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Multiple Processes Predict Motor Learning and Impairments After a Stroke

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MULTIPLE PROCESSES PREDICT MOTOR LEARNING AND IMPAIRMENTS AFTER A STROKE

by

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Dedication

This dissertation is dedicated to my late father Michael Stan Perry and grandfather Stanyarn Perry who committed their lives towards community mentorship and leadership. Through their years of guidance, I have learned the valuable qualities of servitude and leadership needed to carry their legacy forward into future generations.

Abstract

Acquiring, refining, and adapting motor skills allows for successful interaction with our environment to perform daily activities such as driving, cooking, and self-care. Those with stroke often exhibit a compromised ability to relearn motor skills affected by their stroke resulting in chronic disability. Previous rehabilitation studies suggest that deficits in skilled limb movement primarily contributes to deficits after a stroke. However, studies in motor skill performance suggests that multiple behavioral features including visual search, eye-hand coordination and visuomotor decisions also contribute to improved performance. Currently, it is not known if refinements in multiple behavioral features independently contribute to motor learning, resulting in a lack of knowledge of how impairments in each behavioral feature contributes to deficits in motor learning after a stroke. In the current study, we used an ethological approach to test the hypotheses that practice-related refinements of multiple behavioral features are independently predictive of motor learning and that deficits in multiple behavioral features are independently predictive of motor impairments in stroke. Healthy individuals and those with a single cerebral stroke used an upper-limb robot with eye tracking to practice six trials of a continuous object hit-and-avoidance task once a week for six consecutive weeks. Participants were instructed to use virtual paddles to hit away 200 target objects and avoided hitting 100 distractor objects that continuously moved towards them from the back of the workspace. Motor learning was inferred from trial-by-trial acquisition and week-by-week retention of improvements on two measures of task performance related to motor execution and motor inhibition. In healthy individuals, refinements in skilled limb movement, visual search, and eye-hand coordination were independently predictive of improvements in motor execution, while refinements in eye-hand coordination was independently predictive of improvements in motor inhibition. In those with stroke, deficits in skilled limb movement, visual search, and eye-hand coordination were independently predictive of impairments in motor execution, while deficits in skilled limb movements and eye-hand coordination were predictive of impairments in motor inhibition. These results provide evidence that practice-related refinements in multiple behavioral features may independently contribute to motor learning and should be considered for inclusion in stroke rehabilitation interventions.

Table of Contents

List of Tables

List of Figures

List of Definitions

Behavioral Features: Kinematic and kinetic movement characteristics of the eyes and arms that represent the functional capacity of non-specific brain networks during motor task performance.

Motor learning: The acquisition and retention of improvements in measures of task performance. In the current study, acquisition is defined as trial-by-trial improvements, and Retention is defined as week-by-week perseverance of improvements.

Motor tasks: All tasks that require skilled limb movements to achieve the task goal. In the current study, the Object Hit-and-Avoidance (OHA) task will be used as our ethological motor task.

Refinements: The short-term (trial-by-trial) and long-term (week-by-week) plastic changes to brain networks, measured by changes in behavioral features.

Chapter 1

Introduction

The ability to acquire and refine motor skills is necessary for accomplishing common motor task goals such as driving, cooking, or self-care. Many survivors of stroke exhibit a compromised ability to adequately relearn motor tasks that were affected by their stroke leading to chronic disability and a loss of autonomy. Motor skill limitations are often attributed exclusively to poor recovery of the motor functions such as skilled arm and hand movements that are used to accomplish task goals, and rehabilitation methods address these limitations accordingly (Krakauer 2006). However, a growing body of evidence suggests that many stroke survivors also exhibit impaired recovery of perceptual and cognitive functions that underly the ability to quickly gather task-relevant information, accurately process that information, and initiate the skilled limb movements needed to accomplish task goals (Bonato et al 2010; Wu et al 2007). Research in our own lab has shown that many stroke survivors have impairments in multiple behavioral features underlying visuomotor skill performance, including visual search, eye-hand coordination and visuomotor planning that are predictive of impaired performance in visuomotor tasks and daily activities involving hand function and mobility (Harrison et al 2020; Singh et al 2017; Singh et al 2018).

Studies of motor skill learning have demonstrated that practicing visuomotor tasks leads to improvements in task performance (i.e. motor learning) that are associated with refinements of skilled limb movements (Darainy and Ostry 2008; Maeda et al 2018; van Beers 2009; Mosier et al 2005; Cohen and Sternad 2009; Shmuelof et al 2012; Huber et al 2016), visual search (Land and McLeod 2000; Williams et al 2002; Vickers and Lewinski 2012; Causer et al 2011; Wilson et al 2011; Vine et al 2013), eye-hand coordination (Ma-Wyatt et al 2010; Zhang et al 2012; Sailer et al 2005; Rand and Stelmach 2011; Foerster et al 2011; Säfström et al 2014), and visuomotor planning (Brown et al 2007; McGregor and Gribble 2015). However, the extent to which refinements in each behavioral feature is associated with motor learning independent of covariation with each of the other refinements is not well known. Thus, we do not know if refinements of skilled limb movements, visual search, eye-hand coordination, and visuomotor planning independently predict motor learning, nor do we know if impairments in these behavioral features are independently associated with deficits in motor learning in those with stroke.

The lack in knowledge of how multiple behavior features affect motor learning is a major barrier for reducing chronic disability in stroke because we do not know which perceptual and cognitive functions should also be targeted by interventions designed to improve relearning of motor tasks affected by stroke. Here, these knowledge gaps are addressed through an innovative, ethologically based study that examines the extent to which practice-related refinements of skilled limb movement, visual search, eye-hand coordination and visuomotor planning independently predict motor learning in healthy and survivors of stroke. To accomplish this, an upper-limb robotic device with eye tracking were employed to quantify objective behavioral measures of skilled limb movement, visual search, eye-hand coordination, and visuomotor planning that were simultaneously used to perform our continuous, visuomotor task to test the central hypothesis that refinements of multiple behavioral features will independently predict motor learning in our ethological paradigm, and impairments in the multiple behavioral features after stroke will be predictive of deficits in motor learning.

The first aim of this study was to validate that our novel ethological paradigm produced observable refinements in multiple behavioral features including limb movement, visual search, eye-hand coordination, and visuomotor planning and then determine if these refinements independently predict motor learning. This was accomplished through the utilization of a longitudinal ethological visuomotor learning paradigm involving young, healthy individuals. This population was selected to control for any potential medical conditions or age-related factors that may affect normal motor learning. The second aim of this study was to determine if stroke-related deficits in multiple behavioral features were predictive of impairments in motor learning in those with chronic stroke. This was accomplished through a cohort analysis of survivors of a single cerebral stroke and healthy age-matched controls performing the validated visuomotor paradigm from the first aim.

Chapter 2

Review of literature

Previous studies involving healthy adults have shown that practicing a motor task can lead to refinements in multiple behavioral features. Studies of skilled limb movements have shown that practicing motor tasks leads to trial-by-trial improvements in the coordination and efficiency of movement kinetics and muscle activations (Thoroughman and Shadmehr 1999; Burdet et al. 2001; Darainy and Ostry 2008; Maeda et al. 2018). Other studies of skilled limb movements have observed trial-by-trial and day-to-day improvements on kinematic features, such as the speed, accuracy, smoothness, and variability of movements (Flament et al. 1999; Novak et al. 2003; van Beers 2009,Mosier et al. 2005; Cohen and Sternad 2009; Shmuelof et al. 2012; Huber et al. 2016). Research on eye movements has found that experts at different visuomotor tasks have better patterns of eye movements and fixations than their novice counterparts (Mourant and Rockwell 1972; Vickers 1992; Land and McLeod 2000; Williams et al. 2002; Vickers and Lewinski 2012). Other studies of eye movements have demonstrated that interventions designed to teach expert-level patterns of eye movements and attention lead to better performance of visuomotor tasks in novices (Shapiro and Raymond 1989; Harle and Vickers 2001; Causer et al. 2011; Wilson et al. 2011; Vine et al.2013). Studies of eye-hand coordination have also found that patterns of eye-hand coordination depend on task demands (Ma-Wyatt et al. 2010; Zhang et al. 2012) and refinements of eye-hand coordination depend on the motor task that is being practiced (Sailer et al. 2005; Rand and Stelmach 2011; Foerster et al. 2011; Säfström et al. 2014). Studies of perceptual processes have observed that improvements in visuomotor performance result from task practice (Brown et al. 2007) and action observation (McGregor and Gribble 2015) are associated with improvements in visual processing. These studies provide evidence that multiple behavioral features predict and potentially contribute to motor learning. However, these studies were not designed to investigate the covariation between each behavioral feature. As a result, it is not known if each behavioral feature independently contributes to motor learning, or if covariation between one or more behavioral features explains these study findings.

Research on stroke has found that many survivors of stroke have impairments of behavioral features that are predictive of motor learning. Stroke survivors exhibit impairments affecting initiation, direction, distance, speed, and smoothness of skilled reaching movements with both arms (Wu et al. 2000; Schaffer et al. 2007, 2009; Coderre et al. 2010; Tyryshkin et al. 2014; Semrau et al. 2017). Stroke survivors also exhibit impairments of visuomotor planning that affect their ability to select appropriate limb movements during a demanding motor tasks (Bonato et al 2010, Wu et al 2007). Furthermore, we have previously demonstrated that many stroke survivors exhibit impairments of visual search that are associated with deficits in performing a visuomotor task (Trail Making Test) that is a good predictor of driving performance (Singh et al. 2017). We have also found that saccadic eye movements performed during reaching are associated with decreases in speed and smoothness of reaching movements (Singh et al. 2018). Finally, we have shown that impairments of skilled limb movement, visual search, visuomotor planning, and eye-hand coordination are associated with chronic deficits in performing visuomotor tasks and activities of daily living that involve hand function and mobility (Singh et al. 2018; Harrison et al. 2020). Overall, these studies provide indirect evidence that impairments of multiple behavioral features predict and may contribute to deficits in relearning motor tasks after a stroke.

Clinical trials in rehabilitation have traditionally focused on relearning how to execute skilled limb movements (Krakauer 2006). For example, constraint induced movement therapy (CIMT), which is designed to restore upper-limb function, has demonstrated some success in retraining upper-limb function after a stroke (Wolf et al 2006, Wolf et al 2008). More recent clinical trials on interventions designed specifically to restore skilled limb movement with intensive task-based practice (Winstein et al. 2016), upper-limb robotics (Lo et al 2010, Wolf et al 2015), body-weight supported treadmills (Duncan et al 2011, reviewed in Klamroth et al 2012, DePaul et al 2015) and virtual reality (Meldrum et al 2015, Saposnik et al 2016) have failed to find evidence for greater benefits than traditional therapy. Intervention studies designed to improve eye movements and visual search have shown improvements in daily activities in stroke survivors with visuospatial neglect and/or visual field defects (Pambakian et al 2004; Keller et al 2010; Kerkhoff et al 2013; Carrick et al 2016). However, little is known of how impairments to multiple behavioral features independently predict motor learning deficits after a stroke.

Chapter 3

Methods

Participant Recruitment

Participants were recruited from the University of South Carolina and surrounding areas through fliers, word of mouth, and from a database of previous participants who expressed an interest in participating in future research studies. All participants signed an informed consent that was approved by the University of South Carolina's Institutional Review Board prior to their participation.

Clinical Assessments

Prior to participation, participants were screened for normal dexterity, cognitive function, and visual acuity through the completion of the Box and Blocks Test (Mathiowetzet al 1985), the Montreal Cognitive Assessment (Nasreddine et al 2005), and a Snellen chart respectively. Visual correction was provided to those that required it in the form of custom eye-tracking compatible glasses with lens that matched to the nearest ±0.25 of their prescription.

Apparatus

A bilateral, upper-limb robot (Figure 3.1a, KINARM EndPoint Lab, KINARM Technologies, Kingston, Canada) with an integrated augmented-reality workspace and remote, monocular eye-tracker (EyeLink1000, SR Research, Ottawa, Canada) were used to collect experimental data. Participants sat in a custom chair that used floor-mounted tracks and a hydraulic lift to align their head with the forehead rest for stabilized eye tracking. To perform the task, participants grasped two near-frictionless manipulanda (handles) that allowed them to make planar, two-dimensional hand movements within the 80cm by 80cm workspace. The augmented-reality system used an inverted-monitor to project visual stimuli at 60 Hz through a semi-transparent mirror into the same workspace dimensions as the robotic manipulanda. An opaque shield and fabric covering was used to prevent direct vision of the hands and arms. Hand and gaze position were sampled at 1000 and 500 Hz, respectively, recorded at 200 Hz, and filtered with a 20 Hz, low-pass cutoff. Cartesian gaze position in the horizontal plane was estimated using proprietary calibration algorithms (BKIN Technologies, Kingston, Canada) that provide accurate eye tracking within the central portion of the workspace (approximately 50cm by 50cmin Cartesian space or 55°by 40° in visual space) where all visual stimuli were presented.

Task

Participants practiced six trials of a continuous visuomotor task, Object Hit and Avoid (Figure 3.1b, OHA, Bourke et al 2016), once a week for six consecutive weeks. In each OHA trial, 300 red objects comprised of eight geometric shapes (e.g., square, circle, triangle, etc.) moved along ten parallel paths (5 cm center-to-center spacing) from the back of the workspace towards the participants at a constant speed. Two shapes were predefined as “Targets” and the other six shapes will be predefined as “Distractors”. Each parallel path will contain 20 Targets (n=200) and 10 Distractors (n=100) that were released in random order. During each trial, the average number of objects that were simultaneously present in the workspace and the average speed that objects moved were gradually increased over time resulting in increased task difficulty during each trial.

However, the overall difficulty of each trial remained constant. Each trial ended when the final object passed through the workspace (~2 min).

Participants were scheduled on the same day of the week and at the same time of day to prevent confounds related to circadian rhythms or varying amounts of time between each session. Ambient illumination of the room was maintained at a constant level for all trials.

Participants received standardized instructions before each trail to use the two green paddles (2.5 cm wide) located on top of each hand to hit away as many Targets as possible and to avoid hitting as many Distractors as possible until the trial ended. Paddle size, object size, and spacing between paths were sized so that participants could not simultaneously hit two objects with one paddle. When participants hit a Target object with either paddle, the robot applied a small perturbation (10 Newtons for 50ms) to their hand in the opposite direction of paddle movement as the Target object rebounded off the paddle in the same direction and speed as the paddle movement. When participants contacted a Distractor with either paddle, no perturbation was applied to their hand and the Distractor object passed through the paddle with an unaltered direction and speed. The difference between the haptic and visual information provided after hitting Targets and Distractors provided participants with real-time feedback regarding correct and incorrect hitting actions.

Six combinations of Target sand Distractor objects were used to create six distinct OHA variants, that were pseudo-randomized and counter-balanced between participants each week (Figure 3.1c). Specifically, each of the six variants were assigned to different participants each week, and each participant performed six trials of a different variant each week. Before starting each trial, the two Target shapes were presented in the middle of workspace until participants confirm that they had memorized the shapes and were ready to begin the trial. After each trial was complete, participants were offered a rest period that lasted until they verbally confirm that they were ready to start the next trial.

Gaze Processing and Classification

Gaze data was processed and classified using published methods developed in our lab (Singh et al 2016). In summary, gaze data was preprocessed to remove: 1) blink artifacts, 2) spikes caused by incorrect corneal detection, and 3) outliers when gaze moved outside the eye-tracking workspace. We then used our novel geometric method to transform gaze position data in Cartesian coordinates into angular data in ocular coordinates. Finally, we used our adaptive thresholding methods to classify eye movements into saccades (rapid eye movements between targets) and smooth pursuits (eye movements that follow moving targets).

Measures

Hand and gaze kinematics were collected from each trial of OHA to compute measures of Task Performance and behavioral features of Skilled Limb Movement, Visual Search, Eye-Hand Coordination, and Visuomotor Planning. Our measures of task performance consisted of the percent of targets that participants correctly hit away and the percent of distractors that were avoided without paddle contact. Targets Hit (%) was our measure of motor execution, defined as the percent of all targets (N=200) that are hit with a paddle such that they move towards the back of the workspace. Distractors Avoided (%) was our measure of motor inhibition, defined as the percent of all Distractors (N=100) that passed through the workspace without ever contacting a paddle.

$$Targets\ Hit\ (\%) = \frac{Number\ Targets\ Hit}{200\ Targets} * 100 \tag{1}$$

$$Distractors\ Avoided\ (\%) = \frac{Number\ Distractors\ Not\ Hit}{100\ Distractors} * 100 \tag{2}$$

Five measures quantified skilled limb movement (Equations 3-7). Mean Hand-Speed (cm/s) was measured as the average speed of right-and left-hand movements. Mean Hand-Area (cm^2) was measured as the average area covered by movements of the right and left hands. The area covered by each hand was defined as the area contained within the convex hull of left-and right-hand movements. Target Contact Speed (cm/s) was measured as the average hand-speed at the onset of paddle-contact with each target. Hand-Speed Bias was measured as the relative difference between the average movement speed of the right and left hands. Hand-Area Bias was measured as the relative difference between the area covered by movements of the right and left hands. The measures of Hand-Speed Bias and Hand-Area Bias also served as measures of bimanual coordination. Values near zero indicated equal use of both hands and values greater than zero indicated greater use of one hand than the other.

$$Mean\ Hand\ Speed = \frac{(Right\ Mean\ Hand\ Speed + Left\ Mean\ Hand\ Speed)}{2\ Hands} \tag{3}$$

$$Mean\ Hand - Area = \frac{(Right\ Hand\ Area + Left\ Hand\ Area)}{2\ Hands} \tag{4}$$

$$Target\ Contact\ Speed = \frac{\sum_1^N Hand-Speed_{Target\ Contact}}{N_{Targets\ Hit}} \tag{5}$$

$$Hand\ Speed\ Bias = \frac{|Mean\ Right\ Hand\ Speed - Mean\ Left\ Hand\ Speed|}{Mean\ Hand\ Speed} \tag{6}$$

$$Hand\ Area\ Bias = \frac{|Right\ Mean\ Area - Left\ Mean\ Area|}{|Right\ Mean\ Are + Left\ Mean\ Area|} \tag{7}$$

Three measures of visual search were computed (Equations 8-10). Objects Foveated (%) was measured as the percent of all 300 objects that participants foveated with pursuit eye movements for at least 40ms (Singh et al 2016). If an object was pursued more than once, it was only counted one time. Spatial Foveation Bias was measured as the relative difference between the number of objects foveated on the right and left sides of the workspace. Extrafoveal Hits (%) was measured as the use parafoveal and peripheral vision percent of targets that were "Hit" but were not previously "Foveated". Other measures of visual search were not computed because catch-up saccades during pursuit prevented accurate quantification of other valid measures.

$$Objects\ Foveated = \frac{Objects\ pursued}{300} * 100 \tag{8}$$

$$Spatial\ Foveation\ Bias = \left| \frac{N_{Objects\ Foveated\ on\ Right} - N_{Objects\ Foveated\ on\ Left}}{N_{Objects\ Foveated\ on\ Right} + N_{Objects\ Foveated\ on\ Left}} \right| \tag{9}$$

$$Extrafoveal\ Hits = \frac{(\#\ targets\ hit\ |\ not\ foveated)}{\#\ targets\ not\ foveated} \tag{10}$$

Two measures were computed to quantify eye-hand coordination (Equations 11-12). Gaze-Hand Distance (cm) measured the distance between gaze and hand position at the onset of paddle-contact with each target. Gaze-Hand Latency (ms) measured the interval between the initial time of each target hit and final time that gaze foveated the target. If a target was "Hit" more than once, only the first instance was included in these calculations. If a target was "Never Foveated" or was "Hit" before being "Foveated", it was excluded from these calculations.

$$Gaze - Hand\ Distance = \sqrt{(Eye\ X - Target\ X)^2 + (Eye\ Y - Target\ Y)^2} \tag{11}$$

$$Gaze - Hand\ Latency = \frac{\sum_1^N (Time_{Initial\ Contact} - Time_{Final\ Foveation})}{N_{Targets\ Hit}} \tag{12}$$

Three measures were used to quantify visuomotor planning (Equations 13-15). Target Foveation Time (ms) and Distractor Foveation Time (ms) measured the average duration that subjects foveated targets or distractors. If a target or distractor was foveated more than one time, the total time of all foveations were included. Both measures quantified the average time used to recognize and classify shapes as a target or distractor. However, Target Foveation Time included the average time needed to initiate hand movements, whereas Distractor Foveation Time included the average time needed to inhibit hand movements. Foveation Time Difference (ms) quantified the difference between target and distractor foveation times. Assuming the amount of time needed to recognize and classify shapes are the same for both targets and distractors, this measure quantified the difference between time used to initiate and inhibit hand movements.

$$Target\ Pursuit\ Time = \frac{Time\ foveating\ targets}{\#\ targets\ foveated} \tag{13}$$

$$Distractor\ Pursuit\ Time = \frac{Time\ foveating\ distractors}{\#\ distractors\ foveated} \tag{14}$$

$$Pursuit\ Time\ Difference = \frac{Time\ foveating\ targets}{\#\ targets\ foveated} - \frac{Time\ foveating\ distractors}{\#\ distractors\ foveated} \tag{15}$$

All measures were input into robust regressions to compare eight different linear mixed-effects models that quantified common motor learning patterns of trial-by-trial acquisition and week-by-week retention of those refinements (Figure 3.2, Eqs. 16–23). The first four models implemented different combinations of linear and logarithmic growth rates (linear–linear, linear–logarithmic, logarithmic–linear, logarithmic–logarithmic) to quantify trial-by-trial acquisition and week-by-week retention of refinements. The other four models added an interaction term that quantified trial-by-trial changes across weeks.

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 Week_k + \epsilon_{ijk} \tag{16}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 Week_k + \epsilon_{ijk} \tag{17}$$

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 \log Week_k + \epsilon_{ijk} \tag{18}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 \log Week_k + \epsilon_{ijk} \tag{19}$$

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 Week_k + \ \beta_3 \left(Trial_j * Week_k\right) + \epsilon_{ijk} \tag{20}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 Week_k + \ \beta_3 \left(\log Trial_j * Week_k\right) + \epsilon_{ijk} \tag{21}$$

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 \log Week_k + \beta_3 \left(Trial_j * \log Week_k\right) + \epsilon_{ijk} \tag{22}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 \log Week_k + \beta_3 \left(\log Trial_j * \log Week_k\right) + \epsilon_{ijk} \tag{23}$$

In Equations 16-23, Y_{ijk} represents each measure obtained from participant i, in trial j of week k, b_i is a random intercept for each participant, β_1 describes the estimate in trial-by-trial refinements, β_2 describes the estimate in week-by-week refinements, and ϵ_{ijk} is the error term. In Equations 20-23, β_3 is an interaction term that describes estimate differences in trial-by-trial refinements across weeks. The model with the lowest Bayesian Information Criterion (BIC) was used to quantify differences in trial-by-trial (β_1) and week-by-week (β_2) refinements. After finding the best-fit model for each measure, we verified that additional transformations were not required by visually inspecting the fit between the predicted and actual outcomes and by testing the residuals for normality with Kolmogorov-Smirnoff tests. Measures with at least a small effect size ($f^2 \geq 0.02$) for trial-by-trial (β_1) or week-by-week (β_2) refinements were determined to show significant changes in refinement.

Figures

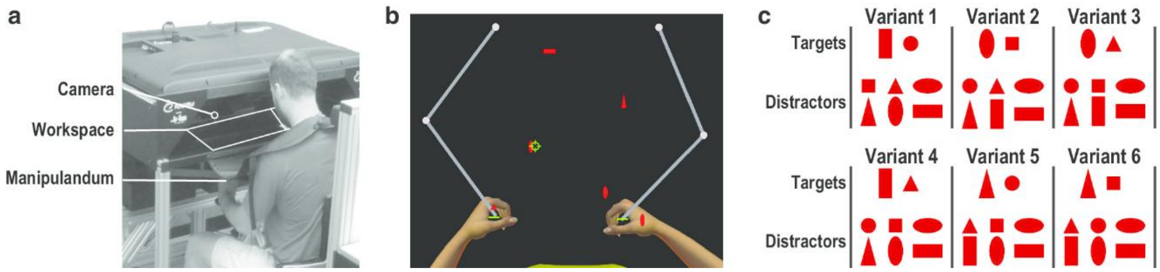

Figure 3.1 Experimental Apparatus. a: Bilateral, upper-limb robot (manipulandum), monocular eye-tracker (camera) and augmented-reality environment (workspace) used for data collection. **b:** Overhead view of the Object Hit and Avoid (OHA) task, showing the arms and hands, robotic manipulanda, two green paddles and six red objects (geometric shapes). Participants used the two paddles to hit away 200 target objects and avoid hitting 100 distractor objects that moved toward them from the back of the workspace. The augmented-reality environment presented the paddles and objects in the same horizontal plane as the robotic workspace. Participants were unable to see their arms and hands or the robotic manipulanda. **c:** The six OHA variants comprised of six combinations of target objects (one small, one large) and distractor objects (2 small, 4 large).

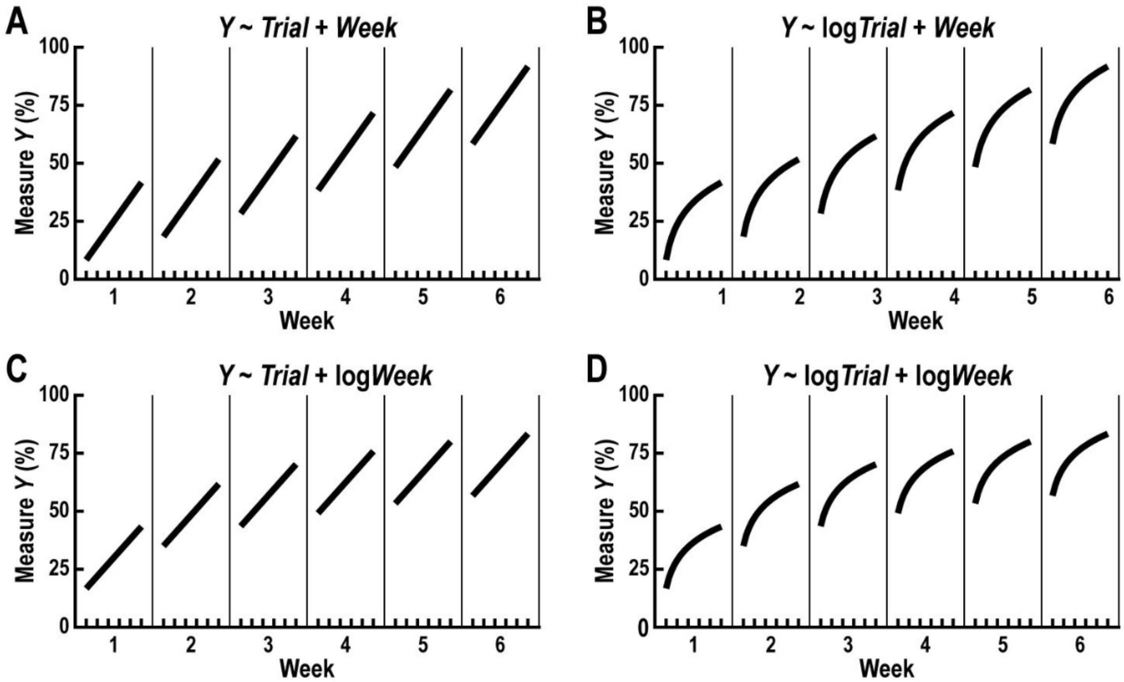

Figure 3.2 Motor Learning Models. Theoretical models used to quantify trial-by-trial acquisition and week-by-week retention of refinements. **a:** Linear trial-by-trial and linear week-by-week refinements. **b:** Logarithmic trial-by-trial and linear week-by-week refinements. **c:** Linear trial-by-trial and logarithmic week-by-week refinements. **d:** Logarithmic trial-by-trial and logarithmic week-by-week refinements.

Chapter 4

Multiple processes independently predict motor learning

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Abstract

Our ability to acquire, refine and adapt skilled limb movements is a hallmark of human motor learning that allows us to successfully perform many daily activities. The capacity to acquire, refine and adapt other features of motor performance, such as visual search, eye-hand coordination and visuomotor decisions, may also contribute to motor learning. However, the extent to which refinements of multiple behavioral features and their underlying brain networks independently contribute to motor learning remains unknown. In the current study, we used an ethological approach to test the hypothesis that practice-related refinements of multiple behavioral features would be independently predictive of motor learning. Eighteen healthy, young adults used an upper-limb robot with eye-tracking to practice six trials of a continuous, visuomotor task once a week for six consecutive weeks. Participants used virtual paddles to hit away 200 "Targets" and avoid hitting 100 "Distractors" that continuously moved towards them from the back of the workspace. Motor learning was inferred from trial-by-trial acquisition and week-by-week retention of improvements on two measures of task performance related to motor execution and motor inhibition. Adaptations involving underlying brain networks were inferred from trial-by-trial acquisition and week-by-week retention of refinements on measures of skilled limb movement, visual search, eye-hand coordination and visuomotor decisions. We tested our hypothesis by quantifying the extent to which refinements on measures of multiple behavioral features (predictors) were independently predictive of improvements on our two measures of task performance (outcomes) after removing all shared variance between predictors. We found that refinements on measures of skilled limb movement, visual search and eye-hand coordination were independently predictive of improvements on our measure of task performance related to motor execution. In

contrast, only refinements of eye-hand coordination were independently predictive of improvements on our measure of task performance related to motor inhibition. Our results provide indirect evidence that refinements involving multiple, behavioral features may independently contribute to motor learning, and distinct behavioral features may underlie improvements in task performance related to motor execution and motor inhibition. This also suggests that refinements involving multiple, behavioral features may contribute to motor recovery after stroke, and rehabilitation interventions should be designed to produce refinements of all behavioral features that may contribute to motor recovery.

Introduction

Humans learn to perform a broad repertoire of motor tasks that often require diverse and adaptable limb movements (i.e., skilled limb movements) to interact with our outside world. Many motor tasks, such as cooking, walking and driving, also employ diverse and adaptable patterns of eye movements (i.e., visual search) to actively gather visual information for planning and execution of skilled limb movements. Information gathered by visual search is also used to decide what skilled limb movements should be performed to achieve task goals (i.e., visuomotor decisions). Conversely, patterns of visual search are influenced by the available repertoire of skilled limb movements that can be used to achieve task goals. These interactions between skilled limb movements and visual search lead to coordinated patterns of eye and limb movements (e.g., eye-hand coordination). Overall, skilled limb movements, visual search, eye-hand coordination and visuomotor decisions may all contribute to learning and performance of motor tasks. However, we do not know the extent to which these behavioral features and their underlying behavioral features are independently refined to produce improvements in task performance.

Given that many concepts in motor learning have unclear or ambiguous definitions, we will define several concepts based on how they are used in this study. “Motor tasks” refer to all tasks that require skilled limb movements to achieve their task goal. Accordingly, most activities of daily living (e.g., cooking, walking, driving) are considered motor tasks even if they engage perceptual, cognitive and motor functions. “behavioral features” refer to movements of the eyes and limbs that are the result of brain networks that manipulate perceptual, cognitive and motor information to perform motor tasks. “Motor learning” refers to acquisition and retention of practice-related improvements in task performance, where “task performance” refers to outcomes that are specific to achieving task goals and “improvements” necessitate increased achievement of task goals. Motor learning results from neural adaptations that produce refinements of behavioral features of motor tasks (e.g., skilled limb movements, visual search, eye-hand coordination, visuomotor decisions), where “refinements” are practice-related changes that do not occur in a particular direction.

Traditional studies of motor learning have examined how skilled limb movements are refined during practice of motor tasks (Shadmehr et al 2010; Krakauer and Mazzoni 2011, Wolpert et al 2011). Studies of movement dynamics have found that muscle activations, joint torques and endpoint forces exhibit trial-by-trial refinements of coordination and efficiency (Thoroughman and Shadmehr 1999; Burdet et al 2001; Darainy and Ostry 2008). Similarly, studies of movement kinematics have observed trial-by-trial refinements of speed, accuracy, smoothness and variability of skilled limb movements (Flament et al 1999; Novak et al 2003; van Beers 2009), and these refinements exhibit good day-by-day retention (Mosier et al 2005; Cohen and Sternad 2009; Shmuelof et al 2012; Huber et al 2016). However, these studies were not designed to investigate if refinements of other behavioral features, such as visual search, eye-hand coordination and visuomotor decisions, contribute to motor learning.

Research on eye movements indicates that refinements of visual search may contribute to motor learning (Land et al 1999; Land and Hayhoe 2001). Observational studies have found that experts at different visuomotor skills have better control of eye movements than novices (Mourant and Rockwell 1972; Vickers 1992; Land and Mcloed 2000; Williams et al 2002; Vickers and Lewinski 2012). Experimental studies have also demonstrated that interventions designed to improve control of eye movements and attention lead to improvements in visuomotor performance (Shapiro and Raymond 1989; Harle and Vickers 2001; Causer et al 2011; Wilson et al 2011; Vine et al 2013). While none of these studies examined trial-by-trial or week-by-week refinements of eye movements, there is ample evidence that visual search is refined during practice of perceptual tasks (Chun and Jiang 1998; van Asselen et al 2011; Jones and Kaschak 2012; Li et al 2016; Hoppe and Rothkopf 2016). However, these studies did not examine any relationships between refinements of visual search and improvements in task performance, nor did they investigate refinements of other behavioral features. Thus, we do not know if refinements of visual search independently contribute to motor learning.

Studies of spatiotemporal coupling between eye and hand movements have provided evidence that refinements of eye-hand coordination may contribute to motor learning. Patterns of eye-hand coordination vary with task demands (Ma-Wyatt et al

2010; Zhang et al 2012) and are refined during motor learning in a task-dependent manner (Sailer et al 2005; Rand and Stelmach 2011; Foerster et al 2011; Säfström et al 2014). However, it remains unclear if refinements of eye-hand coordination independently contribute to improvements in task performance, or if they result from refinements of skilled limb movements and visual search but do not actually contribute to motor learning.

It is widely accepted that sensory processes contribute to planning and execution of skilled limb movements (Scott 2016). In addition, information from sensory feedback provides reinforcement that is known to play an important role in motor learning (Krakauer and Mazzoni 2011). Recent studies have also found that motor learning can induce changes in visual processing that are associated with refinements of skilled limb movement (Brown et al 2007; McGregor and Gribble 2015). This suggests that adaptations of visual and visuomotor processing contribute to motor learning. However, these studies were not designed to investigate the extent to which refinements of other behavioral features, such as visual search, eye-hand coordination and visuomotor decisions, may independently contribute to motor learning.

Despite evidence that refinements of multiple features might underlie motor learning, we do not know the extent to which they independently contribute to motor learning. Traditional experiments cannot easily address this problem because they are designed to isolate individual processes. In contrast, ethological approaches that study real-time, natural behavior can overcome this limitation by leveraging individual patterns of variability exhibited by several behavioral features (Cisek and Kalaska 2010). However, this approach requires carefully controlling for any covariation between different features. For example, two or more processes may be associated with motor learning, but their individual patterns of variability might exhibit substantial covariance. This shared variance can cause regression analyses to produce incorrect estimates of the contributions made by each process. Accurate estimates of the individual contributions can only be obtained from the independent variance that remains after removing all shared variance.

The objective of the current study was to investigate the extent to which multiple behavioral features might independently contribute to motor learning. Healthy young adults used an upper-limb robot with eye tracking to complete six weeks of practice of a novel, visuomotor task designed to mimic the richness of real-world visuomotor tasks. Motor learning was inferred from trial-by-trial acquisition and week-by-week retention of improvements on measures of task performance. Adaptations of brain networks were inferred from trial-by-trial acquisition and week-by-week retention of refinements on measures of behavioral features including skilled limb movement, visual search, eye-hand coordination and visuomotor decisions. Our first hypothesis was that practicing our novel, visuomotor task would elicit trial-by-trial acquisition and week-by-week retention of improvements in task performance that are mirrored by concurrent refinements of skilled limb movements, visual search, eye-hand coordination and visuomotor decisions. Our second hypothesis was that refinements related to multiple behavioral features would be independently predictive of improvements in task performance.

Methods

Participants

We recruited healthy, young adults (18–35 years old) from the University of South Carolina and surrounding areas. Participants were excluded if they reported any history of a central or peripheral neurological disorder or an ongoing musculoskeletal issue affecting either arm or hand. The study protocol was approved by the University of South Carolina's Institutional Review Board and all participants provided informed consent to participate.

Apparatus

Data were collected with a bilateral, upper-limb robot (Figure 3.1a, KINARM EndPoint Lab, KINARM, Kingston, Canada) and monocular eye-tracker (EyeLink 1000, SR Research Ltd., Ottawa, Canada) that were integrated with an augmented-reality workspace (Singh et al 2016). Participants sat in a custom chair that used floor-mounted tracks and hydraulics to align them with a forehead rest, which stabilized the head for eye tracking. Participants grasped two near-frictionless manipulanda, which allowed them to make two-dimensional hand movements within an 80 cm wide by 80 cm deep workspace. An opaque shield and fabric cover prevented direct vision of the hands and arms. Hand and gaze position in the robotic workspace were respectively sampled at 1000 and 500 Hz, recorded at 200 Hz, and filtered offline using a low-pass filter with a 20 Hz cutoff.

The augmented-reality environment was created in the same horizontal plane as the robotic workspace by using an inverted-monitor to project visual stimuli at 60 Hz through a semi-transparent mirror. Cartesian gaze position in the horizontal plane was estimated using proprietary calibration algorithms (Kinarm, Kingston, Canada) that provided accurate eye tracking within a workspace of approximately 50 cm wide by 50 cm deep. All visual stimuli were presented within this portion of the robotic workspace. A nonlinear mapping corresponded to a visual area approximately 55° wide by 40° deep in which stimuli located closer to participants comprised larger visual angles.

Task

Participants practiced six trials of a continuous, visuomotor task, Object Hit and Avoid (OHA) (Bourke et al 2016), once a week for six consecutive weeks. Each participant was scheduled at a consistent time of day on the same weekday to avoid potential confounds caused by circadian rhythms and to assure a consistent retention interval between sessions. Illumination of the room was maintained at a constant level for the duration of the study.

In each trial of the OHA task, 300 red objects comprised of eight geometric shapes (e.g., square, circle, triangle, etc.) moved from the back of the workspace towards the participants along ten parallel paths (5 cm center-to-center spacing) (Figure 3.1b). Two shapes were predefined as “Targets” and six shapes were predefined as “Distractors”. Each parallel path contained 20 Targets ($n = 200$) and 10 Distractors ($n = 100$) that were released in random order. The average number of objects that were simultaneously present in the workspace and the average speed that objects moved progressively increased over time. As a result, task difficulty increased within each trial, whereas the overall difficulty of each trial was consistent. Each trial ended after all 300 objects had passed through the workspace (~ 2 min).

Participants received standardized instructions to use two green paddles (2.5 cm wide) located on top of each hand to hit away as many Targets and to avoid hitting as many Distractors as possible. When participants made paddle contact with Targets, the robot applied a small perturbation (10 Newtons for 50 ms) to the participant's hand and Targets rebounded from the paddle with the same direction and speed as the paddle movement. When participants made paddle contact with Distractors, no perturbation was applied to the participant's hand and Distractors passed unaltered through the paddle. Paddle size, object size and the spacing between adjacent paths prevented participants from simultaneously hitting two objects with the same hand.

We employed six distinct variants of targets and distractors to prevent overlearning of a specific variant from causing plateaus in task performance (Figure 3.1c). Each variant was pseudo-randomized and counter-balanced between participants each week and was never practiced by a participant in more than one week. Specifically, each of the six variants was assigned to three different participants each week, and each participant performed six trials of a different variant each week. Before starting each trial, the two target shapes were presented in the middle of workspace until participants confirmed that they had memorized the shapes and were ready to begin. After each trial, participants were offered a rest period until they were ready to start the next trial.

Gaze classification

Gaze data were processed and classified using the procedures of a validated methodology for processing gaze data our group previously published (Singh et al 2016). In brief, the methodology involves preprocessing gaze data to remove blink artifacts, one sample spikes caused by incorrect corneal detection, and outliers that occurred when gaze moved outside the eye-tracking workspace. We subsequently use a novel geometric method to transform gaze position data into rotational kinematics of the eye. Finally, we use adaptive thresholding methods to classify eye movements into saccades (rapid eye movements between targets) and smooth pursuits (eye movements that followed moving targets with foveal vision). Our previous manuscript demonstrated that our methodology for gaze processing and classification correctly classifies approximately 90% of saccades and smooth pursuits and misclassifies approximately 5% of saccades and smooth pursuits when compared with manual classification (gold standard) (Singh et al 2016).

Measures

We used hand and gaze data to compute measures of Task Performance, Skilled Limb Movement, Visual Search, Eye-Hand Coordination and Visuomotor Decisions for each OHA trial.

Task performance We computed two measures of task performance (Eqs. 1 and 2). Targets Hit (%) quantified goal achievement resulting from successful execution of hand movements to hit targets (motor execution). It was calculated as the percent of all 200 targets that participants “hit”, where a target was counted as “hit” if either paddle made contact with the target, causing it to move toward the back of the workspace. Only one “hit” was counted if a target was hit more than once. Distractors Avoided (%) quantified goal achievement resulting from successful inhibition of hand movements to avoid distractors. It was calculated as the percent of all 100 Distractors that were “not hit”, where a distracter was counted as “not hit” if neither paddle made contact with the distractor or if a paddle made contact but caused the distractor to move toward the front of the workspace.

$$Targets\ Hit\ (\%) = \frac{Number\ Targets\ Hit}{200\ Targets} * 100 \quad (1)$$

$$Distractors\ Avoided\ (\%) = \frac{Number\ Distractors\ Not\ Hit}{100\ Distractors} * 100 \quad (2)$$

Skilled limb movement We computed five measures of skilled limb movement (Eqs. 3-7). Mean Hand-Speed (cm/s) quantified the overall execution speed of all hand movements by computing the average speed of right- and left-hand movements. Mean Hand-Area (cm^2) quantified the overall spatial distribution of all hand movements by calculating the average area covered by right- and left-hand movements, where each area was obtained by computing the convex hull of left- and right-hand movements. Target Contact Speed (cm/s) quantified the execution speed of skilled hand movements by computing the average speed of hand movements at the onset of paddle-contact with each target that was successfully hit. Hand-Speed Bias quantified bimanual coordination by computing inter-limb differences in movement speed. It was calculated as the normalized difference between the average speed of right- and left-hand movements. Hand-Area Bias quantified bimanual coordination by computing inter-limb differences in the spatial distributions of hand movements. It was calculated as the normalized difference between the area covered by movements of the right and left hands. Values of hand-speed bias or hand-area bias near zero indicate equal use of both hands and increasingly higher values indicate greater use of one hand than the other. We were unable to quantify many traditional measures of skilled limb movement, such as time to peak velocity, peak acceleration or smoothness, because we could not identify a distinct start or end point of most limb movements due to the continuous nature of our task.

$$Mean\ Hand\ Speed = \frac{(Right\ Mean\ Hand\ Speed + Left\ Mean\ Hand\ Speed)}{2\ Hands} \quad (3)$$

$$Mean\ Hand - Area = \frac{(Right\ Hand\ Area + Left\ Hand\ Area)}{2\ Hands} \quad (4)$$

$$Target\ Contact\ Speed = \frac{\sum_1^N Hand - Speed_{Target\ Contact}}{N_{Targets\ Hit}} \quad (5)$$

$$Hand\ Speed\ Bias = \frac{|Mean\ Right\ Hand\ Speed - Mean\ Left\ Hand\ Speed|}{Mean\ Hand\ Speed} \quad (6)$$

$$Hand\ Area\ Bias = \frac{|Right\ Mean\ Area - Left\ Mean\ Area|}{|Right\ Mean\ Are + Left\ Mean\ Area|} \quad (7)$$

Visual search We computed three measures of visual search (Eqs. 8–10). Objects Foveated (%) quantified the overall efficiency of visual search by calculating the percent of all 300 objects that participants "foveated" with pursuit eye movements, where an object was counted as "foveated" if the object was followed with foveal vision for at least 40 ms (Singh et al 2016). If an object was foveated more than once, it was only counted once. Spatial Foveation Bias quantified spatial biases in the distribution of visual search by computing the normalized difference between the number of objects foveated on the right and left sides of the workspace. Extrafoveal Hits (%) quantified covert use of parafoveal and peripheral vision for visual search by calculating the percent of targets that were hit but were not previously foveated. We were unable to compute other measures of visual search because a large number of catch-up saccades during pursuit prevented accurate calculation of other valid measures.

$$Objects\ Foveated = \frac{Objects\ Pursued}{300} * 100 \quad (8)$$

$$Spatial\ Foveation\ Bias = \left|\frac{N_{Objects\ Foveated\ on\ Right} - N_{Objects\ Foveated\ on\ Left}}{N_{Objects\ Foveated\ on\ Right} + N_{Objects\ Foveated\ on\ Left}}\right| \quad (9)$$

$$Extrafoveal\ Hits = \frac{(\#\ targets\ hit\ |\ not\ foveated)}{\#\ targets\ not\ foveated} \quad (10)$$

Eye–hand coordination We computed two measures of eye-hand coordination (Eqs. 11-12). Gaze-Hand Distance (cm) quantified spatial coupling between the eyes and hands by calculating the distance between gaze and hand position at the onset of paddle-contact with each target (Sailer et al 2005). Gaze-Hand Latency (ms) quantified temporal coupling between eyes and hands by calculating the interval between the initial time of each target hit and final time that gaze foveated the target (Sailer et al 2005; Rand and Stelmach 2011; Foerster et al 2011; Säfström et al 2014; Neggers and Bekkering 2000). If a target was hit more than once, only the first hit was included in these calculations. If a target was not foveated or was hit before it was foveated, it was excluded from these calculations.

$$Gaze - Hand\ Distance = \sqrt{(Eye\ X - Target\ X)^2 + (Eye\ Y - Target\ Y)^2} \tag{11}$$

$$Gaze - Hand\ Latency = \frac{\sum_1^N (Time_{Initial\ Contact} - Time_{Final\ Foveation})}{N_{Targets\ Hit}} \tag{12}$$

Visuomotor decisions We computed three measures of visuomotor decisions (Eqs. 13-15). Target Foveation Time (ms) quantified the amount of time used for making decisions to hit targets and was calculated as the average duration that participants foveated targets. Distractor Foveation Time (ms) quantified the amount of time used for making decisions to avoid distractors and was calculated as the average duration that participants foveated distractors. If a target or distractor was foveated more than one time, we included the total time of all foveations. Both measures quantified the average time used to recognize and classify shapes as a target or distractor. However, Target Foveation Time included the average time used to initiate hand movements, whereas Distractor Foveation Time included the average time used to inhibit hand movements. Foveation Time Difference (ms) quantified differences between the amount of time used for making decisions to hit targets and avoid distractors and was calculated as the difference between target and distractor foveation times.

$$Target\ Pursuit\ Time = \frac{Time\ foveated\ targets}{\#\ targets\ foveated} \tag{13}$$

$$Distractor\ Pursuit\ Time = \frac{Time\ foveating\ distractors}{\#\ distractors\ foveated} \tag{14}$$

$$Pursuit\ Time\ Difference = \frac{Time\ foveating\ targets}{\#\ targets\ foveated} - \frac{Time\ foveating\ distractors}{\#\ distractors\ foveated} \tag{15}$$

Analysis

All analyses were performed using Matlab 2017b (Mathworks Inc., Natick, MA).

Validation of Measures

Since most of our measures were novel, we first examined each measure for uniqueness of information and for the presence of outliers. We confirmed that each measure quantified unique information by examining the covariance between each pair of measures. If we found a moderate Pearson correlation coefficient between any pair of measures ($|r| \geq 0.707$, $r^2 \geq 0.5$), we excluded the measure with the highest coefficient of variance from further analyses (McDonald 2009). We subsequently performed a visual inspection of our data, which revealed the presence of a small number of outliers in several measures. For all subsequent analyses, we minimized the potential influence of outliers by performing robust regression with a Welsch weighting function (Holland and Welsch 1977). Finally, we standardized each measure to obtain a mean of zero and standard deviation of one, which allowed us to compare measures with different units.

Practice-related refinements

Our first hypothesis was that practice would induce trial-by-trial and week-by-week refinements of skilled limb movement, visual search, eye-hand coordination and visuomotor decisions that mirror improvements in task performance. We tested this hypothesis by using robust regression to compare eight different linear mixed-effects models that quantified trial-by-trial acquisition and week-by-week retention of refinements (Eqs. 16-23). The first four models implemented different combinations of linear and logarithmic growth rates (linear–linear, linear–logarithmic, logarithmic–linear, logarithmic–logarithmic) to quantify trial-by-trial acquisition and week-by-week retention of refinements (Figure 3.2). The other four models added an interaction term that quantified trial-by-trial changes across weeks.

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 Week_k + \epsilon_{ijk} \tag{16}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 Week_k + \epsilon_{ijk} \tag{17}$$

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 \log Week_k + \epsilon_{ijk} \tag{18}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 \log Week_k + \epsilon_{ijk} \tag{19}$$

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 Week_k + \beta_3 \left(Trial_j * Week_k\right) + \epsilon_{ijk} \tag{20}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 Week_k + \beta_3 \left(\log Trial_j * Week_k\right) + \epsilon_{ijk} \tag{21}$$

$$Y_{ijk} = b_i + \beta_1 Trial_j + \beta_2 \log Week_k + \beta_3 \left(Trial_j * \log Week_k\right) + \epsilon_{ijk} \tag{22}$$

$$Y_{ijk} = b_i + \beta_1 \log Trial_j + \beta_2 \log Week_k + \beta_3 \left(\log Trial_j * \log Week_k\right) + \epsilon_{ijk} \tag{23}$$

In Eqs. 16-23, Y_{ijk} represents each measure obtained from participant i, in trial j of week k, b_i is a random intercept for each participant, β_1 describes trial-by-trial acquisition of refinements, β_2 describes week-by-week retention of refinements, and ϵ_{ijk} is the error term. In Eqs. 20-23, β_3 is an interaction term that describes changes in trial-by-trial refinements across weeks. The model with the lowest Bayesian Information Criterion (BIC) was used to examine trial-by-trial acquisition and week-by-week retention of refinements. After finding the best-fit model for each measure, we verified that additional transformations were not required by visually inspecting the fit between the predicted and actual outcomes and by testing the residuals for normality with Kolmogorov-Smirnoff tests. Measures with at least a small effect size ($f^2 \geq 0.02$; (Cohen 1988) for trial-by-trial acquisition (β_1) or week-by-week retention (β_2) of refinements were subsequently included as "predictor measures" in the following analyses of our second hypothesis.

Prediction of motor learning

Our second hypothesis was that refinements related to multiple behavioral features would be independently predictive of improvements in task performance. We tested this hypothesis by using multiple regression to quantify the extent to which refinements of predictor measures were independently predictive of improvements on our two measures of task performance (outcome measures). Before performing these multiple regression analyses, we first reduced the number of predictor measures included in each model by using bivariate regression to confirm that each predictor measure that was individually related to improvements on our two measures of task performance (i.e., at least a small effect size, $f^2 \geq 0.02$). We then examined each predictor measure for multicollinearity by computing the Tolerance of each measure, which is the proportion of variance not explained by linear combinations of all other predictors (i.e., $1–R^2$) (Allison

1990). We subsequently performed multiple regression using linear mixed-effects models that only included the predictor measure identified in the previous step (Eq. 24).

$$Y_{ijk} = b_i + \beta_1 X_{1(ijk)} + \beta_2 X_{2(ijk)} + \cdots + \beta_N X_{N(ijk)} + \epsilon_{ijk} \tag{24}$$

In Eq. 24, Y_{ijk} represents task performance of participant i in trial j of week k, b_i are random intercepts for each participant, coefficients β_1–β_N are estimated relationships between each predictor measure (X_1–X_n) and the respective measure of task performance, and ϵ_{ijk} is the error term.

We finally identified each predictor measure that was independently predictive of improvements on our two measures of task performance. Importantly, the values of coefficients β_1–β_N in Eq. 24 are influenced by variance that is independent of all other predictors and variance that is shared with other predictors. Figure 4.1 illustrates conceptual representations of independent and shared variance for four theoretical regression models that include one, two, three, or four predictors of motor learning. If only one predictor is examined (a), it might be assumed that all variance related to motor learning (dark grey area) is independently predictive of motor learning. However, if multiple predictors are examined (b–d), part of each predictor's variance related to motor learning would be independent of all other predictors (dark grey area) and part would be shared with other predictors (light grey area). The relationships between each predictor's independent variance and motor learning are described by semipartial coefficients of determination (sr^2). For the purpose of our second hypothesis, we calculated semipartial coefficients of determination (sr^2), semipartial effect sizes (sf^2), and semipartial *p*-values (sp) to examine the relationships between the independent variance of each predictor measure and improvements on our two measures of task performance. We considered measures with at least a small semipartial effect size ($sf^2 \geq 0.02$) as meaningful predictors of motor learning, though we recognize that this could underestimate the amount of motor learning that should be attributed to each predictor.

For the purpose of rigor and reproducibility, we validated our multiple regression results by performing forward and backward stepwise regression with the same set of predictor measures used in our multiple regression analyses. We used the BIC to determine which predictor to add or remove at each step. This resulted in a final model with a minimum BIC.

Results

Participants

We enrolled 18 healthy, young adults (8 male, 10 female; 24.2 ± 3.7 years old; 17 R-handed, 1 L-handed; Box-and_Block: 66.4 ± 10.7 R-hand, 66.1 ± 9.1 L-hand; VICA: 19.1 ± 1.1) in the study. One participant was unable to complete the sixth week of the study. We included the participant's data without replacement of the sixth week.

Exemplar OHA performance

Figure 4.2 illustrates pursuit and saccadic eye movements (pink and gold lines) and left- and right-hand movements (blue and red lines) made by an exemplar participant at four time points, $Week_1 \cdot Trial_1$ (a), $Week_1 \cdot Trial_6$ (b), $Week_6 \cdot Trial_1$ (c), and $Week_6 \cdot Trial_6$ (d). At each time point, the participant's eye movements covered an area of approximately 50 cm wide (X) by 40 cm deep (Y). The center-of-mass was consistently located near the midline but shifted distally from around 30 cm on $Week_1 \cdot Trial_1$ (a), to 35 cm on $Week_1 \cdot Trial_6$ (b), and 40 cm on $Week_6 \cdot Trial_1$ and $Week_6 \cdot Trial_6$ (c, d). Combined movements of both hands covered an area that was around 50 cm wide and consistently centered near the midline. However, the range of hand movements in depth increased from around 15 cm on $Week_1 \cdot Trial_1$ (a) to 20 cm on the other three trials (b–d). The center-of-mass also shifted distally from under 10 cm on $Week_1 \cdot Trial_1$ (a) to over 15 cm on the other three trials (b–d). Left- and right-hand movements covered similar areas and were largely constrained to their respective sides.

Figure 4.2 also displays grids of rectangles that represent each Target (upper grids: 20 × 10) and Distractor (lower grids: 10 × 10) that was foveated and hit (left hand: dark blue, right hand: dark red), foveated but not hit (grey), not foveated but hit (left hand: light blue, right hand: light red), or neither foveated nor hit (white). The participant failed to foveate several targets and distractors on $Week_1 \cdot Trial_1$ (e) but foveated the majority of targets and distractors on the other three trials (f–h). Similarly, the participant failed hit a number of targets on $Week_1 \cdot Trial_1$ (e) but hit the majority of targets on the other three trials (f–h). In contrast, the participant hit several distractors in the first week (e, f) but very few in the last week (f–h). At all four time points, the participant hit more targets with the right-hand, including several targets on the left side of the workspace.

Validation of measures

Targets Hit and Distractors Avoided exhibited a low correlation ($r = 0.03$), indicating that they quantified unique aspects of task performance. Both measures were included in our subsequent analyses. We also examined each pair of predictor measures for high correlations ($|r| \geq 0.707$) indicative of redundant information (Table 4.1). Two pairs exhibited high correlations, Mean Hand-Speed and Target Contact Speed ($r = 0.89$) and Gaze-Hand Distance and Gaze-Hand Latency ($r = 0.89$). Target Contact Speed and

Gaze-Hand Latency were excluded from all remaining analyses because they had the highest coefficients of variance in each pair (McDonald 2009).

Confirmation of motor learning

Before testing our two hypotheses, we first confirmed that our participants demonstrated trial-by-trial acquisition and week-by-week retention of improvements in task performance (Table 4.2). Targets Hit exhibited moderate trial-by-trial increases (β_1=0.26, f^2=0.23, $p<10^{-6}$), large week-by-week increases (β_2=0.49, f^2=0.82, $p<10^{-6}$), and small trial-by-trial decreases across weeks (β_3=-0.16, f^2=0.09, $p<10^{-6}$) (Fig. 4.3a). We also observed small, week-by-week increases on Distractors Avoided (β_2=0.20, f^2=0.11, $p<10^{-6}$) (Fig. 4.3b). These finding show that practice-related improvements in motor execution (Targets Hit) and motor inhibition (Distractors Avoided) contributed to improvements in task performance.

Practice-related refinements

We tested our first hypothesis by examining trial-by-trial acquisition and week-by-week retention of refinements on our measures of skilled limb movement, visual search, eye-hand coordination and visuomotor decisions (Table 4.2). Three measures of skilled limb movement (Mean Hand-Speed, Hand-Speed Bias, and Hand-Area Bias) displayed practice-related refinements. Mean Hand-Speed exhibited small trial-by-trial increases (β_1=0.09, f^2=0.03, $p<10^{-4}$) and small week-by-week increases (β_2=0.21, f^2=0.14, $p<10^{-6}$) (Fig. 4.4a). Hand-Speed Bias demonstrated small week-by-week increases (β_2=0.14, f^2=0.03, $p<10^{-5}$) and Hand-Area Bias showed small trial-by-trial increases (β_1=0.14, f^2=0.03, $p<10^{-4}$). Two measures of visual search (Objects Foveated and Extrafoveal Hits) exhibited practice-related refinements. Objects Foveated displayed small trial-by-trial increases (β_1=0.12, f^2=0.04, $p<10^{-6}$), moderate week-by-week increases (β_2=0.32, f^2=0.29, $p<10^{-6}$), and small trial-by-trial decreases across weeks (β_3=− 0.12, f^2=0.04, $p<10^{-6}$) (Fig. 4.4b). Extrafoveal Hits exhibited small trial-by-trial increases (β_1=0.22, f^2=0.12, $p<10^{-6}$) and large week-by-week increases (β_2=0.38, f^2=0.36, $p<10^{-6}$) (Fig. 4.4c). Our only measure of eye-hand coordination, Gaze-Hand Distance, demonstrated large week-by-week increases (β_2=0.33, f^2=0.69, $p<10^{-6}$) (Fig. 4.4d). All three measures of visuomotor decisions (Target Foveation Time, Distractor Foveation Time and Foveation Time Difference) displayed practice-related refinements. Target Foveation Time showed moderate week-by-week decreases (β_2=− 0.27, f^2=0.20, $p<10^{-6}$) (Fig. 4.4e). Distractor Foveation Time displayed small week-by-week increases (β_2=0.11, f^2=0.04, $p<10^{-6}$). Foveation Time Difference exhibited moderate week-by-week decreases (β_2=− 0.41, f^2=0.25, $p<10^{-6}$) (Fig. 4.4f). One measure of skilled limb movement (Mean Hand-Area) and one measure of visual search (Spatial Foveation Bias) did not exhibit practice-related refinements and were excluded from further analyses.

Prediction of motor learning

We initially used bivariate regression to identify predictor measures that were individually related to improvements on our two measures of task performance (i.e., at least a small effect size, $f^2 \geq 0.02$) (Table 4.3). We identified six predictor measures that were individually related to improvements in Targets Hit. They included Extrafoveal Hits (β=0.70, f^2=1.52, $p<10^{-6}$) (Fig. 4.5a), Objects Foveated (β=0.59, f^2=0.80, $p<10^{-6}$) (Fig. 4.5b), Gaze-Hand Distance (β=0.58, f^2=0.65, $p<10^{-6}$) (Fig. 4.5c), Mean Hand-Speed (β=0.50, f^2=0.48, $p<10^{-6}$) (Fig. 4.5d), Target Foveation Time (β=-0.46, f^2=0.41, $p<10^{-6}$), and Foveation Time Difference (β=0.23, f^2=0.09, $p<10^{-6}$). We also identified six predictor measures that were individually related to improvements in Distractors Avoided. They included Gaze-Hand Distance (β=0.29, f^2=0.25, $p<10^{-6}$), Target Foveation Time (β=− 0.11, f^2=0.04, $p<10^{-3}$), Hand-Speed Bias (β=0.11, f^2=0.03, $p<10^{-3}$), Extrafoveal Hits (β=0.11, f^2=0.03, $p<10^{-3}$), Foveation Time Difference (β=− 0.09, f^2=0.02, $p<10^{-3}$), and Objects Foveated (β=0.09, f^2=0.02, $p<0.01$).

We subsequently tested our second hypothesis by using multiple regression to analyze the extent to which refinements on the preceding predictor measures were independently predictive of improvements in Target Hits and Distractors Avoided (i.e., at least a small semipartial effect size, $f^2 \geq 0.02$) (Table 4.4). Our multiple regression identified two measures of visual search (Extrafoveal Hits: β=0.54, f^2=0.61, $sp<10^{-6}$; Objects Foveated: β=0.32, f^2=0.16, $sp<10^{-6}$), one measure of eye-hand coordination (Gaze-Hand Distance: β=0.22, f^2=0.07, $sp<10^{-3}$), and one measure of skilled limb movement (Mean Hand-Speed: β=0.14, f^2=0.03, sp=0.02) that were independently predictive of improvements in Target Hits (Fig. 4.5a). In contrast, our multiple regression only identified a single measure of eye-hand coordination (Gaze-Hand Distance: (β=0.24, f^2=0.04, sp=0.01) that was independently predictive of improvements on Distractors Avoided (Fig. 4.5b).

Finally, our stepwise regression analyses confirmed the results obtained from our multiple regression analyses. Specifically, the final model for Targets Hit only included the same measures of visual search (Extrafoveal Hits, Objects Foveated), eye-hand coordination (Gaze-Hand Distance) and skilled limb movement (Mean Hand-Speed). Furthermore, the final model for Distractors Avoided only included Gaze-Hand Distance.

Discussion

Multiple processes independently predict motor learning

The results of this study provide indirect evidence that practice-related refinements involving multiple behavioral features may contribute to motor learning. Notably, we observed that measures of skilled limb movement, visual search and eye-hand coordination underwent practice-related refinements (Hypothesis 1) that were independently predictive of improvements in task performance (Hypothesis 2). Importantly, in drawing this conclusion, trial-by-trial and week-by-week refinements exhibited by measures of skilled limb movement, visual search and eye-hand coordination infer that practice produced refinements involving multiple behavioral features. Furthermore, motor learning could be inferred from trial-by-trial and week-by-week improvements exhibited by measures of task performance.

Other studies have provided evidence that both sensory and motor processes contribute to motor learning (Ostry and Gribble 2016), but these studies were not designed to investigate the extent to which these processes are independent predictors of motor learning. As result, we do not know the extent to which relationships with motor learning reflected independent or shared variance. In the current study, we addressed the issue of covariation by examining independent predictions of motor learning after removing all shared variance. This analysis showed that skilled limb movements, visual search and eye-hand coordination are independent predictors of motor learning, indicating that studies of motor learning should account for the various processes that may influence improvements in task performance.

Skilled limb movements independently predict motor learning

Increases in Mean Hand-Speed were associated with increases in Targets Hit, indicating that participants learned to hit more targets by quickly moving their hands to different areas of the workspace. Although faster movements are more variable and less accurate (Krakauer and Mazzoni 2011; van Beers 2009), any decreases in movement accuracy were not associated with increases in the proportion of hand movements that failed to make paddle-contact with targets. Alternatively, it is possible that optimization of intermuscular coordination may have allowed participants to move faster without incurring greater movement variability. In either case, increases in movement speed had a positive effect on task performance, thus our results are consistent with the principles of optimal feedback control (Todorov and Jordan 2002).

Visual search independently predicts motor learning

Increases in Extrafoveal Hits and Objects Foveated were the strongest independent predictors of increases in Targets Hits. These findings indicate that refinements of visual search led to better task performance by optimizing how participants gathered information with foveal and extrafoveal vision. This is consistent with evidence that visual search is highly adaptive to different task demands and environments, such as environments in which task-relevant objects are more likely to appear at certain locations (Neider and Zelinsky 2006; Wolfe et al 2011).

The association between Extrafoveal Hits and Target Hits indicates that participants learned to use extrafoveal information to guide hand movements used to hit targets. This is consistent with a previous study of visual search, which found that practice led to improvements in using extrafoveal vision to search for objects with task-relevant features (Wu and Spence 2013). In addition, cortical areas known to process peripheral visual information exhibit greater involvement during motor tasks (Prado et al 2005). However, to our knowledge, our study is the first to show that refinements of extrafoveal visual processing are predictive of motor learning.

The association between Targets Foveated and Target Hits suggests that refinements used to maximize the number of objects that participants foveated with visual search led to improvements in hitting targets. The modest correlation between Objects Foveated and Target Foveation Time ($r = -0.31$; Table 4.1) also indicates that, at least in part, decreases in the time spent foveating targets freed up time to foveate more objects. In contrast, studies of "quiet eye" have found that experts at motor tasks have longer foveations on task-relevant objects than novices (Vickers 1992; Williams et al 2002; Vickers and Lewinski 2012). Furthermore, training interventions designed to increase foveation durations have produced improvements in motor performance (Harle and Vickers 2001; Causer et al 2011; Wilson et al 2011; Vine et al 2013). These divergent findings suggest that both increases and decreases in foveation times can benefit motor performance, depending on the task demands and environment. As a result, we predict that practice will lead to increases in target foveation times in tasks with high demands on accuracy and low demands on speed of visual processing, whereas practice will produce decreases in foveation times in tasks with low demands on accuracy and high demands on speed of visual processing.

Eye-hand coordination independently predicts motor learning

Increases in Gaze-Hand Distance were associated with increases in Targets Hits, indicating that looking away from targets before hitting them led to improvements in task performance. Although this contrasts with studies showing rigid coupling between initiation of eye movements and completion of hand movements (Neggers and Bekkering 2000), other studies have found that this rigid coupling decreases with practice (Sailer et al 2005; Rand and Stelmach 2011; Foerster et al 2011; Säfström et al 2014). We suggest that increases in Gaze-Hand Distance may reflect a transition from an early reliance on visual feedback for accurate execution of hand movements to a subsequent reliance on kinesthetic feedback for accurate execution of hand movements. This would have allowed visual search to gather task-relevant information with greater efficiency (Sailer et al 2005). Specifically, looking away from targets before hitting them would have disrupted visual feedback used to accurately guide hand movements toward targets. However, it would have enabled earlier and longer foveations of objects, thereby facilitating more efficient decisions whether to hit or avoid objects by either executing or inhibiting skilled limb movements. Importantly, any negative effects resulting from disruption of visual feedback of hand movements could be offset by a greater reliance on kinesthetic feedback, which is known to improve during motor learning (Cressman and Henriques 2009; Haith et al 2008; Ostry et al 2010) and may directly contribute to motor learning (Beets et al 2012; Wong et al 2012; Bernardi et al 2015; Sidarta et al 2016).

Distinct predictors of motor execution and inhibition

We found that motor execution (Targets Hit) and motor inhibition (Distractors Avoided) exhibited distinct patterns of improvements. Notably, Targets Hit showed trial-by-trial and week-by-week improvements, whereas Distractors Avoided displayed only week-by-week improvements. We also found that different processes were independently predictive of improvements in motor execution and inhibition. Refinements of skilled limb movements (Mean Hand-Speed), visual search (Objects Foveated, Extrafoveal Hits) and eye-hand coordination (Gaze-Hand Distance) were independently predictive of improvements in Targets Hit. In contrast, eye-hand coordination (Gaze-Hand Distance) was the only independent predictor of improvements in Distractors Avoided. Given that avoiding distractors mainly involved inhibition rather than execution of hand movements, it is not surprising that increases in Mean Hand-Speed were not predictive of increases in Distractors Avoided. In contrast, increased Gaze-Hand Distance would have facilitated both motor execution and inhibition by allowing participants more time to make decisions whether to initiate or inhibit movements. It is perhaps surprising that increases in Objects Foveated were not predictive of increases in Distractors Avoided. We would expect that more efficient visual search should lead to improvements in both motor execution and inhibition by allowing more objects to be processed with foveal vision. The lack of a relationship may reflect that participants exhibited smaller improvements on Distractors Avoided. However, if the proportion of targets and distractors was equal or reversed, participants would have a greater demand to foveate and identify distractor objects during task performance. In this case we expect that participants may have shown greater improvements on Distractors Avoided and we may have found a meaningful relationship.

Limitations

By examining patterns of variability exhibited by measures related to multiple behavioral features, we found that refinements of multiple processes were independently predictive of motor learning. However, our paradigm and analyses were not designed to make causal inferences. This requires measuring motor learning while experimentally manipulating one process and controlling for interactions with all other processes. For example, masking objects that are not located within foveal vision would neutralize the contributions of extrafoveal hits on motor learning. If this reduced motor learning without affecting refinements of other processes, it would show that refinements of extrafoveal processing are causally linked to motor learning.

Another limitation of the current study is that we did not examine practice-related refinements of proprioception. This is an important limitation because improvements in planning and executing skilled limb movements may involve refinements that alter the processing of proprioceptive feedback (Scott 2016). In agreement with this hypothesis, previous studies have demonstrated that motor learning is associated with modifications of rapid responses to proprioceptive feedback (Cluff and Scott 2013) and improvements in kinesthesia (Prado et al 2005; Cressman and Henriques 2009; Haith et al 2008). Although we do not know if refinements involving proprioceptive processing contribute to motor learning in the current study, we suggests they may have facilitated increases in Gaze-Hand Distance by reducing reliance on visual feedback used to accurately execute skilled limb movements. A future study utilizing a repeated measures proprioceptive task in addition to the current paradigm would provide additional evidence that refinements in proprioception contribute to motor learning in the current paradigm.

Task demands and environmental features are known to alter motor learning (Wright and Shea 1991; Kurtzer et al 2003). However, we did not investigate how task demands, performance feedback, and environmental features influence the extent to which different processes are predictive of motor learning. In the current paradigm, for example, we would expect that refinements of skilled limb movements would be a greater predictor of motor learning if the demands on skilled limb movements were increased by reducing the size of the paddles or by imposing mechanical perturbations on the hands. In addition, changing the probability or feedback received from target and distractor objects may alter refinements behavioral features and their respective association with improvements in task performance. For example, if the proportion of targets and distractors were reversed, we would expect to see a larger improvement in our task performance measure of Distractors Avoided and refinements in its unique predictor of Hand-Speed Bias.

Although our behavioral measures probed several behavioral features involved in motor learning, we did not directly investigate the underlying neural mechanisms of motor learning. Numerous studies of motor learning have explored changes in brain regions and networks related to refinements of skilled limb movement (Ghilardi et al 2000; Frutiger et al 2000; Muellbacher et al 2002). Other studies have investigated the brain regions and networks associated with visual search during perceptual and cognitive tasks (Gitelman et al 2002; Egner et al 2008; Weidner et al 2009; Huang and Grossberg 2010; Wei et al 2019). However, we are unaware of any studies that have examined the extent to which brain regions and networks that underlie multiple processes are associated with motor learning.

Conclusions

Our findings indicate that motor learning may result from refinements of multiple behavioral features. We found many behavioral features were refined with practice, however not all behavioral features were independently predictive of improvements in task performance. In addition, we found differences in the behavioral features that predicted each of our task performance measures, indicating that different task demands may drive refinements in different behavioral features. This new knowledge can be applied to rehabilitation interventions of clinical populations, such as stroke, that exhibit impairments in task performance and motor learning.

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Table 4.1 Variance and covariance of predictor measures.

Measure	Coefficient of Variance	Covariance Matrix												
		MHS	MHA	TCS	HSB	HAB	OF	FB	EH	GHD	GHL	TFT	DFT	FTD
Mean Hand-Speed (MHS)	0.30	1												
Mean Hand-Area (MHA)	0.29	0.58	1											
Target Contact Speed (TCS)	**0.44**	**0.89**	0.35	1										
Hand-Speed Bias (HSB)	0.59	-0.11	-0.06	-0.08	1									
Hand-Area Bias (HAB)	0.68	-0.02	-0.07	0.05	0.67	1								
Objects Foveated (OF)	0.09	0.12	0.15	-0.03	-0.04	-0.01	1							
Foveation Bias (FB)	0.93	0.08	0.05	0.02	-0.01	-0.16	0.07	1						
Extrafoveal Hits (EH)	0.58	0.09	0.07	-0.06	0.05	-0.08	0.13	0.21	1					
Gaze-Hand Distance (GHD)	0.28	-0.06	-0.32	0.12	0.05	0.09	0.13	-0.09	0.19	1				
Gaze-Hand Latency (GHL)	**0.47**	-0.26	-0.39	-0.06	0.11	0.08	0.03	-0.05	0.20	**0.89**	1			
Target Foveation Time (TFT)	0.12	-0.32	-0.27	-0.22	0.12	0.11	-0.31	-0.19	-0.33	-0.14	-0.09	1		
Distractor Foveation Time (DFT)	0.16	-0.16	-0.16	-0.01	0.08	0.08	-0.20	-0.14	-0.22	0.11	0.12	0.66	1	
Foveation Time Difference (FTD)	0.36	-0.18	-0.11	-0.24	0.04	0.03	-0.12	-0.05	-0.12	-0.30	-0.26	0.36	-0.46	1

Table 4.2 Practice-related improvements of outcome and predictor measures.

Category	Measure	Full Model			Trial x Trial						Week x Week						Interaction				
		R^2	**F^2**	**p**	**Fit**	**β**	**SE**	**sr^2**	**sf^2**	**sp**	**Fit**	**β**	**SE**	**sr^2**	**sf^2**	**sp**	**β**	**SE**	**sr^2**	**sf^2**	**sp**
Task	**TH**	0.72	2.49	$<10^{-6}$	log	0.26	0.02	0.07	**0.23**	$<10^{-6}$	log	0.49	0.02	0.24	**0.82**	$<10^{-6}$	–0.16	0.02	0.03	0.09	$<10^{-6}$
	DA	0.67	1.99	$<10^{-6}$	log	–0.13	0.02	0.00	0.00	0.17	ln	0.20	0.02	0.04	**0.11**	$<10^{-6}$					
Limb Motor	**MHS**	0.70	2.31	$<10^{-6}$	log	0.09	0.02	0.01	**0.03**	$<10^{-4}$	ln	0.21	0.02	0.04	**0.14**	$<10^{-6}$					
	MHA	0.55	1.21	$<10^{-6}$	log	0.07	0.03	0.00	0.01	0.01	ln	0.07	0.03	0.00	0.01	0.009	–0.08	0.03	0.01	0.01	0.004
Bimanual	**HSB**	0.47	0.88	$<10^{-6}$	ln	0.07	0.03	0.01	0.01	0.01	ln	0.14	0.03	0.02	**0.03**	$<10^{-5}$	0.08	0.03	0.01	0.01	0.005
	HAB	0.33	0.50	$<10^{-4}$	ln	0.14	0.03	0.02	**0.03**	$<10^{-4}$	ln	0.04	0.03	0.00	0.00	0.19					
Visual Search	**OF**	0.65	1.86	$<10^{-6}$	log	0.12	0.02	0.01	**0.04**	$<10^{-6}$	log	0.32	0.02	0.10	**0.29**	$<10^{-6}$	–0.12	0.02	0.01	0.04	$<10^{-6}$
	CH	0.60	1.48	$<10^{-6}$	log	0.22	0.03	0.05	**0.12**	$<10^{-6}$	ln	0.38	0.03	0.15	**0.36**	$<10^{-6}$					
	SFB	0.37	0.60	0.003	log	0.04	0.03	0.00	0.00	0.22	ln	0.10	0.03	0.01	0.01	0.001					
Eye-Hand	**GHD**	0.84	5.14	$<10^{-6}$	log	–0.01	0.02	0.00	0.00	0.65	log	0.33	0.02	0.11	**0.69**	$<10^{-6}$	–0.07	0.02	0.01	0.03	$<10^{-5}$
Visuo-motor	**TFT**	0.63	1.70	$<10^{-6}$	log	–0.06	0.02	0.00	0.01	0.01	log	–0.27	0.02	0.08	**0.20**	$<10^{-6}$	0.11	0.02	0.01	0.03	$<10^{-5}$
	DFT	0.67	1.98	$<10^{-6}$	ln	0.02	0.02	0.00	0.00	0.33	ln	0.11	0.02	0.01	**0.04**	$<10^{-6}$	0.08	0.02	0.01	0.02	0.001
	FTD	0.34	0.53	$<10^{-6}$	log	–0.10	0.03	0.01	0.01	0.002	log	–0.41	0.03	0.16	**0.25**	$<10^{-6}$					

Table 4.3 Bivariate regression between outcome and predictor measures.

Outcome Measures	Predictor Measures	β	SE	R^2	p (K-S residuals)	sr^2	sf^2	sp
Targets Hit	**Extrafoveal Hits**	0.700	0.029	0.680	0.07	0.490	**1.516**	$<10^{-6}$
	Objects Foveated	0.593	0.037	0.562	0.27	0.352	**0.803**	$<10^{-6}$
	Gaze-Hand Distance	0.575	0.053	0.490	0.31	0.331	**0.650**	$<10^{-6}$
	Mean Hand-Speed	0.499	0.047	0.483	0.07	0.249	**0.482**	$<10^{-6}$
	Target Fov Time	–0.459	0.041	0.486	0.14	0.211	**0.412**	$<10^{-6}$
	Fov Time Difference	–0.231	0.033	0.430	0.05	0.053	**0.094**	$<10^{-6}$
	Hand-Speed Bias	0.101	0.041	0.388	0.04	0.010	0.017	0.01
	Distractor Fov Time	–0.061	0.051	0.382	0.07	0.004	0.006	0.23
	Hand-Area Bias	0.017	0.038	0.382	0.10	0.000	0.000	0.65
Distractors Avoided	**Gaze-Hand Distance**	0.294	0.044	0.649	0.65	0.086	**0.245**	$<10^{-6}$
	Target Fov Time	–0.114	0.036	0.630	0.23	0.013	**0.035**	0.001
	Hand-Speed Bias	0.112	0.032	0.632	0.51	0.013	**0.034**	<0.001
	Extrafoveal Hits	0.105	0.031	0.631	0.37	0.011	**0.030**	<0.001
	Fov Time Difference	–0.093	0.027	0.632	0.31	0.009	**0.024**	<0.001
	Objects Foveated	0.086	0.035	0.628	0.21	0.007	**0.020**	0.01
	Distractor Fov Time	0.054	0.041	0.626	0.32	0.003	0.008	0.19
	Hand-Area Bias	0.018	0.030	0.624	0.25	0.000	0.001	0.54
	Mean Hand-Speed	0.004	0.041	0.624	0.14	0.000	0.000	0.92

Table 4.4 Multiple regression between outcome and predictor measures.

Outcome		***DF***	***R^2***	***f^2***	***$P_{(F\text{-}Test)}$***	***P* (K-S residuals)**
Target Hits	Full Model	561	0.948	17.915	$<10^{-6}$	0.122
	Predictors	***VIF***	***B***	***sr^2***	***sf^2***	***sp***
	Number Objects Foveated	1.14	0.567	0.023	**0.442**	$<10^{-5}$
	Extrafoveal Hits	1.20	0.134	0.008	**0.154**	$<10^{-6}$
	Mean Hand-Speed	1.12	0.133	0.004	**0.077**	0.003
	Gaze-Hand Distance	1.20	0.097	0.003	**0.058**	0.002
	Spatial Foveation Bias	1.38	0.026	<0.001	0.006	0.25
	Target Foveation Time	1.38	–0.018	<0.001	0.001	0.60
	Distractor Foveation Time	1.26	<0.001	<0.001	<0.001	0.97
Outcome	**Predictors**	***DF***	***R^2***	***f^2***	***$P_{(F\text{-}Test)}$***	***P* (K-S residuals)**
Distractors Avoided	Full Model	564	0.845	5.479	$<10^{-6}$	0.400
	Predictors	***VIF***	***β***	***sr^2***	***sf^2***	***sp***
	Hand-Speed Bias	1.05	–0.180	0.007	**0.046**	0.014
	Gaze-Hand Distance	1.16	0.129	0.006	**0.038**	0.004
	Foveation Time Difference	1.25	0.082	0.003	0.018	0.036
	Distractor Foveation Time	1.35	–0.058	0.001	0.008	0.208

Figures

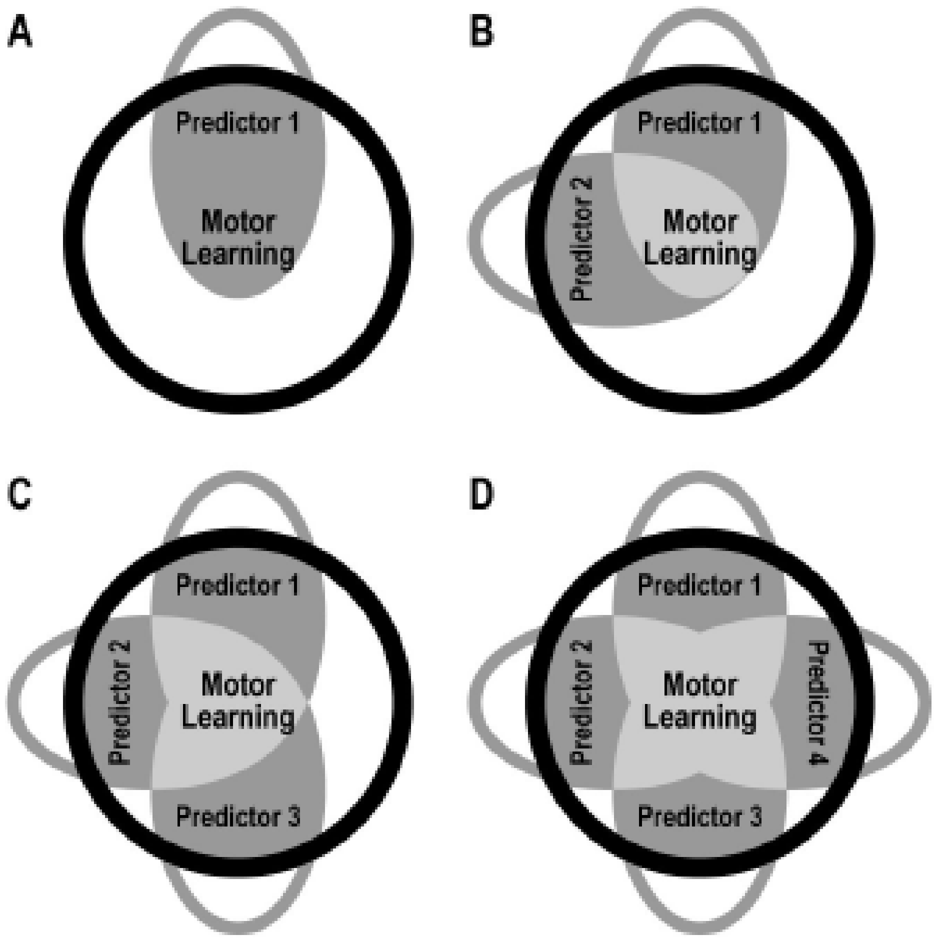

Figure 4.1 Independent and Shared Variance. Conceptual illustrations of regression analyses used to examine motor learning. **a:** Diagram showing how bivariate regression quantifies relationships between an individual predictor and motor learning without removing the variance shared with other potential predictors. **b–d:** Diagrams showing how multiple regression quantifies relationships between two (**b**), three (**c**) or four (**d**) predictors and motor learning. Regression coefficients estimate relationships from the independent and shared variance of each predictor, whereas semipartials estimate relationships from only the independent variance of each predictor. Light grey areas show portions of motor learning that cannot be attributed to a single predictor due to shared variance with other predictors. Dark grey areas show portions of motor learning that can be attributed to a single predictor after removing its shared variance.

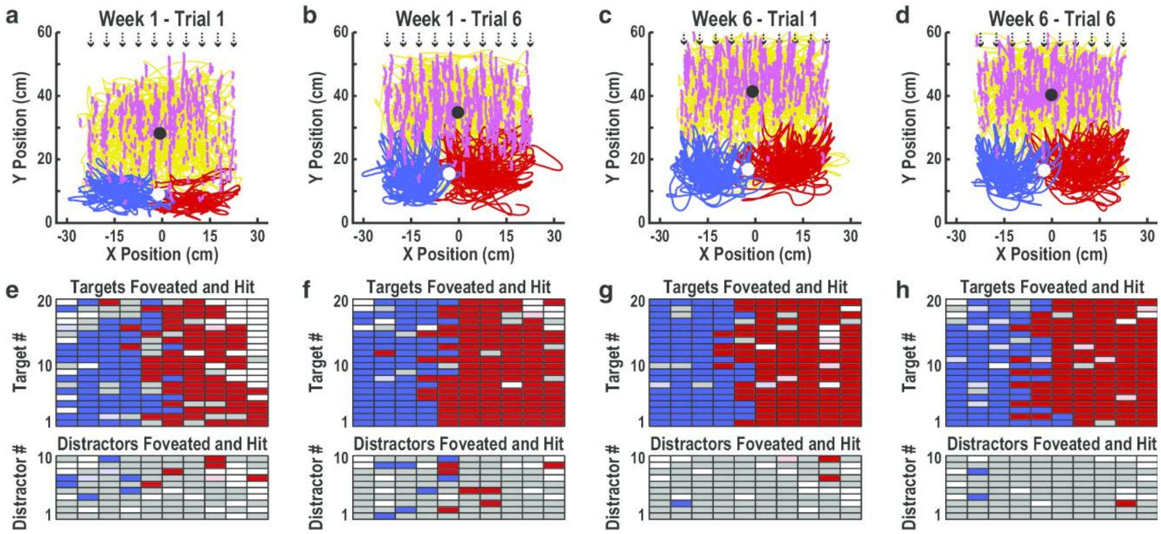

Figure 4.2 Exemplar Trials. Eye and hand movements and target/distractor foveations and hits by an exemplar participant during two trials on Week 1 and two trials on Week 6. (**a–d**). *X* position (width) versus *Y* position (depth) of eye and hand movements on $\text{Week}_1 \cdot \text{Trial}_1$ (**a**), $\text{Week}_1 \cdot \text{Trial}_6$ (**b**), $\text{Week}_6 \cdot \text{Trial}_1$ (**c**), and $\text{Week}_6 \cdot \text{Trial}_6$ (**d**). Colored lines illustrate pursuit eye movements (pink), saccadic eye movements (gold), left-hand movements (blue) and right-hand movements (red). Dashed arrows indicate the ten parallel paths that objects moved along. Black and white circles show the Center-of-Mass of gaze and hand movements, respectively. (**e–h**) Task performance on $\text{Week}_1 \cdot \text{Trial}_1$ (**e**), $\text{Week}_1 \cdot \text{Trial}_6$ (**f**), $\text{Week}_6 \cdot \text{Trial}_1$ (**g**) and $\text{Week}_6 \cdot \text{Trial}_6$ (**h**). The upper grids (20×10) represent each target and the lower grids (10×10) represent each distractor that was foveated and hit with the left hand (dark blue), foveated and hit with the right hand (dark red), foveated but not hit (grey), not foveated but hit with the left hand (light blue), not foveated but hit with the right hand (light red), or neither foveated nor hit (white).

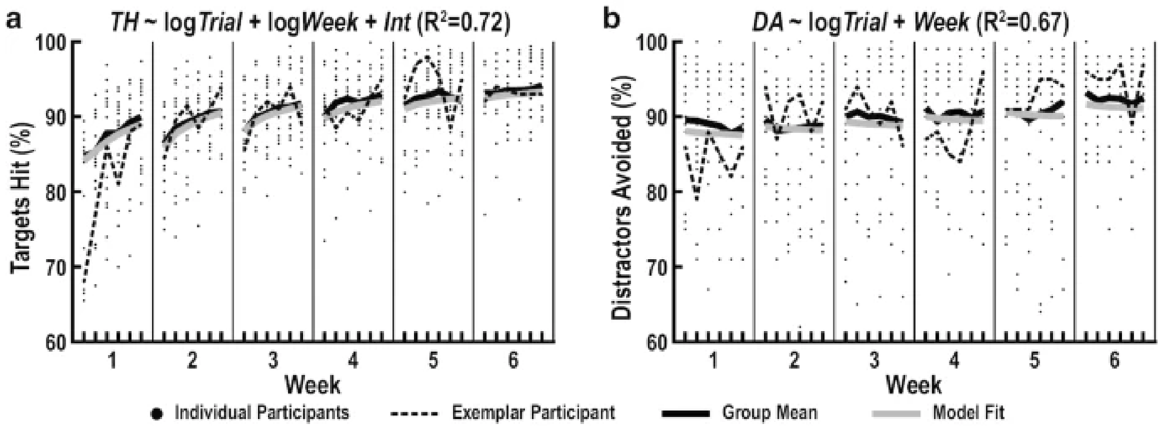

Figure 4.3 Task Performance. Improvements on measures of task performance. Trial-by-trial acquisition and week-by-week retention of improvements on Targets Hit (**a**) and Distractors Avoided (**b**). Each panel shows raw data values of all individual participants (small black dots), raw data values of the exemplar participant in Fig. 4.2 (thin dashed lines), group means of the reweighted participant data (thick black lines), and model predictions (thick grey lines). Reweighted participant data were obtained by applying weights from the robust regression to the raw data values of all participants. The model with the best overall fit (lowest Bayesian Information Criterion) is displayed at the top of each panel

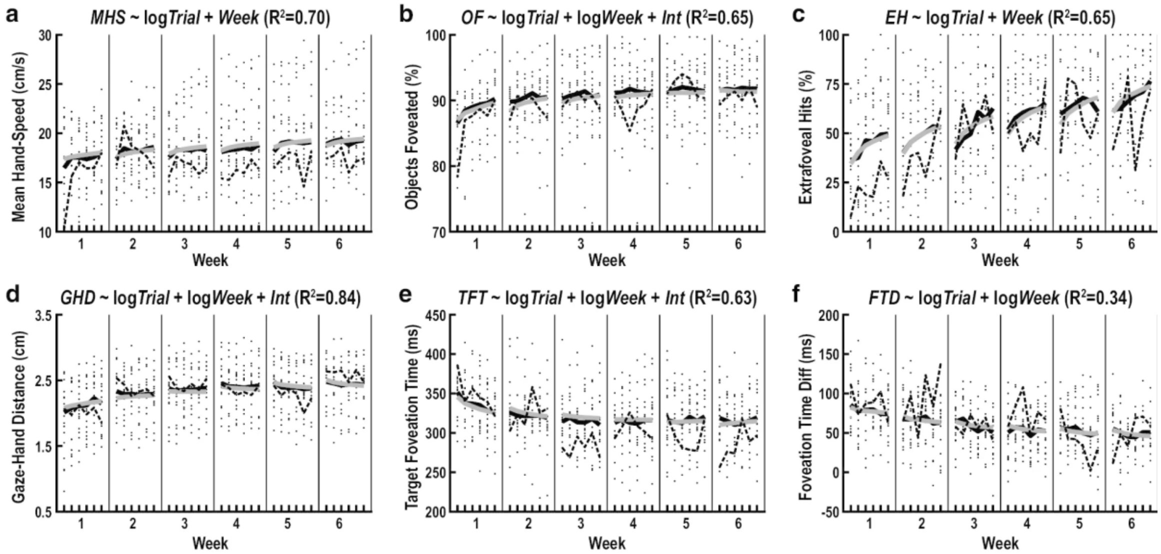

Figure 4.4 Refinements of Behavioral Features. Refinements on measures of behavioral features. Trial-by-trial acquisition and week-by-week retention of refinements on Mean Hand-Speed (**a**), Objects Foveated (**b**), Extrafoveal Hits (**c**), Gaze-Hand Distance (**d**), Target Foveation Time (**e**) and Foveation Time Difference (**f**). Each panel shows raw data values of all individual participants (small black dots), raw data values of the exemplar participant in Fig. 4.2 (thin dashed lines), group means of the reweighted participant data (thick black lines), and model predictions (thick grey lines). Reweighted participant data were obtained by applying weights from the robust regression to the raw data values of all participants. The model with the best overall fit (lowest Bayesian Information Criterion) is displayed at the top of each panel

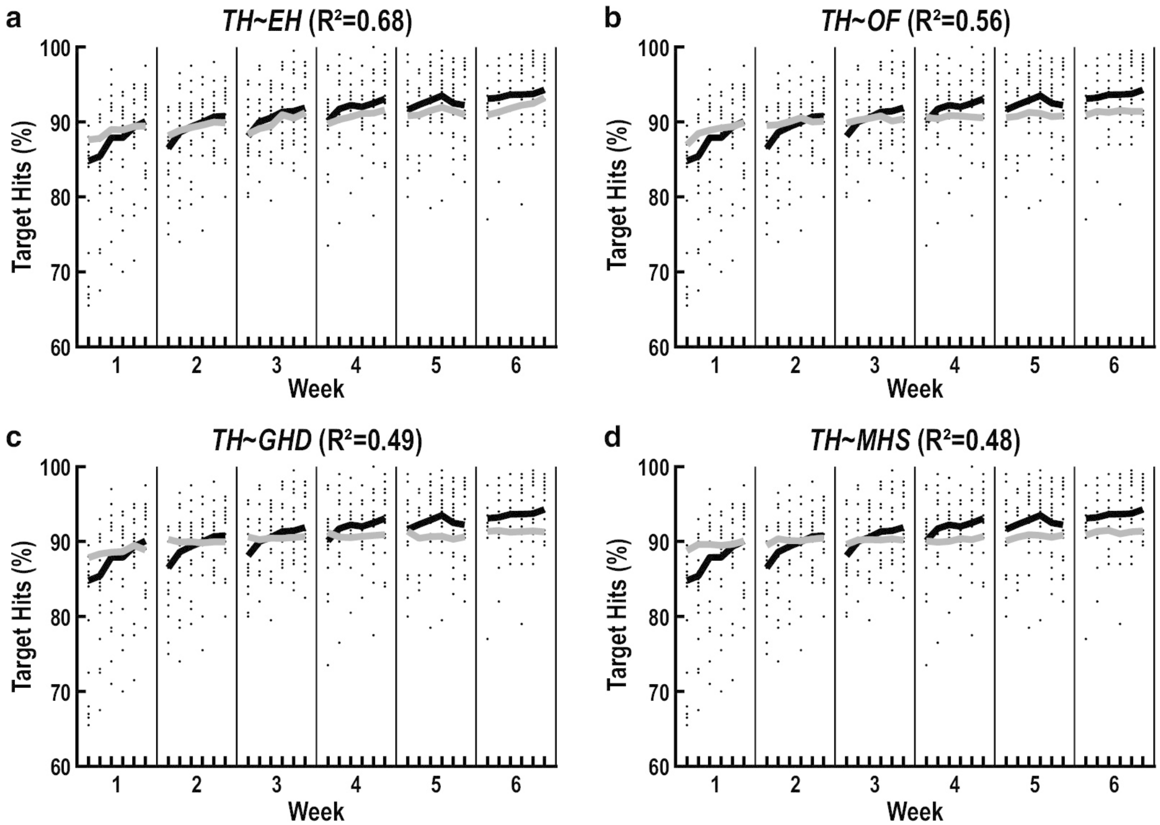

Figure 4.5 Univariate Predictors. Univariate predictions of task performance. Illustrations show the predicted improvements in Targets Hit obtained from bivariate regression models using Extrafoveal Hits (**a**), Objects Foveated (**b**), Gaze-Hand Distance (**c**) and Mean Hand-Speed (**d**) as predictors. Each panel shows raw data values of all individual participants (small black dots), group means of the reweighted participant data (thick black lines), and model predictions (thick grey lines). Reweighted participant data were obtained by applying weights from the robust regression to the raw data values of all participants

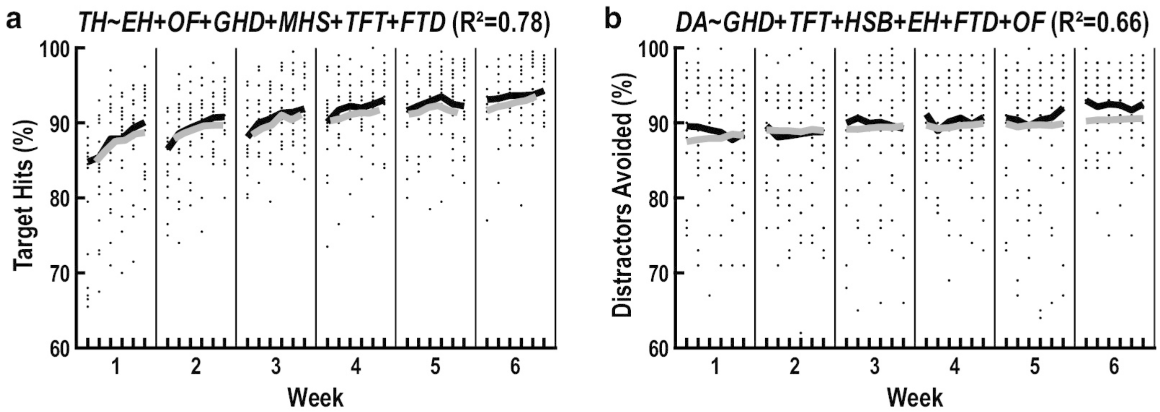

Figure 4.6. Multivariate Models. Multivariate predictions of task performance. Illustrations show the predicted improvements in Targets Hit (**a**) and Distractors Avoided (**b**) obtained from multiple regression. Each panel shows raw data values of all individual participants (small black dots), group means of the reweighted participant data (thick black lines), and model predictions (thick grey lines). Reweighted participant data were obtained by applying weights from the robust regression to the raw data values of all participants

Chapter 5

Multiple processes predict impairments in motor learning in stroke

Abstract

Humans use a combination of skilled eye and limb movements to learn and perform daily motor tasks such as driving a car, preparing food, and self-care. Those who have survived a cerebral stroke must often re-learn motor skills to regain independence and quality of life. However, survivors of stroke often exhibit a compromised ability to relearn motor skills resulting in incomplete recovery and a decreased quality of life. Current research suggests that poor recovery is the result of deficits in the behavioral features underlying motor skill learning. However, it is not known if these deficits independently predict motor learning outcomes. We used a longitudinal motor learning paradigm to investigate if deficits in multiple behavioral features independently predict motor learning in survivors of stroke. Eight survivors of a single cerebral stroke and nine age-matched healthy controls were recruited to perform 6 trials of an object hit-and-avoidance task once a week for six consecutive weeks. During each trail, participants were instructed to use green paddles to hit away 200 “target” objects and avoid hitting 100 “distractor” objects that continuously moved towards them from the top of the screen. Deficits in visual search, limb-movement, eye-hand coordination, and visuomotor planning were investigated as potential predictors of motor learning. We found that

deficits in visual search, limb-movement, and eye-hand coordination in survivors of stroke were independently predictive of motor execution, while deficits in eye-hand coordination and limb-movement were predictive of motor inhibition. This research provides evidence that incomplete recovery after a stroke is may be the result of deficits in multiple behavioral features. To address this, future rehabilitation interventions will need to account for deficits in multiple behavioral features to maximize rehabilitation potential in survivors of stroke.

Introduction

Effective human interaction with the world requires continuous learning and refinement of many adaptable motor skills. Many motor tasks such as driving a car, preparing food, and self-care require refinements of many different behavioral features to accomplish task goals, including those of eye movements used to collect visual information and limb movements used to interact with the environment. However, in cases of a cerebral stroke, deficits in many behavioral features negatively affect motor task performance, requiring survivors to re-learn motor skills to regain independence and quality of life. Previous research has shown that rehabilitation interventions that target observed deficits in stroke promote motor learning, but often does not result in full recovery. We suggest this is due in part to the methodologies of previous motor learning studies that have investigated deficits in individual behavioral features in isolation without accounting for the shared and independent variability from deficits in other behavioral features. This has resulted in an incomplete understanding of how deficits in multiple behavioral features affect rehabilitation outcomes. Here, we address this lack of knowledge by investigating if deficits in multiple behavioral features independently predict motor learning in survivors of stroke.

We will first define many terms and concepts that have been persistently unclear or ambiguous in previous literature on motor learning. “Motor tasks” refers to all tasks that require skilled limb movements to achieve task goals. Most activities of daily living (e.g., cooking, walking, and driving) are considered motor tasks even though they also use visual, perceptual, and cognitive functions to achieve task goals. “Motor learning” refers to the acquisition (trial-by-trial) and retention (week-by-week) of improvements on measures of task performance (outcomes). “Behavioral feature” refers to observable movements of the eyes and hands that result from brain networks that manipulate perceptual, cognitive, and motor information to plan, execute, and/or coordinate eye and limb movements. Practice-related changes in brain networks will be inferred from measures of behavioral features involved in limb and eye movements. “Refinements” refer to short-term (trial-by-trial) and long-term (week-by-week) changes to behavioral features. We infer that refinements of behavioral features contribute to improvements in task performance, but we do not infer that a particular direction of refinement is associated with improvements in a specific behavioral feature. “Deficits” refers to differences in the rate of refinements when comparing those with stroke against age-matched healthy controls.

Previous studies in stroke rehabilitation have primarily investigated how mitigating deficits in skilled limb-movements improve task performance (Krakauer 2006; Lang et al 2009). Studies investigating the effects of repetition of skilled limb-movements have shown that higher volumes of movement practice contribute to improvements in functional motor skill performance (ie. Fugl-Myer) after completing weekly training sessions with significant effects still observed during retention tests (Lohse et al 2014; Oujamma et al 2009; Hsieh et al 2011). Studies of constraint-induced movement therapy of the upper-limbs have shown increased changes in cortical plasticity of the practiced limb and improvements in function and movement quality (Fugl-Myer, Motor Activity Log), reaction times, reaching movement times, movement variability, and grip strength (Wu et al 2007; Yadav et al 2016; Sawaki et al 2008; Wu et al 2007). Interventions investigating virtual reality and robotic-assisted movement interventions found improvements in muscle strength, coordination of muscle activation, range of motion, acceleration, smoothness of movement, accuracy of reaching, and upper-extremity Fugl-Meyer scores (Fasoli et al 2003, 2012; Masiero et al 2007; Lo et al 2017; Grimm et al 2016; Jang et al 2005; Rand et al 2014). However, these motor learning studies were not designed to account for the effects of deficits in other behavioral features such as visual search, eye-hand coordination, and visuomotor planning. Thus, we do not know if deficits in limb-movements independently contribute to motor learning.

Studies investigating deficits in the behavioral features underlying visual search have focused on explaining how deficits in eye movements patterns negatively affect task performance. Many with stroke exhibit altered or impaired visual search patterns that include increased number of fixations, fixation durations, and inefficient search patterns that are indicative of impaired spatial planning, working memory, and decreased performance (Singh et al 2017; Alves et al 2014; Ten Brink et al 2016). Previous work in our lab has shown that the number of stimuli foveated with the eyes is predictive of improved or decreased task performance, dependent upon task type (Singh et al 2018;

Harrison et al 2020). However, these studies have not investigated if visual search independently contributes to motor learning, nor have they investigated if refinements in other behavioral features independently predict to motor learning deficits.

Studies of eye-hand coordination and visuomotor planning involving survivors of stroke have investigated how deficits in spatial and temporal patterns of eye and hand movements impair task performance. When performing eye-hand coordination tasks, survivors of stroke show increases in movement planning time, movement time, and decreases in endpoint accuracy with these effects being exacerbated with increases in task complexity (Tsang et al 2013; Fang et al 2007; Singh et al 2018). It has also been shown that survivors of stroke are more reliant on vision when performing reaching movements to reduce movement variability and increase accuracy compared (Torre et al 2013). In addition, survivors of stroke exhibit latent gaze onset to informational stimuli that is associated with increased latency in the initiation of limb-motor movements (Lamontagne and Fung 2009). However, these studies did not examine if deficits in eye-hand coordination and visuomotor planning can be refined with practice to improve motor learning outcomes.

Previous research in stroke rehabilitation suggests that motor learning often results in improved, but incomplete recovery. However, it is not known if deficits in multiple behavioral features independently predict motor learning outcomes in survivors of stroke. We have previously shown that deficits in behavioral features of visual search, limb-movement, eye-hand coordination and visuomotor planning are predictive of task performance in a single session of a continuous bimanual object hit and avoidance task (Harrison et al. 2020). Here we utilized a similar task to create a motor learning paradigm to investigate if deficits in multiple behavioral features predict motor learning outcomes in survivors of stroke. Our first hypothesis was that survivors of stroke would exhibit deficits in the rate of refinements in the behavioral features of visual search, limb-movements, eye-hand coordination, and visuomotor processing. Our second hypothesis was that deficits in behavioral features would be independently predictive of motor learning outcomes in survivors of stroke.

Methods

Participants

We recruited survivors of a single unilateral stroke and age-matched healthy adults from the University of South Carolina, surrounding areas, and from recruitment lists of previous study participants. Participants were included if 1) there were no additional neurological conditions affecting the central or peripheral nervous system (self-reported) other than a single unilateral cerebral stroke (verified with MRI) that occurred greater than 6 months prior to their experimental date, 2) were free of any musculoskeletal conditions affecting their ability to perform daily tasks (Box-and-Block, Stroke Impact Scale), 3) were free of any visual deficits that could not be corrected with glasses (Visual confrontation, Snellen Chart, Presbyopia Screen), 4) exhibited normal cognition (Letter Cancellation, VICA, TULIA, Shape Recall), and 5) were free of any conditions affecting their ability to sit upright and perform light exercise for 1 hour (self-reported). The study protocol was approved by the University of South Carolina's Institutional Review Board and all participants provided informed consent to participate.

Apparatus

Data were collected with a bilateral, upper-limb robot (KINARM EndPoint Lab, KINARM, Kingston, Canada) and monocular eye-tracker (EyeLink 1000, SR Research Ltd., Ottawa, Canada) that were integrated with an augmented-reality workspace (Figure 3.1a). Participants sat in a custom chair that used floor-mounted tracks and hydraulics to align them with a forehead rest, which stabilized the head for eye tracking. Participants grasped two near-frictionless manipulanda, which allowed them to make two-dimensional hand movements within an 80cm wide by 80cm deep workspace. A support strap was supplied to those with stroke if they experienced any difficulty maintaining a firm grasp on the manipulandum handle. An opaque shield and fabric cover prevented direct vision of the hands and arms. Hand and gaze position in the robotic workspace were respectively sampled at 1000 and 500 Hz, recorded at 200 Hz, and filtered offline using a low-pass filter with a 20 Hz cutoff.

The augmented-reality environment was created in the same horizontal plane as the robotic workspace by using an inverted-monitor to project visual stimuli at 60 Hz through a semi-transparent mirror. Cartesian gaze position in the horizontal plane was estimated using proprietary calibration algorithms (BKIN Technologies, Kingston, Canada) that provided accurate eye tracking within a workspace of approximately 50cm wide by 50cm deep. All visual stimuli were presented within this portion of the robotic workspace. A nonlinear mapping corresponded to a visual area of approximately 55° wide by 40° deep in which stimuli located closer to participants comprised larger visual angles.

Task

All participants practiced six repetitions of a continuous, visuomotor task, Object Hit and Avoid (OHA, Bourke et al 2016), once a week for six consecutive weeks. Participants were scheduled at a consistent time of day and day of week to avoid potential performance confounds related to circadian rhythms or different amounts of time between sessions. Illumination of the room was maintained at a constant level for the duration of the study.

In each OHA repetition, 300 red objects comprised of eight geometric shapes (e.g., square, circle, triangle, etc.) moved from the back of the workspace towards the participants along ten parallel paths (5 cm center-to-center spacing) (Figure 3.1b). Two shapes were predefined as “Targets” and six shapes were predefined as “Distractors”. Each parallel path contained 20 Targets (n=200) and 10 Distractors (n=100) that were released in random order. Within each repetition, the average number of objects that were simultaneously present in the workspace and the average speed that objects moved progressively increased over time. As a result, task difficulty increased within each repetition, whereas task difficulty remained consistent between repetitions. Each repetition ended after all 300 objects had passed through the workspace (~2 min).

Participants received standardized instructions to use two green paddles (2.5 cm wide) located on top of each hand to hit away as many Targets and to avoid hitting as many Distractors as possible. When participants made paddle contact with Targets, the robot applied a small perturbation (10 Newtons for 50 ms) to the participant’s hand and Targets rebounded from the paddle with the same direction and speed as the paddle movement. When participants made paddle contact with Distractors, no perturbation was applied to the participant's hand and Distractors passed unaltered through the paddle. Paddle size, object size and the spacing between adjacent paths prevented participants from simultaneously hitting two objects with the same hand.

We employed six distinct variants of targets and distractors to prevent overlearning of a specific variant from causing plateaus in task performance (Figure 3.1c) Each variant was pseudo-randomized and counter-balanced between participants each week. Specifically, each of the six variants was assigned different participants each week, such that each participant performed six repetitions of a different variant each week. Before starting each repetition, the two target shapes were presented in the middle of workspace until participants confirmed that they had memorized the shapes and were ready to begin. After completing each repetition, participants were offered a rest period until they were ready to start the next trial.

Gaze classification

Gaze data were processed and classified using the procedures of a validated methodology for processing gaze data our group previously published (Singh et al 2016). In brief, the methodology involves preprocessing gaze data to remove blink artifacts, one sample spikes caused by incorrect corneal detection, and outliers that occurred when gaze moved outside the eye-tracking workspace. We subsequently use a novel geometric method to transform gaze position data into rotational kinematics of the eye. Finally, we use adaptive thresholding methods to classify eye movements into saccades (rapid eye movements between targets) and smooth pursuits (eye movements that followed moving targets with foveal vision). Our previous manuscript demonstrated that our methodology for gaze processing and classification correctly classifies approximately 90% of saccades and smooth pursuits and misclassifies approximately 5% of saccades and smooth pursuits when compared with manual classification (gold standard).

Measures

We used hand and gaze data to compute measures of Task Performance, Skilled Limb Movement, Visual Search, Eye-Hand Coordination and Visuomotor Decisions for each repetition of OHA.

Task Performance: We computed two measures of task performance (Equations 1 and 2). *Targets Hit (%)* quantified successful execution of reaching movements required to achieve the task goal of hitting targets. It was calculated as the percent of all 200 targets that participants "Hit", where "Hit" indicated that a paddle made contact with a target causing it to move toward the back of the workspace. *Distractors Avoided (%)* quantified successful inhibition of reaching movements required to achieve the task goal of avoiding distractors. It was calculated as the percent of all 100 Distractors that were "Not Hit", where "Not Hit" indicated that neither paddle made contact a distractor or a paddle made contact but caused the distractor to move toward the bottom of the workspace.

$$Targets\ Hit = \frac{N_{Targets\ Hit}}{200\ Targets} * \ 100\% \tag{1}$$

$$Distractors\ Avoided = \frac{N_{Distractors\ Not\ Hit}}{100\ Distractors} * \ 100\% \tag{2}$$

Skilled Limb Movements: We computed three measures of skilled limb movement (Equations 3-5). *Mean Hand-Speed (cm/s)* quantified movement speed by computing the average speed of right- and left-hand movements. *Hand-Speed Bias* quantified inter-limb differences in movement speed by calculating the relative difference between the average movements speed of the right and left hands in controls and affected and unaffected hands in stroke. *Hand-Area Bias* quantified inter-limb differences in the spatial distributions of movements by calculating the relative difference between the area covered by movements of the right and left hands in controls and affected and unaffected hands in stroke. Hand-Area Bias quantified bimanual coordination of skilled limb movements, where values near zero indicate equal use of both hands and values greater than zero indicate greater use of one hand than the other. We were unable to quantify accuracy, smoothness and other traditional measures of skilled limb movement because hand movements used to hit targets were highly variable due to the continuous and random nature of the task.

$$Mean\ Hand\text{–}Speed = \frac{\overline{Hand\text{–}Speed_{Right}} + \overline{Hand\text{–}Speed_{Left}}}{2\ Hands} \tag{3}$$

$$Hand\text{–}\ Speed\ Bias = \left|\frac{\overline{Hand\text{–}Speed_{Right}} - \overline{Hand\text{–}Speed_{Left}}}{\overline{Hand\text{–}Speed_{Right}} + \overline{Hand\text{–}Speed_{Left}}}\right| \tag{4}$$

$$Hand\text{–}\ Area\ Bias = \left|\frac{Hand\text{–}Area_{Right} - Hand\text{–}Area_{Left}}{Hand\text{–}Area_{Right} + Hand\text{–}Area_{Left}}\right| \tag{5}$$

Visual Search: We computed three measures of visual search (Equations 6-8). *Objects Foveated (%)* quantified efficiency of visual search by calculating the percent of all 300 objects that participants “Foveated” with pursuit eye movements, where “Foveated” indicated that the object was followed with foveal vision for at least 40ms (Singh et al 2016). If an object was pursued more than once, it was only counted one time. *Spatial Foveation Bias* quantified spatial biases in the distribution of visual search by computing the relative difference between the number of objects foveated on the right and left sides of the workspace. *Extrafoveal Hits (%)* quantified covert use of parafoveal and peripheral vision for visual search by calculating the percent of targets that were “Hit” but were not previously “Foveated”. We were unable to compute other measures of visual search because large numbers of catch-up saccades during pursuit prevented accurate calculation of other valid measures.

$$Objects\ Foveated = \frac{N_{Objects\ Pursued}}{300\ Objects} * 100\% \tag{6}$$

$$Spatial\ Foveation\ Bias = \left|\frac{N_{Objects\ Foveated\ on\ Right} - N_{Objects\ Foveated\ on\ Left}}{N_{Objects\ Foveated\ on\ Right} + N_{Objects\ Foveated\ on\ Left}}\right| \tag{7}$$

$$Extrafoveal\ Hits = \frac{N_{Targets\ Hit \cap Not\ Foveated}}{N_{Targets\ Not\ Foveated}} * 100\% \tag{8}$$

Eye-Hand Coordination: We computed one measure of eye-hand coordination (Equation 9). *Gaze-Hand Distance (cm)* quantified spatial coupling between the eyes and hands by calculating the distance between gaze and hand position at the onset of paddle-contact with each target. If a target was “Hit” more than once, only one instance was included in this calculation. If a target was “Not Foveated” or was “Hit” before it was “Foveated”, it was excluded from this calculation.

$$Gaze\text{–}Hand\ Distance = \frac{\sum_1^N \sqrt{(X_{Gaze} - X_{Target})^2 + (Y_{Gaze} - Y_{Target})^2}}{N_{Targets\ Hit}} \tag{9}$$

Visuomotor Decisions: We computed three measures of visuomotor decisions (Equations 10-12). *Target Foveation Time (ms)* quantified the speed of making visuomotor decisions to hit targets by calculating the average duration that subjects foveated targets. *Distractor Foveation Time (ms)* quantified the speed of making visuomotor decisions to avoid distractors by calculating the average duration that subjects foveated distractors. If a target or distractor was foveated more than one time, we included the total time of all foveations. Both measures quantified the average time used to recognize and classify shapes as a target or distractor. However, Target Foveation Time included the average time used to initiate hand movements, whereas Distractor Foveation Time included the average time used to inhibit hand movements. *Foveation Time Difference (ms)* quantified differences in the speed of making visuomotor decisions to hit targets and avoid distractors by calculating the difference between target foveation time and distractor foveation time. Assuming the amount of time needed to recognize and classify shapes was the same for both targets and distractors, this measure quantified the difference between times for deciding whether to initiate or inhibit hand movements.

$$Target\ Foveation\ Time = \frac{\sum_1^N Target\ Foveated\ Time}{N_{Targets\ Foveated}} \tag{10}$$

$$Distractor\ Foveation\ Time = \frac{\sum_1^N Distractor\ Foveated\ Time}{N_{Distractors\ Foveated}} \tag{11}$$

$$Fov\ Time\ Diff = Target\ Foveated\ Time - Distractor\ Foveated\ Time \tag{12}$$

Analysis

All analyses were performed using Matlab 2017b (Mathworks Inc., Natick, MA).

Validation of measures

Since most of our measures were novel and there were some instances of performance difficulties in the stroke group, we examined the data for the presence of performance outliers and uniqueness of information. We used Tukey's method to identify performance outlier trials, which were values that were three times the interquartile range greater than the 75th percentile or three times the interquartile range less than the 25th percentile (Tukey, 1977). Across all measures, we identified 8 trials that qualified as performance outliers (1.39% of all trials); all outlier trials were from 8 different stroke participants (2.78% of stroke trials). For all subsequent analyses, we minimized the potential influence of outliers in our measures by performing robust regression with a Welsch weighting function (Holland and Welsch 1977). In the previous experiment, we tested each measure for unique information by applying Pearson correlations between each pair of measures. If a measure pair had a moderate Pearson correlation coefficient $|r|\geq 0.707$ ($r^2\geq 0.5$), the measure with the highest coefficient of variance was excluded from further analyses in the previous and current analysis (McDonald 2009). This process was performed again in the current experiment to ensure unique information from each measure. Finally, we standardized each measure to obtain a mean of zero and standard deviation of one, which allowed us to compare measures with different units.

Practice-related refinements

Our first hypothesis was that the stroke group would exhibit deficits in the rate of refinements in the behavioral features of visual search, limb-movements, eye-hand coordination, and visuomotor processing. We tested this hypothesis by using robust regression to compare eight different linear mixed-effects models that quantified differences in trial-by-trial and week-by-week refinements between the stroke and control group (Equations 13-20). The first four models (Figure 3.2) used different combinations of linear and logarithmic (*log*) learning rates (linear-linear, linear-logarithmic, logarithmic-linear, logarithmic-logarithmic). The other four models added an interaction term to investigate changes in trial-by-trial learning across weeks.

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 T_j + \beta_3 W_k + \beta_4 G T_j + \beta_5 G W_k + \epsilon_{ijk} \tag{13}$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 \log T_j + \beta_3 W_k + \beta_4 G \log T_j + \beta_5 G W_k + \epsilon_{ijk} \tag{14}$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 T_j + \beta_3 \log W_k + \beta_4 G T_j + \beta_5 G \log W_k + \epsilon_{ijk} \quad (15)$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 \log T_j + \beta_3 \log W_k + \beta_4 G \log T_j + \beta_5 G \log W_k + \epsilon_{ijk} \quad (16)$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 T_j + \beta_3 W_k + \beta_4 G T_j + \beta_5 G W_k + \beta_6 T_j W_k + \epsilon_{ijk} \quad (17)$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 \log T_j + \beta_3 W_k + \beta_4 G \log T_j + \beta_5 G W_k + \beta_6 \log T_j \, W_k + \epsilon_{ijk} \quad (18)$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 T_j + \beta_3 \log W_k + \beta_4 G T_j + \beta_5 G \log W_k + \beta_6 T_j \log W_k + \epsilon_{ijk} \quad (19)$$

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 \log T_j + \beta_3 \log W_k + \beta_4 G \log T_j + \beta_5 G \log W_k \ldots \quad (20)$$

$$+\beta_6 \log T_j \log W_k + \epsilon_{ijk}$$

In Equations 13-20, Y_{ijk} represents each measure obtained from participant i, in trial (*T*) j of week (*W*) k, b_i is a random intercept for each participant, β_2 describes group differences in trial-by-trial refinements, β_3 describes group differences in week-by-week refinements, *Group* (*G*) is the logic term for the control (*Group* = 0) or stroke (*Group* = 1) groups, and ϵ_{ijk} is the error term. In Equations 17-20, β_3 is an interaction term that describes group differences in trial-by-trial refinements across weeks. The model with the lowest Bayesian Information Criterion (BIC) was used to quantify differences in trial-by-trial (β_2) and week-by-week (β_3) refinements. After finding the best-fit model for each measure, we verified that additional transformations were not required by visually inspecting the fit between the predicted and actual outcomes and by testing the residuals for normality with Kolmogorov-Smirnoff tests. Measures with at least a small effect size ($f^2 \geq 0.02$) for trial-by-trial (β_2) or week-by-week (β_3) refinements were determined to show group differences in the rate of refinement.

Prediction of motor learning

Our second hypothesis was that the observed deficits in the refinements of behavioral features would be independently predictive of motor learning outcomes in survivors of stroke. We tested this hypothesis by using multiple regression to quantify the extent to which group differences in refinements of our predictor measures were independently predictive of motor learning. To do this, we first reduced the number of predictors by using the age-matched control groups data to test each measure as a predictor in a bivariate regression to determine if it had a meaningful relationship (i.e., small effect size; $f^2 \geq 0.02$) with our task performance measures. Second, we performed a multiple regression using the linear mixed-effects models that only included the reduced set of predictor measures (Equation 21).

$$Y_{ijk} = b_i + \beta_1 G + \beta_2 G X_{1(ijk)} + \beta_3 G X_{2(ijk)} + \cdots + \beta_N G X_{n(ijk)} + \epsilon_{ijk} \qquad (21)$$

In Equation 21, Y_{ijk} represents task performance of participant i in trial j of week k, b_i are random intercepts for each participant, coefficients β_2-β_N are the coefficient differences between groups for each predictor measure (X_1-X_n) and task performance, *Group (G)* is the logic term for control (*Group* = 0) and stroke (*Group* = 1) groups, and ϵ_{ijj} is the error term.

Importantly, the values of coefficients β_1-β_N in Equation 21 are influenced by variance that is independent of all other predictors and variance that is shared with other predictors. Figure 4.1 illustrates conceptual representations of independent and shared variance for four theoretical regression models with one, two, three, or four predictors of motor learning. If only one predictor is examined (a), it might be assumed that all variance related to task performance (dark grey area) is independently predictive of motor learning deficits. However, if multiple predictors are examined (b-d), part of each predictor's variance related to task performance deficits would be independent of all other predictors (dark grey area) and part would be shared with other predictors (light grey area). The relationships between the independent variance of each predictor and measures of task performance are described by semipartial coefficients of determination (sr^2). For our second hypothesis, we examined the relationships between the independent variance of each predictor measure and motor learning outcomes by calculating semipartial coefficients of determination (sr^2), semipartial effect sizes (sf^2), and semipartial *p*-values (*sp*). We considered measures with at least a small semipartial effect size ($sf^2 \geq 0.02$) as meaningful predictors of motor learning, though we recognize that this might underestimate the amount that each deficit should be attributed to each predictor.

For rigor and reproducibility, we also validated our multiple regression results by performing forward and backward stepwise regression with the same set of predictor measures used in our multiple regression analyses. We used the BIC to determine which predictor to add or remove at each step. This resulted in a final model with a minimum BIC.

Results

Participants

We enrolled 8 survivors of stroke (Table 5.1; 6 male, 2 female; 61 ± 11.7 y/o; 6 left, 2 right hemisphere strokes; 2 left handed, 6 right handed; 9.5 ± 3.2 years since stroke) and 9 healthy, age-matched controls (2 male, 7 female; 54.6 ± 8.59 years; 7 R-handed, 2 L-handed) to participate in the study. All participants completed the full 6 week paradigm.

Exemplar OHA performance

Figure 5.1 illustrates exemplars of pursuit and saccadic eye movements (pink and gold lines) and left- and right-hand movements (blue and red lines) made by an age-matched controls and a survivor of stroke participant at four time points, $Week_1 \bullet Trial_1$ (a, i), $Week_1 \bullet Trial_6$ (b, j), $Week_6 \bullet Trial_1$ (c, k), and $Week_6 \bullet Trial_6$ (d, h). For both exemplar participants, the eye and hand center-of-mass shifted distally from $Week_1 \bullet Trial_1$ (a) to $Week_6 \bullet Trial_6$ (b).

Fig. 5.1 also displays grids of rectangles (e-h, m-p) that represent each Target (upper grids: 20x10) and Distractor (lower grids: 10x10) that was *foveated and hit* (left hand: dark blue, right hand: dark red), *foveated but not hit* (grey), *not foveated but hit* (left hand: light blue, right hand: light red), or *neither foveated nor hit* (white). The participant failed to foveate several targets and distractors on $Week_1 \bullet Trial_1$ (e, m) but foveated the majority of targets and distractors by $Week_6 \bullet Trial_6$ (h, p). Similarly, the participant failed hit a number of targets and avoid a number of distractors on Week-$_1 \bullet Trial_1$ (e, m) but hit the majority of targets and avoided the majority of distractors by $Week_6 \bullet Trial_6$ (h, p).

Validation of measures

Targets Hit and Distractors Avoided exhibited a low correlation (r=0.24), indicating that they quantified unique aspects of task performance. Both measures were included in our subsequent analyses. We also examined each pair of predictor measures for high correlations ($|r|\geq0.707$) indicative of redundant information (Table 5.2). One pair of measures, Hand-Speed Bias and Hand-Area Bias, exhibited a high correlation

(r=0.88). In accordance, Hand-Speed Bias was excluded from all remaining analyses due to it having the higher coefficient of variance (McDonald 2009).

Group differences in task performance

Impaired motor learning in the stroke group were observed in our measures of task performance. Targets Hit (Table 5.3, Figure 5.2 a, b) exhibited deficits in the main effect ($\beta=-0.78$ $sf^2=7.54$, $sp<0.01$) and across weeks ($\beta=-0.07$ $sf^2=0.05$, $sp=0.006$) with no observable deficit in trial-by-trial refinements ($\beta=0.02$ $sf^2=0.00$, $sp<0.51$). Distractors Avoided (Figure 5.2 c, d) exhibited deficit in the main effect ($\beta=-0.41$ $sf^2=1.03$, $sp=0.18$) and in trial-by-trial refinements ($\beta=0.07$ $sf^2=0.03$, $sp=0.05$) with no observable deficit in weekly retention ($\beta=-0.04$ $sf^2=0.01$, $sp<0.23$).

Group differences in refinements of behavioral features

We tested our first hypothesis by examining differences in practice-related refinements in the behavioral features of skilled limb movement, visual search, eye-hand coordination and visuomotor planning (Figure 5.3, Table 5.3). All measures except for Spatial Foveation Bias ($sf^2\leq0.02$) exhibited deficits in the stroke group.

Both measures of Limb-Movement exhibited significant deficits in the stroke group. Mean Hand Speed exhibited a deficit in the main effect (Figure 5.3 a, b: $\beta=0.10$ $sf^2=0.04$, $sp=0.75$) and in weekly retention ($\beta=-0.09$ $sf^2=0.03$, $sp=0.04$), but no observable deficit in trial-by-trial refinements ($\beta=0.04$ $sf^2<0.01$, $sp<0.33$). Hand Speed Bias exhibited a deficit in the main effect ($\beta=-0.78$ $sf^2=4.96$, $sp=0.004$) and in trial-by-trial refinements ($\beta=-0.07$ $sf^2=0.04$, $sp=0.02$) with no observable deficit in weekly retention ($\beta=0.02$ $sf^2<0.01$, $sp=0.41$).

Two of our measures for Visual Search exhibited deficits in the stroke group. Objects Foveated exhibited a deficit in the main effect (Figure 5.3 c, d: β=-0.77 sf^2=6.63, sp=0.004) and in weekly retention (β=-0.06 sf^2=0.04, sp=0.017), but no observable deficit in trial-by-trial refinements (β=0.01 sf^2<0.01, sp=0.67). Extrafoveal Hits exhibited a deficit in the main effect (Figure 5.3 e, f: β=-0.29 sf^2=0.14, sp=0.14) and in weekly retention (β=-0.29 sf^2=0.14, sp<0.001), but no observable deficit in trial-by-trial refinements (β=0.06 sf^2<0.01, sp=0.38).

Our one measure of Eye-Hand Coordination, Gaze-Hand Distance, exhibited a deficit in the a main effect (Figure 5.3 g, h: β=-0.34 sf^2=0.62, sp=0.19), in trial-by-trial refinements (β=-0.02 sf^2=0.02, sp=0.08), and in weekly retention (β=-0.19 sf^2=0.19, sp<0.001).

All three measures of visuomotor processing exhibited deficits in the stroke group. Target Foveation exhibited a deficit in the main effect (Figure 5.3 i, j: β=0.13 sf^2=0.06, sp=0.63) and in weekly retention (β=0.30 sf^2=0.31, sp<0.001), but no observable deficit in trial-by-trial refinements (β<0.01 sf^2<0.01, sp=0.91). Distractor Foveation Time exhibited deficits in the main effect (Figure 5.3 k, l: β=0.46 sf^2=0.53, sp<0.05), trial-by-trial refinements (β=-0.12 sf^2=0.04, sp=0.02), and in weekly retention (β=0.24 sf^2=0.14, sp<0.001). Foveation Time Difference exhibited deficits in the main effect (β=-0.27 sf^2=0.15, sp=0.25) and trial-by-trial refinements (β=0.14 sf^2=0.04, sp=0.02), with no observable deficit in weekly retention (β=0.07 sf^2<0.01, sp=0.28).

Confirmation of motor learning

To test our second hypothesis, we initially used bivariate regression to identify which measures of behavioral features were associated with motor learning outcomes using a criterion of $sp \leq 0.02$ (Figure 5.4, Table 5.4). In our performance measure of Targets Hit, we found that Mean Hand Speed (Figure 5.4 a, b:, $\beta=0.32$ $sf^2=0.78$, $sp<0.001$), Objects Foveated (Figure 5.4 c, d: $\beta=0.76$ $sf^2=7.22$, $sp<0.001$), Extrafoveal Hits (Figure 5.4 e, f: $\beta=0.22$ $sf^2=0.39$, $sp<0.001$), Gaze-Hand Distance (Figure 5.4 g, h: $\beta=0.33$ $sf^2=0.98$, $sp<0.001$), Target Foveation Time (Figure 5.4 i, j: $\beta=-0.26$ $sf^2=0.54$, $sp<0.001$), Distractor Foveation Time (Figure 5.4 k, l: $\beta=-0.19$ $sf^2=0.27$, $sp<0.001$), and Spatial Foveation Bias ($\beta=0.09$ $sf^2=0.06$, $sp<0.001$) showed significant association. In our performance measure of Distractors Avoided, we found that Mean Hand Speed ($\beta=-0.16$ $sf^2=0.148$, $sp<0.001$), Gaze-Hand Distance ($\beta=0.13$ $sf^2=0.10$, $sp<0.001$), Foveation Time Difference ($\beta=0.09$ $sf^2=0.05$, $sp<0.001$), and Distractor Foveation Time ($\beta=-0.09$ $sf^2=0.05$, $sp<0.001$) showed significant associations.

Prediction of motor learning

We subsequently tested our second hypothesis by examining the extent to which deficits in our measures of behavioral features were independently predictive of motor learning (Figure 5.5, Table 5.5). Our multiple regression models identified two measures of visual search (Extrafoveal Hits: $sf^2=0.154$, $sp<10^{-6}$; Objects Foveated: $sf^2=0.442$, $sp<10^{-6}$), one measure of eye-hand coordination (Gaze-Hand Distance: $sf^2=0.058$, $sp<0.01$), and one measure of skilled limb movement (Mean Hand-Speed: $sf^2=0.077$, $sp<0.01$) that were independently predictive of Target Hits (Figure 5.5 a, b). In addition, our multiple regression identified one measure of limb-movement (Mean Hand Speed:

sf^2=0.046, sp=0.01) and one measure of eye-hand coordination (Gaze-Hand Distance: sf^2=0.038, sp<0.01) that were independently predictive of Distractors Avoided (Figure 5.5 c, d).

Finally, our stepwise regression analyses confirmed the results obtained from our multiple regression analyses. Specifically, the final model for Targets Hit included the same measures of visual search (Extrafoveal Hits, Objects Foveated), eye-hand coordination (Gaze-Hand Distance) and skilled limb movement (Mean Hand-Speed) that were significant in our multiple regression model. Furthermore, the final model for Distractors Avoided included the same measurements for limb-movement (Mean Hand Speed) and eye-hand coordination (Gaze-Hand Distance) as the multiple regression model.

Discussion

Multiple processes independently predict motor learning

The results of this study provide indirect evidence that deficits in multiple behavioral features may independently affect motor learning outcomes. The first aim of this study was to identify deficits in multiple behavioral features in survivors of stroke. We found deficits in both of our task performance measures (Targets Hit and Distractors Avoided) as well as in our measures of behavioral features in visual search, limb-movement, eye-hand coordination, and visuomotor planning (Hypothesis 1). Our second aim was to determine if these deficits were independently predictive of motor learning outcomes. We found that measures of behavioral features in visual search, limb-movement, and eye-hand coordination were independent predictors of targets hit, and measures of limb-movement and eye-hand coordination were independent predictors of distractors avoided (Hypothesis 2).

Previous studies have provided evidence that deficits in limb-movements, visual search, eye-hand coordination, and visuomotor planning result in impaired task performance. However, these studies were not designed to investigate the extent to which deficits in these behavioral features are independently predictive of motor learning outcomes. As a result, we do not know the extent to which impairments in motor learning is linked to the independent or shared variance in deficits of multiple behavioral features. In the current study, we addressed the issue of covariance by examining independent measures of behavioral features as predictors of motor learning outcomes by removing all shared variance between each measure. This analysis showed that deficits in the behavioral features of skilled limb movements, visual search and eye-hand coordination are each independent predictors of motor learning outcomes, indicating that studies of motor learning in survivors of stroke should account for deficits in multiple behavioral features.

Deficits in skilled limb movements independently predict motor learning

Deficits in Mean Hand-Speed were independently predictive of impairments in Targets Hits and Distractors Avoided. By learning to increase hand speed, survivors of stroke were able to hit away more target objects, but also mistakenly hit away more distractor objects. A possible explanation for this effect is that increased movement speed resulted in more variable and erroneous limb movements, resulting in the unintentional hitting of additional objects. Previous literature on speed/accuracy trade-off in healthy individuals supports this by showing that faster limb movements are more variable and less accurate than slower movements (Hammerbeck et al 2017, Plamondon and Alimi 1997). However, it has also been shown that the speed/accuracy trade-off is exacerbated in survivors of stroke but can be mitigated through task practice (Hardwick et al 2017). Perhaps additional practice sessions in the current experiment would have eventually shown reduced movement variability leading to greater motor learning outcomes in Targets Hit and Distractors Avoided.

Deficits in visual search independently predicts motor learning

Deficits in Objects Foveated and Extrafoveal Hits were associated with impairments in Targets Hits. Survivors of stroke who refined their visual search patterns were more likely to hit away more target objects. This is likely due to increased amount of visual information being collected through foveal and extrafoveal vision. We have previously shown in two previous studies where greater number of objects foveated during task performance is a strong predictor of positive performance outcomes (Singh et al 2017, Harrison et al 2020). In addition, survivors of stroke who refined extrafoveal vision likely adopted more efficient visual search patterns that incorporated guidance from working memory and spatial planning (Singh et al 2017). Or perhaps increased utilization of extrafoveal vision allowed survivors of stroke to identify target objects in advance without removing foveal vision used to monitor hand position during reaching movements (Alves et al 2014, Torre et al 2013).

Deficits in eye-hand coordination independently predicts motor learning

Deficits in Gaze-Hand Distance were associated with Targets Hit and Distractors Avoided. This likely reflects a greater dependence on gaze-locking behavior where rigid coupling exists between the initiation of eye movements needed to continue visual search and completion of hand movements as participants intercept target objects (Armstrong et al 2013, Gowen and Miall 2006). However, our findings align with previous studies that have found that rigid coupling of the eyes and hands decreases with practice, allowing the eyes to gather information in advance of the hand movements (Sailer et al 2005, Säfström et al 2014). We suggest that survivors of stroke who refined Gaze-Hand Distance with practice were better able to rely on somatosensory feedback to monitor hand position while utilizing visual search patterns to find and identify task objects rather than monitoring hand position. (Torre et al 2013, Meyer et al 2014). In this case, an increase in objects foveated would also be expected.

Deficits in visuomotor processing independently predicts motor learning

Deficits in target foveation time and distractor foveation time were predictive of Target Hits, distractor foveation time and foveation time difference were also predictive of Distractors Avoided. Those who refined target and distractor foveation time were associated with hitting more target objects. In addition, those who refined distractor foveation time and foveation time difference were likely to perform better in Distractors Avoided. We suggest refinements in these measures reflect an increased ability to identify task objects, plan appropriate motor plans to hit or avoid the object, and initiate that motor plan (Wu et al 2000, 2007; Schaffer et al 2007, 2009; Coderre et al 2010; Tyryshkin et al 2014, Semrau et al 2017, Bonato et al 2010). We also suggest that foveating each object for a lesser duration allows the eyes more time to foveate additional objects in the workspace. In this case, we would expect increases in objects foveated.

Distinct predictors of in motor execution and inhibition

Using our multiple regression models, we found that deficits in the behavioral features of Visual Search (Extrafoveal Hits, Objects Foveated), Eye-Hand Coordination (Gaze-Hand Distance), and Limb-Movements (Mean Hand Speed) were independently predictive of Targets Hit. In Addition, deficits in Eye-Hand Coordination (Gaze-Hand Distance) and Limb-Movements (Mean Hand Speed) were independently predictive of Distractors Avoided. It is not surprising that deficits in Mean Hand Speed and Gaze-Hand Distance are common predictors of impairments both performance measures. The ability to quickly move hands around the workspace to hit or avoid objects and the ability to mitigate gaze-locking effects for advanced recognition of objects is crucial for task performance. However, it is surprising that deficits in Objects Foveated and Extrafoveal Hits were not independently predictive of Distractors Avoided. We would expect that lesser number of objects foveated and lesser reliance on extrafoveal vision to identify objects and guide visual search would decrease the number of Distractors Avoided. This lack of association may reflect a smaller impairment in Distractors Avoided. If the proportion of targets and distractors in our paradigm were equal or reversed, perhaps we would observe a greater impairment in Distractors Avoided and additional measures to predict this effect.

Limitations

By examining patterns of variability exhibited in multiple behavioral features, we found that deficits in visual search, limb-movement, and eye-hand coordination were independently predictive of motor learning in survivors of stroke. However, our paradigm and analyses were not designed to make causal inferences on the effects of deficits in behavioral features. This would require measuring deficits during motor learning while experimentally manipulating the deficits in one behavioral feature and controlling for interactions with deficits in all other behavioral features. For example, requiring participants to foveate target objects until the point of paddle contact would neutralize processes involved in Gaze-Hand Distance. If this paradigm adaptation decreased motor learning outcomes without affecting deficits in other behavioral features, it would show that deficits in Gaze-Hand Distance are causally linked to motor learning.

Another limitation of the current study is that we did not examine potential deficits in proprioception as a predictor of motor learning. Planning and executing skilled limb movements may be impaired in survivors of stroke and therefore alter proprioceptive feedback during task performance (Torre et al 2013; Meyer et al 2014). In support of this view, studies have demonstrated that improvements in kinesthesia contribute to motor learning (Bernardi et al 2015; Sidarta et al 2016) and modifications of rapid responses to proprioceptive feedback are linked to motor learning (Cluff and Scott 2013). Although we do not know if deficits involving proprioceptive processing contribute to motor learning in the current study, we suggest they may have facilitated increases in Gaze-Hand Distance by reducing reliance on visual feedback used to accurately execute skilled limb movements. A future study utilizing a proprioceptive task in addition to the current paradigm would provide additional evidence that deficits in proprioception may predict motor learning in survivors of stroke.

Task demands and environmental features are known to alter motor learning (Wright and Shea 1991; Kurtzer et al 2003). However, we did not investigate how task demands, performance feedback, and environmental features influence the extent to which behavioral features predict motor learning. In the current paradigm, for example, we would expect deficits of skilled limb movements would be a stronger predictor of motor learning if the demands on skilled limb movements were increased by reducing the size of the paddles or by imposing mechanical perturbations on the hands. In addition, changing the probability, or feedback from target and distractor objects may alter refinements in behavioral features and their respective association with motor learning. For example, if both targets and distractors provided the same amount of feedback (visual and haptic), we may see a larger improvement in our task performance measure of Distractors Avoided.

The inclusion criteria for those with stroke was generalized, primarily focusing on those with approximately normal cognitive and physical function. However, additional factors such as prescription medication may affect refinements in behavioral features and motor learning outcomes. Many medications have documented positive or negative effects on functional performance in survivors of stroke, but these effects were not investigated in the current study (Conroy et al 2005). In addition, the effects of lesion characteristics such as lesion size or location were not investigated in the current study (Shelton & Reding 2001). A future study with a larger sample size could investigate differential effects of medication or injury characteristics in motor learning.

Although our measures of behavioral features probed motor learning, we did not directly investigate the underlying impaired neural mechanisms of each behavioral feature. Numerous studies of motor learning have explored changes in brain regions and networks related to refinements of skilled limb movement (Ghilardi et al 2000; Frutiger et al 2000; Muellbacher et al 2002; Grafton et al 1994; Tomassini et al 2011). Other studies have investigated the brain regions and networks associated with visual search during perceptual and cognitive tasks (Gitelman et al 2002; Egner et al 2008; Weidner et al 2009; Huang and Grossberg 2010). However, we are unaware of any studies that have examined the extent to which impaired brain regions and networks that underlie multiple behavioral features are associated with motor learning.

Conclusions

Our findings indicate that deficits of multiple behavioral features can predict motor learning outcomes. However, future studies are needed to determine how deficits of different behavioral features affect motor learning and recovery. For example, if a survivor of stroke undergoes an intervention that is designed to improve limb-movements, will deficits in Visual Search, Gaze-Hand Distance, or other behavioral features also be affected?

Systematic modification to the methods of this study could be used to advance the knowledge of motor learning in survivors of stroke. For example, modifying the proportions of target and distractors objects would allow for the investigation of how refinements in behavioral features differ when task demands change. In addition, controlling for various participant characteristics (ex. Lesion location, medication) would provide valuable predictive information on which participants respond to motor learning interventions. Finally, quantifying additional behavioral features such as proprioception would provide new knowledge on its contribution to other behavioral features and motor learning.

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Tables

Table 5.1 Participant demographics and clinical screens.

		Stroke		Controls	
		Right	**Left**	**Right**	**Left**
Affect Side		6	2	-	-
Handedness		6	2	7	2
Tulia		11.3 ± 2.0	12 ± 0	-	-
		Unaffected	**Affected**	**Dominant**	**Non-Dominant**
Box-and-Block		55.9 ± 9.0	38.6 ± 15.5	64.6 ± 7.9	62.9 ± 5.7
VICA		15.8 ± 3.5		19.1 ± 1.0	
MOCA		19.9 ± 5.8		27.1 ± 2.3	
SIS					
	Physical (20)	12.3 ± 2.2		-	
	Memory/Thinking (35)	30.1 ± 4.7		-	
	Emotions (45)	36.1 ± 5.8		-	
	Communications (35)	27.8 ± 5.3		-	
	ADLs (50)	44.6 ± 6.3		-	
	Mobility (45)	38.9 ± 5.1		-	
	Affected Hand (25)	17.9 ± 5.0		-	
	Occupation (40)	34.0 ± 8.6		-	
	Stroke Recovery (100)	70.0 ± 15.4		-	

Table 5.2 Variance and covariance of predictor measures.

Measure	CoV of Cof	Covariance Matrix									
		MHS	HSB	HAB	OF	SFB	EH	GHD	TFT	DFT	FTD
Mean Hand-Speed (MHS)	0.30	1									
Hand-Speed Bias (HSB)	0.59	0.10	1								
Hand-Area Bias (HAB)	0.68	0.18	**0.88**	1							
Objects Foveated (OF)	0.09	0.11	0.55	0.53	1						
Spatial Foveation Bias (SFB)	0.93	–0.31	–0.33	–0.50	–0.19	1					
Extrafoveal Hits (EH)	0.58	0.11	0.14	0.13	0.31	–0.04	1				
Gaze-Hand Distance (GHD)	0.28	–0.14	0.23	0.13	0.50	0.15	0.22	1			
Target Foveation Time (TFT)	0.12	–0.45	–0.36	–0.38	–0.47	0.45	–0.25	–0.24	1		
Distractor Foveation Time (DFT)	0.16	–0.11	–0.44	–0.38	–0.60	0.12	–0.23	–0.50	0.66	1	
Foveation Time Difference (FTD)	0.36	–0.44	0.03	–0.05	0.08	0.44	–0.05	0.26	0.53	-0.29	1

Table 5.3 Practice-related improvements of outcome and predictor measures.

Category / Measure		Full Model			Group				Trial					Week					Group x Trial				Group x Week			
		R^2	**F^2**	**p**	**β**	**sr^2**	**sf^2**	**sp**	**Fit**	**β**	**sr^2**	**sf^2**	**sp**	**Fit**	**β**	**sr^2**	**sf^2**	**sp**	**β**	**sr^2**	**sf^2**	**sp**	**β**	**sr^2**	**sf^2**	**sp**
Task	TH	0.92	11.5	$<10^{-6}$	**-0.78**	**0.61**	**7.54**	**<0.01**	**log**	**0.10**	**0.01**	**0.12**	**$<10^{-6}$**	**log**	**0.28**	**0.08**	**0.94**	**$<10^{-6}$**	0.02	<0.01	0.00	0.51	**-0.07**	**0.01**	**0.05**	**0.006**
	DA	0.84	5.17	$<10^{-6}$	**-0.41**	**0.17**	**1.03**	**0.18**	**log**	**-0.10**	**0.01**	**0.07**	**$<10^{-5}$**	**log**	**0.05**	**<0.01**	**0.02**	**0.03**	**0.07**	**<0.01**	**0.03**	**0.05**	-0.04	<0.01	0.01	0.23
Limb-Motor	MHS	0.77	3.23	$<10^{-6}$	**0.10**	**0.01**	**0.04**	**0.75**	log	0.01	$<10^{-3}$	$<10^{-3}$	0.60	**ln**	**0.09**	**<0.01**	**0.03**	**<0.01**	0.04	<0.01	<0.01	0.33	**-0.09**	**<0.01**	**0.03**	**0.04**
Bimanual	HSB	0.88	7.18	$<10^{-6}$	**-0.78**	**0.61**	**4.96**	**0.004**	ln	0.02	$<10^{-3}$	<0.01	0.38	ln	0.02	$<10^{-3}$	<0.01	0.29	**-0.07**	**<0.01**	**0.04**	**0.02**	0.02	$<10^{-3}$	<0.01	0.41
Visual Search	OF	0.91	10.2	$<10^{-6}$	**-0.77**	**0.59**	**6.63**	**0.004**	**log**	**0.07**	**<0.01**	**0.05**	**$<10^{-3}$**	**log**	**0.22**	**0.05**	**0.53**	**$<10^{-6}$**	0.01	<0.01	<0.01	0.67	**-0.06**	**<0.01**	**0.04**	**0.017**
	EH	0.40	0.66	$<10^{-6}$	**-0.29**	**0.08**	**0.14**	**0.14**	log	0.04	<0.01	<0.01	0.36	**ln**	**0.40**	**0.16**	**0.27**	**$<10^{-6}$**	0.06	<0.01	<0.01	0.38	**-0.29**	**0.09**	**0.14**	**$<10^{-5}$**
	SFB	0.58	1.38	$<10^{-6}$	-0.04	<0.01	<0.01	0.89	ln	<0.01	$<10^{-5}$	$<10^{-4}$	0.94	**log**	**0.12**	**0.01**	**0.03**	**$<10^{-3}$**	-0.04	<0.01	<0.01	0.51	0.01	$<10^{-3}$	$<10^{-3}$	0.86
Eye-Hand	GHD	0.82	4.48	$<10^{-6}$	**-0.34**	**0.11**	**0.62**	**0.19**	**log**	**0.11**	**0.01**	**0.07**	**$<10^{-5}$**	**log**	**0.55**	**0.31**	**1.67**	**$<10^{-6}$**	**-0.02**	**<0.00**	**0.02**	**0.08**	**-0.19**	**0.03**	**0.19**	**$<10^{-6}$**
Visuomotor	TFT	0.71	2.45	$<10^{-6}$	**0.13**	**0.02**	**0.06**	**0.63**	**log**	**-0.16**	**0.02**	**0.08**	**$<10^{-6}$**	**ln**	**-0.36**	**0.13**	**0.44**	**$<10^{-6}$**	<-0.01	$<10^{-4}$	$<10^{-4}$	0.91	**0.30**	**0.09**	**0.31**	**$<10^{-6}$**
	DFT	0.59	1.46	$<10^{-6}$	**0.46**	**0.22**	**0.53**	**<0.05**	log	-0.03	$<10^{-3}$	<0.01	0.42	**log**	**-0.28**	**0.08**	**0.19**	**$<10^{-6}$**	**-0.12**	**0.02**	**0.04**	**0.02**	**0.24**	**0.05**	**0.14**	**$<10^{-4}$**
	FTD	0.49	0.96	$<10^{-6}$	**-0.27**	**0.08**	**0.15**	**0.25**	**log**	**-0.15**	**0.02**	**0.04**	**$<10^{-3}$**	**ln**	**-0.10**	**0.01**	**0.02**	**0.01**	**0.14**	**0.02**	**0.04**	**0.02**	0.07	<0.01	<0.01	0.28

Table 5.4 Bivariate regression between outcome and predictor measures.

Outcome Measures	Predictor Measures	β	SE	R^2	p *(K-S residuals)*	sr^2	sf^2	sp
Targets Hit	**Objects Foveated**	**0.76**	**0.03**	**0.92**	**0.56**	**0.58**	**7.219**	**$<10^{-6}$**
	Gaze-Hand Distance	**0.33**	**0.02**	**0.89**	**0.51**	**0.11**	**0.984**	**$<10^{-6}$**
	Mean Hand-Speed	**0.32**	**0.03**	**0.87**	**0.04**	**010**	**0.775**	**$<10^{-6}$**
	Target Fov Time	**-0.26**	**0.02**	**0.87**	**0.51**	**0.07**	**0.538**	**$<10^{-6}$**
	Extrafoveal Hits	**0.22**	**0.02**	**0.88**	**0.14**	**0.05**	**0.387**	**$<10^{-6}$**
	Distractor Fov Time	**-0.19**	**0.02**	**0.87**	**0.61**	**0.04**	**0.265**	**$<10^{-6}$**
	Spatial Foveation Bias	**0.09**	**0.02**	**0.85**	**0.31**	**<0.01**	**0.056**	**$<10^{-3}$**
	Hand-Speed Bias	0.04	0.05	0.85	0.30	<0.01	0.011	0.37
	Fov Time Difference	-0.04	0.02	0.85	0.34	<0.01	0.008	0.12
Distractors Avoided	**Mean Hand-Speed**	**–0.16**	**0.04**	**0.083**	**0.53**	**0.02**	**0.148**	**$<10^{-5}$**
	Gaze-Hand Distance	**0.13**	**0.03**	**0.84**	**0.38**	**0.02**	**0.096**	**$<10^{-5}$**
	Fov Time Difference	**0.09**	**0.02**	**0.83**	**0.32**	**<0.01**	**0.053**	**$<10^{-4}$**
	Distractor Fov Time	**-0.09**	**0.03**	**0.83**	**0.28**	**<0.01**	**0.050**	**$<10^{-3}$**
	Hand-Speed Bias	0.06	0.05	0.83	0.24	<0.01	0.019	0.25
	Objects Foveated	-0.03	0.05	0.83	0.17	$<10^{-3}$	0.005	0.52
	Extrafoveal Hits	0.01	0.02	0.83	0.15	$<10^{-3}$	<0.001	0.63
	Spatial Foveation Bias	0.01	0.03	0.83	0.18	$<10^{-3}$	<0.001	0.70
	Target Fov Time	0.01	0.03	0.83	0.16	$<10^{-3}$	<0.001	0.71

Table 5.5 Multiple regression between predictor and outcome measures. Bold indicates measures that measure exhibited meaningful relationships with group differences in Targets Hit or Distractors Avoided ($sf^2 \geq 0.02$).

Outcome		***DF***	$\boldsymbol{R^2}$	$\boldsymbol{f^2}$	$\boldsymbol{P}$ ***(F-Test)***	$\boldsymbol{P}$ **(K-S residuals)**
Target Hits	Full Model	561	0.95	17.92	$<10^{-6}$	0.12
	Predictors	***VIF***	$\boldsymbol{\beta}$	$\boldsymbol{sr^2}$	$\boldsymbol{sf^2}$	***sp***
	Extrafoveal Hits	1.02	0.134	0.008	**0.154**	$<10^{-6}$
	Objects Foveated	1.47	0.567	0.023	**0.442**	$<10^{-5}$
	Gaze-Hand Distance	1.01	0.097	0.003	**0.058**	<0.01
	Mean Hand-Speed	1.02	0.133	0.004	**0.077**	<0.01
	Target Foveation Time	1.00	-0.018	$<10^{-3}$	0.002	0.60
	Distractor Foveation Time	1.00	$<10^{-3}$	$<10^{-6}$	$<10^{-4}$	0.97
	Spatial Foveation Bias	1.00	0.026	$<10^{-3}$	0.006	0.25
Outcome	**Predictors**	***DF***	$\boldsymbol{R^2}$	$\boldsymbol{f^2}$	$\boldsymbol{P}$ ***(F-Test)***	$\boldsymbol{P}$ **(K-S residuals)**
Distractors Avoided	Full Model	561	0.85	5.48	$<10^{-6}$	0.40
	Predictors	***VIF***	$\boldsymbol{\beta}$	$\boldsymbol{sr^2}$	$\boldsymbol{sf^2}$	***Sp***
	Mean Hand-Speed	**1.03**	**-0.180**	**0.007**	**0.046**	**0.01**
	Gaze-Hand Distance	**1.02**	**0.129**	**0.006**	**0.038**	**<0.01**
	Foveation Time Difference	1.01	0.083	0.003	0.018	0.04
	Distractor Foveation Time	1.00	-0.058	0.001	0.008	0.21

Figures

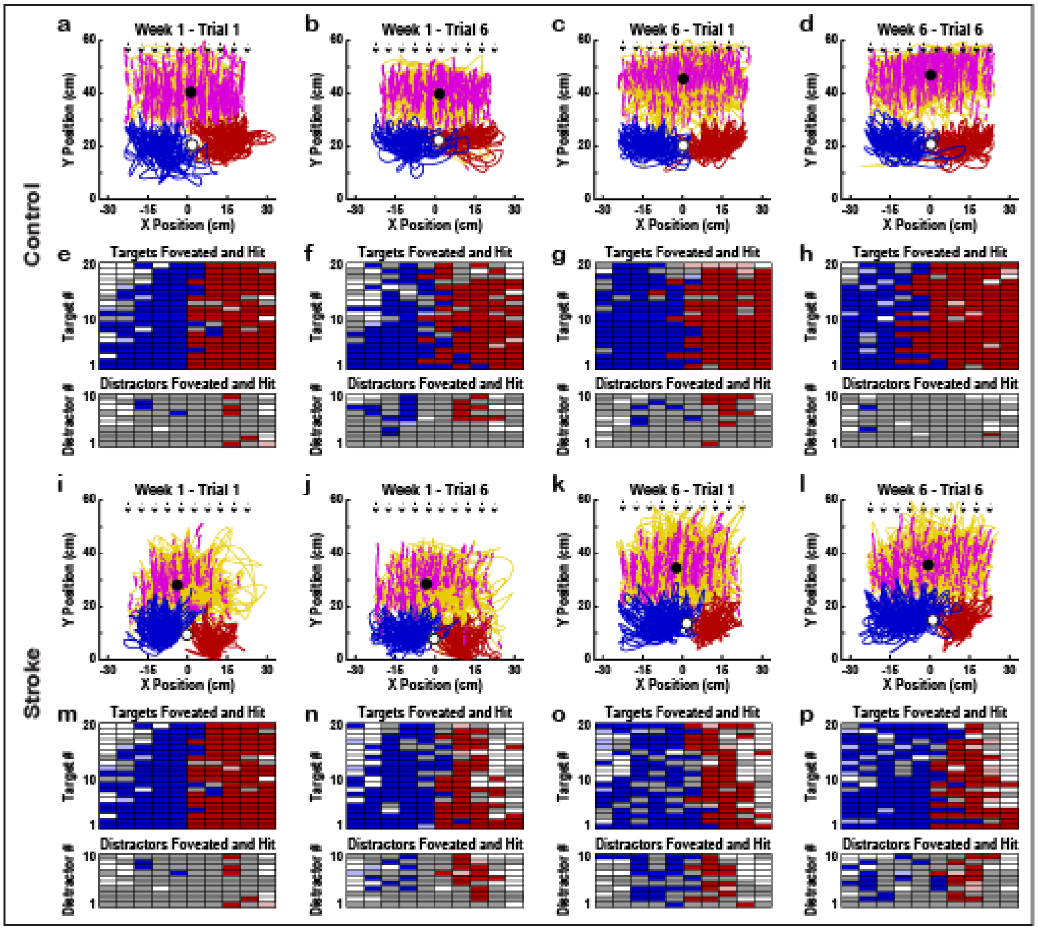

Figure 5.1. Exemplar Trials. Eye and hand movements and target/distractor foveations and hits by one exemplar age-matched control participant (**a-h**) and one exemplar stroke participant (**i-p**) during the first and last trials on Week 1 and Week 6. *X* position (width) versus *Y* position (depth) of eye and hand movements on $Week_1 \cdot Trial_1$ (**a, i**), $Week_1 \cdot Trial_6$ (**b, j**), $Week_6 \cdot Trial_1$ (**c, k**), and $Week_6 \cdot Trial_6$ (**d, l**). Colored lines illustrate pursuit eye movements (pink), saccadic eye movements (gold), left-hand movements (blue) and right-hand movements (red). Dashed arrows indicate the ten parallel paths that objects moved along. Black and white circles show the Center-of-Mass of gaze and hand movements, respectively. Task performance on $Week_1 \cdot Trial_1$ (**e, m**), $Week_1 \cdot Trial_6$ (**f, n**), $Week_6 \cdot Trial_1$ (**g, o**) and $Week_6 \cdot Trial_6$ (**h, p**). The upper grids (20×10) represent each target and the lower grids (10×10) represent each distractor that was foveated and hit with the left hand (dark blue), foveated and hit with the right hand (dark red), foveated but not hit (grey), not foveated but hit with the left hand (light blue), not foveated but hit with the right hand (light red), or neither foveated nor hit (white).

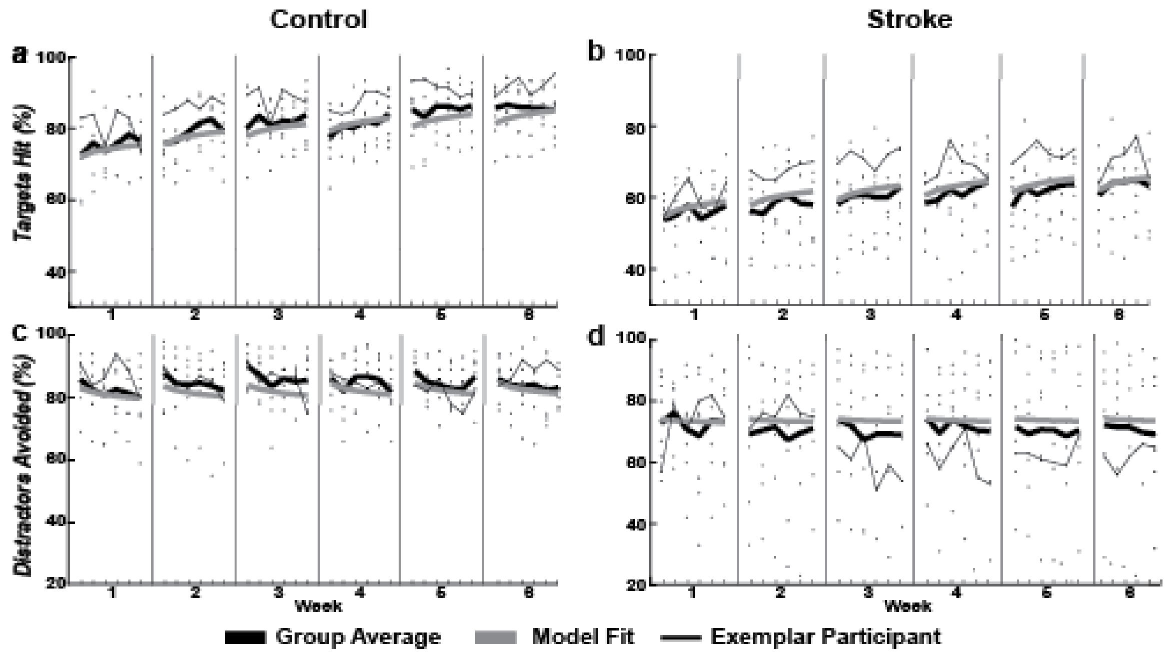

Figure 5.2 Task Performance. Trial-by-trial acquisition and week-by-week retention of improvements by the age-matched controls (left column) and stroke survivors (right column) on Targets Hit (**a, b:** $TH \sim G + logT + logW + G{*}logT + G{*}logW$, $R^2 = 0.92$) and Distractors Avoided (**c, d:** $DA \sim G + logT + logW + G{*}logT + G{*}logW$, $R^2 = 0.84$). Each panel displays raw data values of all participants (small black dots), exemplar participant performance (**fig. 5.1**, thin black lines), group means of reweighted data (thick black lines), and the regression model (thick grey lines). Reweighted participant data was calculated by applying weights from the robust regression model to the raw data values.

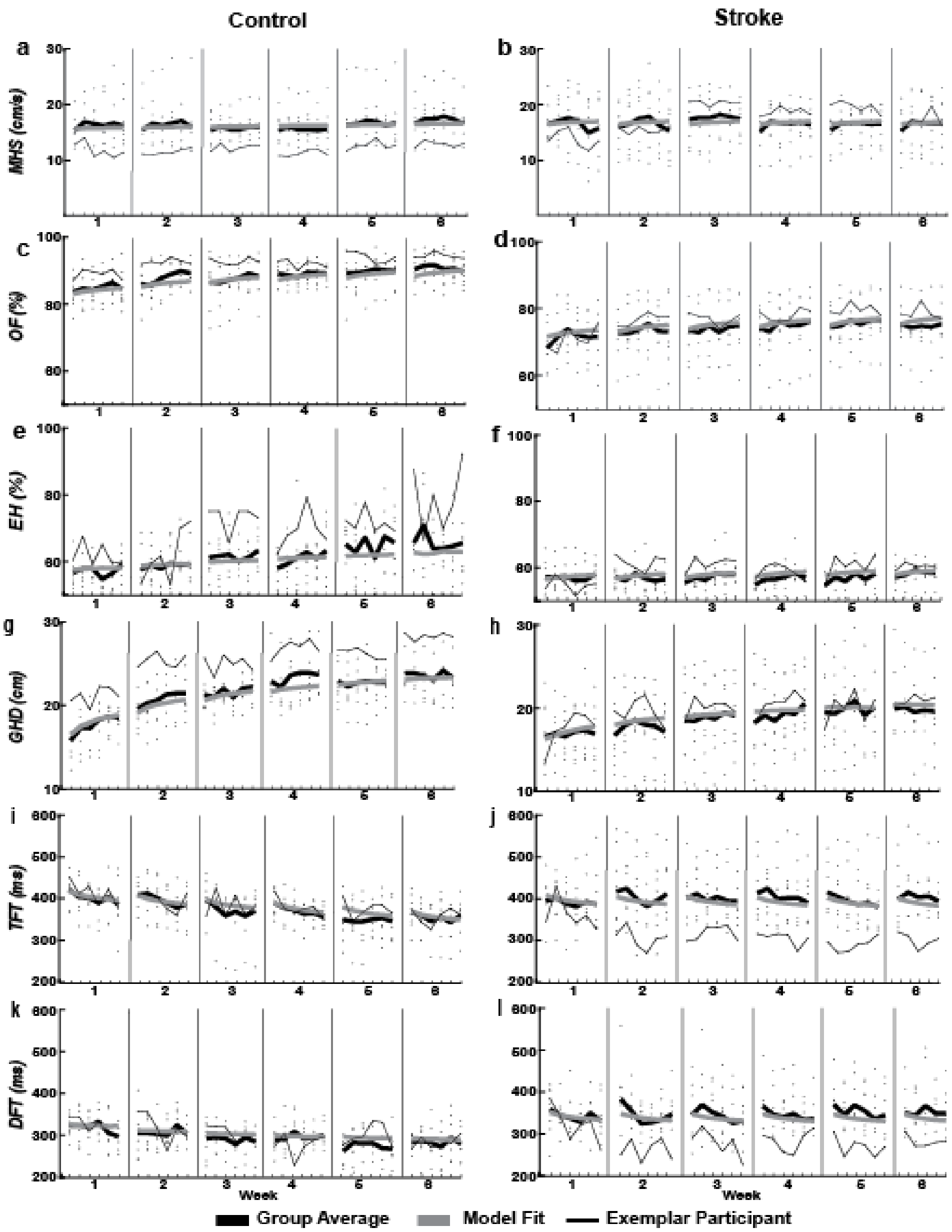

Figure 5.3 Refinements of Behavioral Features. Trial-by-trial acquisition and week-by-week retention of refinements by the age-matched controls (left column) and stroke survivors (right column) on Mean Hand-Speed (**a, b:** *MHS ~ G + logT + W + G*logT + G*W*, R^2 = 0.77), Objects Foveated (**c ,d:** *OF ~ G + logT + logW + G*logT + G*logW*, R^2 = *0.91*), Extrafoveal Hits (**e, f:** *EH ~ G + logT + W + G*logT + G*W*, R^2 = *0.40*), Gaze-Hand Distance (**g, h:** *GHD ~ G + logT + logW + G*logT + G*logW + logT*logW*, R^2 = 0.82), Target Foveation Time (**i, j:** *TFT ~ G + logT + W + G*logT + G*W*, R^2 = *0.71*) and Distractor Foveation Time (**k, l:** *DFT ~ G + logT + logW + G*logT + G*logW*, R^2 = *0.59*).

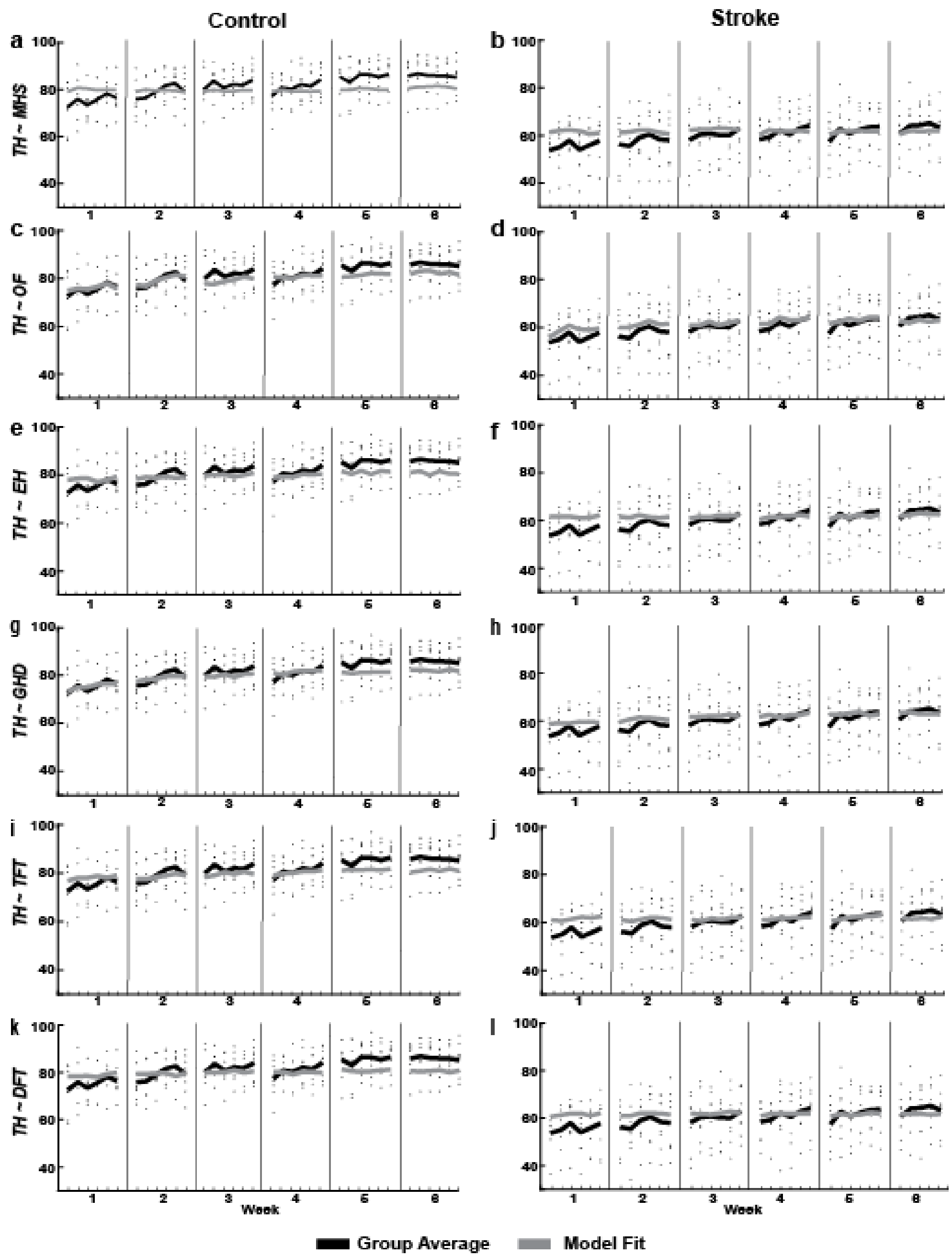

Figure 5.4 Univariate Predictors. Trial-by-trial and week-by-week retention of predictors by the age-matched controls (left column) and stroke survivors (right column) on Targets Hit. Bivariate regression models of Targets Hit using Mean Hand Speed (**a, b:** TH ~ MHS, $R^2 = 0.87$), Objects Foveated (**c, d:** TH ~ OF, $R^2 = 0.92$), Extrafoveal Hits (**e, f:** TH ~ EH, $R^2 = 0.88$), Gaze Hand Distance (**g, h:** TH ~ GHD, $R^2 = 0.89$), Target Foveation Time (i, j: TH ~ TFT, $R^2 = 0.87$), and Distractor Foveation Time (k, l: TH ~ DFT, $R^2 = 0.87$) as predictors.

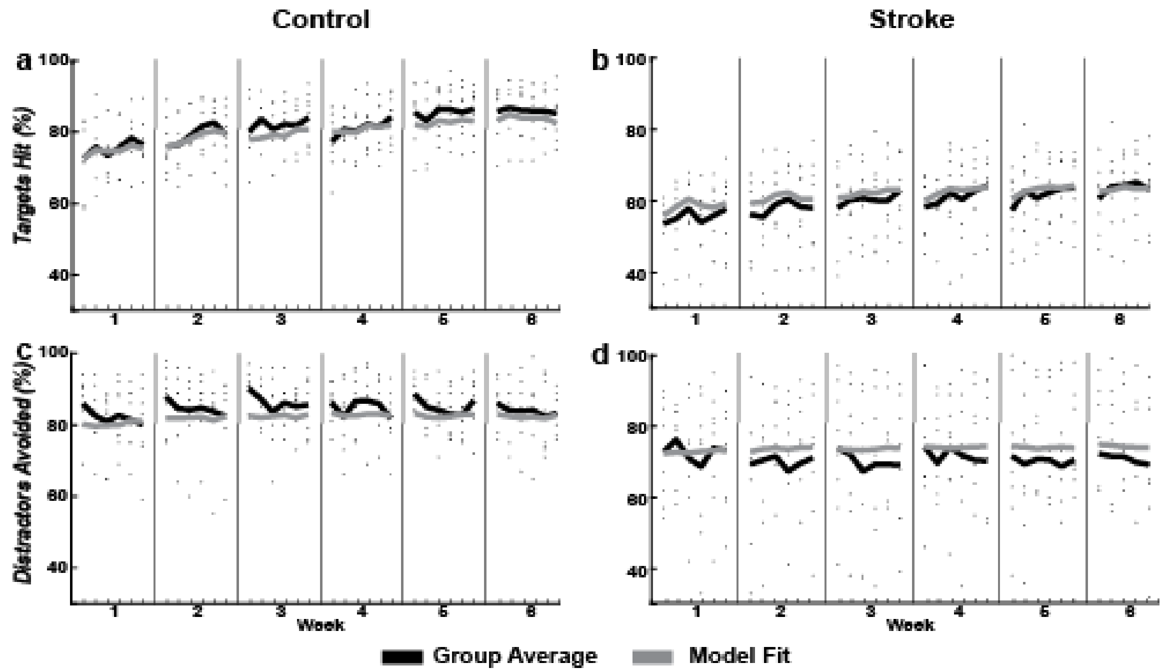

Figure 5.5 Multivariate Models. Illustrations show the predicted improvements by the age-matched controls (left column) and stroke survivors (right column) on Targets Hit (**a, b:** *TH ~ MHS + OF + GHD + EH*, $R^2=0.95$) and Distractors Avoided (**c, d:** *DA ~ MHS + GHD*, $R^2=0.85$) calculated with multiple regression.

Chapter 6

Summary of findings

Multiple behavioral features independently predict motor learning

In our first experiment we investigated the role of refinements in multiple behavioral features in motor learning by quantifying the independent variation between behavioral features. We observed practice-related refinements in skilled limb movement, visual search and eye-hand coordination were independently predictive of improvements in task performance. Our findings are supported by previous research studies that have shown that refinements in sensory and motor processes contribute to motor learning (Ostry and Gribble 2016).

Our second experiment aimed to determine if deficits in multiple behavioral features predict motor learning outcomes in survivors of stroke. Results showed that the stroke group exhibited deficits in the behavioral features of visual search, limb-movement, and eye-hand coordination that were independently predictive of Targets Hit, and our behavioral features of limb-movement and eye-hand coordination were independently predictive of distractors avoided. These findings are in accordance with previous studies that have shown that deficits in behavioral features of limb-movements (Krakauer 2006; Lang et al 2009, Lohse et al 2014; Oujamma et al 2009; Hsieh et al 2011), visual search (Singh et al 2017; Alves et al 2014; Ten Brink et al 2016), eye-hand coordination

(Tsang et al 2013; Fang et al 2007; Singh et al 2018), and visuomotor planning (Singh et al 2018) may result in decreased task performance.

Skilled limb movements independently predict motor learning

In the first experiment, increases in Mean Hand-Speed were associated with increases in Targets Hit, indicating that participants learned to increase the speed of their hands to hit more targets. Previous research suggests that faster movements are more variable and less accurate (Krakauer and Mazzoni 2011, van Beers 2009), however a decrease in accuracy (defined as targets hit) was not observed in the first experiment. It is possible that optimization of intermuscular coordination allowed participants to move faster without incurring greater movement variability (Todorov and Jordan 2002, Todorov 2004).

Survivors of stroke exhibited a Mean Hand-Speed greater than the control group that was predictive of Targets Hit and Distractors Avoided. We suggest this indicates that the abnormally high hand movement speeds in survivors of stroke exceeded their ‘optimum’ hand movement speed for task performance, resulting in excessive movement variability and unintentionally hitting additional target and distractor objects. Previous literature of speed-accuracy trade-off supports this hypothesis through the general notion that faster, more rapid movements are more variable and less accurate, and that this effect is exacerbated in those with stroke (Hammerbeck et al 2017, Plamondon and Alimi 1997). However, some evidence exists that suggests that the disproportionate speed/accuracy trade-off in survivors of stroke can be mitigated with task practice (Hardwick et al 2016).

Visual search independently predicts motor learning

Refinements in our measures of Extrafoveal Hits and Objects Foveated were the strongest independent predictors of Targets Hits. We suggest that task performance was optimized by participants gathering increased amounts of information with foveal and extrafoveal vision. This is consistent previous studies that suggest that visual search is highly adaptive to different task demands and environments, such as environments in which task-relevant objects are more likely to appear at certain locations (Neider and Zelinsky 2006, Wolfe et al 2011).

The association between Extrafoveal Hits and Target Hits indicates that participants refined extrafoveal vision to guide the hand movements used to hit targets. Previous studies of visual search have also found that task practice leads to improvements in extrafoveal vision to search for task-relevant features (Wu and Spence 2013). In addition, cortical areas associated with peripheral visual information exhibit greater activity task performance (Prado et al 2005).

Survivors of stroke exhibited deficits in Objects foveated and Extrafoveal Hits that were predictive of Targets Hit. We have previously shown that greater number of objects foveated during task performance is predictive of task outcomes (Singh et al 2017, Harrison et al 2020). This same effect was observed in experiment 1 and 2, with refinements more objects were foveated and extrafoveal vision was utilized to a greater extent during task performance.

Eye-hand coordination independently predicts motor learning

Refinements in Gaze-Hand Distance were associated with increases in Targets Hits, indicating that looking away from targets earlier before paddle contact was beneficial for task performance. Our findings contrast with some studies that show rigid eye-hand coupling between the initiation of eye movements and the completion of hand movements (Neggers and Bekkering 2000). However, other studies have provided evidence that eye-hand coupling decreases with practice (Sailer et al 2005, Rand and Stelmach 2011, Foerster et al 2011, Säfström et al 2014). Our findings reflect a transition from an early reliance on visual feedback for accurate hand movements to a subsequent reliance on kinesthetic feedback, allowing visual search to gather task-relevant information with greater efficiency (Sailer et al 2005, Cressman and Henriques 2009, Haith eta l 2008, Ostry et al 2010, Beets et al 2012, Wong et al 2012, Bernardi et al 2015, Sidarta et al 2016).

Survivors of stroke exhibited a deficits in Gaze-Hand Distance that were associated with Targets Hit and Distractors Avoided. This effect closely resembles the findings of gaze-locking studies that describe rigid coupling between initiation of eye movements that are contingent on the near completion of hand reaching movements (Armstrong et al 2013; Gowen and Miall 2006). It should be noted that some studies have provided evidence that gaze-locking can decrease with practice, allowing earlier separation of the eyes and hands to visually search for task-relevant objects (Sailer et al 2005; Säfström et al 2014). We suggest that the greater gaze-locking behavior observed in the stroke group may reflect a greater reliance on visual feedback for accurate execution of hand movements (Alves et al 2014; Torre et al 2013). It is known that somatosensory feedback is often impaired in survivors of stroke, resulting in decreased proprioception and kinesthesia (Torre et al 2013; Meyer et al 2014). In this case, a decrease in objects foveated would be expected as the participants' vision would spend more time viewing their hand position and less time viewing falling objects.

Distinct predictors of motor execution and inhibition

Our first experiment showed that motor execution (Targets Hit) and motor inhibition (Distractors Avoided) exhibited distinct patterns of improvements with practice of our novel paradigm. Targets Hit showed trial-by-trial and week-by-week improvements, whereas Distractors Avoided only displayed week-by-week improvements. We also found that different behavioral features were independently predictive of motor learning. Refinements of skilled limb movements (Mean Hand-Speed), visual search (Objects Foveated, Extrafoveal Hits) and eye-hand coordination (Gaze-Hand Distance) were independently predictive of improvements in Targets Hit. In contrast, eye-hand coordination (Gaze-Hand Distance) was the only independent predictor of Distractors Avoided.

Our second experiment found deficits in motor execution (Targets Hit) and motor inhibition (Distractors Avoided). Notably, survivors of stroke exhibited deficits in weekly retention of Targets Hits and in trial-by-trial refinements in Distractors. We also found that deficits in the behavioral features of Visual Search (Objects Foveated and Extrafoveal Hits), Eye-Hand Coordination (Gaze-Hand Distance), and Limb-Movement (Mean Hand Speed) were independently predictive of Targets Hit. In addition, we found that Eye-Hand Coordination (Gaze-Hand Distance) and Limb-Movement (Mean Hand Speed) were independently predictive of Distractors Avoided.

Dissertation Conclusions

The goal of this research was to investigate the link between multiple behavioral features and motor learning in healthy individuals and survivors of stroke. Our first study provided evidence that multiple behavioral features involved in limb-motor, visual search, and eye-hand coordination are refined during practice and independently predict motor learning. Our second experiment expanded on these findings by providing evidence that survivors of stroke exhibited deficits in multiple behavioral features that are predictive of motor learning.

The new knowledge gained through these studies is an important step forward in developing novel rehabilitation interventions that better address deficts observed in survivors of stroke. Using similar methods, clinical assessments can be created to identify deficits in multiple behavioral features during practice of functional tasks such as driving a car or preparing food. By identify deficits and quantifying their contribution towards motor learning, targeted rehabilitation interventions can be prescribed that address each deficit.

Future studies should focus on systematically altering the methods of this paradigm to better understand the effects that task parameters and participant selection have on motor learning. Changing task demands such as target and distractor object proportions, or feedback may impact the refinements of behavioral features. This would provide new information on how refinements in each behavioral feature is associated with motor learning. Participant groups can be experimentally controlled to explore the effects of medications and lesion characteristics to better understand if, and by how much individual participants will respond to motor learning interventions.

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