR & rVGR
Path Length Ratio	Ratio of a) the distance traveled by the hand between movement onset and movement offset and b) the straight-line distance between those two hand positions	VGR & rVGR
Movement Time	Total time elapsed from movement onset to movement offset	VGR & rVGR
Speed Maxima Count	Number of maxima in hand speed between movement onset and movement offset	VGR & rVGR
Posture Speed	Median hand speed when the hand should be at rest. The median value of all trials is reported.	rVGR
Direction Errors	The number of times the subject initially moved the cursor away from the end target	rVGR
Correction Time	For direction errors, the mean time before the subject starts to move toward the end target	rVGR

Note. Definitions were gathered from the Kinarm Dexterit-E User Guide 3.10 (BKIN Technologies, 2023).

3 Results

3.1 Global Motor Performance Measures

Ten factorial ANOVAs were completed to compare group performance between the VGR and rVGR tasks. Four measures of interest were picked based on results from Hawkins and Sergio (2014): reaction time, initial direction angle, initial distance ratio and, initial speed ratio (Fig. 1).

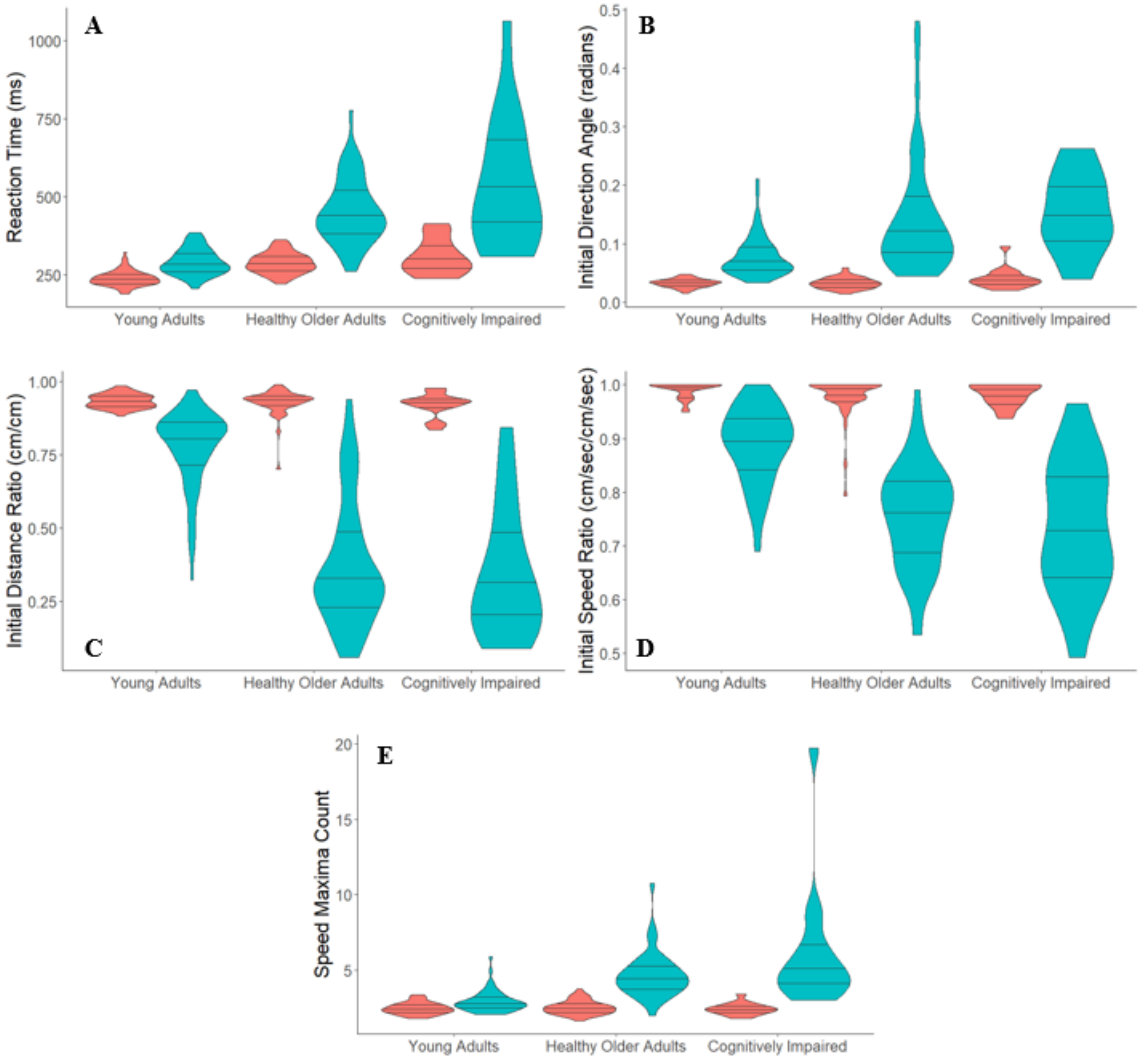

Figure 1. Overall Performance on VGR and rVGR Tasks. Red violins show performance on VGR task, teal show rVGR performance. Bars on each violin show quartiles.

These measures are expected to show a significant difference between healthy older adults and the CI group given the results from Hawkins and Sergio (2014). For reaction time, there was a main effect of task ($F(1) = 96.18$, $p < .01$, $\eta_p^2 = .27$), a main effect of group ($F(2) = 52.21$, $p < .01$, $\eta_p^2 = .29$), and an interaction between the task and group ($F(2) = 19.02$, $p < .01$, $\eta_p^2 = .13$). A post-hoc Tukey test revealed that younger adults had shorter reaction time than healthy older adults ($p < .001$, $d = 2.12$), and healthy older adults had shorter reaction time than the CI group ($p < .001$, $d = .55$). These findings suggest that CI adults move the slowest out of the three groups, and young adults react the fastest. Initial direction angle had a main effect of task ($F(1) = 23.02$, $p < .001$, $\eta_p^2 = .08$), a main effect of group ($F(2) = 6.20$, $p < .01$, $\eta_p^2 = .05$), and an interaction between the two ($F(2) = 5.54$, $p < .01$, $\eta_p^2 = .04$). A post-hoc Tukey test revealed that younger adults did not differ significantly from healthy older adults ($p = .12$, $d = 2.12$) but there was a marginally significant difference between older adults and CI ($p = .056$, $d = .29$). This suggests that larger initial direction angles might be indicative of cognitive impairment. For initial distance ratio there was a main effect of task ($F(1) = 502.76$, $p < .001$, $\eta_p^2 = .67$), a main effect of group ($F(2) = 80.53$, $p < .001$, $\eta_p^2 = .40$), and an interaction between the two ($F(2) = 74.93$, $p < .001$, $\eta p^2 = .38$). A post-hoc Tukey test revealed that there was a significant effect of age ($p < .001$, $d = 2.29$), but the CI group did not differ from healthy older adults. Initial speed ratio showed a main effect of task ($F(1) = 407.39$, $p < .001$, $\eta_p^2 = .63$), a main effect of group ($F(2) = 41.02$, $p < .001$, $\eta_p^2 = .25$), and an interaction between the two ($F(2) = 30.05$, $p < .001$, $\eta p^2 = .20$). The post-hoc Tukey test revealed that younger adults differed from healthy older adults and CI ($p < .001$, $d = 1.74$) but the two older groups did not differ. We were also interested in speed maxima count as a measure of corrective movements. Speed maxima count measures the number of peaks in velocity over the course of a trial. For speed maxima count we found a main effect of task ($F(1) = 83.27$, $p < .001$, $\eta p^2 = .25$), a main effect of group ($F(2) = 26.30$, $p < .001$, $\eta p^2 = .18$), and an interaction between the two ($F(2) = 26.09$, $p < .001$, $\eta p^2 = .17$). A post-hoc Tukey test revealed that younger adults differed from older adults ($p < .001$, $d = 1.16$) older adults differed from CI ($p < .01$, $d = 1.29$). The number of corrective movements in the rVGR task increased with age and those with cognitive impairment tended to make more corrections (Fig. 1E). Across the five remaining measures there was a main effect of task (all $p < .01$) and three of the five showed a main effect of age ($p < .05$), but none showed an interaction (all $p > .05$). These results are presented in Table 2. Between the groups, the younger adults performed better than the older adults in every measurement (Fig. 1 and Fig. 2) which is especially apparent in the rVGR performance.

Table 2. Global Performance Metrics.

Measure	Task	Mean (*SD*)			Factor	*F*(df)	Sig.	η_p^2
		Younger Adults	Healthy Older Adults	Cognitively Impaired				
Posture Speed	VGR	.14(.08)	.12(.11)	.15(.12)	Group	1.87(2)	.16	.01
					Task	17.27(1)	<.001	.07
	rVGR	.09(.06)	.08(.07)	.11(.13)	Interaction	0.26(2)	.77	.002
Min/Max Speed Difference	VGR	1.73(.67)	1.35(.64)	1.44(.78)	Group	5.26(2)	<.01	.04
					Task	7.62(1)	<.01	.03
	rVGR	2.07(1.17)	1.70(1.05)	1.59(1.17)	Interaction	0.16(2)	.85	.001
Movement Time	VGR	.92(.13)	1.06(.17)	1.01(.23)	Group	28.48(2)	<.001	.19
					Task	144.28(1)	<.001	.37
	rVGR	1.27(.26)	1.85(.66)	1.97(.81)	Interaction	13.49(2)	<.001	.10
Path Length Ratio	VGR	1.13(.05)	1.11(.05)	1.11(.04)	Group	3.68(2)	.02	.03
					Task	29.86(1)	<.001	.11
	rVGR	1.21(.10)	1.44(.63)	1.40(.38)	Interaction	5.03(2)	<.01	.04
Max Speed	VGR	34.70(8.59)	27.55(7.64)	28.16(8.91)	Group	26.48(2)	<.001	.18
					Task	116.81(1)	<.001	.32
	rVGR	24.14(7.87)	16.71(7.70)	15.75(6.83)	Interaction	0.17(2)	.84	.001

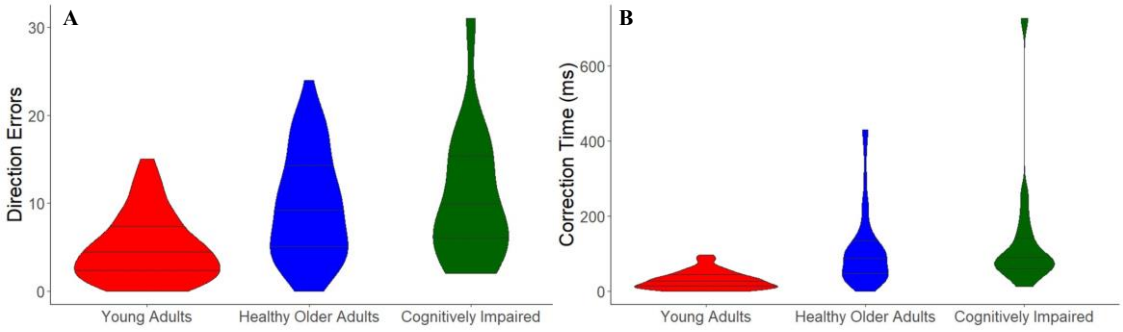

Figure 2. Overall Performance on rVGR-Specific Measures. Bars on violins show quartiles.

The two rVGR-specific metrics, direction errors and correction time (Fig. 2), were analyzed using one-way ANOVAs. Given the results from Hawkins and Sergio (2014; 2016) these rVGR measures should be sensitive to changes in cognitive impairment. Direction errors showed a significant effect of group ($F(2,123) = 16.47$, $p < .001$, $\eta_p^2 = .21$). A post-hoc Tukey test revealed that this finding is driven by age ($p < .001$, $d = 1.03$), not cognitive impairment ($p = .86$, $d = .11$). Correction time also showed a significant effect of group ($F(2,123) = 8.21$, $p < .001$, $\eta_p^2 = .12$). The post-hoc Tukey test showed that age was the driving factor ($p < .001$, $d = .67$), not cognitive impairment ($p = .99$, $d = .02$). Both older groups exhibited more direction errors during the task and took longer to correct their mistakes than younger adults. See Table 3 for Post-Hoc tests on the rest of the measures.

Table 3. Global rVGR Performance Metrics TukeyHSD Post-Hoc test.

Measure	Comparison	Mean Difference	Sig.	d
Posture Speed	YA- OA	.00009	.99	.15
	YA-CI	.0002	.95	.20
	OA – CI	.0003	.82	.29
Min/Max Speed Difference	YA- OA	.378	.29	.33
	YA-CI	.481	.43	.41
	OA – CI	.103	.99	.10
Movement Time	YA- OA	.585	<.001	1.16
	YA-CI	.704	<.001	1.16
	OA – CI	.120	.90	.16
Path Length Ratio	YA- OA	.224	<.01	.51
	YA-CI	.186	.20	.68
	OA – CI	.038	.99	.08
Max Speed	YA- OA	7.435	<.001	.95
	YA-CI	8.393	<.01	1.14
	OA – CI	.959	.99	.13

Note. Significance was found using Tukey HSD post hoc tests. Young Adults (YA), Healthy Older Adults (HOA), Cognitively Impaired (CI).

3.2 Learning Curve Assessment

Seventeen rVGR performance measures were separated into 12 bins, each representing the average of four consecutive trials, to examine learning across the task. Visually the largest and most consistent difference between the healthy older adults and CI group occured in the earliest stages of the task (Fig. 3). The healthy older adults appear slower in the first bin, which is contradictory to the findings in the global measures of performance (Fig. 3A).

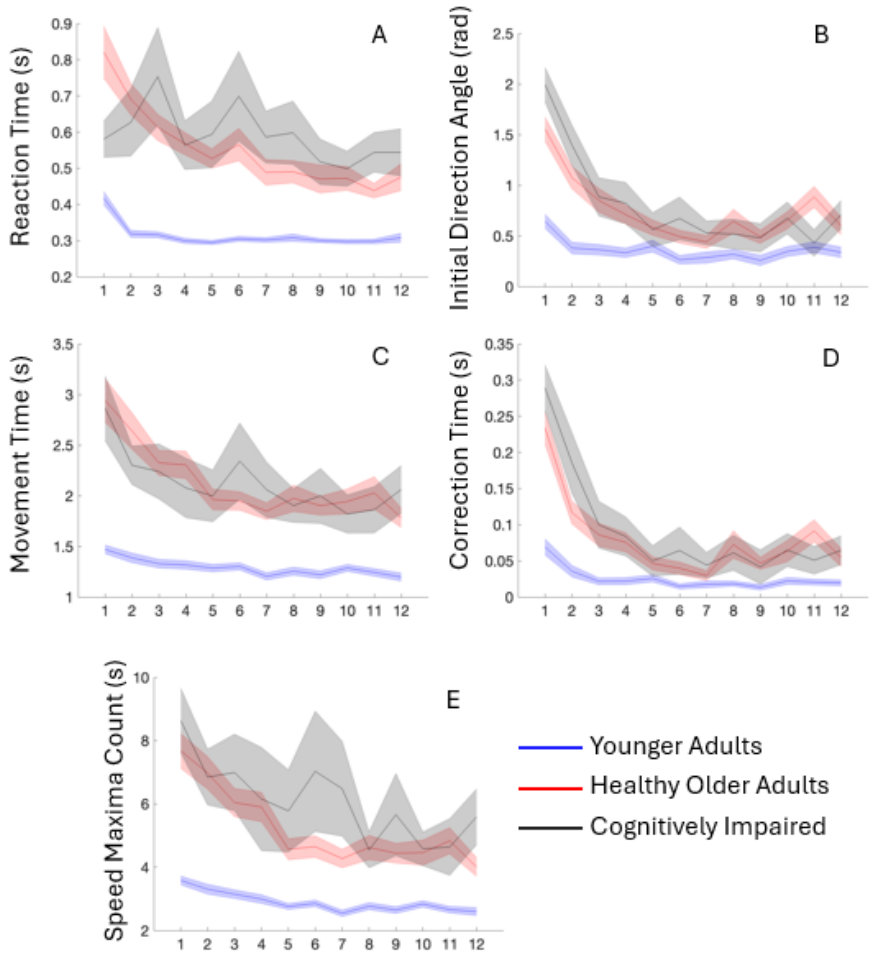

Figure 3. rVGR Learning Curves Separated by Bins. Error bars show standard error for each bin.

To evaluate differences in early learning curves between healthy older adults and those living with cognitive impairment we calculated the slope of the linear, least-square fit of the first half of the rVGR task and compared the slope between groups in independent samples *t*-tests. The slope of reaction time was significantly different between the healthy older adults and CI group ($t(62) = 2.58$, $p < .01$, $d = .74$). The CI group appeared to have a larger initial direction angle and higher correction time than the healthy older adults in the first few bins (Fig. 3BD). There was a trend towards a significant difference in the slope for the initial direction angle ($t(62) = 1.89$, $p = .06$, $d = .54$) and correction time ($t(62) = 1.90$, $p = .06$, $d = .55$) measures. For the first half of the task, it appears that the CI group had a higher speed maxima count than the healthy older group (Fig. 3E). The slope was not significantly different between those groups ($t(62) = 1.04$, $p = .30$, $d = .30$). Movement time does not appear to show a difference between the two groups (Fig. 3C). The movement time slope difference between healthy older adults and CI group was not significant ($t(62) = 1.21$, $p = .23$, $d = .35$). The CI group appears to perform worse than

their healthy counterparts in the earlier bins as described above. The exception to this is reaction time, where in bin 1 the healthy older adults are slower than the CI adults (Fig. 3A). Visually, the CI group shows little change in reaction time and speed maxima count until bin 7, which is unlike the healthy older adults who seem to improve consistently throughout the first half of the task (Fig. 3A,E). None of the other variables had significantly different slopes (Table 4).

Table 4. Learning Curve Slope Analysis.

Measure	Mean Difference	t(62)	Sig,	d
Direction	.0639	1.25	.22	.36
Distance	.0007	.50	.62	.15
Distance Error	.0022	1.40	.17	.40
Distance Ratio	.0002	.02	.98	.01
Max Speed	.0011	.269	.79	.08
Max Speed Ratio	.0161	1.46	.15	.42
Hitch Count	.0620	.63	.53	.18
Min/Max Speed Difference	.0011	1.09	.28	.32
Path Length	.0002	.03	.97	.01
Path Length Ratio	.0398	.41	.68	.12

Note. Slope was calculated across the first 6 bins of the learning curve. Significance is two-tailed.

Given prior literature on the sensitivity of the early stages of sensorimotor adaptation to cognitive impairment, the next analysis focused on this early stage which can be defined here as the first bin.

3.3 Bin 1 Measures

To further characterize early learning during the rVGR task, 17 *t*-tests were performed to analyze differences between healthy older adults and CI adults in the first bin. The CI group had on average quicker reaction times compared to the healthy adults (Fig. 4A); this relationship was approaching significance ($F(1, 60) = 2.87$, $p = .10$, $\eta_p^2 = .05$).

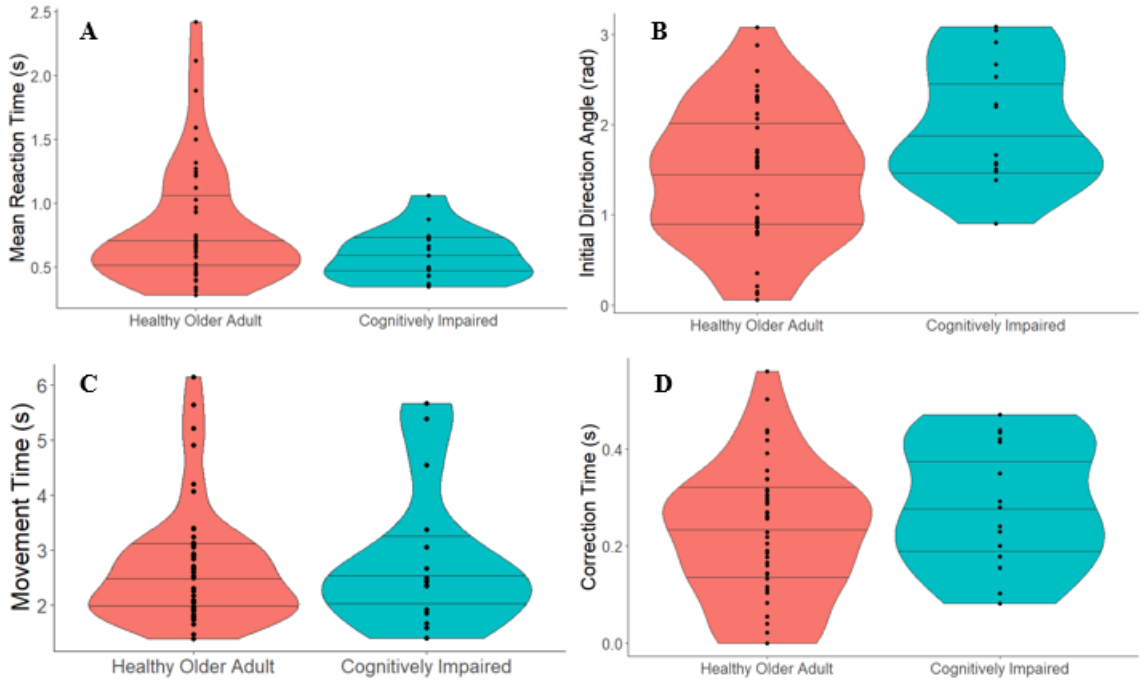

Figure 4. Bin 1 rVGR Performance Measurements of Interest. Points show individual performance. Bars on violins show quartiles.

This finding contradicts overall reaction time which found that the CI group was significantly slower than the healthy groups. In Bin 1, they exhibited significantly larger initial direction angles ($F(1, 60) = 4.29$, $p = .01$, $\eta_p^2 = .07$) compared to the healthy older adults. The CI group is beginning their movements with a larger initial angular error compared to the healthy older adults (Fig. 4B). Movement time was not significantly different between the older groups ($F(1, 60) = 0.50$, $p = .48$, $\eta_p^2 = .008$). Correction time was also not significantly different between the healthy older group and CI group ($F(1, 60) = 1.98$, $p = .16$, $\eta_p^2 = .03$). None of the additional tests were statistically significant; however, a few were approaching significance (Table 5). The variables that stand out in bin 1 are reaction time and initial direction angle: the older groups do not have a significant difference in reaction time, but the CI group has larger initial direction angles compared to the healthy older adults.

Table 5. Bin 1 rVGR Performance Metrics

Measure	Healthy Older Adults	Cognitively Impaired			
	Mean(*SD*)	Mean(*SD*)	*F*(60)	Sig.	η_p^2
Direction	3.12(0.87)	3.08(0.91)	.026	.87	.0004
Distance	.04(.02)	.04(.02)	.004	.95	.00007
Distance Error	.1(.02)	.11(.03)	3.581	.06	.06
Distance Ratio	.23(.19)	.19(.15)	.606	.44	.01
Max Speed	.12(.08)	.13(.07)	.215	.64	.0035
Max Speed Ratio	.58(.18)	.61(.24)	.220	.64	.004
Hitch Count	2.12(1.56)	2.44(2.81)	.318	.58	.005
Min/Max Speed Difference	.029(.016)	.038(.037)	1.483	.23	.02
Max Speed	.218(.11)	.23(.07)	.124	.73	.002
Speed Maxima Count	7.03(3.0)	8.5(4.2)	2.309	.13	.04
Path Length	.22(.13)	.24(.12)	.302	.58	.005
Path Length Ratio	2.17(1.34)	2.34(1.12)	.213	.65	.003
Wrong Direction Time	.45(.54)	.53(.52)	.299	.59	.005

Note. Significance was found using Tukey HSD post hoc tests.

3.4 Global Metrics Excluding Bin 1

We looked at performance on the rVGR task after bin 1 was removed to check if observed changes in early learning affected the overall analysis. The four measures of interest in bin 1 were used in this analysis. Removing bin 1 changed the overall performance very little on three of the four measures (Fig. 5). However, by removing bin 1 performance the CI group showed significantly slower reaction time on the rVGR task ($F(1, 59) = 8.23$, $p < .01$, $\eta_p^2 = .13$). This affirms the finding from the global performance measure section. Initial direction angle was not significantly different between the older groups ($F(1, 59) = .0004$, $p = .99$, $\eta_p^2 = .000002$). This contrasts with the Bin 1 finding, which showed a significant difference between these groups. Movement time was not significantly impacted by cognitive impairment ($F(1, 59) = 1.04$, $p = .31$, $\eta_p^2 = .02$). Correction time was not significant when bin 1 was excluded ($F(1, 59) = 0.19$, $p = .67$, $\eta_p^2 = .003$). Findings when Bin 1 was excluded are consistent with the global measures analysis.

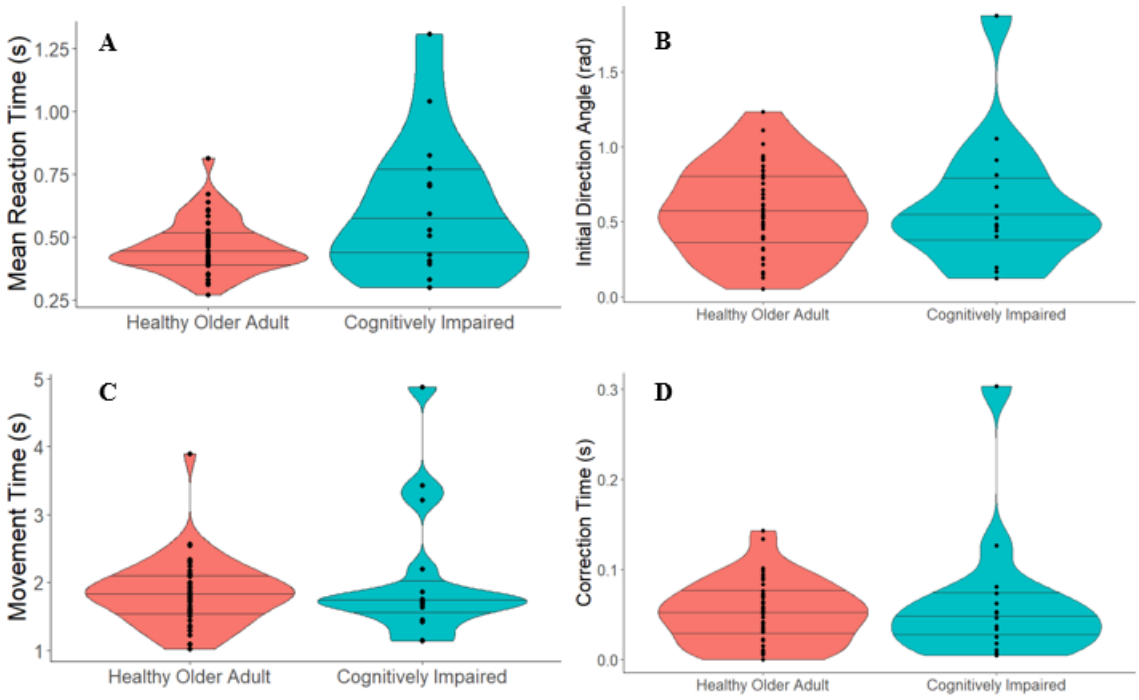

Figure 5. Overall rVGR Performance Excluding Bin 1. Points show individual performances. Bars on violins show quartiles.

3.5 Neuropsychological Correlates

Previous literature has demonstrated a relationship between measures of memory and cognitive control and visuomotor rotation performance in older adults. Here, we assessed the bivariate correlations between measures of memory (i.e., word list recall and recognition) and cognitive control (i.e., verbal fluency, Stroop, and Trail making tests) from the neuropsychological test battery and performance measures on the rVGR task. In Figures 6 and 7 we present correlations with a subset of rVGR performance measures of interest for overall and bin 1 measures, respectively.

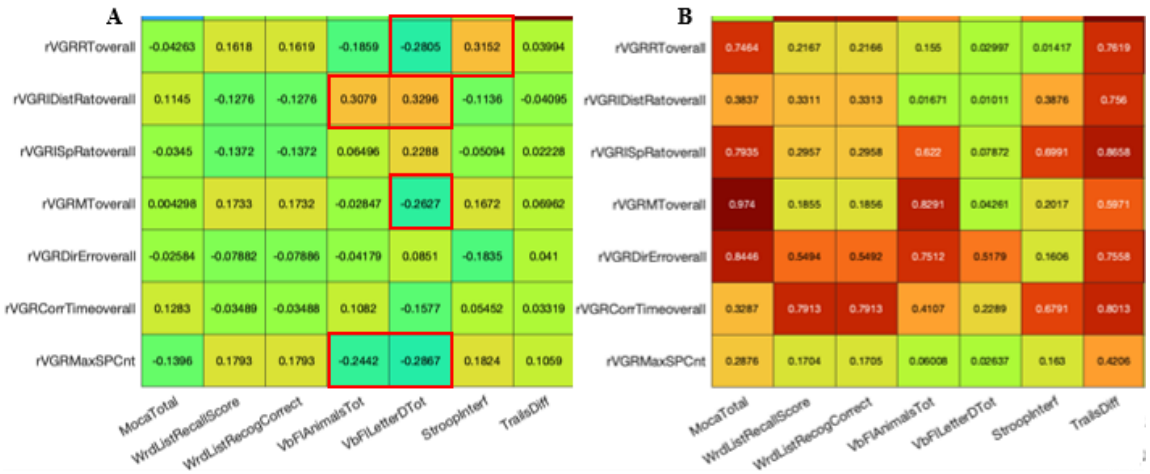

Figure 6. Overall rVGR Measurements and Neuropsychological Battery Test Correlation Matrix. Relationships highlighted in red ($p < .05$). A shows correlations, B shows *p*-values.

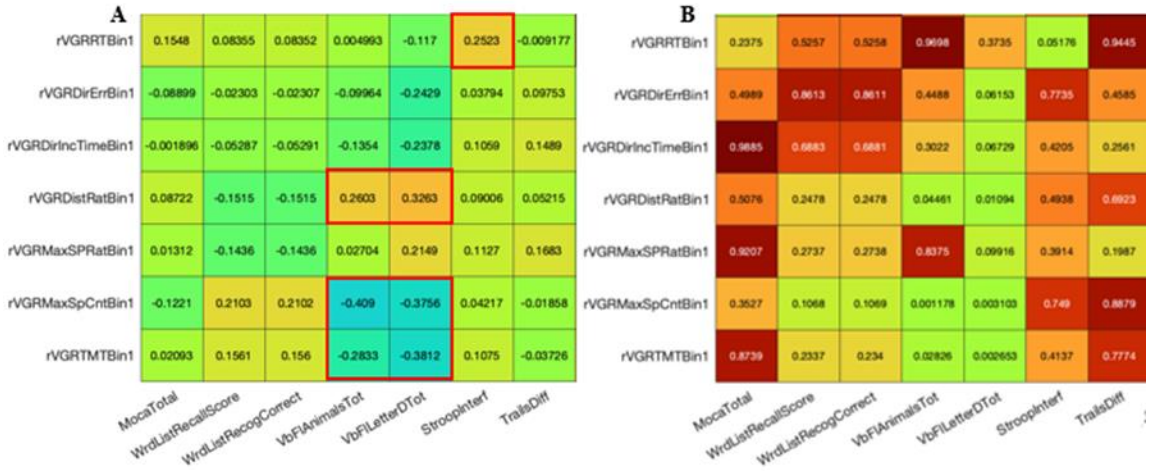

Figure 7. Bin1 rVGR Measurements and Neuropsychological Battery Test Correlation Matrix. Relationships highlighted in red ($p < .05$). A shows correlations, B shows *p*-values.

The bivariate correlations among all neuropsych and rVGR performance measures are shown in Appendix A. Both overall (Fig. 6) and Bin 1 (Fig. 7) rVGR measures showed small to moderate correlations with performance on both verbal fluency tasks. Both the Bin 1 and overall measures of reaction time were also correlated with poor performance on the Stroop task. Overall reaction time was negatively correlated with verbal fluency letter (Fig. 6). This suggests poor performance on the verbal fluency task might indicate

longer planning for movements in the rVGR task. Performance on both verbal fluency tests was negatively correlated with movement time and speed maxima count but positively correlated with distance ratio. This suggests that strong performance on the verbal fluency tasks correlates with less corrective movements and faster movement times. Reaction time was positively correlated with the Stroop task. Distance ratio was positively correlated with performance on the verbal fluency tasks, which may suggest that better verbal fluency scores indicate on average less distance error. These correlations show that both initial and overall rVGR performance is broadly correlated with measures of cognitive control, but none of the memory measures were significantly correlated with any of the rVGR measures across healthy older adults and those living with cognitive impairment.

4 Discussion

The current work sought to characterize performance differences between younger adults, healthy older adults, and individuals living with early stages of cognitive impairment in a rVGR task. This study was aimed at extending prior research on rVGR performance in older adults with high versus low risk of developing Alzheimer's Disease (Hawkins & Sergio, 2014). Our first key finding was that younger adults outperformed older adults in every measure of performance on both VGR and rVGR tasks. Younger adults tended to react more quickly, made fewer directional errors, and made smoother movements (ex. smaller path length). Older Adults were more prone to error and exhibited higher variability in their movements. Our second key finding was that the cognitively impaired group had the largest reaction times and most corrective movements (speed maxima count) across the whole task. Thirdly, in the early-learning stages of the rVGR task, the cognitively impaired group made significantly more angular direction errors, but after the first bin, there was no significant difference between the cognitively impaired group and older adults. Our final analyses revealed that both Bin 1- and global- performance measures were correlated with measures of cognitive control but not measures of memory.

This work sought to expand upon the findings of Hawkins & Segio (2014) by extending their findings with adults at-risk of developing AD by assessing individuals living with cognitive impairment (i.e. MCI, early-AD). In their study, those with a high-risk of developing Alzheimer's Disease showed increased direction reversals, poor reaction time and slower movements overall (Hawkins & Sergio, 2014). It was expected that these findings would be exacerbated in participants experiencing cognitive impairment however, we failed to observe strong differences between healthy older adults and the cognitively impaired group. The current findings do corroborate their findings to some extent given that individuals with cognitive impairment exhibited slower reaction times and larger angular errors. These increases in reaction time are consistent with other investigations that involve the rVGR task (Tippet & Sergio, 2006; Hawkins & Sergio, 2014; 2016). Visual reaction time represents the amount of time between the target illuminating and the participant initiating their movement, and includes processing related to the planning of the aiming movement. Longer reaction times in our cognitively impaired group suggests that they take longer to plan their movement compared to the healthy groups. Secondly, we found that the cognitively impaired group exhibited an increased number of overall corrective movements (speed maxima count). This observation strengthens the view that individuals living with cognitive impairment have difficulty planning the entire reaching movement in advance, before initiating the reach.

In both the VGR and rVGR task there was a significant effect of age across most of the measures. These differences in performance were exacerbated by the difficulty of the rVGR task compared to the VGR task. Watral and Trewartha (2021) found that age differences in performance of a rapid, bimanual coordination task are largest when the task imposes cognitive control demands on the participants. Similarly, visuomotor rotation tasks rely heavily on spatial working memory resources which decline with age (Anguera et al., 2010; Anguera et al., 2011). The rVGR task is a specific type of

visuomotor rotation that likely demands spatial working memory resources to make appropriate adjustments to reach the target. Participants likely use spatial working memory to remember details about the movement made on the previous trial, and any errors associated with it, to make appropriate adjustments to their movements during the current trial. This view is consistent with well-established mathematical models of sensorimotor adaptation (e.g., Smith et al., 2006). Older participants exhibit more directional errors and have greater variability in movements, which demand more corrective movements to reach the targets. Indeed, healthy aging has been shown to impact performance in sensorimotor adaptation tasks (Fernandez-Ruiz et al., 2000; Trewartha et al., 2014) and these differences may be especially evident when working memory demands are high (Rajeshkumar & Trewartha, 2019). Our findings show that young adults not only exhibit smoother and more consistent movements, but they also move quicker than older adults in the rVGR task. These findings add to a growing literature showing that age differences in motor tasks are larger for more complex motor tasks that require working memory and cognitive control resources than for simple motor tasks like the VGR task.

Our assessment of early learning found that cognitively impaired individuals learn differently from healthy older adults. While global measurements of performance distinguish between healthy aging well, we decided to look at learning across the rVGR task to investigate how cognitive impairment impacts learning to adapt to the rVGR perturbation. It has been shown that early learning during sensorimotor adaptation tasks relies on declarative memory resources (Keisler & Shadmehr, 2010), and more recent work has emphasized the importance of working memory resources in particular (e.g., Anguera et al., 2010; Anguera et al., 2011; Rajeshkumar & Trewartha, 2019; Trewartha et al., 2014). In the current study, we quantified early learning by calculating the slope of the learning curve over the first half of the task. The cognitively impaired group displayed a smaller slope for the reaction time measure compared to the healthy adults. Slower improvement in the cognitively impaired group suggests that they take longer to learn the task well enough to shorten planning time during rVGR trials. One possible explanation for this trend stems from diminished declarative learning processes in early AD (Gabrieli et al., 1993; Sutter et al., Preprint 2024). In support of this, we see marginally significant differences between healthy older adults and those living with cognitive impairment in the slope of the learning curves for initial direction angle and correction time measures as well. These findings build off prior literature of motor slowing and dyscoordination in Alzheimer's patients (Aggarwal et al., 2006; Camicioli et al., 1998; Mitchell et al., 2022; Yan et al., 2008). We suspect that these findings in early learning are a result of impairments in the fast, declarative stage of learning. Declarative processes rely on cognitive control to keep previous trials in-mind while trying to adjust in a sensorimotor adaptation task (McDougle, Bond & Taylor, 2015). The cognitively impaired group’s poor reaction time on the rVGR task might be explained by worsened cognitive control related to planning processes.

To probe this explanation, we isolated the first bin and found that the cognitively impaired group showed higher angular error, but reaction time was not significantly different between the impaired and healthy older group. The cognitively impaired group

exhibited slightly faster reaction times than the healthy group, which is contradictory to the rest of the task. This effect was approaching significance and considering that expected performance was flipped between the groups highlights a novel finding about early learning. This finding also contradicts prior literature which suggests that people living with early AD should exhibit slower reaction times to healthy controls (Tippet & Sergio, 2006; Hawkins & Sergio, 2014). The healthy participants may be taking more time to plan their movements while the impaired group does not. This movement planning deficit may contribute to higher angular errors in the cognitively impaired group. When bin 1 was removed from analysis, the findings were consistent with the global measurements of performance. These findings suggest that cognitively impaired individuals struggle during the early (declarative) stages of learning where the participant must decide to move in the opposite direction of the target to reach it. These changes could suggest that the group with cognitive impairment is over-compensating by reacting faster and adjusting their movements instead of making planned movements. These findings support the notion that cognitive impairment and early stages of AD likely cause subtle changes to the early stages of learning in a novel motor task due to difficulty planning the movement.

Further evidence in support of a cognitive control explanation for performance differences in rVGR comes from the correlation results. We found that the rVGR global measures and isolated bin 1 measures were correlated with multiple measures of cognitive control from the neuropsychological test battery. We found this to be consistent with current literature on the rVGR task (Lowrey et al., 2022). Interestingly, performance on the tasks was not correlated with any measures of declarative memory (i.e., word list recall and recognition). Both verbal fluency tasks and the Stroop task involve following a set rule to complete the task much like the single rule set for rVGR: the cursor moves opposite of the user's hand. Strong performance on these tests correlates with faster and smoother (less distance error) movements on the rVGR task. People living with MCI and early AD exhibit more erratic (less-smooth) movements compared with healthy adults (Yan et al., 2008). Changes in motor control reflect changes in cognitive control (Buchman & Bennet, 2011; McDougle, Bond & Taylor, 2015), which might explain the higher amounts of angular error and speed maxima count in the cognitively impaired group in the current data. Findings from the neuropsychological test battery highlight the relationship between cognitive control and rVGR task performance in healthy aging and cognitive impairment.

This work looked at cognitive impairment more generally, rather than focusing on early Alzheimer's Disease directly. Due to recruitment issues stemming from the COVID-19 pandemic, we were unable to obtain a large enough sample of patients diagnosed with early-AD to isolate that group for analysis. The cognitively impaired group consisted of self-reported healthy individuals who scored poorly on a neuropsychological test battery, 3 patients diagnosed with mild cognitive impairment and 2 early-AD patients. With only ¼ of our cognitively impaired group having a clinical diagnosis, we cannot speak definitively to Alzheimer's Disease specifically. In the future, we hope to recruit more early-AD patients and separate them as their own group to specifically characterized changes between general cognitive impairment and the early stages of Alzheimer's

disease. To validate whether the rVGR task is sensitive-enough to aid in the clinical diagnosis of early-AD, more work with that specific population is required. Ideally, we would like to utilize various classification methods to distinguish between healthy and cognitively impaired adults. Lastly, we would like to differentiate between AD and other forms of cognitive impairment that may impact performance on the rVGR task such as Parkinson's disease.

The findings from this investigation suggest that the rVGR task might be a time-efficient test of cognitive impairment. Globally, people living with cognitive impairment show slower reaction times, make more corrective movements, and learn more slowly than healthy older adults. In the earliest stages of learning cognitively impaired group showed larger angular error but contradictory to current literature, did not have slower reaction times compared to healthy adults. Lastly, measures of cognitive control, and not memory, in the neuropsychological test battery were correlated with performance on the rVGR task. These findings improve our general understanding of the impact of the earliest stages of Alzheimer's Disease on motor behavior. If the rVGR task can distinguish between healthy aging and early AD, the task could be used as an effective diagnostic tool to improve the reliability of standard neuropsychological test batteries. Mixing neuropsychological test batteries with measures of motor behavior can improve accuracy of diagnosing cognitive impairment (Kluger et al., 1997). This work could be extended using a computer or tablet application, which could provide accessibility to clinicians who lack access to a Kinarm (Watral et al., 2023). Future work using the rVGR task with early-AD patients this task may prove useful in improving diagnostic sensitivity in the earliest stages of Alzheimer's Disease.

5 Reference List

Aggarwal, N. T., Wilson, R. S., Beck, T. L., Bienias, J. L., & Bennett, D. A. (2006). Motor Dysfunction in Mild Cognitive Impairment and the Risk of Incident Alzheimer Disease. *Archives of Neurology*, *63*(12), 1763. https://doi.org/10.1001/archneur.63.12.1763

Agosta, F., Rocca, M. A., Pagani, E., Absinta, M., Magnani, G., Marcone, A., Falautano, M., Comi, G., Gorno-Tempini, M. L., & Filippi, M. (2009). Sensorimotor network rewiring in mild cognitive impairment and Alzheimer's disease. *Human Brain Mapping*, NA-NA. https://doi.org/10.1002/hbm.20883

Albert, M.S., DeKosky, S.T., Dickson, D., Dubois, B., Feldman, H.H., Fox, N.C., Gamst, A., Holtzman, D.M., Jagust, W.J., Petersen, R.C., Snyder, P.J., Carrillo, M.C., Thies, B., Phelps, C.H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging and Alzheimer's Association workgroup. *Alzheimer's & Dementia*, *7*, 270-279. https://doi.org/10.1016/j.jalz.2011.03.008

Anguera, J. A., Reuter-Lorenz, P. A., Willingham, D. T., & Seidler, R. D. (2010). Contributions of Spatial Working Memory to Visuomotor Learning. *Journal of Cognitive Neuroscience*, *22*(9), 1917–1930. https://doi.org/10.1162/jocn.2009.21351

Anguera, J. A., Reuter-Lorenz, P. A., Willingham, D. T., & Seidler, R. D. (2011). Failure to Engage Spatial Working Memory Contributes to Age-related Declines in Visuomotor Learning. *Journal of Cognitive Neuroscience*, *23*(1), 11–25. https://doi.org/10.1162/jocn.2010.21451

BKIN Technologies (2023). Dexterit-E User Guide 3.10. Retrieved March 24, 2024, from https://kinarm.com/download/dexterit-e-user-guide-3-10/

Buch, E. R., Young, S., & Contreras-Vidal, J. L. (2003). Visuomotor Adaptation in Normal Aging. *Learning & Memory*, *10*(1), 55–63. https://doi.org/10.1101/lm.50303

Buchman, A. S., & Bennett, D. A. (2011). Loss of motor function in preclinical Alzheimer's disease. *Expert Review of Neurotherapeutics*, *11*(5), 665–676. https://doi.org/10.1586/ern.11.57

Camicioli, R., Howieson, D., Oken, B., Sexton, G., & Kaye, J. (1998). Motor slowing precedes cognitive impairment in the oldest old. *Neurology*, *50*(5), 1496–1498. https://doi.org/10.1212/WNL.50.5.1496

Caselli, R. J., Beach, T. G., Knopman, D. S., & Graff-Radford, N. R. (2017). Alzheimer Disease. *Mayo Clinic Proceedings*, *92*(6), 978–994. https://doi.org/10.1016/j.mayocp.2017.02.011

Dick, M. B., Hsieh, S., Bricker, J., & Dick-Muehlke, C. (2003). Facilitating acquisition and transfer of a continuous motor task in healthy older adults and patients with Alzheimer's disease. *Neuropsychology*, *17*(2), 202–212. https://doi.org/10.1037/0894-4105.17.2.202

Eslinger, P., & Damasio, A. (1986). Preserved motor learning in Alzheimer's disease: Implications for anatomy and behavior. *The Journal of Neuroscience*, *6*(10), 3006–3009. https://doi.org/10.1523/JNEUROSCI.06-10-03006.1986

Fernández-Ruiz, J., Hall, C., Vergara, P., & Díaz, R. (2000). Prism adaptation in normal aging: Slower adaptation rate and larger aftereffect. *Cognitive Brain Research*, *9*(3), 223–226. https://doi.org/10.1016/S0926-6410(99)00057-9

Fillenbaum, G. G., van Belle, G., Morris, J. C., Mohs, R. C., Mirra, S. S., Davis, P. C., Tariot, P. N., Silverman, J. M., Clark, C. M., Welsh-Bohmer, K. A., & Heyman, A. (2008). Consortium to Establish a Registry for Alzheimer's Disease (CERAD): The first twenty years. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *4*(2), 96–109. https://doi.org/10.1016/j.jalz.2007.08.005

Gabrieli, J. D. E., Corkin, S., Mickel, S. F., & Growdon, J. H. (1993). Intact acquisition and long-term retention of mirror-tracing skill in Alzheimer's disease and in global amnesia. *Behavioral Neuroscience*, *107*(6), 899–910. https://doi.org/10.1037/0735-7044.107.6.899

Ghilardi, M.-F., Alberoni, M., Marelli, S., Marina Rossi, Franceschi, M., Ghez, C., & Fazio, F. (1999). Impaired movement control in Alzheimer's disease. *Neuroscience Letters*, *260*(1), 45–48. https://doi.org/10.1016/S0304-3940(98)00957-4

Hawkins, K. M., & Sergio, L. E. (2014). Visuomotor Impairments in Older Adults at Increased Alzheimer's Disease Risk. *Journal of Alzheimer's Disease*, *42*(2), 607–621. https://doi.org/10.3233/JAD-140051

Hawkins, K. M., & Sergio, L. E. (2016). Adults at Increased Alzheimer's Disease Risk Display Cognitive-Motor Integration Impairment Associated with Changes in Resting-State Functional Connectivity: A Preliminary Study. *Journal of Alzheimer's Disease*, *53*(3), 1161–1172. https://doi.org/10.3233/JAD-151137

Hegele, M., & Heuer, H. (2010). Implicit and explicit components of dual adaptation to visuomotor rotations. *Consciousness and Cognition*, *19*(4), 906–917. https://doi.org/10.1016/j.concog.2010.05.005

Hegele, M., & Heuer, H. (2013). Age-related variations of visuomotor adaptation result from both the acquisition and the application of explicit knowledge. *Psychology and Aging*, *28*(2), 333–339. https://doi.org/10.1037/a0031914

Heuer, H., & Hegele, M. (2008). Adaptation to visuomotor rotations in younger and older adults. *Psychology and Aging*, *23*(1), 190–202. https://doi.org/10.1037/0882-7974.23.1.190

Keisler, A., & Shadmehr, R. (2010). A Shared Resource between Declarative Memory and Motor Memory. *Journal of Neuroscience*, *30*(44), 14817–14823. https://doi.org/10.1523/JNEUROSCI.4160-10.2010

Kluger, A., Gianutsos, J. G., Golomb, J., Ferris, S. H., George, A. E., Franssen, E., & Reisberg, B. (1997). Patterns of Motor Impairment in Normal Aging, Mild Cognitive Decline, and Early Alzheimer' Disease. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *52B*(1), P28–P39. https://doi.org/10.1093/geronb/52B.1.P28

Lowrey, C. R., Dukelow, S. P., Bagg, S. D., Ritsma, B., & Scott, S. H. (2022). Impairments in Cognitive Control Using a Reverse Visually Guided Reaching Task Following Stroke. *Neurorehabilitation and Neural Repair*, *36*(7), 449–460. https://doi.org/10.1177/15459683221100510

McDougle, S. D., Bond, K. M., & Taylor, J. A. (2015). Explicit and Implicit Processes Constitute the Fast and Slow Processes of Sensorimotor Learning. *Journal of Neuroscience*, *35*(26), 9568–9579. https://doi.org/10.1523/JNEUROSCI.5061-14.2015

McDougle, S. D., Ivry, R. B., & Taylor, J. A. (2016). Taking Aim at the Cognitive Side of Learning in Sensorimotor Adaptation Tasks. *Trends in Cognitive Sciences*, *20*(7), 535–544. https://doi.org/10.1016/j.tics.2016.05.002

McKhann, G.M., Knopman, D.S., Chertkow, H., Hyman, B.T., Jack, C.R. Jr., Kawas, C.H., Klunk, W.E., Koroshetz, W.J., Manly, J.J., Mayeux, R., Mohs, R.C., Morris, J.C., Rossor, M.N., Scheltens, P., Carillo, M.C., Thies, B., Weintraub, S., Phelps, C.H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup. *Alzheimer's & Dementia, 7*, 263-269. https://doi.org/10.1016/j.jalz.2011.03.005

Mitchell, A. G., Rossit, S., Pal, S., Hornberger, M., Warman, A., Kenning, E., Williamson, L., Shapland, R., & McIntosh, R. D. (2022). Peripheral reaching in Alzheimer's disease and mild cognitive impairment. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *149*, 29–43. https://doi.org/10.1016/j.cortex.2022.01.003

Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment: MOCA: A BRIEF

SCREENING TOOL FOR MCI. *Journal of the American Geriatrics Society*, *53*(4), 695–699. https://doi.org/10.1111/j.1532-5415.2005.53221.x

Porsteinsson, A.P., Isaacson, R.S., Knox, S. *et al.* Diagnosis of Early Alzheimer's Disease: Clinical Practice in 2021. *J Prev Alzheimers Dis* **8**, 371–386 (2021). https://doi.org/10.14283/jpad.2021.23

Rajeshkumar, L., & Trewartha, K. M. (2019). Advanced spatial knowledge of target location eliminates age-related differences in early sensorimotor learning. *Experimental Brain Research*, *237*(7), 1781–1791. https://doi.org/10.1007/s00221-019-05551-w

Rossetti, H. C., Munro Cullum, C., Hynan, L. S., & Lacritz, L. H. (2010). The CERAD Neuropsychologic Battery Total Score and the Progression of Alzheimer Disease. *Alzheimer Disease & Associated Disorders*, *24*(2), 138–142. https://doi.org/10.1097/WAD.0b013e3181b76415

Schmitz, G., Dierking, M. & Guenther, A. Correlations between executive functions and adaptation to incrementally increasing sensorimotor discordances. *Exp Brain Res* **236**, 3417–3426 (2018). https://doi.org/10.1007/s00221-018-5388-y

Seidler, R. D. (2007). Aging affects motor learning but not savings at transfer of learning. *Learning & Memory*, *14*(1–2), 17–21. https://doi.org/10.1101/lm.394707

Shabbott, B.A., Sainburg, R.L. Learning a visuomotor rotation: simultaneous visual and proprioceptive information is crucial for visuomotor remapping. *Exp Brain Res* **203**, 75–87 (2010). https://doi.org/10.1007/s00221-010-2209-3

Smith, M. A., Ghazizadeh, A., & Shadmehr, R. (2006). Interacting Adaptive Processes with Different Timescales Underlie Short-Term Motor Learning. *PLoS Biology*, *4*(6), e179. https://doi.org/10.1371/journal.pbio.0040179

Sperling, R.A., Aisen, P.S., Beckett, L.A., Bennett, D.A., Craft, S., Fagan, A.M., Iwatsubo, T., Jack, C.R., Kaye, J., Montine, T.J., Park, D.C., Reiman, E.M., Rowe, C.C., Siemers, E., Stern, Y., Yaffe, K., Carilloa, M.C., Thies, B., Morrison-Bogorad, M., Wagster, M.V., Phelps, C.H. (2011). Toward defining the preclinical stages of Alzheimer"s disease: Recommendations from the National Institute on Aging and the Alzheimer"s Association workgroup. *Alzheimer's & Dementia*, *7*, 280-292. https://doi.org/10.1016/j.jalz.2011.03.003

Sutter, K., Oostwoud, W. L., Beers, RJ., Claassen, J.A.H.R., Kessels, R.P.C., & Medendorp, W.P. (2024). Does early-stage Alzheimer's disease affect the dynamics of motor adaptation? *bioRxiv*, 2024.01.16.575820. https://doi.org/10.1101/2024.01.16.575820

Suzumura, S., Osawa, A., Nagahama, T., Kondo, I., Sano, Y., & Kandori, A. (2016). Assessment of finger motor skills in individuals with mild cognitive impairment and

patients with Alzheimer's disease: Relationship between finger-to-thumb tapping and cognitive function. *Japanese Journal of Comprehensive Rehabilitation Science*, *7*(0), 19–28. https://doi.org/10.11336/jjcrs.7.19

Squire, L. R. (2009). The Legacy of Patient H.M. for Neuroscience. *Neuron*, *61*(1), 6–9. https://doi.org/10.1016/j.neuron.2008.12.023

Tippett, W. J., & Sergio, L. E. (2006). Visuomotor integration is impaired in early stage Alzheimer's disease. *Brain Research*, *1102*(1), 92–102. https://doi.org/10.1016/j.brainres.2006.04.049

Trewartha, K. M., Garcia, A., Wolpert, D. M., & Flanagan, J. R. (2014). Fast But Fleeting: Adaptive Motor Learning Processes Associated with Aging and Cognitive Decline. *Journal of Neuroscience*, *34*(40), 13411–13421. https://doi.org/10.1523/JNEUROSCI.1489-14.2014

Vega, A. (1969). Use of Purdue Pegboard and finger tapping performance as a rapid screening test for brain damage. *Journal of Clinical Psychology*, *25*(3), 255–258. https://doi.org/10.1002/1097-4679(196907)25:3<255::AID-JCLP2270250306>3.0.CO;2-V

Wang, L., Rand, M. K., & Müsseler, J. (2013). Spatial realignment in sensorimotor adaptation: Taking the efficiency into account. *Journal of Experimental Psychology: Human Perception and Performance*, *39*(6), 1763-1774. https://doi.org/10.1037/a0032123

Watral, A. T., Morley, A., Pastel, R., & Trewartha, K. M. (2023). Comparing mouse versus trackpad input in a web-based app for assessing motor learning. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*.

Watral, A. T., & Trewartha, K. M. (2021). Measuring age differences in executive control using rapid motor decisions in a robotic object hit and avoid task. *Psychology and Aging*, *36*(8), 917–927. https://doi.org/10.1037/pag0000641

Willingham, D. B., Peterson, E. W., Manning, C., & Brashear, H. R. (1997). Patients with Alzheimer's disease who cannot perform some motor skills show normal learning of other motor skills. *Neuropsychology*, *11*(2), 261–271. https://doi.org/10.1037/0894-4105.11.2.261

Wolpe, N., Ingram, J. N., Tsvetanov, K. A., Henson, R. N., Wolpert, D. M., Rowe, J. B., Tyler, L. K., Brayne, C., Bullmore, E. T., Calder, A. C., Cusack, R., Dalgleish, T., Duncan, J., Matthews, F. E., Marslen-Wilson, W. D., Shafto, M. A., Campbell, K., Cheung, T., Davis, S., … Villis, L. (2020). Age-related reduction in motor adaptation: Brain structural correlates and the role of explicit memory. *Neurobiology of Aging*, *90*, 13–23. https://doi.org/10.1016/j.neurobiolaging.2020.02.016

Yan, J. H., Rountree, S., Massman, P., Doody, R. S., & Li, H. (2008). Alzheimer's disease and mild cognitive impairment deteriorate fine movement control. *Journal of Psychiatric Research*, *42*(14), 1203–1212. https://doi.org/10.1016/j.jpsychires.2008.01.006

A Appendix

A.1 Global rVGR Neuropsycholgical Correlates

See below for bivariate correlation matrices between all global measures of rVGR and all neuropsychological test battery measures.

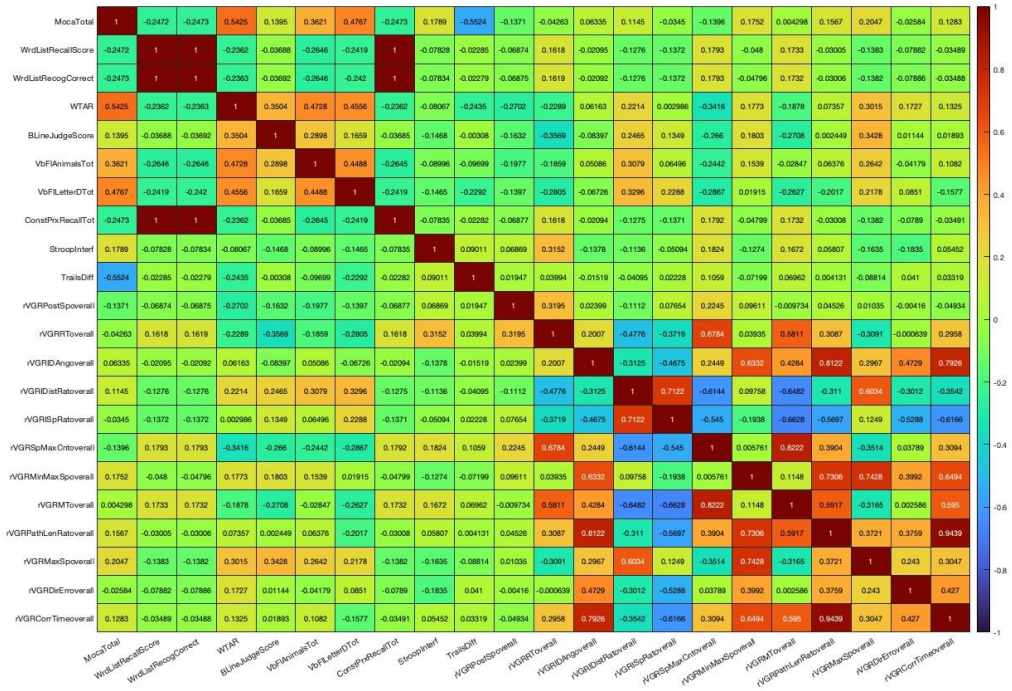

Figure 9. Overall correlations

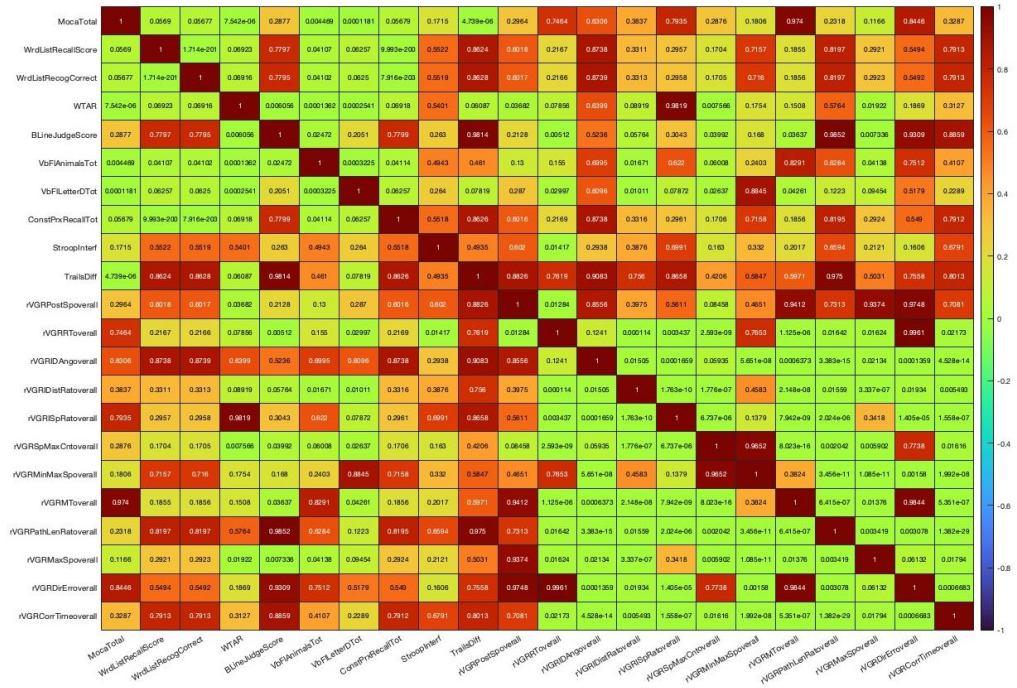

Figure 10. overall *p*-values

A.2 Bin 1 rVGR Neuropsycholgical Correlates

See below for bivariate correlation matrices between all global measures of rVGR and all neuropsychological test battery measures.

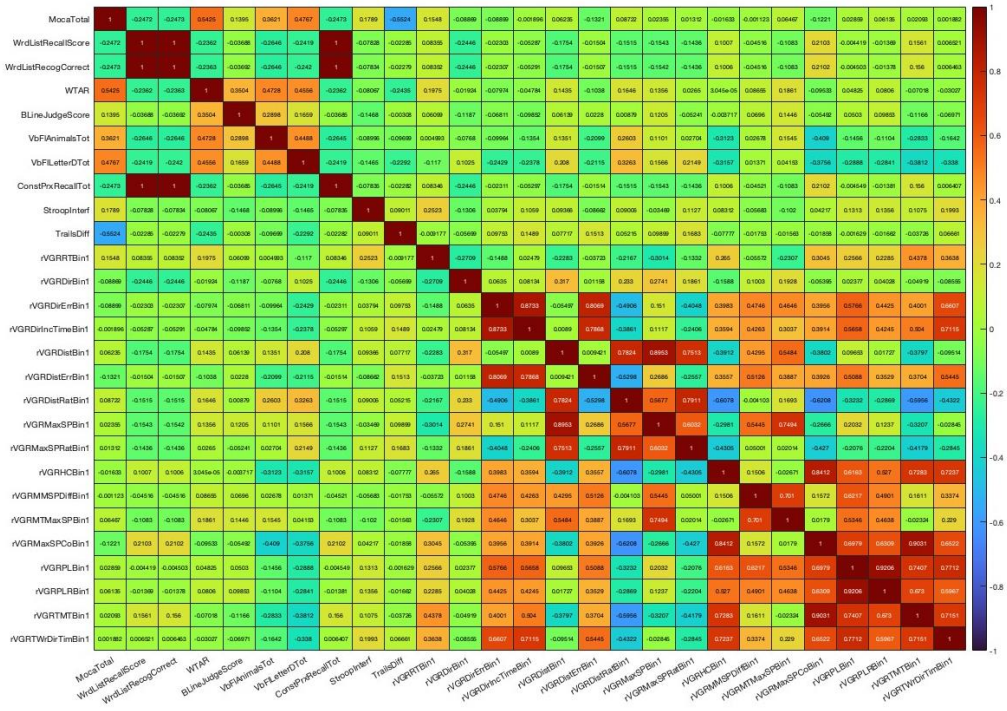

Figure 11. Bin 1 Correlations

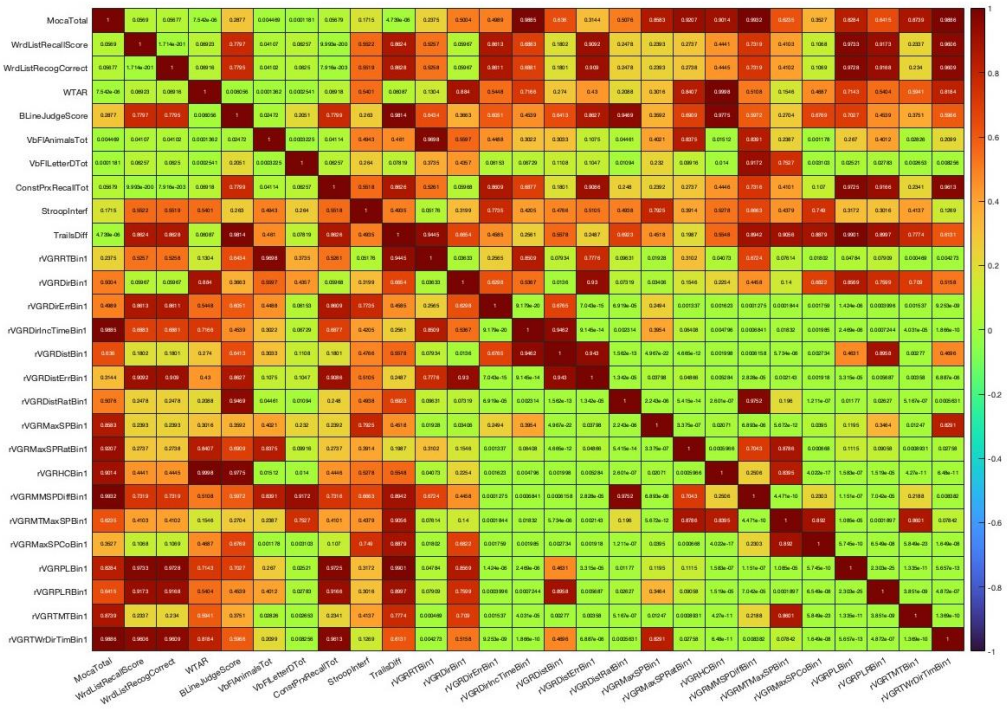

Figure 12. Bin 1 *p*-values