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## Rehabilitation of Poststroke Cognition

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### Abstract

Given the increasing rates of stroke and our aging population, it is critical that we continue to foster innovation in stroke rehabilitation. Although there is evidence supporting cognitive rehabilitation in stroke, the set of cognitive domains effectively addressed to date represents only a small subset of the problems experienced by stroke survivors. Further, a gap remains between investigational treatments and our evolving theories of brain function. These limitations present opportunities for improving the functional impact of stroke rehabilitation. The authors use a case example to encourage the reader to consider the evidence base for cognitive rehabilitation in stroke, focusing on four domains critical to daily life function: (1) speech and language, (2) functional memory, (3) executive function and skilled learned purposive movements, and (4) spatial-motor systems. Ultimately, they attempt to draw neuroscience and practice closer together by using translational reasoning to suggest possible new avenues for treating these disorders.

### Introduction

Rehabilitation is considered a standard for poststroke health care in the United States. At its best, clinical rehabilitation is a deductive, scientific process, guided by the known brain basis for clinical syndromes. Targeted assessment of modular and domain-specific information processing systems (our working definition of cognition) allows clinicians to form hypotheses about the nature of dysfunction and plan targeted treatments. However, current stroke rehabilitation often emphasizes compensatory strategies. In such circumstances, cognition is inadequately assessed, and as a result, disorders are tragically not diagnosed.<sup>[1]</sup> Similarly, treatments for cognitive disorders are underprescribed and underutilized. When treatments are implemented, they may be guided by models that have not kept pace with developments in behavioral science and neuroscience. Knowledge gaps between basic research and stroke rehabilitation can limit the efficacy of tools and opportunities available for cognitive rehabilitation.

On the brighter side, these limitations present an opportunity for improving stroke rehabilitation techniques. Using a case example in a postacute rehabilitation setting, we encourage the reader to consider the evidence base for clinical applications. We briefly review four cognitive domains critical to daily life function: (1) speech and language, (2) functional memory, (3) executive function and skilled learned purposive movements, and (4) spatial-motor systems. We then illustrate the impact of stroke on these domains and the brain basis of common symptoms, emphasizing key concepts regarding information input, how it is represented internally, and how it is used for action preparation. Finally, we attempt to draw neuroscience and practice closer together, and suggest possible new avenues for treating these disorders.

## Clinical Case

KR is a right-handed, 81-year-old, college-educated woman who suffered a large left middle cerebral artery (MCA) distribution infarction. Prior to her stroke, KR lived alone, managing her own finances, medications, and housekeeping. She tended to be sedentary and enjoyed reading.

### Speech and Language

Most theories of language production and comprehension are predicated on the concept of modularity—the idea of a language system or network of distinct cognitive components, supported by left brain systems.<sup>[2]</sup> Patients like KR can benefit from linguistic assessment, using tasks that allow for observing and dissociating the known behavioral components of speech and language.

KR demonstrated stroke-related aphasia, with severely limited verbal and written language production. KR's speech output was initially limited to inconsistent functional use of well-articulated single words and occasional short phrases; no phonological errors were noted. KR's comprehension (yes/no responses) was relatively spared, as was repetition of words and phrases. KR was able to follow simple three-step commands easily, but made syntactic errors (e.g., confusing "or" with "and" and "on" with "next to") with more complex commands.

KR's symptoms were consistent with transcortical motor aphasia. Because the major deficit is fluency, excellent recovery is possible.<sup>[3]</sup> Most patients with transcortical motor aphasia syndrome have lesions affecting left anterior brain regions, and this is frequently associated with lesions that involve frontal cortical structures outside the classic perisylvian language areas.<sup>[4]</sup> KR's brain magnetic resonance imaging (MRI) results were consistent with this, which demonstrated primary areas of infarction in the left basal ganglia and prefrontal cortex.

### Functional Memory

Functional everyday memory depends not only on efficient information storage and retrieval, but also on process functions associated with executive systems. KR's assessment included attention, working memory (ability to hold information in mind temporarily), problem solving, and recall of newly learned facts. Although KR was able to spell a five-letter word backward, working memory for more unstructured, naturalistic material was impaired. This was demonstrated by inconsistent reporting during the course of a conversation. Executive functioning was notable for intrusions—inappropriate responses incorporating elements of a preceding task. For example, when asked to copy overlapping pentagons, KR first drew a pair of eyes. This was interpreted as an intrusion as it followed a command to follow the written instruction: "CLOSE YOUR EYES." In problem-solving tasks, KR tended to overestimate her performance accuracy. She therefore required cues to attend to detail and to monitor herself. KR's problems with working memory and self-awareness were considered important because they adversely affected her ability to compensate for comprehension errors. This in turn adversely affected her memory.

KR's functional memory profile is very typical for patients with a left dorsolateral frontal stroke, which affects regions that help organize linguistic and quantitative information, mental sequencing, and self-monitoring.<sup>[5]</sup> The dorsolateral prefrontal cortex also supports integration of contextual information with memory content (e.g., how the information was presented and by whom), to create rich detail in episodic and autobiographical memory.<sup>[6]</sup> Improving these processes may improve task tracking and performance in everyday life (e.g., "Did I turn off the stove? Or did I just intend to do so?").

### **Executive Functioning/Skilled Purposeful Movement Planning**

Left parietal and supplementary motor areas (SMA) are critical for producing skilled purposive movements (praxis). Tasks like gesturing (e.g., waving goodbye) or pantomiming object use (e.g., using scissors or a screwdriver) require dedicated cognitive systems to store concepts of praxis and to execute these movements.<sup>[7,8]</sup> Dorsolateral and dorsomedial SMA frontal cortical systems also mediate motor sequencing, which can be tested by asking patients to perform the Luria hand commands (imitating a short hand-gesture sequence: "fist, palm, edge").<sup>[9]</sup> KR demonstrated not only severe contralateral (right) arm paralysis, but also mild ipsilateral (left) upper extremity impairment typifying ideomotor apraxia.<sup>[10]</sup> She was unable to pantomime tool use in response to verbal commands. Her gestures were recognizable, but imprecise to the point of violating the physical properties of the tool. Over time, KR's ability to use tools improved sufficiently such that she could answer her cell phone, eat, and groom herself independently when set up. However, she continued to require assistance to initiate a phone call.

Only limited information is available on the natural spontaneous recovery of apraxia. KR's progression is consistent with observations of greater recovery from apraxia among patients with lesions sparing the posterior (parietal-temporal-occipital) cortex.<sup>[11]</sup> Not surprisingly, less-severe ideomotor apraxia has been associated with more complete recovery.<sup>[12]</sup>

### **Spatial Motor Functioning**

The motor system in the healthy brain comprises the primary motor cortex, subcortical pyramidal/corticospinal connections, and cognitive systems supporting functional movement. Cognitive systems include the praxis system (see above) and also right brain mediators of spatial perception, imagery, and action.<sup>[13]</sup> These systems report, respond, and orient to spatial information (especially in left space) to compute body orientation and position of objects around us when we carry out visuomotor movements.

Compromise of spatial motor systems can be evaluated through strength and movement coordination testing, and by observing motor behavior in three-dimensional space. Patients with spatial neglect (i.e., failure to report, respond, or orient to stimuli located in contralateral space), have deficits beyond those accounted for by simple weakness. Although neglect is common after nondominant hemispheric stroke, the right side of the body and right hemispace also can be affected by a left hemisphere stroke.<sup>[13]</sup> KR was weak on the right with a plegic hand and paretic arm/shoulder. With rehabilitation, she was able to use her right arm to stabilize herself with a walker. Although lower extremity range of motion was satisfactory bilaterally, her right leg remained weaker. It was possible that some

of her weakness might be accounted for by right-sided motor neglect; her right-hand weakness decreased when she moved it into the left body space.

As is the case in approximately 10% of stroke patients, KR demonstrated impaired control of vertical-horizontal body postures and actions (pusher syndrome).<sup>[14]</sup> When seated, she actively leaned toward her weak, contralesional (right) side. When repositioned to upright, she braced forcefully with her ipsilesional (left) leg, attempting to reassume a right-leaning orientation.

Spatial neglect greatly increases functional disability and slows recovery from hemiparesis after stroke.<sup>[15]</sup> As part of the neglect syndrome, patients can have a primary problem with moving one arm in one direction (or hemispace), without visual or perceptual deficits (i.e., aiming or motor-intentional spatial neglect). This can occur with frontal and subcortical right brain lesions.<sup>[16]</sup> Spatial-motor neglect after left brain stroke can affect the “unaffected” left arm, so that it is weaker when operating in the neglected, right hemispace.<sup>[17]</sup> Impaired trunk control and body orientation can also be associated with spatial neglect and right brain stroke given its association with damage that includes the left inferior frontal gyrus, middle temporal gyrus, inferior parietal lobule, and/or parietal white matter.<sup>[18]</sup>

## Current Methods of Care or Management

Recovery of function following stroke depends on either restoration or compensatory reorganization of the damaged neural/computational modules supporting particular cognitive domains. Our ability to identify faulty systems and syndromes, however, has outpaced the development and evaluation of specific treatments for these symptoms. Evidence is available for only a limited complement of targeted cognitive rehabilitation treatments.<sup>[19]</sup> Most clinicians are trained to apply generic treatments, and treatment selection may be largely based on their experience and preferences.

In postacute settings, treatments for stroke may focus heavily on compensatory versus restorative strategies.<sup>[20]</sup> This practice dovetails with the rehabilitation field’s heavy reliance on the Functional Independence Measure (FIM) to assess the burden of care caused by an impairment or condition. It is commonly used to provide structure for setting individual treatment goals, evaluating patients’ progress, and facilitating discharge planning (e.g., as reflected in clinical practice guidelines). Unfortunately, the FIM does not distinguish between improvement stemming from recovery of an impaired function versus increased use of compensatory “workarounds” that avoid using the impaired system. Prioritizing compensatory training to attain short-term, general objectives may preclude more resource and time-intensive restorative treatments. In this section, both compensatory and restorative therapies are described.

## Speech and Language

Aphasia affects up to 38% of stroke survivors and responds to speech therapy provided in the early stages of stroke recovery.<sup>[21]</sup> Frequently, speech–language pathologists use both compensatory and restorative approaches to treatment. In an effort to address KR’s

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transcortical motor aphasia (poor fluency, with relatively spared comprehension and relatively spared speech repetition), her speech therapist engaged her with an array of general intervention tasks based on information processing.<sup>[19]</sup> Examples of therapeutic activities included naming objects and describing their function, conversing with the therapist, answering yes/no questions about material read by the therapist, completing sentence stems, selecting words to fit a category, and generating words to match a definition.

KR's therapist addressed concurrent treatment goals; reducing KR's frustration by using compensatory strategies, while also supporting her desire to restore vocal speech. KR's therapist encouraged her to use elliptical speech (i.e., economizing by producing a partial sentence if a full sentence was too difficult).<sup>[22]</sup> She also provided simple compensatory assistive devices, including letter and picture boards that could be used with pointing.

Even with speech therapy, around half of patients with aphasia have persistent problems after one year.<sup>[23]</sup> Compensatory training may contribute to these difficulties. From an information-processing perspective, patients with transcortical motor aphasia benefit most from intensively producing full sentences, accurately including modifiers, conjunctions, and prepositions to the greatest degree possible (i.e., rebuilding the "bottleneck" to speech output).

By practicing alternative methods of communication (e.g., writing words or articulating incomplete, elliptical sentences) during a critical period for stroke recovery, functional remodeling of the impaired information processing stages may be blocked. Notably, if there is a minimum threshold of use required for functional changes in the impaired brain pathway, reaching this level may require more practice trials than can be achieved in the time allotted for speech therapy. In other words, varying tasks within one session (a training approach that is recommended to reduce boredom or frustration) may not provide sufficient intensity of restorative effort. The best outcomes ultimately may be produced by targeting one specific area of function. As an example, KR's therapy session might have eliminated training single-word naming, and instead focused nearly exclusively on sentence generation.

### **Functional Memory**

Deficits in memory caused by stroke can present a significant barrier to independence, especially among patients who do not have family or friends available to provide support. Patients and families are typically familiar with the concept of explicit memory—the ability to intentionally recall information for use. In actuality, the range of cognitive skills affecting functional memory is much broader. For example, deficits in attention may decrease the efficiency with which new information can be processed, and difficulties with problem-solving may cause inefficiencies in developing and using memory search strategies. Together, these can result in retrieval difficulties experienced as "forgetting."

KR's rehabilitation focused on two approaches. First, her physical therapist used repeated practice to teach her ways to safely perform daily activities (e.g., locking wheels before attempting to transfer from the wheelchair). This "overlearning" approach is often combined with a strategic decrease in cuing and increased expectancy that patients can verbalize process steps prior to engaging in the activity. Once taught, KR's safety routines were

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encouraged by all disciplines within the inpatient setting. Additionally, her speech therapist attempted to teach compensatory use and implementation of memory-enhancing tools and cues. These strategies can include memory notebooks or calendars to remember important dates or events, or pillboxes to help patients remember to take their medications. KR was encouraged to use memory tools in the rehabilitation setting. However, she had limited success in applying these independently, due to her self-awareness deficits. KR's family was educated about providing external structure and cuing, such as reminder calls, so that appropriate expectations and plans could be put into place for the next stages of recovery.

A potential problem with rehabilitation strategies used for KR is that training top-down processes depend on the survivor's ability to detect memory failures. KR's unawareness of her deficits, which was evident in her tendency to overestimate her memory accuracy, is common after stroke and affects health and safety.<sup>[24]</sup> When stroke survivors are unaware of cognitive errors, relying on top-down, strategic cuing interventions is inadvisable and additional resources for external support should be explored.

### **Executive Functioning/Skilled Purposive Movement Planning**

Praxis and motor planning systems provide processing efficiency via access to previously constructed complex action programs. If these programs are unavailable, they must be reconstructed each time we encounter the same task.<sup>[25]</sup> Ideomotor apraxia contributes to disability through clumsiness when handling objects.<sup>[26]</sup> Studies using kinematic analysis to deconstruct movement patterns in ideomotor apraxia show abnormal joint angles and limb trajectories when patients pantomime tool use, and the spatial and temporal aspects of their movements are poorly synchronized.<sup>[27]</sup> Remarkably, there has been very little research on treatments for apraxia. Although KR's initial apraxia was mild, it increased the time she needed to complete self-care activities. With therapy, KR regained functional independence for several simple and straightforward daily activities. In contrast, she was unable to master complex tool use or problem-solving tasks (e.g., making an outgoing call).

### **Spatial-motor Functioning**

Occupational and physical therapists used neurodevelopmental training (NDT) approaches with KR. Neurodevelopmental training refers to practices that aim to facilitate motor recovery by capitalizing on neuroplastic processes. Several approaches, including the Bobath Concept that is a core element of NDT training, are based on how children learn movement.<sup>[28]</sup> In recent decades, NDT concepts for stroke have attempted to refocus on neurologic recovery patterns.<sup>[29]</sup> KR's spatial-motor problems—pushing syndrome and impaired spatial-motor limb activation—presented barriers to her returning home even with family assistance. Her therapy used guided practice in an attempt to improve strength, endurance, and standing weight-shifts. After postacute care, she received less intensive therapy but she remained at high risk for falls and accidents during transfers, dressing, and toileting.

## Evidence-based Compensatory or Restorative Treatments

We highlight selected evidence-based treatments and encourage the reader to consult key references, such as the systematic reviews conducted by the Cognitive Rehabilitation Task Force (CRTF) of the American Congress of Rehabilitation Medicine and the Brain Injury Interdisciplinary Special Interest Group. In the 2011 report, 370 studies published from 1971 to 2008 were reviewed, and recommendations made for both TBI and stroke rehabilitation.<sup>[19]</sup>

### Speech and Language

Clinical guidelines for stroke endorse both restorative and compensatory aphasia treatment strategies, and early treatment is recommended.<sup>[30]</sup> Although intensive treatment may improve outcomes, the active components for the most effective treatment are not yet fully characterized.<sup>[21]</sup> One approach to aphasia rehabilitation is *constraint-induced language/aphasia therapy* (CILT/CIAT). This method, which is based on intensive, constraint protocols for arm paralysis (i.e., CIMT),<sup>[31]</sup> proposes that treatment efficacy may be improved by constraining compensatory communication such as gesturing, drawing, or elliptical speech. A typical CIAT intervention follows an intensive activity-training schedule to encourage and shape verbal communication (typically using a card game similar to Go Fish). Studies suggest that even chronic stroke patients can make functionally relevant gains.<sup>[31,32]</sup> However, there is debate about whether current evidence supports broad use of this technique.<sup>[33]</sup>

### Functional Memory

Stages of consciously and intentionally retrieving information (i.e., explicit memory) include encoding, storage, and retrieval. Intact attention and executive control systems are needed to orchestrate these basic processes in everyday functional memory.<sup>[34]</sup> Unfortunately, attempts to use repetitive exercises and drills typically demonstrate that subjects can learn specific material if practiced sufficiently. But improvement rarely generalizes to new contexts.<sup>[35]</sup> In contrast, successes have been demonstrated with approaches targeting attentional and executive control processes. Approaches to enhancing memory may aim to reduce distraction, or increase efficiency of encoding and retrieval. Memory strategy training can include teaching internalized mnemonic strategies<sup>[36]</sup> and behavioral strategies (e.g., always keeping keys in the same place),<sup>[37]</sup> and also external compensatory strategies and tools (e.g., receiving cues during the learning process, then gradually eliminating cues; memory notebook).<sup>[35,38]</sup> For patients with mild to moderate memory deficits, teaching internalized strategies results in improved performance on memory tests.<sup>[39]</sup> However, teaching internalized strategies is ineffective for patients with poor self-awareness, where external compensations such as memory books are recommended instead.<sup>[19]</sup>

Other treatment options include *errorless learning*, in which the therapist structures the learning process to avoid errors. This can be contrasted with *trial-and-error learning*, which encourages guessing.<sup>[40]</sup> Errorless learning may activate implicit memory systems, improving performance even without awareness, even in patients with severe memory problems. In at least one study, it has led to generalized improvements on

neuropsychological tasks.<sup>[41,42]</sup> Targeting interventions to each domain may be needed when multiple areas of attention are affected (i.e., vigilance training to address vigilance deficits, selective attention training for selective attention deficits). Consistent with this reasoning, *attention process training* (ATP) uses a hierarchically organized approach to exercise different components of attention, and has been shown to improve performance after brain injury.<sup>[43]</sup> Interestingly, trials combining ATP with pharmacotherapy or psychotherapy have shown complementary effects, with improvements noted in working and other memory skills, as well as in executive control.<sup>[44]</sup> When impaired executive control manifests as problem-solving deficits and distraction, self-monitoring and self-regulation are critical for learning to live independently with stroke-related disability (e.g., remembering safety instructions when using a walker). *Metacognitive strategy training* strives to enhance these skills and is the practice standard for executive dysfunction in brain injury.<sup>[19,43]</sup>

### **Executive Function/Skilled Purposive Movement Planning**

As reviewed above, stroke may lead to problems organizing and sequencing complex motor tasks independent of attention. Because limb apraxia can reflect a loss of prepared movement programs for familiar motor acts, it reduces movement efficiency. New movement programs are needed for every task, no matter how familiar. Inefficiency results in errors in gain, orientation, and coordination of skilled movement, which risks increased functional impairment and caregiver burden.<sup>[45]</sup> At present, there is not enough evidence from intervention studies to compare treatments conclusively. Recent reviews suggest possible benefits from several approaches. *Strategy training* includes verbal cuing by the therapist to aid action initiation and action execution.<sup>[46]</sup> *Direct training*, a therapist-supported method of training daily activities, aims to anticipate and prevent errors, as in errorless training.<sup>[47]</sup> *Gesture training* uses contextual pictures, demonstrated gestures, and pictured gestures to prompt pantomimes.<sup>[48]</sup> The premise is that improved competence in daily life activities will be more likely if gesture training occurs with training for the context in which the gestures are used.<sup>[49]</sup>

### **Spatial-motor Skills**

Spatial-motor function is essential for motor recovery,<sup>[50]</sup> transfers, wheelchair ambulation, self-toileting, and community mobility.<sup>[51]</sup> Spatial-motor capability, and not simply strength, therefore critically influences independence.<sup>[52]</sup> Definitive trials are limited, but there is emerging evidence for treatments of spatial neglect and pusher syndrome, both of which are common in stroke and have significant impact on prognosis. Unfortunately, spatial-motor disorders can be easily missed if visual-spatial screening focuses exclusively on perceptual tasks (e.g., Rey-Osterrieth complex figure). Although many right-hemisphere stroke survivors demonstrate classic “where” unawareness of left-sided stimuli and events, others manifest spatial-motor intention-deficient leftward “aiming” of movements, or problems activating their left side.<sup>[13]</sup>

Visual scanning training, which targets “where” neglect deficits, has been identified as a standard of care.<sup>[19]</sup> Though many variations are used, the crux of visual scanning training is to encourage patients to scan the contralateral visual environment. Unfortunately, methods

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in postacute care may drastically reduce treatment time in comparison with research protocols. Also, if taught directly to patients as a self-initiated and self-monitored strategy, right brain survivors lacking awareness of their spatial neglect are unlikely to be successful with it.<sup>[53]</sup>

Emerging evidence suggests that prism adaptation training may improve spatial-motor intentional “aiming” deficits and the improvements can potentially generalize to real-world functioning.<sup>[7,54]</sup> In prism adaptation training, patients do visual-manual exercises, such as repeated pointing, while seated and wearing prism lenses. The lenses are worn only in session, and “shift” the external world approximately 11 degrees rightward. Success, which is experience-dependent rather than strategic in nature, comes as the patient learns to shift their arm leftward.<sup>[54]</sup>

Although studies examining prism adaptation training in pusher syndrome are not yet available, postural imbalance has been shown to improve after prism adaptation for spatial neglect.<sup>[55]</sup> KR had significant difficulty reaching into left space with her left arm without triggering pushing; prism training might have altered her body-spatial computations. In contrast, KR’s therapist used an NDT approach, in which she encouraged “testing” her sense of upright using environmental cues.<sup>[56]</sup> She was given goal-directed activities, requiring her to reach and grasp objects placed progressively further into left hemispace while seated. In contrast with *explicit* hypothesis-testing, this activity may have introduced *implicit* learning, as her therapist helped her to practice leaning leftward without asking her to do so consciously.

## Interesting Developments in the Therapeutic Pipeline

### Speech and Language

Subcortical and cerebellar network components may influence speech and language. For example, aphasia has been associated with injury to the cerebellar vermis and putamen.<sup>[57,58,59]</sup> These regions are critical components of the extended motor system, and may be particularly important for functions that occur more automatically. To date, improving speech-related, automatic, motor processing has not been a widely implemented focus of stroke rehabilitation. However, when external cuing and implicit learning are components of treatment, such as when training people with aphasia to use “scripts” for common daily life situations,<sup>[60]</sup> putaminal, cerebellar, and other procedural learning systems may be activated.

### Functional Memory

Innovative approaches to training functional memory could exploit the existence of multiple brain memory systems. Procedural or implicit learning (by which we retain how to do something versus what we learned), is motor behavior-based and supported by subcortical brain networks.<sup>[61,62]</sup> Although these systems respond to errorless learning, it is difficult to develop challenging treatment tasks while also preventing errors. In another vein, Libet reported a simple reaction-time experiment, showing motor-related potentials that preceded conscious awareness of volitional action, the results of which suggest that “early decisions” for actions are made automatically within the motor system.<sup>[63]</sup> Treatment could capitalize

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on this process by altering motor cortical activity (e.g., via a brain modulation technique such as transcranial magnetic stimulation) to increase the likelihood that subjects respond correctly during a motor task.<sup>[64]</sup> For instance, if using a forced-choice recall test format where the left-hand option is correct, the trial could be coordinated with right motor cortical stimulation. Procedures to increase errorless responding and help instantiate automatic, procedural memories need to be explored in future research.

### **Executive Function/Skilled Purposive Movement Planning**

Innovative treatments for stroke-related limb apraxia may use new knowledge about brain regions supporting skilled learned purposive movement. Traditional views focus narrowly on the posterior left hemisphere in supporting pantomime to verbal command.<sup>[65]</sup> Gesture pantomime asymmetrically engages left parietal, premotor, and prefrontal structures in right-handers, processes that are independent of the hand used for performing the gestures.<sup>[66,67]</sup> In patients with apraxia who have difficulty pantomiming, the left inferior frontal cortex is a common region of damage.<sup>[68]</sup> Even left-handers (i.e., right hemisphere motor dominance) exhibit left parietal dominance for gestures,<sup>[69]</sup> although this covaries with degree of left speech lateralization.<sup>[70]</sup> The dissociation between praxis and motor dominance is also supported by investigations of left-handed apraxia.<sup>[66,71]</sup> However, we have likely underestimated the role of the right hemisphere in planning and performing daily activities. Goldenberg and colleagues<sup>[72]</sup> provide compelling evidence that planning and organizing daily activities can be compromised by injuries to either hemisphere.<sup>[73]</sup> It is possible that motor behavioral treatments already in use, which propose to stimulate premotor and prefrontal regions bilaterally (e.g., intensive task practice with one or both hands,<sup>[74]</sup> motor imagery,<sup>[75]</sup> or physiologic stimulation of premotor and prefrontal areas<sup>[76]</sup>) might improve action planning and limb praxis in poststroke apraxia. Focused clinical research is needed to investigate limb praxis and functional outcomes.

### **Spatial-motor Skills**

An innovative approach to treating spatial-motor dysfunction includes facilitating the beneficial input of the left hemisphere to accelerate recovery. Several key studies strongly indicate that the left brain can mediate spatial judgments and movements in right versus left body space.<sup>[17,77]</sup> Physiological approaches could be used to stimulate left-brain spatial systems, but tasks that promote left-brain engagement, such as linguistic activities or specific limb movement, might also promote neglect recovery by these mechanisms; additional research is needed. Animal models of poststroke spatial neglect may inform new treatment approaches on the horizon. For example, in rats spatial neglect recovery is accelerated by light deprivation.<sup>[78]</sup> Also, though right cortical networks support many aspects of spatial function, the midbrain (i.e., intermediate and deep layers of the superior colliculus) maps head and eye orienting movements.<sup>[79]</sup> Innovative treatments to improve spatial-motor function might target and modulate collicular-cortical spatial networks.<sup>[80]</sup> In patients with stroke and severe spatial-motor deficits, future treatments might include deep-brain stimulation, or even radioablation to suppress hyperactive subcortical orienting systems.<sup>[81]</sup>

## Summary

Although there is evidence supporting cognitive rehabilitation in stroke, the set of cognitive domains effectively addressed to date has been only a small subset of the problems experienced by stroke survivors. The literature frequently fails to address long-term outcomes and generalization of treatments to typical daily activities. Importantly, a gap remains between investigational treatments and our evolving theories of brain function. Underdevelopment of the evidence base is due, at least in part, to the difficulties associated with conducting large, well-controlled, randomized studies in rehabilitation settings and the challenges presented by individual differences. Given the increasing rates of stroke and our aging population, it is critical that we continue to foster innovation in stroke rehabilitation. Ideally, theoretical developments, including consideration of less traditional brain functions such as those we have discussed, will drive this needed innovation. For the purpose of early investigation, single-subject studies, targeting specific deficits, and with emphasis on long-term functional outcomes, may be a good alternative. Larger, controlled group studies may be most useful when the specifics of treatment efficacy at the individual level are well defined.

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