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Research Notes

Added cognitive demand from increased sensorimotor complexity resulted in better goal-directed movement following stroke: a novel finding in post-stroke recovery

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HIGHLIGHTS
• Two cases post-stroke showed unique behavior on robotic reaching assessment tasks.
• Both had better performance on the reaching task with added cognitive demand.
• Improved reaching performance may be associated with "dual-task benefit".
• Findings have clinical implications, including informing rehabilitation strategies.
• Highlights utility of robotic tools to objectively identify unique patterns of post-stroke impairments.

ABBREVIATIONS

DWI	Diffusion weighted imaging
RVGR	Reverse Visually Guided Reaching
T1 to T4	4 time points
T1-T3	Collected in the subacute phase (1-24 weeks post-stroke)
T4	Collected in the chronic phase of recovery
VGR	Visually Guided Reaching

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BACKGROUND: Stroke often causes impairments in goal-directed movements, which are commonly assessed using goal-directed reaching tasks. Here we present two individuals post-stroke who performed two robotic reaching tasks: 1. Visually Guided Reaching (VGR); reaching a cursor representing the fingertip to virtual targets, 2. Reverse Visually Guided Reaching (RVGR); where the cursor moves in the opposite direction of hand motion, requiring a novel cognitive rule. Participants are typically more successful at reaching targets in the simple VGR task compared to the more complex RVGR task (~92% of our database). The two cases are notable as they performed better on RVGR compared to VGR.
CASE DESCRIPTIONS: Case 1: 80-year-old patient with left hemorrhagic thalamic stroke, with interventricular extension, presenting with right hemiparesis/reduced motor control. They were unable to complete reaches to any targets in VGR (0/40 targets), but were able to reach ~30% of the targets (15/48) in RVGR. Case 2: 76-year-old patient with a left ischemic pontine stroke, presenting with right hemiparesis/reduced motor control. They were unable to complete reaches to any targets in VGR (0/40) but were able to reach ~60% of the targets in RVGR (29/48).
INTERPRETATION: Better performance in RVGR compared to VGR may be associated with a "dual-task benefit" and has potential clinical implications, including informing neuro-rehabilitative strategies, potentially by including tasks with added complexity or cognitive components. These findings also highlight the utility of robotic tools to provide novel environments within which to identify unique patterns of impairments and abilities.

KEYWORDS: Stroke | Reaching | Impairment | Pontine | Thalamus | Case report

INTRODUCTION

A common impairment following stroke is a decreased ability to make goal-directed movements with the arms [1–5]. Robotic tools for neurological assessment are part of a recent shift towards objective measures of motor performance following stroke, including kinematics and kinetics to quantify motor behaviors like reaching [6]. Such highly repeatable and objective measures lend themselves to the identification of impairments in a single patient. Further, we can compare individual performance to statistical models of healthy control performance collected on the same robotic tasks to identify if performance falls outside what is typically expected for an individual of similar age, sex and handedness [7].

A further advantage of robotic, computerized technology is the ability to use virtual/augmented reality to create tasks to probe specific aspects of motor control not easily assessed using traditional clinical tools. We recently investigated cognitive and motor integration following stroke using a Reverse Visually Guided Reaching (RVGR) task [8] where visual feedback of the hand is mirror-reversed, thus requiring a novel cognitive rule to reach in the opposite direction of the visual goal [9,10] (Figure 1B). We found that 75% of individuals with stroke (44/59) showed impairments in both RVGR and a simple Visually Guided Reaching (VGR) task with their affected arm. However, it was more common to see higher impairment in RVGR compared to VGR (Figure 1C,D) due to the added cognitive load of the novel task rules in RVGR. Only 6 participants out of 59 completed less reaches in VGR compared to RVGR (Figure 1C) and of these 6 participants, 2 stood out as having disproportionately poorer performance in VGR compared to RVGR, completing no successful reaches to any targets in the simple VGR task, but successfully reaching to 30-60% of targets in the more complex RVGR (Figure 1C,D).

The aim of this case report is to present the novel impairment profiles of these two individuals. We present case details, robotic and clinical assessments in the acute and chronic stages, and consider underlying mechanisms, future research and therapeutic implications.

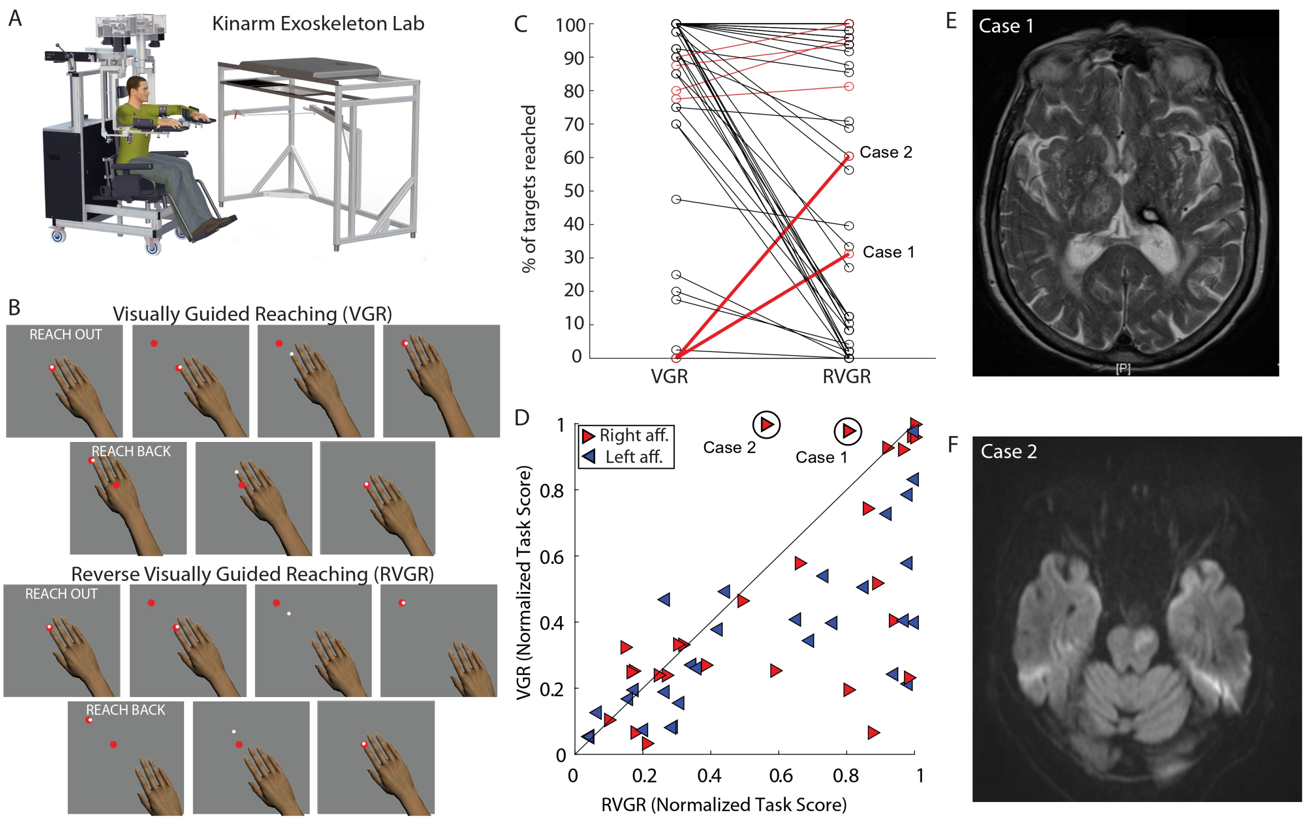

Figure 1. (A) Schematic illustration of the Kinarm Exoskeleton Lab robotic testing setup. Participants were seated in a height-adjustable chair and their arms rested in exoskeletons with adjustable arm and hand troughs. Shoulder and elbow joints were aligned with the robotic arm linkages to allow for free arm movement in the horizontal plane. (B) Schematic illustration of the Visually Guided Reaching (VGR) and the Reverse Visually Guided Reaching (RVGR) tasks. Note that the tasks were performed in the horizontal plane. Participants were required to stabilize the white cursor that represented their fingertip location in the red central target. A peripheral target appeared and the goal of the task was to move the white cursor into the peripheral target as quickly and accurately as possible. In VGR, the cursor paralleled the fingertip location but in RVGR the cursor moved in the mirror opposite direction to finger motion. Note that in VGR and RVGR, vision of the limb was occluded and participants could only see the virtual objects on the screen. (C) The percentage of the total targets reached in each task for a larger group of participants with stroke (N=59). Black circles and lines show participants who reached less targets in RVGR than VGR (or an equal amount in both tasks). Red circles and lines show participants who reached less targets in VGR than RVGR. The thick red lines indicate the two cases presented here. (D) Normalized Task Scores compared across both tasks for a larger group of participants with stroke. Right-facing red triangles represent participants whose right side was the most affected side following stroke. Left-facing blue triangles represent participants whose left side was the most affected side following stroke. (E) Magnetic resonance imaging (MRI), T2 sequence for Case 1. (F) MRI, diffusion weighted imaging (DWI) for Case 2.

METHODS

Case Details

Case 1: 80-year-old female admitted for inpatient stroke rehabilitation following left-hemisphere thalamic, hemorrhagic stroke, secondary to hypertension. Key deficits at rehabilitation admission included right hemiparesis/reduced motor control, right hemisensory loss (touch/pinprick), mild dysarthria, expressive aphasia (able to follow instructions), dysphagia and cognitive changes (processing speed, memory, higher-level attention, executive function, and ideomotor apraxia).

Case 2: 76-year-old female transitioned to inpatient stroke rehabilitation from acute care following left-hemisphere brainstem/pontine, ischemic stroke, secondary to small vessel disease. Key deficits at admission included right hemiparesis/reduced motor control, mild dysarthria, dysphagia and mild cognitive changes (memory, attention). See Table 1 for summary of clinical features.

Table 1. Clinical Information

	Case 1		Case 2	
Lesion location	Left thalamus (with interventricular extension)		Left brainstem (pons)	
Stroke type (etiology)	Hemorrhagic (hypertension)		Ischemic (small vessel disease)	
Demographics	F, 80-years-old		F, 76-years-old	
Testing time points (weeks post stroke)	T1: 10 weeks T2: 11 weeks T3: 16 weeks T4: 44 weeks		T1: 3.5 weeks T2: 6 weeks T3: 12 weeks T4: 27.5 weeks	
Chedoke McMaster Stroke Assessment (CMSA) (/7)	ARM aff/less aff	HAND aff/less aff	ARM aff/less aff	HAND aff/less aff
	T1: 3/5 T2: not done* T3: 3/5 T4: 3/6	T1: 5/6 T2: not done T3: 5/6 T4: 5/6	T1: 3/5 T2: 4/5 T3: 5/6 T4: 5/6	T1: 5/6 T2: 5/6 T3: 5/6 T4: 6/6
Functional Independence Measure (FIM)	T1: 83 T2: not done T3: 95 T4: 106		T1: 105 T2: 110 T3: 116 T4: 121	
Montreal Cognitive Assessment (MoCA)	T1: 22 T2: not done T3: 25 T4: 23		T1: 25 T2: 22 T3: 23 T4: 24	
Visual Acuity (T1)	Left eye: 20/20(corrected) Right eye: 20/25 (corrected)		Left eye: 20/30 Right eye: 20/40	
Visual fields / Visual inattention / Extra-ocular movements (T1)	Intact / None noted / Intact		Intact / None noted / Intact	
Behavioral Inattention Task (conventional) (BITc)	T1: not done T2: not done T3: 144 T4: 144		T1: 137 T2: 142 T3: 143 T4: 143	
Purdue Pegboard (PPB)	T1: 9.5 T2: not done T3: 10 T4: 7.5		T1: 13.5 T2: 10.5 T3: 17 T4: 17	

* clinical tests were not repeated for Case 1 at T2 because it was within a week from T1.

Experiments

Participants completed tasks using the Kinarm Exoskeleton Lab (Figure 1A). Details of the set-up have been described previously [3,11]. We obtained informed consent from participants and ethics were approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (#ANAT042-05). Part of these data have been published elsewhere [8]. Individuals were recruited from an inpatient Stroke Rehabilitation program at Providence Care Hospital, Kingston, Ontario, and were assessed by a trained physiotherapist.

Participants completed the VGR [3] and RVGR [8] tasks (Figure 1B) and were required to move a white virtual cursor to red circular targets as quickly and accurately as possible. In VGR the cursor paralleled the movement of the index finger whereas in RVGR, the cursor moved in the opposite direction (full task description in Supplemental Methods). In these tasks, a "successful" reach was considered moving to, and stabilizing within, a target. Data were collected at 4 time points T1-T4. T1-T3 were in the subacute phase (1-24 weeks post-stroke) and T4 was in the chronic phase of recovery. Between T1-T3, each participant received the standard of therapeutic care from the in-patient rehabilitation team, including physical/occupational/speech therapy up to 3 hours per weekday (as tolerated) for 6 (Case 1) and 4 (Case 2) weeks.

Data Analysis

Position and velocity of the robots were recorded at 1000Hz (Dexterit-E software; version 3.6.4, Kinarm, Kingston, Ontario, Canada) and filtered (sixth-order double-pass Butterworth low-pass filter, 10Hz cutoff). Position, speed, and acceleration of the hands were calculated and analyzed using Dexterit-E software (version 3.9, Kinarm, Kingston, Ontario, Canada).

Task Parameters were calculated from kinematic signals (see supplemental Table 1 for full description). Participant performance was compared to normalized models calculated from a large database of healthy controls [7]. "Task Scores" were calculated using parameter Z-scores to provide an overall measure of task performance [7]. Performance was identified as impaired if it fell outside of 95% of controls; i.e., a Task Score >1.96.

RESULTS

Case 1 displayed highly variable hand paths in VGR with the most affected (right) arm (Figure 2A). Of note, despite moving around the targets, hand paths rarely touched the targets themselves. Case 1 made 0 successful reaches to any targets. In RVGR with the most affected arm, hand paths appear slightly less variable, and the hand spent more time in the targets, (15/48 targets successfully reached). Of note, Case 1 was able to reach to all targets with the less affected (left) arm (Task Score=1.54, no impairment compared to a population of healthy controls).

Case 2 demonstrated less variable hand paths than Case 1 but hand paths rarely touched the targets, often undershooting them in the medial-lateral plane (Figure 2B). In RVGR with the most affected (right) arm, hand paths were highly variable but with more time spent in the targets (29/48 targets reached). Of note, in contrast to Case 1, Case 2 did not reach any targets in VGR with the less affected (left) arm. Case 2 did reach almost all targets in RVGR with the less affected arm (41/48 targets).

No meaningful task parameters were able to be calculated for either case in VGR because no reaches were completed. Task parameter Z-scores for RVGR are reported in Supplemental Table 2. In RVGR, Case 1 was impaired in 11/16 parameters (affected arm). Case 2 was impaired in 10/16 parameters in RVGR (affected arm).

Longitudinal data

Case 1 was assessed at 4 time points (affected and less affected arms; 10, 11, 16 and 44 weeks post-stroke; Figure 2C). For the affected arm, Case 1 reached 0 targets in VGR at each time point, but was able to reach some targets in RVGR. VGR Task Scores were 14.01(T1), 14.17(T2), 14.17(T3), 14.17(T4). RVGR Task Scores were 8.97(T1), 8.60(T2), 9.37(T3), 10.68(T4). For the less affected arm, Case 1 was able to reach all targets in VGR at every time point, but only some targets in RVGR. Task Scores in VGR were 1.54(T1), 2.61(T2), 1.76(T3), 1.18(T4). Task Scores for RVGR were 6.84(T1), 6.64(T2), 4.33(T3), 4.01(T4).

Case 2 was assessed at 3.5, 6, 12 and 27.5 weeks post-stroke (Figure 2D). For the affected arm, by 6 weeks post-stroke Case 2 completed successful reaches to all targets in VGR and to most targets in RVGR. Task Scores for VGR were 14.3(T1), 3.52(T2), 3.41(T3), 2.40(T4). Task Scores for RVGR were 6.27(T1), 5.33(T2), 6.82(T3), 7.05(T4). For the less affected arm, by 6 weeks Case 2 reached to all targets in both tasks. Task Scores for VGR were 14.3(T1), 1.88(T2), 1.21(T3), 1.08(T4). Task Scores for RVGR were 3.94(T1), 1.69(T2), 1.35(T3), 1.40(T4).

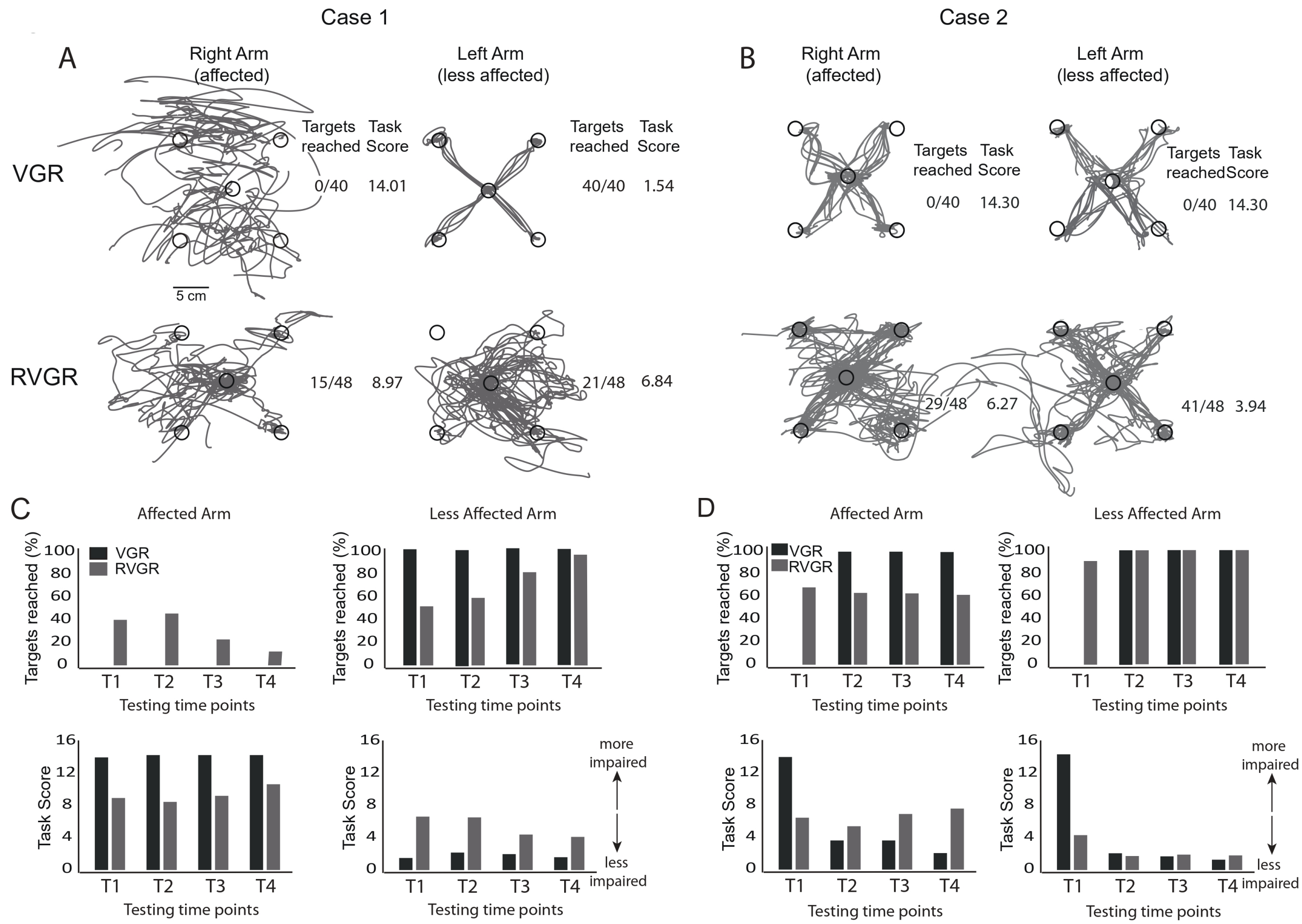

Figure 2. (A) Hand path traces for Case 1. Left traces are for the affected side (right arm) and right traces are for the less affected side (right arm). Circles represent the peripheral targets that appeared in a pseudorandom pattern during the trials. Targets reached represent the number of targets successfully reached to and stabilized within. (B) Same as A but for Case 2. (C) Longitudinal data for Case 1. Upper left: percentage of trials where the end target was successfully reached for VGR and RVGR at each testing time point for the affected arm. Upper right: percentage of trials where the end target was successfully reached for VGR and RVGR at each testing time point for the less affected arm. Lower left: Task Scores for VGR and RVGR at each testing time point for the affected arm. Lower right: Task Scores for VGR and RVGR at each testing time point for the less affected arm. (D) Longitudinal data for Case 2. Upper left: percentage of trials where the end target was successfully reached for VGR and RVGR at each testing time point for the affected arm. Upper right: percentage of trials where the end target was successfully reached for VGR and RVGR at each testing time point for the less affected arm. Lower left: Task Scores for VGR and RVGR at each testing time point for the affected arm. Lower right: Task Scores for VGR and RVGR at each testing time point for the less affected arm. Note that T1-T4 time points were different for each case participant: Case 1: T1 = 10 weeks, T2 = 11 weeks, T3 = 16 weeks and T4 = 44 weeks post-stroke. Case 2: T1 = 3.5 weeks, T2 = 6 weeks, T3 = 12 weeks and T4 = 27.5 weeks post-stroke.

DISCUSSION

Here we present two individuals post-stroke with novel performances on robotic reaching assessments. When initially assessed post-stroke, each participant was unable to successfully reach any targets in a simple reaching task (VGR), but were able to successfully reach a portion of targets in the more complex reaching task, (RVGR).

Inability to reach targets in VGR is not uncommon, since ~25% of participants with stroke we have tested are unable to successfully reach more than half the targets [3,8]. However, the problems that typically lead to deficits in VGR (e.g. hemiparesis/hemi-neglect/apraxia) almost always result in the same or worse deficits in RVGR [8]. Since the physical movements required for RVGR are identical to VGR, issues such as limited range of motion or weakness did not create this difference in performance. Similarly, even though hand feedback was reversed in RVGR, visual demands were similar between tasks, suggesting that differences in visual demand between the two tasks did not play a role.

Localization/multi-sensory integration

Underlying deficits experienced by each case, at least in VGR, may be explained by lesion location. Both cases involved sub-cortical strokes (Case 1: thalamus; Case 2: pons). Generally, sub-cortical lesions are associated with greater motor impairment and poorer motor recovery compared to purely cortical lesions [12]. Typically, the thalamus is considered a passive relay center, transferring sensory information to cortical and subcortical structures. However, recent work has suggested that some thalamic nuclei may influence motor learning directly. Neurons in the posteromedial thalamic nuclei of rodents were more active during correct trials than during incorrect trials in a goal-directed movement, thereby potentially encoding correct movements and influencing learning [13]. Thus, a lesion in the thalamic area in Case 1 could have led to challenges in learning a new motor task, (i.e., reaching to targets in virtual environments). Lesions to the pontine nuclei can lead to visual and sensorimotor impairments [14] and have recently been linked to dexterity in voluntary movements. In rodents, disrupting the pontine nuclei affected skill and precision in trained reach-to-grasp movements, causing decreases in success rate and increases in endpoint variability [15]. Therefore, a lesion in the pons for Case 2 may have led to the endpoint errors observed in VGR. However, in both cases it is unclear why these impairments would be less evident in RVGR, a parallel task with added cognitive load.

Alternatively, these individuals may have a specific difficulty with directly integrating visual and proprioceptive information to guide motor action [16]. In contrast to VGR, RVGR requires the integration of vision and proprioception in a conflicting way, where visual feedback of the arm is equal and opposite to arm motion. The specific profile of impairments in multisensory integration could be teased out by quantifying whether reaching performance improves in a reaching task without a cursor representing hand position compared to the VGR task where such visual feedback is provided.

Cognitive dual-task

Everyday activities often require the simultaneous performance of motor and cognitive tasks and numerous studies have noted this dual-task condition is detrimental to performance for older adults [17,18] as well as post-stroke [19], (i.e., "dual-task cost"/cognitive-motor interference [17,19]). However, certain dual-task circumstances can facilitate motor performance, reflecting a dual-task benefit [18,19,20]. This may involve facilitated activation of motor planning circuitry (e.g., dorsal premotor cortex), added utilization of attentional resources to enhance encoding of the motor task (i.e., the positive vigilance effect) [18], and greater automatization of the primary motor task[20]. Further, the timing of the cognitive demand (i.e., during the motor preparatory phase) may be an important factor [18]. Since the cognitive load imposed in RVGR comes in the preparatory phase of movement, increased activation of planning circuitry could have improved reaching performance. Case 1 featured noted apraxia or impairment in motor planning, and thus this mechanism may explain the greater and sustained dual-task benefit in RVGR. In both cases, it is also possible that attentional resourcing, vigilance and automatization played a role.

Robotic Tasks

It is important to note that it would have been less likely to identify the complexity of these impairments using traditional clinical assessment tools. The use of the robotic tasks, specifically RVGR, was able to provide a novel scenario where visual feedback of the arm was not directly linked to the exact position of the arm. The similarity of the VGR and RVGR tasks, along with the objective measures of behavior, allowed for the direct comparison of the two tasks that uncovered the paradoxical behavior.

Limitations

VGR was always performed prior to RVGR which could lead to enhanced performance on RVGR, as participants become accustomed to the robotic environment. However, this would likely lead to more targets missed in the first trials of VGR and improvement in performance as the trials progressed, which did not occur.

CONCLUSION

This report outlines novel patterns of impairment in goal-directed movements following stroke. These findings highlight the use of robotic technologies to uncover novel impairment profiles in individual participants. Potential neuro-rehabilitative and therapeutic strategies that include a cognitive component could be explored to maximize post-stroke functional recovery.

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