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STROKE REHABILITATION (P RAGHAVAN, SECTION EDITOR)

Post-Stroke Cognitive Impairments and Responsiveness to Motor Rehabilitation: A Review

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Abstract

Purpose of Review This review discusses the prevalence of cognitive deficits following stroke and their impact on responsiveness to therapeutic intervention within a motor learning context.

Recent Findings Clinical and experimental studies have established that post-stroke cognitive and motor deficits may impede ambulation, augment fall risk, and influence the efficacy of interventions. Recent research suggests the presence of cognitive deficits may play a larger role in motor recovery than previously understood.

Summary Considering that cognitive impairments affect motor relearning, post-stroke motor rehabilitation therapies may benefit from formal neuropsychological testing. For example, early work suggests that in neurotypical adults, cognitive function may be predictive of responsiveness to motor rehabilitation and cognitive training may improve mobility. This sets the stage for investigations probing these topics in people post-stroke. Moreover, the neural basis for and extent to which these cognitive impairments influence functional outcome remains largely unexplored and requires additional investigation.

Keywords Cognitive decline · Rehabilitation · Stroke · Falls · Gait · Function

Introduction

Motor learning is important for motor rehabilitation as individuals must often relearn lost motor skills [1]. Evidence from clinical and experimental studies have long supported that specific cognitive abilities such as attention, working memory, and visuospatial ability are related to both performance and performance improvement on novel motor tasks (i.e., procedural learning) [2–10]. This may be problematic for stroke survivors, as these same domains are often impacted post-stroke. While the reporting of cognitive data has become more customary in stroke rehabilitation studies, these data are often limited to global cognitive screening tools that provide only a cursory glimpse into cognitive function and are typically used only to exclude individuals with low scores. Moreover, a comprehensive understanding of specific cognitive impairments in stroke survivors, and the extent to which they interfere with gait rehabilitation remains a critical knowledge gap.

Here, we will briefly summarize key points regarding the effects of stroke on gait and posture, and discuss a novel, less-studied area of research regarding the extent to which cognitive impairments may interfere with motor learning and rehabilitation. We first review common neuropsychological assessments used to evaluate cognition, particularly those relevant to the stroke survivor population, and discuss the limitations and broader implications of using these assessments. We then discuss the role of stroke-specific cognitive deficits in gait and postural control and how these deficits may influence the degree of improvement in motor behaviors. Finally, we discuss our understanding of how specific cognitive deficits may impact stroke rehabilitation and propose that thorough neuropsychological evaluation be integrated into stroke protocols (rather than serve as exclusion criteria) to clarify cognition's role in recovery and relearning of motor skills.

This article is part of the Topical Collection on *Stroke Rehabilitation*

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What Are Common Cognitive Impairments Associated with Stroke and How Can They Be Measured?

While cognitive impairment following stroke is certainly linked to the lesion location and/or size [11, 12•, 13], clinical studies indicate that impairments in attention, executive function, and processing speed are the most prevalent across stroke survivors [12, 14]. In fact, stroke survivors are tenfold more likely to show impaired memory, orientation, language, and attention, compared with age-matched non-stroke individuals, with prevalence rates of 35% vs 3%, respectively [15]. Moreover, these impairments may be differentially impacted throughout neurological recovery. For instance, attention and executive functions may be most susceptible to impairment at the time of stroke diagnosis [16], whereas impairments in memory, executive, and visuospatial functions are notable 3 months post-stroke [17]. Interestingly, these cognitive deficits persisted in patients with no apparent physical or cognitive disability as screened by the modified Rankin Scale and Mini-Mental State Exam, respectively [17], suggesting subtle cognitive impairments may remain undetected if evaluated with a brief global cognitive screen.

However, there is no gold standard for the diagnosis of post-stroke cognitive impairment (i.e., vascular cognitive impairment) [12], which obfuscates the selection of clinical cognitive screening and assessments. For instance, the Mini-Mental State Exam (MMSE) has been widely used as a clinical diagnostic tool of cognitive impairment since its advent in 1975, despite its authors' warnings it cannot be used exclusively to diagnose impairment [18]. In fact, it excludes an evaluation of executive function and has poor sensitivity in Mild Cognitive Impairment detection [19]. The Montreal Cognitive Assessment (MoCA) is also commonly used, and although it provides a measure of executive function and may be more reliable in Mild Cognitive Impairment detection [19], it has poor sensitivity in quantifying cognitive function of the domains it asserts to evaluate [20]. Moreover, these brief clinical assessments do not provide standardized age-adjusted scoring (although recent work has attempted to address this limitation [21]), which may be particularly important considering the preponderance of older adults among the stroke population [22].

The National Institutes of Health (NIH) developed the National Institutes of Health Stroke Scale [23], a measure of activities of consciousness, movement, sensation, response, and advanced neurological function in stroke patients, and is a reliable indicator of stroke severity [24]. Similar to other global cognitive screens, however, it yields a global measure of cognition that may be insensitive to cognitive deficits [25]; it is also susceptible to floor effects and biased towards hemisphere-specific lesions [26]. The NIH has proposed a validated, standardized, robust measure of cognitive function, namely the NIH Toolbox Cognitive Battery [27]; however, it is only appropriate for research applications and does not serve as a substitution for formal neuropsychological or other clinical testing. At present, the battery has only been validated in healthy populations while the work to validate it in traumatic brain injury, spinal cord injury, and stroke cases remain ongoing [28•, 29, 30]. In the interim, implementing formal neuropsychological testing, specifically tests that thoroughly evaluate cognitive domains particularly relevant to motor-related outcomes (e.g., executive function and functional outcome in stroke patients [31]; spatial working memory with procedural learning [32]) may provide critical prognostic insight into stroke rehabilitation outcomes. This aligns with the first recommendation by the Cognition Working Group, which convened as part of the second international Stroke Recovery and Rehabilitation Roundtable [33••].

How Is Cognition Typically Measured?

Global cognition broadly encompasses six domains of cognitive function, namely attention, executive function, learning and memory, language, perceptual-motor function, and social cognition, with each domain being further stratified into subdomains [34]. As previously mentioned, the MoCA and MMSE are ubiquitous clinical tools used to quickly screen global cognitive status by cursorily evaluating attention, language, memory, and visuospatial/executive functions. Although these global screening tools are relatively quick (approximately 5–10 min) and easy to administer, they may have differential sensitivity to premorbid abilities [34] and are subject to age, educational, and cultural background confounds [35]. More extensive neuropsychological assessments that rigorously test each cognitive domain may provide a more robust estimation of cognitive status (e.g., Repeatable Battery for Neuropsychological Status [36], Weschler Adult Intelligence Scale [37]), yet often require costly instrumentation, appropriate licensure, and longer administration periods (approximately 30 and 75 min, respectively). Unlike the MoCA or MMSE (or similar), these assessments can evaluate individual domains (e.g., complex attention, language) and subdomains (e.g., long-term memory, working memory). For instance, the Repeatable Battery for Neuropsychological Status and Weschler Adult Intelligence Scale yields an age-adjusted composite score comprising multiple index scores, each validated to represent a specific cognitive domain.

If the function of a single cognitive domain is of interest to a clinician, they can utilize individual neuropsychological tests. For example, the Rey-Osterrieth Complex Figure test is a widely used paper-and-pencil examination that measures visuospatial construction, immediate visuospatial memory, and delayed visuospatial memory [38] and has also been shown to evaluate latent constructs such as graphomotor function, object use and planning, visuomotor transformation, and visuospatial perception [39]. One major advantage of using standardized cognitive assessments is that normative data, user qualifications, administration instructions, and results reporting are generally well-documented, and reputable online databases that thoroughly review important considerations of individual neuropsychological assessments (such as cost, test/retest reliability, cutoff scores, normative data, etc.) are publicly accessible, much like many physical/motor assessments that physical and occupational therapists use (e.g., https://www.sralab.org/rehabilitation-measures, Shirley Ryan AbilityLab). We take the time to summarize this point here to encourage future studies to utilize standardized, validated assessments alongside (or in place of) novel experimental methods for characterizing cognition post-stroke.

When formal neuropsychological testing is unavailable or infeasible, the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders provides a list of brief assessments that can provide insight into each subdomain. For example, to evaluate planning ability (a subdomain of executive function), the examinee should demonstrate the ability to find the exit to a maze and/or interpret a sequential picture or object arrangement [34]. Similarly, while researchers may develop experimental approaches that provide insight into a specific cognitive domain (e.g., [32]), one caveat to experimenter-derived assessments is that they are not necessarily standardized (i.e., generalizable), potentially complicating the comparison and replication of research findings among laboratories.

We also want to briefly acknowledge a recent study demonstrated that years of education explained differences in cognitive factors such as executive function, working memory, global cognition, and alertness, as well as motor function (as measured by the modified Rankin Scale) among stroke survivors with right-hemispheric lesion [40]. Education served as a proxy for cognitive reserve (i.e., the brain's resilience to neuropathological damage [41]), which is a very feasible variable to collect, and may be an important factor to consider or control for in motor rehabilitation trials. Notably, results of this study also highlight the complex interplay between cognitive function, cognitive reserve, and motor behavior.

What Is the Effect of Stroke and Cognitive Impairment on Gait and Balance?

Gait and balance deficits are common post-stroke, and directly contribute to poor mobility, increased falls, and reduced quality of life [42, 43]. Given that a stroke can result in heterogeneous sensory and motor deficits such as muscle weakness, altered movement selection, spasticity, and altered sensation and integration of proprioceptive signals, the severity of balance and/or gait changes observed post-stroke is largely variable among individuals. In general though, slower ambulation increased variability [44] and asymmetry [45], shorter, wider steps [46], and large anterior-posterior and lateral deviations of the trunk and pelvis [47•] are common gait impairments following stroke. Like gait, impairments in balance are similarly broad in scope and may include asymmetric and increased sway [48, 49], poor weight transfer [50], a reduced limit of stability [51], and poor reactive postural control (i.e., the ability to quickly react to imbalance) [52•]. As proprioceptive capacity is typically diminished following stroke, many stroke survivors may also become more reliant on visual information to maintain appropriate postural control [48].

Nearly 60% of older adults with cognitive impairment experience at least one fall annually [53], more than twofold that of their cognitively intact peers [54]. Indeed, the link between cognition and motor behavior has been well established, but to what extent do stroke-related cognitive impairments affect gait and balance? Recent research has shown that the Stroop Color Word Test (a measure of inhibition of cognitive interference) and errors made on part B of the Trail Making Test (a measure of attention switching) predict fall risk in stroke survivors [55]. Furthermore, when compared with age-matched controls, stroke survivors tend to have the highest levels of cognitive-motor interference (i.e., the relative cost of dual-tasking) when performing concurrent working memory and balance tasks [56]; results indicated that working memory, but not semantic memory, had a disproportionately negative impact on cognitive-motor interference for the stroke group compared with controls. Interestingly, the stroke survivors had similar cognitive scores (i.e., score > 10 on the Short Orientation–Memory–Concentration Test of Cognitive Impairment [57]) as age-matched controls, suggesting that individuals with stroke may require greater attentional resources due to their motor impairment(s), to perform as well as their age-matched counterparts. Collectively, these findings suggest that working memory, attention switching, and inhibition may be the most pertinent cognitive domains for proper balance control and encourages future work to discern if the presence (or absence) of selective cognitive impairments following stroke may, in part, explain inter-individual differences in motor behavior (e.g., balance and gait).

Does Cognitive Impairment Interfere with Motor Rehabilitation?

Given that an estimated 40–50% of all physical rehabilitation patients currently receiving care in the USA are over age 65 [58], it is imperative that today's therapies are effective for older adults [59]. And while it is difficult to precisely quantify the amount of elderly stroke survivors seeking some form of motor rehabilitation, the Centralized Open-Access Rehabilitation Database for Stroke (SCOAR) [22] approximates that ~33% of motor rehabilitation trials for stroke have an average participant age of 65 or older. Carefully chosen rehabilitation interventions can improve mobility, even in older stroke survivors [60•, 61].

However, improvements through rehabilitation can be variable, with some survivors improving more than others or at different rates. Thus, an important factor to consider is the likelihood that many older patients may present with cognitive impairments. Rigorous assessment of cognitive capacity may improve rehabilitative care for at least two reasons. First, it can instruct the patient interaction, including the types and modalities of instructions given to the patient. Second, cognitive impairments may interfere with their ability to learn or regain motor skills after stroke or neurological injury. For example, as a proof-of-concept, we recently demonstrated that regardless of primary diagnosis, overall cognitive status affected the extent to which transitional care patients improved their gait speed over their length of stay [62] (see also [63]). This trend persisted in a stroke-specific sample as well over 1 year post-stroke [64•]. Importantly, this does not suggest that cognitively impaired individuals should not participate in motor therapy, given they may still experience significant gains [65, 66, 67••]. Instead, it advocates for (1) developing more personalized or targeted physical therapeutic interventions that are effective in cases of specific cognitive impairments post-stroke (e.g., [68]) and (2) conducting additional research that investigates which post-stroke cognitive impairments interfere most with motor skill learning. However, the field of stroke rehabilitation has only recently begun to investigate the impact of cognitive deficits on therapeutic responsiveness. In a recent meta-analysis of 215 stroke rehabilitation randomized controlled clinical trials (RCTs) from SCOAR, only 31% of the studies reported collecting cognitive information from participants (as measured by the MMSE), and nearly half of those studies used this information to *exclude* participants with cognitive deficits [22]. Overall, the use of cognitive assessments is encouraging, as it indicates that cognitive data are being collected in stroke motor rehabilitation, and could theoretically be used in retrospective, secondary analyses of clinical trial data. For example, Dobkin et al. [69] conducted secondary analyses on the Locomotor Experience Applied Post Stroke (LEAPS) RCT [70] and reported that attentional switching (measured as the difference in performance on trails A and B) at baseline predicted participants' change in gait speed in response to a partial bodyweight-supported intervention involving both treadmill and over-ground walking. These analyses occurred retrospectively, after the initial LEAPS trial reported equivalent walking outcomes for both the treadmill and over-ground walking intervention and home-based exercise (that did not emphasize walking). However, given that the most common cognitive assessments reported among stroke rehabilitation RCTs are global cognitive screens, there remains an opportunity for scientific inquiry regarding which, when, and to what extent specific cognitive deficits affect the motor rehabilitative process.

Are There Specific Cognitive Impairments that Can Affect Motor Skill Learning After Stroke?

As summarized above, considerable work has demonstrated the relationship between cognition and gait/posture performance. However, an equally pertinent question for clinicians is whether cognitive factors affect *responsiveness* to gait training (which is driven by mechanisms of motor learning) are less understood. Although there remains a relative dearth of information on this topic, several recent studies have begun to provide insight into this knowledge gap. For example, evidence from a small (6-study) meta-analysis by Mullick et al. [71] suggests that both executive function and attention deficits after stroke can affect the amount of improvement in upper-extremity motor function following training, although there may be stronger cognitive-motor learning associations when kinematic outcomes (i.e., peak velocity or endpoint accuracy [72]) are used rather than clinical scales (e.g., the Action Research Arm Test or the Wolf Motor Function Test [73]). Visuospatial impairments also influence how much motor task performance improves following upper-extremity task-specific training [6–8, 74], as well as the amount and rate of functional improvement (measured with the Functional Independence Measure motor subscale) [31]. Provocative findings from Schweighofer and colleagues [10, 75] also implicate visuospatial working memory in upper-extremity motor learning after stroke, particularly the role of contextual interference. Moreover, the post-stroke integrity of functional networks that are critical for visuospatial function (namely, frontoparietal) can predict how responsive individuals will be to upper-extremity motor training [76].

However, it is likely that the cognitive processes underlying the learning of upper vs. lower extremity movements are distinct. For example, while evidence supports the impact of visuospatial deficits on upper-extremity motor learning, such deficits may be less detrimental to gait and/or postural training. At present, there are limited studies that investigate cognitive factors related to lower- vs. upper-extremity motor learning, and no studies that have systematically compared across cognitive domains and body effectors. Moreover, it is plausible that different types of motor learning (implicit vs. explicit, [77]) are more reliant on different cognitive domains, which suggests the cognitive impairments that interfere with learning discrete upper-extremity skills (like reaching, grasping, or object manipulation) would likely differ from those that interfere with adaptations of gait and posture.

McDowd et al. [78] suggest that attention (divided and switching, specifically) may be the most critical for determining the amount of improvement made during gait training in stroke. This has also led to an important area of research regarding whether engaging in concurrent cognitive tasks during gait training is more efficacious that simply walking (see [79]). For example, gait training while solving a problem using visual feedback has been shown to improve both gait and some aspects of cognition (namely, backwards visual digit span) but not others (auditory digit span) [80]. Such findings do not, however, directly address the question of whether attentional deficits post-stroke result in poorer gait relearning or slower recovery of balance, per se, although there is evidence of this in upper-extremity recovery (see [81] for review). If so, therapists could use different strategies, such as internal or external loci of attention [82], to enhance gait and balance rehabilitation via an attention mechanism/intervention.

Can Cognitive Rehabilitation Improve Motor Rehabilitation After Stroke?

The correlative relationship observed between cognition and balance suggests it is plausible that cognitive training (or, motor rehabilitation paired with a cognitive task) could enhance motor performance improvement (i.e., relearning). However, while early evidence in healthy adults suggests cognitive training may improve some aspects of mobility [83], evidence in stroke survivors is limited and mixed. For example, Helm and colleagues [84] had two groups of stroke survivors perform locomotor training with either constant or variable practice structure, where variable practice requires greater attentional demands compared with constant practice; results indicated there was no difference in performance or retention of the locomotor task between either group. In contrast, Liu and colleagues [85•] evaluated if various dual-task training (i.e., motor-motor: tray-carrying and walking, or cognitive-motor: serial subtraction and walking) would affect different gait parameters in individuals with stroke; results indicated that each dual task had differential effects on stride length and dual-task cost, suggesting that specific dual-task training may address selective cognitive deficits. At present, no studies have reported the effect of specialized training to target select cognitive deficits and its subsequent effect on gait in a neuropathological population (i.e., stroke). Future work is necessary to better understand if cognitive training impacts motor performance and learning.

Conclusions

Cognition is important for motor rehabilitation, particularly domains shown to underlie procedural learning such as attention, working memory, and visuospatial abilities. Global cognitive testing is insensitive to subtle deficits in cognition and may only narrowly establish if an individual is cognitively intact. Neuropsychological tests that thoroughly evaluate the function of select cognitive domains may provide critical prognostic insight into rehabilitation outcomes. For example, recent work suggests that visuospatial deficits are associated with poorer upper-extremity motor recovery. Furthermore, other studies have linked stroke-specific cognitive impairments not only with altered gait and balance performance but also with the degree to which patients improve gait with training as well. Stroke-related research studies should consider incorporating comprehensive neuropsychological testing to further our understanding of cognition's role in recovery and relearning of motor skills.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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