STROKE (B. OVBIAGELE, SECTION EDITOR)

Reversing the Ruin: Rehabilitation, Recovery, and Restoration After Stroke

Melissa D. Stockbridge[1] · Lisa D. Bunker[1] · Argye E. Hillis[1]

Abstract

Purpose of Review Stroke is a common cause of disability in aging adults. A given individual's needs after stroke vary as a function of the stroke extent and location. The purpose of this review was to discuss recent clinical investigations addressing rehabilitation of an array of overlapping functional domains.

Recent Findings Research is ongoing in the domains of movement, cognition, attention, speech, language, swallowing, and mental health. To best assist patients' recovery, innovative research has sought to develop and evaluate behavioral approaches, identify and refine synergistic approaches that augment the response to behavioral therapy, and integrate technology where appropriate, particularly to introduce and titrate real-world complexity and improve the overall experience of therapy.

Summary Recent and ongoing trials have increasingly adopted a multidisciplinary nature — augmenting refined behavioral therapy approaches with methods for increasing their potency, such as pharmaceutical or electrical interventions. The integration of virtual reality, robotics, and other technological advancements has generated immense excitement, but has not resulted in consistent improvements over more universally accessible, lower technology therapy.

Keywords Stroke · Rehabilitation · Physiatry · Aphasia · Technology

Introduction

An estimated 7.6 million American adults have had a stroke, and projections show that by 2030, an additional 3.4 million will, a 20% increase in prevalence over the next 10 years [1, 2]. However, recent advancements have driven an age-adjusted decrease in death from stroke and complementary increase in demand for rehabilitation [3]. A given individual's needs after stroke vary widely as a function of the stroke extent and location. Motor impairments are the most common [4], but post-stroke cognitive impairments have been estimated in as much as half of surviving adults [5, 6] and may include deficits in reasoning, attention [7, 8], memory [9], and language that significantly contribute to a reduced quality of life [10]. Mental health also has been identified as an important mediating factor for rehabilitation success [11, 12].

Post-stroke recovery is impacted by numerous activity-dependent mechanisms including axonal sprouting [13, 14, 15], dendritic spine elaboration [16, 17], and migration of subventricular stem cells to peri-infarct regions [18, 19, 20]. Synaptic plasticity is the dominant mechanism for recovery. Thus, the basic principles of behaviorally supported neuroplasticity apply; frequent, rigorous, specific exercises lead to recovery of function [21]. The standard of care for post-stroke rehabilitation remains characterized by task-specific and task-oriented training strategies facilitated by a clinician and deployed for 30–60 min per day for each domain (physical and cognitive-linguistic) in the acute phase and tapering over time as a function of recovery and ongoing access to services.

The goal of physiatric research is maximizing the effectiveness and efficiency of supported recovery. This work can be broadly classified in one of three ways. First is the development and evaluation of activities and strategies to facilitate behavioral modification. Second is identification and refinement of synergistic approaches to behavioral therapy that decrease the threshold for long-term potentiation and

---

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

Melissa D. Stockbridge and Lisa D. Bunker are co-first authors.

✉ Melissa D. Stockbridge
md.stockbridge@jhmi.edu

1 Department of Neurology, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Phipps 4, Suite 446, Baltimore, MD 21287, USA

depression through direct manipulations like transcranial direct current stimulation (tDCS) [22, 23, 24] or pharmacological adjuncts [25, 26•]. Finally, there is considerable enthusiasm for the introduction of emerging technology, such as robotics, virtual reality (VR), and gamification for the enhancement of therapy, which offer promising ways of improving rehabilitation adherence. These innovations also allow rehabilitation specialists to introduce and titrate real-world complexity and multifaceted demands, particularly in the inpatient setting. Patients may use these tools in conjunction with other technologies. For example, a patient may engage in a gamified version of a therapy task, meaning it integrates elements like scoring points, rules, puzzles, and competition, typically to increase interest and engagement in the activity's goal, but instead of moving a joystick or pressing keys, the interaction with the task is electromyographically directed, meaning the electrical activity in the patient's muscle is the input used to interact with the task.

Here, we will summarize the recent evidence for novel behavioral strategies, synergistic approaches, and technological enhancements across three key domains of function: mobility, cognition, and language. Mobility research has been substantially strengthened by the bench to bedside pipeline. However, there is a relative dearth of cognitive rehabilitation studies targeting attention, executive function, and memory, let alone positive trials. Despite considerable interest, studies targeting post-stroke language rehabilitation, or the treatment of aphasia, are even more niche and, thus, that much more difficult to design and execute. For this reason, we have incorporated both meta-analyses and systematic reviews, which near-ubiquitously note the paucity of well-controlled, sufficiently powered clinical trials, and descriptions of select ongoing trials into our review in order to best reflect the leading edge of physiatry research.

Strength and Movement

Motor rehabilitation was the subject of a recent comprehensive review [27••], which found that the vast majority of novel intervention strategies resulted in *no statistically significant improvement* in motor outcomes relative to "standard" therapy at the primary endpoint. Null improvements were noted in studies of neuromuscular electrical stimulation, functional strength training, task-oriented training, and modified constraint-induced movement therapy (but see [28] for positive evidence of constraint-induced movement therapy). A review of sensory therapies to improve motor recovery also came up with modest results [29]. Authors noted studies supporting mirror therapy [30] and mental imaging [31, 32] but minimal evidence overall. However, even in the absence of demonstrable improvement over conventional therapy, broadening the diversity of available therapies that

are similarly effective provides patients and clinicians with better tools to respond to individual patient needs and preferences, potentially improving overall outcomes. For example, self-rehabilitation of post-stroke motor function is similarly valuable to conventional therapy [33].

Synergistic approaches to motor rehabilitation have included both tDCS [34, 35] and pharmacology [36, 37, 38] with mixed results, leading authors to highlight the potential value of identifying subgroups to facilitate individualized treatment planning [39]. The strongest evidence for drug therapies comes from serotonergic and dopaminergic drugs [37]; however, no clear pharmacological recommendation has emerged [40]. Intravenous cerebrolysin within 3 days of stroke [41] has been associated with significant upper limb motor improvement and remains a focus of ongoing investigation [42, 43, 44, 45].

Technological therapy enhancements for motor rehabilitation often are used in concert to create an overall experience for patients that is challenging and motivating. Robot-assisted regimens include passive and active therapy, including electromyograph driven exoskeletons [46]. However, efficacy of robotic implementation varies as a function of the robot and the patient's needs and may be prohibitively expensive for certain healthcare settings. Recent feasibility study demonstrated the utility of a home-based robotic system for upper limb rehabilitation [47], and the proliferation of robotics into consumer technology may make this a more promising direction for future work. As of this writing, there are a remarkable number of ongoing clinical trials examining enhancements to traditional motor rehabilitation using robotic exoskeletons with (e.g., NeuroExo NCT05374486; NCT04724824; and NCT04599036) and without (e.g., RESTORE NCT04201613; NCT05226988; NCT04054700; and NCT05174676) brain-machine interface. A few trials have demonstrated feasibility of VR [48] alone, VR combined with a gamified therapy activity [49], and VR combined with electrical stimulation and robotics [50] for upper limb motor recovery. However, a systematic review found insufficient evidence to arrive at a conclusion regarding the utility of VR over and above conventional therapy [51]. In contrast, a meta-analysis of 42 trials examining gamified therapy for upper limb rehabilitation found greater, more retained improvements than those from conventional therapy in function, activity, and participation domains [52].

Cognition and Memory

Cognitive rehabilitation strategies most commonly focus on multiple cognitive domains but occasionally target single capacities in isolation. General cognitive protocols have been associated with modest improvements [53, 54, 55, 56], and additional programs are under investigation (e.g., COMPEX

study, NCT04229056). However, a recent Cochrane review failed to find sufficient evidence that cognitive rehabilitation meaningfully improved selective, sustained, or divided attention either immediately or long term [57], with the possible exception of prism adaptation training [58, 59] and visual scanning training [60] for spatial neglect (see section on neglect below). Memory deficits are generally addressed through the use of compensatory strategies and mnemonic aids, sometimes referred to as "cognitive prosthetics." The proliferation of smartphones and personal computers has revolutionized the kind of support individuals with diverse needs can receive from handheld devices [60, 61] and given rise to new computerized memory training protocols under investigation (e.g., the ASCEND-I study, which combines traditional and gamified elements when targeting working memory; NCT04472351).

tDCS and transcranial magnetic stimulation (TMS) combined with frequent, rigorous, and specific activities have been associated with improvements in cognition. Further, these noninvasive brains stimulation approaches have been found to augment the effects of behavioral therapies targeting executive function [62–64]. More recently, studies have been designed to refine our understanding and use of these tools to optimize their effect. For example, an upcoming trial is planned to examine the effect of anodal tDCS combined with computerized cognitive therapy on memory and executive function in individuals with chronic stroke (TIP-SCI trial, NCT05195398), while a similar design is ongoing that examines anodal tDCS combined with execution of an n-back task for the treatment of memory and attention after stroke (TRAINS trial, NCT04897334).

Pharmacological interventions continue to be considered for the treatment of inattention, particularly cholinergic therapies, such as rivastigmine [65, 66], though there is a marked absence of double-blind, randomized clinical trials. Presently, clinical trials targeting general cognitive improvement are underway using levodopa (NCT03735901) and maraviroc (NCT04966429), and rolflumilast is under investigation specifically for treating post-stroke memory impairment (NCT04854811).

The emergence of increasingly sophisticated VR technology has generated tremendous excitement [67, 68, 69]. Two recent meta-analyses of VR in the treatment of cognitive skills found no benefit over standard of care and noted the paucity of adequately powered trials [70, 71], while a third using more liberal inclusion criteria and did find evidence of a benefit of VR on global cognitive measures [72]. Thus, there remains equipoise with regard to the integration of this technology for cognitive benefit. Overwhelmingly, studies have focused on feasibility and failed to generate sufficient information to compare effects with either traditional rehabilitation or spontaneous recovery [73]. As systems become more affordable and commercially available, this is certain

to be an area of continued inquiry (e.g., NCT04441177 and NCT05283369).

Language, Speech, and Communication

Post-stroke communication impairments (e.g., aphasia, dysarthria, and apraxia of speech [AOS]) can exist together with cognitive deficits or in isolation (e.g., *aphasia*, the impairment of language with spared cognitive function). Left hemisphere disorders, such as aphasia, have by far received the most attention in the intervention literature, but disorders associated with right-hemisphere damage (e.g., aprosodia, or the inability to recognize or produce emotional speech) are also common [74] and can be detrimental to an individual's functional communication. Remediation of communication deficits, to date, is almost exclusively comprised of behavioral interventions, typically delivered face-to-face (although the COVID-19 pandemic did create a monumental shift towards more teletherapy in practice and research). However, with approximately 100 h of SLT needed to significantly improve functional communication [75], interest has turned more and more towards alternative approaches to the recovery of communicative function. These alternative approaches, as with the other common post-stroke impairments, include methods of moderating/enhancing neural activity (e.g., non-invasive brain stimulation or medication) and/or using various technological applications to support recovery. These approaches have not replaced traditional behavioral interventions, but rather typically have been applied in conjunction with them (i.e., as an adjuvant). In all cases of adjuvant approaches discussed in subsequent paragraphs, additional evidence from large RCTs is sorely needed to confirm (or disprove) positive effects on language outcomes.

tDCS and repetitive TMS (rTMS) are the most commonly investigated methods of non-invasive brain stimulation in post-stroke aphasia, with only minimal investigation in motor speech disorders (e.g., [76]). Recent reviews and meta-analyses of tDCS and rTMS have shown accumulating evidence of positive effects on specific language targets, such as naming, but neither can be confidently labeled as effective/efficacious (tDCS: [23, 77, 78, 79, 80]; rTMS: [81, 82, 83, 84]). Likewise, additional study of more functional outcomes and individuals in the subacute phase (particularly for tDCS) also is needed. However, evidence is emerging: for tDCS, see Matar et al. [85] for a recent small-N study showing positive results for discourse and functional communication outcomes [85], Sebastian et al. (in review) for positive results of right cerebellar tDCS on functional communication (NCT02901574), or Stockbridge et al. (in review) for positive effects of left anodal tDCS on discourse in an RCT in subacute aphasia (SLISSE trial,

NCT02674490). Several ongoing/planned RCTs hopefully will contribute additional evidence to support the efficacy of tDCS (e.g., NCT03773406 and NCT04166513) and rTMS (e.g., REMAP trial, NCT04102228).

There is no current consensus on the best site(s) for stimulation, but most positive effects have been associated with stimulating left-hemisphere perilesional areas and/or inhibiting intact right-hemisphere homologues or the right cerebellum [86]. Specific stimulation sites are generally theoretically determined (e.g., LIFG) but can sometimes be anatomically individualized using resting-state magnetoencephalography (rsMEG; [87]), functional MRI [88], or functional near-infrared spectroscopy (fNIRS; [89, 90]) to identify targets. A comparison of traditional sponge-based electrodes or high-definition electrodes (HD-tDCS) showed similar results [91], although the effect of HD-tDCS was limited to a 2 mA current in a double-blinded RCT [92]. For rTMS, most evidence supports 1 Hz (inhibitory) rTMS at about 90% of the resting motor threshold over right pars triangularis, although one study has shown improvement on different outcomes when inhibiting right posterior STG compared to right IFG [93].

Considering that both tDCS and rTMS aim to enhance neuroplastic mechanisms, it is as yet unclear if one method of stimulation is superior in terms of recovery. There have been very few comparative studies of rTMS versus tDCS and results are contradictory (although this is unsurprising given the significant differences in study design, quality, and stimulation parameters/targets; [94, 95]). Additional study comparing the various delivery parameters for both tDCS and rTMS, individually, as well as comparisons between these and other adjuvants therapies, using comparable paradigms is needed. As a whole, the evidence does show that tDCS and rTMS are safe and relatively easy to use, but they rarely have been implemented into clinical practice. The lack of consensus for the optimal parameters remains a significant barrier to implementation, as well as the lack of access and training for SLPs. Indeed, most SLPs report feeling uncomfortable with tDCS [96].

Another stimulation technique is just beginning to be investigated in aphasia: transcranial alternating current stimulation (tACS; see NCT04375722, NCT05194566). This method of stimulation is used to increase connectivity between two target sites—thus, it is not difficult to see the appeal that this method would have for language recovery considering the breadth of the network. Thus far, only one study examining feasibility has been reported [97].

With regard to pharmacological adjuvants to speech/language recovery, current evidence has been expertly summarized in several recent reviews [25, 26•, 98]. Currently, there are no FDA-approved medications for the treatment of aphasia, but there are a few dozen trials primarily focused on catecholamines (e.g., dopamine and epinephrine) or

neurotransmitters such as acetylcholine or serotonin. Few trials have been conducted focused specifically on AOS or dysarthria, although early studies showed conflicting results of dopamine on motor speech, see [99] for review. In general, pharmacological studies have been small and the overall results are mixed but encouraging, warranting further investigation (see [25] for a list of specific drugs recommended for continued investigation). Currently, there are only two ongoing registered drug trials for aphasia: an RCT examining the effect of escitalopram in conjunction with computerized naming therapy (ELISA trial, NCT03843463) and a crossover trial of levetiracetam alone (i.e., not in conjunction with behavioral therapy; NCT00227461). While published drug studies in aphasia focus on identifying positive effects of various drugs on recovery, a recent retrospective study of longitudinal data found no *detrimental* effects of cholinergic, GABAergic, or dopaminergic medications on language recovery [100].

With technological advances and widespread access, investigation into teletherapy and electronic-based tasks/self-practice is rising considerably. The main premise in pursuing technology-assisted therapy is to facilitate access (by reducing costs and/or logistical barriers like location/transportation) and/or increase the amount of practice an individual can complete, given the large number of hours needed to facilitate learning. Good compliance, ease-of-use, and satisfaction have been reported with these studies [101, 102, 103], which is encouraging given a primary motivation of increasing total amount of practice time. Results from VR, telerehabilitation, and computer-/tablet-based treatment studies are overwhelmingly positive, but lack of comparison studies and/or adequate control groups/tasks makes it difficult to identify superior protocols or attribute outcomes to the technological component of the treatment [104, 105]. Some studies have shown similar response to remote delivery as in-person, supporting the notion that teletherapy is a viable and effective option [106–108]. There are also limited data showing better outcomes with computerized self-practice than some traditional approaches/tasks [109, 110], but any conclusions that one approach is collectively better than the other are inappropriate or, at least, premature. VR applications have been successfully used to create opportunities for real-time or simulated social or task-specific interactions with caregivers or other persons with aphasia [111, 112]. In the case of AOS, besides mode of delivery/practice, computer-based programs have also been used for [bio] visual feedback [113]. In general, most treatment evidence in this area comes from aphasia and AOS, but there is an ongoing trial examining tablet-based practice in dysarthria (NCT05146765).

Behavioral interventions have been, and continue to be, the primary means of intervention in post-stroke communication disorders. The breadth of treatment protocols and

targets precludes discussion here, but general trends involve establishing higher levels of evidence for some of the most established protocols (e.g., semantic feature analysis [SFA, see NCT04215952], constraint-induced aphasia therapy (CIAT, [114]), or verb network strengthening treatment [VNeST, NCT05152979]) or to examine optimal dose/frequency/intensity, either generally [115] or for specific protocols (e.g., [116]). The latter question has also prompted investigations of intensive treatment programs where a significant amount of treatment (e.g., 30 h) is provided over a relatively brief period of time (e.g., 2 weeks; NCT04957225, [117, 118]). Such programs report favorable outcomes, including the psychological well-being of participants [119, 120], but the optimal timing of such intensive practice is not known (i.e., acute vs. subacute vs. chronic), especially considering feasibility and tolerance concerns during earlier stages of recovery [121, 122].

There has unfortunately been limited investigation of treatment for communication disorders stemming from right-hemisphere stroke [123] besides cognitive deficits (reported above). Response to a single session of training for affective prosody recognition is reported [124] and an RCT crossover trial treating right-hemisphere communication deficits (aprosodia) is planned (NCT04575909). One previous study reported gains in prosody production with either cognitive-linguistic or imitative therapy [125].

Some researchers have examined the combination of multiple approaches, combining medication, neuromodulation, technology, and/or behavioral language therapy in a single interventional program (combination of medication, tDCS, and behavioral therapy: NCT04134416, [126]), but there is insufficient evidence at this time to draw broad conclusions regarding the benefit of such approaches.

A few other intervention approaches to communication do not quite fit into any of the prior categories but may be of interest to specific providers. These include targeting speech/language and/or psychosocial outcomes through social groups [127], singing groups [128], mental health therapies specifically for persons with communication disorders ([129], NCT04984239), and physical exercise [130].

Swallowing

Traditional dysphagia therapy typically involves behavioral interventions as well as training compensatory strategies (e.g., diet modification or postural adjustments), but recent trends include neurostimulation (both peripheral and central) and biofeedback [131]. Peripheral stimulation includes pharyngeal electrical stimulation (PES) and neuromuscular electrical stimulation (NMES). PES—which is applied intrapharyngeally—has had positive results for tracheotomized individuals with dysphagia post-stroke [132]

but mixed results otherwise. Positive outcomes are reported with NMES—which stimulates muscle contractions externally—when paired with traditional therapy [133]. Central stimulations include tDCS and rTMS. For rTMS, best results are associated with high-frequency (i.e., excitatory) rTMS applied to pharyngeal motor cortex—applied bilaterally or contralesionally [134, 135]. Single anode tDCS (applied to ipsilateral pharyngeal motor cortex with the cathode placed suborbitally or on the contralesional pharyngeal motor cortex) offers minimal benefit [134], while bilateral anodal tDCS (anode applied to both hemispheres with cathodes applied to the contralateral suborbital regions) is more promising [136, 137]. As with neurostimulation in the other modalities, optimal parameters are unclear at this time.

Biofeedback for dysphagia typically involves accelerometry, surface electromyography (sEMG), or tongue manometry, and tasks are often gamified to incentivize participation. While individual studies report positive outcomes, a recent review and meta-analysis found that improvements on the behavior targeted did not translate into improved functional swallowing or decreased tube-feeding/oral supplements [138]. Differences in methodological rigor and study parameters may be contributing to the lack of positive findings, thus additional study is needed to determine the benefit (or lack thereof) of biofeedback approaches.

Attention

Neglect is a multifaceted syndrome that can manifest in a variety of ways [139] with most treatment research addressing unilateral visuospatial neglect. While individuals with persistent neglect may be trained to compensate for attentional biases in some contexts (e.g., reading), there is only limited evidence for effective remediation of the impairment [140, 141•]. A lack of consensus stems, in part, from the many differences that exist across treatment study methodologies, participants, outcome measures, etc. Treatment approaches follow other impairments and involve behavioral modification (e.g., prism adaptation, visual scanning, and mirror therapy), adjuvant neuromodulation (e.g., non-invasive brain stimulation and pharmacological treatment), and technology-based interventions (e.g., robotics training), as well as combinations of these approaches.

Prism adaptation is the most common behavioral approach, and the only approach with modest evidence for the treatment of unilateral visuospatial neglect. Prism goggles are worn during therapeutic tasks to shift visual input to the ipsilesional hemispace. While reviews of prism adaptation treatments report positive effects on objective and functional tasks following treatment [58, 59, 142], a meta-analysis of RCTs did not find improvement on subjective ratings or retention of gains beyond 1 month,

relative to controls [142]. However, this may be due to the relatively small amount of total practice (i.e., most studies administered only about 5 h total over 2 weeks), differences in the prism parameters (i.e., degree of visual shift), or heterogeneity of recovery stage. Visual scanning training (VST) has yielded mixed results [60, 141•]. Evidence for other behavioral approaches, such as mirror therapy, are scant [141•, 143].

Several recent reviews of non-invasive brain stimulation in conjunction with behavioral interventions such as prism adaptation for the treatment of neglect [144, 145] paint a promising picture for rTMS, tDCS, and neuromuscular vibration (NMV, a type of peripheral sensory stimulation intended to implicitly shift the center of attentional processing; [146–149]). Unfortunately, sample sizes, stimulation sites, time-post onset, and other parameters vary such that reliable conclusions regarding the effectiveness of these approaches, especially long-term, remain unclear. Some meta-analyses suggest an advantage for rTMS over tDCS, generally, with excitatory stimulation to the ipsilesional hemisphere and inhibitory stimulation to the contralesional hemisphere yielding equally favorable results [146, 148]. However, a recent RCT showed positive effects, relative to sham, with excitatory tDCS to ipsilesional parietal cortex, but not inhibitory tDCS to contralesional parietal cortex [150]. Evidence for another stimulation technique—continuous theta-burst stimulation (a specific variant of TMS)—is less favorable [148], but perhaps only because there are few studies having investigated it.

Investigation of pharmacological adjuvants follows the same theoretical motivations noted previously, but only a few drug trials were conducted in the last 20 years with regard to neglect. Results are conflicting without positive long-term effects [141•]. The most promising results that may warrant further investigation were for rotigotine (a dopamine agonist; [151, 152]) and guanfacine (a noradrenergic agonist; [153]). We are unaware of any ongoing drug trials for the treatment of unilateral hemispatial neglect.

A single RCT has examined use of robotics for treatment of hemispatial neglect. In that study, a sophisticated robotic toy was placed in neglected space and programmed to interact with the person with neglect. As attention to the device improved, it was moved further and further into neglected space. Participants demonstrated significant improvement on measures of neglect, including performance of activities of daily living, relative to controls, but long-term outcomes were no reported. Another similar study, using an interactive humanoid robot, is ongoing (see NCT05152433). VR applications have limited evidence thus far [141•, 154], but there are ongoing studies to treat neglect in a VR environment (NCT03458611, NCT04651335).

Mental Health

An important caveat to rehabilitation is the frequent and common co-occurrence of post-stroke depression and other neuropsychiatric disorders [155, 156], and their impact on therapy participation and success. For an estimated one in three [156] to five [77] individuals with stroke [157], effective pharmacological and counseling is key to patients experiencing the greatest benefit associated with their rehabilitation therapy. As noted in the prior section, new avenues of research are pursuing the direct treatment of these sequelae for individuals with communication disorders that are notoriously difficult to treat and often excluded from research related to these issues [158].

Conclusions

Rehabilitation after stroke is evolving, with a number of innovative stimulation (sometimes called "electroceutical"), pharmacological, and technological approaches to augment traditional behavioral therapies for the myriad of sequelae of stroke. Most of these augmentations still require large RCTs to demonstrate efficacy and substantial effects on daily function or quality of life.

Declarations

Conflict of Interest Authors report no conflict of interest.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, Boehme AK, Buxton AE, Carson AP, Commodore-Mensah Y. Heart disease and stroke statistics—2022 update: a report from the American Heart Association. Circulation. 2022;145(8):e153–639.
2. Ovbiagele B, Goldstein LB, Higashida RT, Howard VJ, Johnston SC, Khavjou OA, Lackland DT, Lichtman JH, Mohl S, Sacco RL. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. Stroke. 2013;44(8):2361–75.
3. National Center for Health Statistics, Centers for Disease Control and Prevention. Multiple cause of death, CDC WONDER online databse.

4. Schaechter JD. Motor rehabilitation and brain plasticity after hemiparetic stroke. Prog Neurobiol. 2004;73(1):61–72.

5. Mellon L, Brewer L, Hall P, Horgan F, Williams D, Hickey A, on behalf of the A-Ssg. Cognitive impairment six months after ischaemic stroke: a profile from the ASPIRE-S study. BMC Neurol.;15(1):31.

6. Cumming TB, Marshall RS, Lazar RM. Stroke, cognitive deficits, and rehabilitation: still an incomplete picture. Int J Stroke. 2013;8(1):38–45.

7. Esposito E, Shekhtman G, Chen P. Prevalence of spatial neglect post-stroke: a systematic review. Ann Phys Rehabil Med. 2021;64(5):101459.

8. Suarez A, Saxena S, Oishi K, Oishi K, Walker A, Rorden C, Hillis AE. Influence of age, lesion volume, and damage to dorsal versus ventral streams to viewer- and stimulus-centered hemispatial neglect in acute right hemisphere stroke. Cortex. 2020;126:73–82.

9. Lugtmeijer S, Lammers NA, de Haan EH, de Leeuw F-E, Kessels RP. Post-stroke working memory dysfunction: a meta-analysis and systematic review. Neuropsychol Rev. 2021;31(1):202–19.

10. King RB. Quality of life after stroke. Stroke. 1996;27(9):1467–72.

11. Olaiya MT, Cadilhac DA, Kim J, Nelson MR, Srikanth VK, Andrew NE, Bladin CF, Gerraty RP, Fitzgerald SM, Phan T. Long-term unmet needs and associated factors in stroke or TIA survivors: an observational study. Neurology. 2017;89(1):68–75.

12. Luker J, Lynch E, Bernhardsson S, Bennett L, Bernhardt J. Stroke survivors experiences of physical rehabilitation a systematic review of qualitative studies. Arch Phys Med Rehabil. 2015;96(9):1698-708 e10.

13. Dancause N, Barbay S, Frost SB, Plautz EJ, Chen D, Zoubina EV, Stowe AM, Nudo RJ. Extensive cortical rewiring after brain injury. J Neurosci. 2005;25(44):10167–79.

14. Overman JJ, Clarkson AN, Wanner IB, Overman WT, Eckstein I, Maguire JL, Dinov ID, Toga AW, Carmichael ST. A role for ephrin-A5 in axonal sprouting, recovery, and activity-dependent plasticity after stroke. Proc Natl Acad Sci. 2012;109(33):E2230–9.

15. Carmichael ST, Kathirvelu B, Schweppe CA, Nie EH. Molecular, cellular and functional events in axonal sprouting after stroke. Exp Neurol. 2017;287:384–94.

16. Brown CE, Murphy TH. Livin' on the edge: imaging dendritic spine turnover in the peri-infarct zone during ischemic stroke and recovery. Neuroscientist. 2008;14(2):139–46.

17. Ueno Y, Chopp M, Zhang L, Buller B, Liu Z, Lehman NL, Liu XS, Zhang Y, Roberts C, Zhang ZG. Axonal outgrowth and dendritic plasticity in the cortical peri-infarct area after experimental stroke. Stroke. 2012;43(8):2221–8.

18. Danilov A, Kokaia Z, Lindvall O. Ectopic ependymal cells in striatum accompany neurogenesis in a rat model of stroke. Neuroscience. 2012;214:159–70.

19. Wang JM. Allopregnanolone and neurogenesis in the nigrostriatal tract. Front Cell Neurosci. 2014;8:224.

20. Merson TD, Bourne JA. Endogenous neurogenesis following ischaemic brain injury: insights for therapeutic strategies. Int J Biochem Cell Biol. 2014;56:4–19.

21. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. 2008.

22. Kang N, Summers JJ, Cauraugh JH. Transcranial direct current stimulation facilitates motor learning post-stroke: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2016;87(4):345–55.

23. Biou E, Cassoudesalle H, Cogné M, Sibon I, De Gabory I, Dehail P, Aupy J, Glize B. Transcranial direct current stimulation in post-stroke aphasia rehabilitation: a systematic review. Ann Phys Rehabil Med. 2019;62(2):104–21.

24. Van Hoornweder S, Vanderzande L, Bloemers E, Verstraelen S, Depestele S, Cuypers K, van Dun K, Strouwen C, Meesen R. The effects of transcranial direct current stimulation on upper-limb function post-stroke: a meta-analysis of multiple-session studies. Clin Neurophysiol. 2021;132(8):1897–918.

25. Berthier ML. Ten key reasons for continuing research on pharmacotherapy for post-stroke aphasia. Aphasiology. 2021;35(6):824–58.

26.• Stockbridge MD. Better language through chemistry: augmenting speech-language therapy with pharmacotherapy in the treatment of aphasia. Handb Clin Neurol. 2022;185:261–72. **Review of the history of drug trials in the treatment of communication.**

27.•• Stinear CM, Lang CE, Zeiler S, Byblow WD. Advances and challenges in stroke rehabilitation. The Lancet Neurology. 2020;19(4):348–60. **Scoping review of recent developments in stroke rehabilitation.**

28. Peurala SH, Kantanen MP, Sjögren T, Paltamaa J, Karhula M, Heinonen A. Effectiveness of constraint-induced movement therapy on activity and participation after stroke: a systematic review and meta-analysis of randomized controlled trials. Clin Rehabil. 2012;26(3):209–23.

29. Arya KN, Pandian S, Joshi AK, Chaudhary N, Agarwal G. Active sensory therapies enhancing upper limb recovery among poststroke subjects: a systematic review. Annals of Neurosciences. 2022:09727531221086732.

30. Arya KN, Pandian S, Puri V. Mirror illusion for sensori-motor training in stroke: a randomized controlled trial. J Stroke Cerebrovasc Dis. 2018;27(11):3236–46.

31. De Diego C, Puig S, Navarro X. A sensorimotor stimulation program for rehabilitation of chronic stroke patients. Restor Neurol Neurosci. 2013;31(4):361–71.

32. Azad A, Mahmodi A, Arani-Kashani Z. Effect of motor imagery training with sensory feedback on sensory-motor function of the upper extremity in patients with chronic stroke. J Babol Univ Med Sci. 2018;20(9):28–35.

33. Everard G, Luc A, Doumas I, Ajana K, Stoquart G, Edwards MG, Lejeune T. Self-rehabilitation for post-stroke motor function and activity—a systematic review and meta-analysis. Neurorehabil Neural Repair. 2021;35(12):1043–58.

34. Elsner B, Kugler J, Pohl M, Mehrholz J. Transcranial direct current stimulation for activities after stroke: what is the updated evidence? Stroke. 2021;52(7):e358–9.

35. Alabdulaali L, Hickman L, Punt TD, Jenkinson N. Effectiveness of transcranial direct current stimulation on hand dexterity in stroke patients: a protocol for a systematic review and meta-analysis. BMJ Open. 2022;12(2):e056064.

36. Viale L, Catoira NP, Di Girolamo G, González CD. Pharmacotherapy and motor recovery after stroke. Expert Rev Neurother. 2018;18(1):65–82.

37. Cramer SC. Drugs to enhance motor recovery after stroke. Stroke. 2015;46(10):2998–3005.

38. Chollet F, Tardy J, Albucher J-F, Thalamas C, Berard E, Lamy C, Bejot Y, Deltour S, Jaillard A, Niclot P. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. The Lancet Neurology. 2011;10(2):123–30.

39. Hordacre B, McCambridge AB, Ridding MC, Bradnam LV. Can transcranial direct current stimulation enhance poststroke motor recovery?: development of a theoretical patient-tailored model. Neurology. 2021;97(4):170–80.

40. Richards LG, Cramer SC. Advances in stroke recovery therapeutics. Stroke. 2022;53(1):260–3.

41. Muresanu DF, Heiss W-D, Hoemberg V, Bajenaru O, Popescu CD, Vester JC, Rahlfs VW, Doppler E, Meier D, Moessler H. Cerebrolysin and recovery after stroke (CARS): a randomized,

placebo-controlled, double-blind, multicenter trial. Stroke. 2016;47(1):151–9.

42. Bornstein NM, Guekht A, Vester J, Heiss W-D, Gusev E, Hoemberg V, Rahlfs VW, Bajenaru O, Popescu BO, Muresanu D. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. Neurol Sci. 2018;39(4):629–40.

43. Guekht A, Heiss D, Gusev E, Vester J, Doppler E, Muresanu D. Cerebrolysin and recovery after stroke (CARS 2): a randomized, placebo-controlled, double-blind, multicenter clinical study. J Neurol Sci. 2015;357:e103.

44. Guekht A, Vester J, Heiss W-D, Gusev E, Hoemberg V, Rahlfs VW, Bajenaru O, Popescu BO, Doppler E, Winter S. Safety and efficacy of Cerebrolysin in motor function recovery after stroke: a meta-analysis of the CARS trials. Neurol Sci. 2017;38(10):1761–9.

45. Chang WH, Lee J, Shin Y-I, Ko M-H, Kim DY, Sohn MK, Kim J, Kim Y-H. Cerebrolysin combined with rehabilitation enhances motor recovery and prevents neural network degeneration in ischemic stroke patients with severe motor deficits. J Personalized Med. 2021;11(6):545.

46. Qassim HM, Wan HW. A review on upper limb rehabilitation robots. Appl Sci. 2020;10(19):6976.

47. Guillén-Climent S, Garzo A, Muñoz-Alcaraz MN, Casado-Adam P, Arcas-Ruiz-Ruano J, Mejías-Ruiz M, Mayordomo-Riera FJ. A usability study in patients with stroke using MERLIN, a robotic system based on serious games for upper limb rehabilitation in the home setting. J Neuroeng Rehabil. 2021;18(1):1–16.

48. Ellis F. Investigation of virtual reality as a new model of delivery for evidence-based stroke rehabilitation: University of East Anglia; 2020.

49. Alves C, Rezende A, Marques I, Silva D, Paiva T, Naves E, editors. Serious games and virtual reality in the treatment of chronic stroke: both sides rehabilitation. Brazilian Congress on Biomedical Engineering; 2022: Springer.

50. Norouzi-Gheidari N, Archambault PS, Monte-Silva K, Kairy D, Sveistrup H, Trivino M, Levin MF, Milot M-H. Feasibility and preliminary efficacy of a combined virtual reality, robotics and electrical stimulation intervention in upper extremity stroke rehabilitation. J Neuroeng Rehabil. 2021;18(1):1–10.

51. Ellis F, Kennedy NC, Hancock NJ, Pomeroy VM. Neurophysiological changes accompanying reduction in upper limb motor impairments in response to exercise-based virtual rehabilitation after stroke: systematic review. Physiotherapy. 2021;113:141–52.

52. Doumas I, Everard G, Dehem S, Lejeune T. Serious games for upper limb rehabilitation after stroke: a meta-analysis. J Neuroeng Rehabil. 2021;18(1):1–16.

53. Bogdanova Y, Yee MK, Ho VT, Cicerone KD. Computerized cognitive rehabilitation of attention and executive function in acquired brain injury: a systematic review. J Head Trauma Rehabil. 2016;31(6):419.

54. Van de Ven RM, Murre JM, Veltman DJ, Schmand BA. Computer-based cognitive training for executive functions after stroke: a systematic review. Front Hum Neurosci. 2016;10:150.

55. Poulin V, Korner-Bitensky N, Bherer L, Lussier M, Dawson DR. Comparison of two cognitive interventions for adults experiencing executive dysfunction post-stroke: a pilot study. Disabil Rehabil. 2017;39(1):1–13.

56. Wolf TJ, Polatajko H, Baum C, Rios J, Cirone D, Doherty M, McEwen S. Combined cognitive-strategy and task-specific training affects cognition and upper-extremity function in subacute stroke: an exploratory randomized controlled trial. Am J Occup Ther. 2016;70(2):7002290010p1-p10.

57. Loetscher T, Potter KJ, Wong D, das Nair R. Cognitive rehabilitation for attention deficits following stroke. Cochrane Database Syst Rev. 2019(11).

58. Champod AS, Frank RC, Taylor K, Eskes GA. The effects of prism adaptation on daily life activities in patients with visuospatial neglect: a systematic review. Neuropsychol Rehabil. 2018;28(4):491–514.

59. Barrett A, Houston K. Update on the clinical approach to spatial neglect. Curr Neurol Neurosci Rep. 2019;19(5):1–8.

60. Cicerone KD, Goldin Y, Ganci K, Rosenbaum A, Wethe JV, Langenbahn DM, Malec JF, Bergquist TF, Kingsley K, Nagele D. Evidence-based cognitive rehabilitation: systematic review of the literature from 2009 through 2014. Arch Phys Med Rehabil. 2019;100(8):1515–33.

61. Charters E, Gillett L, Simpson G. Efficacy of electronic portable assistive devices for people with acquired brain injury: a systematic review. Neuropsychol Rehabil. 2015;25(1):82–121.

62. Yuan-Wen L, Zhong-Hua C, Jing L, Ming-Yu Y, Li-Li L, Yu-De Y, Hai-Qing ZHENG Z-HL, Xi-Quan H. Explore combined use of transcranial direct current stimulation and cognitive training on executive function after stroke. J Rehabil Med. 2021;53(3).

63. Nelson JT, McKinley RA, Golob EJ, Warm JS, Parasuraman R. Enhancing vigilance in operators with prefrontal cortex transcranial direct current stimulation (tDCS). Neuroimage. 2014;85:909–17.

64. Coffman BA, Trumbo M, Flores R, Garcia CM, Van Der Merwe A, Wassermann EM, Weisend MP, Clark VP. Impact of tDCS on performance and learning of target detection: interaction with stimulus characteristics and experimental design. Neuropsychologia. 2012;50(7):1594–602.

65. van der Kemp J, Dorresteijn M, Ten Brink AF, Nijboer TC, Visser-Meily JM. Pharmacological treatment of visuospatial neglect: a systematic review. J Stroke Cerebrovasc Dis. 2017;26(4):686–700.

66. Paolucci S, Nocentini U. An open-label pilot study of the use of rivastigmine to promote functional recovery in patients with unilateral spatial neglect due to first ischemic stroke. Funct Neurol. 2010;25(4):195.

67. Unibaso-Markaida I, Iraurgi I, Ortiz-Marqués N, Amayra I, Martínez-Rodríguez S. Effect of the Wii Sports Resort on the improvement in attention, processing speed and working memory in moderate stroke. J Neuroeng Rehabil. 2019;16(1):1–8.

68. Gamito P, Oliveira J, Coelho C, Morais D, Lopes P, Pacheco J, Brito R, Soares F, Santos N, Barata AF. Cognitive training on stroke patients via virtual reality-based serious games. Disabil Rehabil. 2017;39(4):385–8.

69. Faria AL, Andrade A, Soares L. Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a randomized controlled trial with stroke patients. J Neuroeng Rehabil. 2016;13(1):1–12.

70. Wiley E, Khattab S, Tang A. Examining the effect of virtual reality therapy on cognition post-stroke: a systematic review and meta-analysis. Disabil Rehabil Assist Technol. 2022;17(1):50–60.

71. Khan A, Podlasek A, Somaa F. Virtual reality in post-stroke neurorehabilitation—a systematic review and meta-analysis. Top Stroke Rehabil. 2021:1–20.

72. Chen X, Liu F, Lin S, Yu L, Lin R. Effects of virtual reality rehabilitation training on cognitive function and activities of daily living of patients with post-stroke cognitive impairment: a systematic review and meta-analysis. Arch Phys Med Rehabil. 2022.

73. Champod AS, Eskes GA, Barrett A. Neuropsychological rehabilitation. Neurovascular neuropsychology: Springer; 2020. p. 415–63.

74. Sheppard SM, Stockbridge MD, Keator LM, Murray LL, Blake ML. The company prosodic deficits keep following right hemisphere stroke: a systematic review. J Int Neuropsychol Soc. 2022:1–16.

75. Bhogal SK, Teasell R, Speechley M. Intensity of aphasia therapy, impact on recovery. Database of Abstracts of Reviews of Effects (DARE): quality-assessed reviews [Internet]: Centre for Reviews and Dissemination (UK); 2003.

76. Wang J, Wu D, Cheng Y, Song W, Yuan Y, Zhang X, Zhang D, Zhang T, Wang Z, Tang J, et al. Effects of transcranial direct current stimulation on apraxia of speech and cortical activation in patients with stroke: a randomized sham-controlled study. Am J Speech Lang Pathol. 2019;28(4):1625–37.

77. Elsner B, Kugler J, Mehrholz J. Transcranial direct current stimulation (tDCS) for improving aphasia after stroke: a systematic review with network meta-analysis of randomized controlled trials. J Neuroeng Rehabil. 2020;17:1–11.

78. Alharbi MF, Armijo-Olivo S, Kim ES. Transcranial direct current stimulation (tDCS) to improve naming ability in post-stroke aphasia: a critical review. Behav Brain Res. 2017;332:7–15.

79. Sebastian R, Tsapkini K, Tippett DC. Transcranial direct current stimulation in post stroke aphasia and primary progressive aphasia: current knowledge and future clinical applications. NeuroRehabilitation. 2016;39:141–52.

80. Zettin M, Bondesan C, Nada G, Varini M, Dimitri D. Transcranial direct-current stimulation and behavioral training, a promising tool for a tailor-made post-stroke aphasia rehabilitation: a review. Front Hum Neurosci. 2021;15:742136.

81. Zhang J, Zhong D, Xiao X, Yuan L, Li Y, Zheng Y, Li J, Liu T, Jin R. Effects of repetitive transcranial magnetic stimulation (rTMS) on aphasia in stroke patients: a systematic review and meta-analysis. Clin Rehabil. 2021;35(8):1103–16.

82. Hong Z, Zheng H, Luo J, Yin M, Ai Y, Deng B, Feng W, Hu X. Effects of low-frequency repetitive transcranial magnetic stimulation on language recovery in poststroke survivors with aphasia: an updated meta-analysis. Neurorehabil Neural Repair. 2021;35(8):680–91.

83. Gholami M, Pourbaghi N, Taghvatalab S. Evaluation of rTMS in patients with poststroke aphasia: a systematic review and focused meta-analysis. Neurol Sci. 2022.

84. Yao L, Zhao H, Shen C, Liu F, Qiu L, Fu L. Low-frequency repetitive transcranial magnetic stimulation in patients with poststroke aphasia: systematic review and meta-analysis of its effect upon communication. J Speech Lang Hear Res. 2020;63(11):3801–15.

85. Matar SJ, Newton C, Sorinola IO, Pavlou M. Transcranial direct-current stimulation as an adjunct to verb network strengthening treatment in post-stroke chronic aphasia: a double-blinded randomized feasibility study. Front Neurol. 2022;13:722402.

86. Sebastian R, Kim JH, Brenowitz R, Tippett DC, Desmond JE, Celnik PA, Hillis AE. Cerebellar neuromodulation improves naming in post-stroke aphasia. Brain Communications. 2020;2(2).

87. Shah-Basak PP, Sivaratnam G, Teti S, Francois-Nienaber A, Yossofzai M, Armstrong S, Nayar S, Jokel R, Meltzer J. High definition transcranial direct current stimulation modulates abnormal neurophysiological activity in post-stroke aphasia. Sci Rep. 2020;10(1):19625.

88. Szaflarski JP, Nenert R, Allendorfer JB, Martin AN, Amara AW, Griffis JC, Dietz A, Mark VW, Sung VW, Walker HC, et al. Intermittent theta burst stimulation (iTBS) for treatment of chronic post-stroke aphasia: results of a pilot randomized, double-blind, sham-controlled trial. Med Sci Monit. 2021;27:e931468.

89. Hara T, Abo M, Kakita K, Mori Y, Yoshida M, Sasaki N. The effect of selective transcranial magnetic stimulation with functional near-infrared spectroscopy and intensive speech therapy on individuals with post-stroke aphasia. Eur Neurol. 2017;77(3–4):186–94.

90. Chang WK, Park J, Lee J-Y, Cho S, Lee J, Kim W-S, Paik N-J. Functional network changes after high-frequency rTMS over the most activated speech-related area combined with speech therapy in chronic stroke with non-fluent aphasia. Front Neurol. 2022;13.

91. Richardson J, Datta A, Dmochowski J, Parra LC, Fridriksson J. Feasibility of using high-definition transcranial direct current stimulation (HD-tDCS) to enhance treatment outcomes in persons with aphasia. NeuroRehabilitation. 2015;36(1):115–26.

92. Fiori V, Nitsche MA, Cucuzza G, Caltagirone C, Marangolo P. High-definition transcranial direct current stimulation improves verb recovery in aphasic patients depending on current intensity. Neuroscience. 2019;406:159–66.

93. Ren C, Zhang G, Xu X, Hao J, Fang H, Chen P, Li Z, Ji Y, Cai Q, Gao F. The effect of rTMS over the different targets on language recovery in stroke patients with global aphasia: a randomized sham-controlled study. Biomed Res Int. 2019;2019:4589056.

94. Razmyslovich A, Buivolova O, Samoukina A, Abramova T, Iskra E, Ivanova E, Ivanova M, Pakholiuk O, Pozdniakova V, Shlyakhova A, et al. Combination of verb network strengthening treatment with TMS and tDCS: preliminary results. Russian J Cognitive Sci. 2021;8(3):33–45.

95. Zumbansen A, Black SE, Chen JL, Edwards JD, Hartmann A, Heiss W-D, Lanthier S, Lesperance P, Mochizuki G, Paquette C, et al. Non-invasive brain stimulation as add-on therapy for subacute post-stroke aphasia: a randomized trial (NORTHSTAR). European Stroke J. 2020;5(4):402–13.

96. Keator LM, Basilakos A, Rorden C, Elm J, Bonilha L, Fridriksson J. Clinical implementation of transcranial direct current stimulation in aphasia: a survey of speech-language pathologists. Am J Speech Lang Pathol. 2020;29(3):1376–88.

97. Keator L. Transcranial alternating current stimulation as an adjuvant for nonfluent aphasia therapy: a proof of concept study. Scholar Commons: University of South Carolina; 2022.

98. Picano C, Quadrini A, Pisano F, Marangolo P. Adjunctive approaches to aphasia rehabilitation: a review on efficacy and safety. Brain Sci. 2021;11(1):41.

99. Small SL. Pharmacotherapy of aphasia. A critical review Stroke. 1994;25(6):1282–9.

100. Stockbridge MD, Keser Z, Bunker LD, Hillis AE. No evidence of impediment by three common classes of prescription drugs to post-stroke aphasia recovery in a retrospective longitudinal sample. PLoS ONE. 2022;17(6):e0270135.

101. De Cock E, Batens K, Feiken J, Hemelsoet D, Oostra K, De Herdt V. The feasibility, usability and acceptability of a tablet-based aphasia therapy in the acute phase following stroke. J Commun Disord. 2021;89:106070.

102. Cherney LR, Lee JB, Kim K-YA, van Vuuren S. Web-based oral reading for language in aphasia (Web ORLA®): a pilot randomized control trial. Clin Rehabil. 2021;35(7):976–87.

103. Mitchell C, Bowen A, Tyson S, Conroy P. A feasibility randomized controlled trial of ReaDySpeech for people with dysarthria after stroke. Clin Rehabil. 2017;32(8):1037–46.

104. Repetto C, Paolillo MP, Tuena C, Bellinzona F, Riva G. Innovative technology-based interventions in aphasia rehabilitation: a systematic review. Aphasiology. 2021;35(12):1623–46.

105. Weidner K, Lowman J. Telepractice for adult speech-language pathology services: a systematic review. Perspect ASHA Spec Interes Groups. 2020;5(1):326–38.

106. Peñaloza C, Scimeca M, Gaona A, Carpenter E, Mukadam N, Gray T, Shamapant S, Kiran S. Telerehabilitation for word retrieval deficits in bilinguals with aphasia: effectiveness and reliability as compared to in-person language therapy. Front Neurol [Internet]. 2021 2021; 12:[589330 p.].

107. Cacciante L, Kiper P, Garzon M, Baldan F, Federico S, Turolla A, Agostini M. Telerehabilitation for people with aphasia: a systematic review and meta-analysis. J Commun Disord. 2021;92:106111.

108. Meltzer JA, Baird AJ, Steele RD, Harvey SJ. Computer-based treatment of poststroke language disorders: a non-inferiority study of telerehabilitation compared to in-person service delivery. Aphasiology. 2018;32(3):290–311.

109. Braley M, Pierce JS, Saxena S, De Oliveira E, Taraboanta L, Anantha V, Lakhan SE, Kiran S. A virtual, randomized, control trial of a digital therapeutic for speech, language, and cognitive intervention in post-stroke persons with aphasia. Front Neurol [Internet]. 2021 2021; 12:[626780 p.].

110 Elhakeem ES, Saeed SSGM, Elsalakawy RNA-E, Elmaghraby RM, Ashmawy GAHO. Post-stroke aphasia rehabilitation using computer-based Arabic software program: a randomized controlled trial. Egyptian J Otolaryngol. 2021;37(1):77.

111. Marshall J, Booth T, Devane N, Galliers J, Greenwood H, Hilari K, Talbot R, Wilson S, Woolf C. Evaluating the benefits of aphasia intervention delivered in virtual reality: results of a quasi-randomised study. PLoS ONE. 2016;11(8):e0160381.

112. Grechuta K, Rubio Ballester B, Espín Munne R, Usabiaga Bernal T, Molina Hervás B, Mohr B, Pulvermüller F, San Segundo R, Verschure P. Augmented dyadic therapy boosts recovery of language function in patients with nonfluent aphasia. Stroke. 2019;50(5):1270–4.

113. Wambaugh JL. An expanding apraxia of speech (AOS) treatment evidence base: an update of recent developments. Aphasiology. 2021;35(4):442–61.

114. Szaflarski JP, Ball AL, Vannest J, Dietz AR, Allendorfer JB, Martin AN, Hart K, Lindsell CJ. Constraint-induced aphasia therapy for treatment of chronic post-stroke aphasia: a randomized, blinded, controlled pilot trial. Med Sci Monit. 2015;21:2861–9.

115. Harvey S, Carragher M, Dickey MW, Pierce JE, Rose ML. Dose effects in behavioural treatment of post-stroke aphasia: a systematic review and meta-analysis. Disabil Rehabil. 2022;44(12):2548–59.

116. Wambaugh JL, Wright S, Nessler C, Mauszycki SC, Bunker L, Boss E, Zhang Y, Hula WD, Doyle PJ. Further study of the effects of treatment intensity on outcomes of sound production treatment for acquired apraxia of speech: does dose frequency matter? Am J Speech Lang Pathol. 2020;29(1):263–85.

117. Breitenstein C, Grewe T, Flöel A, Ziegler W, Springer L, Martus P, Huber W, Willmes K, Ringelstein EB, Haeusler KG, et al. Intensive speech and language therapy in patients with chronic aphasia after stroke: a randomised, open-label, blinded-endpoint, controlled trial in a health-care setting. The Lancet. 2017;389(10078):1528–38.

118. Menahemi-Falkov M, Breitenstein C, Pierce JE, Hill AJ, O'Halloran R, Rose ML. A systematic review of maintenance following intensive therapy programs in chronic post-stroke aphasia: importance of individual response analysis. Disabil Rehabil. 2021:1–16.

119. Griffin-Musick JR, Off CA, Milman L, Kincheloe H, Kozlowski A. The impact of a university-based Intensive Comprehensive Aphasia Program (ICAP) on psychosocial well-being in stroke survivors with aphasia. Aphasiology. 2021;35(10):1363–89.

120. Babbitt EM, Worrall L, Cherney LR. "It's like a lifeboat": stakeholder perspectives of an intensive comprehensive aphasia program (ICAP). Aphasiology. 2022;36(3):268–90.

121. Carpenter J, Cherney LR. Increasing aphasia treatment intensity in an acute inpatient rehabilitation programme: a feasibility study. Aphasiology. 2016;30(5):542–65.

122. Godecke E, Armstrong E, Rai T, Ciccone N, Rose ML, Middleton S, Whitworth A, Holland A, Ellery F, Hankey GJ, et al. A randomized control trial of intensive aphasia therapy after acute stroke: the Very Early Rehabilitation for SpEech (VERSE) study. Int J Stroke. 2020;16(5):556–72.

123. Blake LM. Cognitive communication deficits associated with right hemisphere brain damage. In: Kimbarow ML, editor. Cognitive communication disorders. 3rd ed. San Diego, CA: Plural Publishing; 2021. p. 153–206.

124. Durfee AZ, Sheppard SM, Meier EL, Bunker L, Cui E, Crainiceanu C, Hillis AE. Explicit training to improve affective prosody recognition in adults with acute right hemisphere stroke. Brain Sci. 2021;11(5):667.

125. Rosenbek JC, Rodriguez AD, Hieber B, Leon SA, et al. Effects of two treatments for aprosodia secondary to acquired brain injury. J Rehabil Res Dev. 2006;43(3):379–90.

126. Keser Z, Dehgan MW, Shadravan S, Yozbatiran N, Maher LM, Francisco GE. Combined dextroamphetamine and transcranial direct current stimulation in poststroke aphasia. Am J Phys Med Rehabil. 2017;96(10).

127. Moss B, Behn N, Northcott S, Monnelly K, Marshall J, Simpson A, Thomas S, McVicker S, Goldsmith K, Flood C, et al. "Loneliness can also kill:" a qualitative exploration of outcomes and experiences of the SUPERB peer-befriending scheme for people with aphasia and their significant others. Disabil Rehabil. 2021:1–10.

128. Tarrant M, Carter M, Dean SG, Taylor R, Warren FC, Spencer A, Adamson J, Landa P, Code C, Backhouse A, et al. Singing for people with aphasia (SPA): results of a pilot feasibility randomised controlled trial of a group singing intervention investigating acceptability and feasibility. BMJ Open. 2021;11(1):e040544.

129. Northcott S, Simpson A, Thomas S, Barnard R, Burns K, Hirani SP, Hilari K. "Now I am myself": exploring how people with poststroke aphasia experienced solution-focused brief therapy within the SOFIA trial. Qual Health Res. 2021;31(11):2041–55.

130. Harnish SM, Rodriguez AD, Blackett DS, Gregory C, Seeds L, Boatright JH, Crosson B. Aerobic exercise as an adjuvant to aphasia therapy: theory, preliminary findings, and future directions. Clin Ther. 2018;40(1):35-48.e6.

131. Jones CA, Colletti CM, Ding M-C. Post-stroke dysphagia: recent insights and unanswered questions. Curr Neurol Neurosci Rep. 2020;20(12):61.

132. Dziewas R, Stellato R, van der Tweel I, Walther E, Werner CJ, Braun T, Citerio G, Jandl M, Friedrichs M, Nötzel K, et al. Pharyngeal electrical stimulation for early decannulation in tracheotomised patients with neurogenic dysphagia after stroke (PHAST-TRAC): a prospective, single-blinded, randomised trial. The Lancet Neurology. 2018;17(10):849–59.

133. Alamer A, Melese H, Nigussie F. Effectiveness of neuromuscular electrical stimulation on post-stroke dysphagia: a systematic review of randomized controlled trials. Clin Interv Aging. 2020;15:1521–31.

134. Pisegna JM, Kaneoka A, Pearson WG, Kumar S, Langmore SE. Effects of non-invasive brain stimulation on post-stroke dysphagia: a systematic review and meta-analysis of randomized controlled trials. Clin Neurophysiol. 2016;127(1):956–68.

135. Liao X, Xing G, Guo Z, Jin Y, Tang Q, He B, McClure MA, Liu H, Chen H, Mu Q. Repetitive transcranial magnetic stimulation as an alternative therapy for dysphagia after stroke: a systematic review and meta-analysis. Clin Rehabil. 2017;31(3):289–98.

136. Ahn YH, Sohn H-J, Park J-S, Ahn TG, Shin YB, Park M, Ko S-H, Shin Y-I. Effect of bihemispheric anodal transcranial direct current stimulation for dysphagia in chronic stroke patients: a randomized clinical trial. J Rehabil Med. 2017;49(1):30–5.

137. Li Y, Feng H, Li J, Wang H, Chen N, Yang J. The effect of transcranial direct current stimulation of pharyngeal motor cortex on swallowing function in patients with chronic dysphagia after stroke: a retrospective cohort study. Medicine (Baltimore). 2020;99(10):e19121.

138. Benfield JK, Everton LF, Bath PM, England TJ. Does therapy with biofeedback improve swallowing in adults with dysphagia?

A systematic review and meta-analysis. Arch Phys Med Rehabil. 2019;100(3):551–61.

139. Vuilleumier P. Mapping the functional neuroanatomy of spatial neglect and human parietal lobe functions: progress and challenges. Ann N Y Acad Sci. 2013;1296(1):50–74.

140. Pierce J, Saj A. A critical review of the role of impaired spatial remapping processes in spatial neglect. Clin Neuropsychol. 2019;33(5):948–70.

141.• Umeonwuka C, Roos R, Ntsiea V. Current trends in the treatment of patients with post-stroke unilateral spatial neglect: a scoping review. Disabil Rehabil. 2022;44(11):2158–85. **Thorough review of recent interventions for attention.**

142. Li J, Li L, Yang Y, Chen S. Effects of prism adaptation for unilateral spatial neglect after stroke: a systematic review and meta-analysis. Am J Phys Med Rehabil. 2021;100(6).

143. Tavaszi I, Nagy AS, Szabo G, Fazekas G. Neglect syndrome in post-stroke conditions: assessment and treatment (scoping review). Int J Rehabil Res. 2021;44(1).

144. Müri RM, Cazzoli D, Nef T, Mosimann UP, Hopfner S, Nyffeler T. Non-invasive brain stimulation in neglect rehabilitation: an update. Front Hum Neurosci. 2013;7:248.

145. Làdavas E, Giulietti S, Avenanti A, Bertini C, Lorenzini E, Quinquinio C, Serino A. a-tDCS on the ipsilesional parietal cortex boosts the effects of prism adaptation treatment in neglect. Restor Neurol Neurosci. 2015;33:647–62.

146. Kashiwagi FT, El Dib R, Gomaa H, Gawish N, Suzumura EA, da Silva TR, Winckler FC, de Souza JT, Conforto AB, Luvizutto GJ, et al. Noninvasive brain stimulations for unilateral spatial neglect after stroke: a systematic review and meta-analysis of randomized and nonrandomized controlled trials. Neural Plast. 2018;2018:1638763.

147. Lucente G, Valls-Sole J, Murillo N, Rothwell J, Coll J, Davalos A, Kumru H. Noninvasive brain stimulation and noninvasive peripheral stimulation for neglect syndrome following acquired brain injury. Neuromodulation Technol Neural Interface. 2020;23(3):312–23.

148. Fan J, Li Y, Yang Y, Qu Y, Li S. Efficacy of noninvasive brain stimulation on unilateral neglect after stroke: a systematic review and meta-analysis. Am J Phys Med Rehabil. 2018;97(4).

149. Salazar APS, Vaz PG, Marchese RR, Stein C, Pinto C, Pagnussat AS. Noninvasive brain stimulation improves hemispatial neglect after stroke: a systematic review and meta-analysis. Arch Phys Med Rehabil. 2018;99(2):355-66.e1.

150. da Silva TR, de Carvalho Nunes HR, Martins LG, da Costa RDM, de Souza JT, Winckler FC, Sartor LCA, Modolo GP, Ferreira NC, da Silva Rodrigues JC, et al. Non-invasive brain stimulation can reduce unilateral spatial neglect after stroke: ELETRON trial. Ann Neurol. 2022.

151. Swayne OB, Gorgoraptis N, Leff A, Ajina S. Exploring the use of dopaminergic medication to treat hemispatial inattention during in-patient post-stroke neurorehabilitation. J Neuropsychol. 2022;n/a(n/a).

152. Gorgoraptis N, Mah Y-H, Machner B, Singh-Curry V, Malhotra P, Hadji-Michael M, Cohen D, Simister R, Nair A, Kulinskaya E, et al. The effects of the dopamine agonist rotigotine on hemispatial neglect following stroke. Brain. 2012;135(8):2478–91.

153. Dalmaijer ES, Li KMS, Gorgoraptis N, Leff AP, Cohen DL, Parton AD, Husain M, Malhotra PA. Randomised, double-blind, placebo-controlled crossover study of single-dose guanfacine in unilateral neglect following stroke. J Neurol Neurosurg Psychiatry. 2018;89(6):593–8.

154. Ogourtsova T, Souza Silva W, Archambault PS, Lamontagne A. Virtual reality treatment and assessments for post-stroke unilateral spatial neglect: a systematic literature review. Neuropsychol Rehabil. 2017;27(3):409–54.

155. Edelkraut L, López-Barroso D, Torres-Prioris MJ, Starkstein SE, Jorge RE, Aloisi J, Berthier ML, Dávila G. Spectrum of neuropsychiatric symptoms in chronic post-stroke aphasia. World J Psychiatry. 2022;12(3):450–69.

156. Mitchell AJ, Sheth B, Gill J, Yadegarfar M, Stubbs B, Yadegarfar M, Meader N. Prevalence and predictors of post-stroke mood disorders: a meta-analysis and meta-regression of depression, anxiety and adjustment disorder. Gen Hosp Psychiatry. 2017;47:48–60.

157. Burvill P, Johnson G, Jamrozik K, Anderson C, Stewart-Wynne E, Chakera T. Prevalence of depression after stroke: the Perth Community Stroke Study. Br J Psychiatry. 1995;166(3):320–7.

158. Strong KA, Randolph J. How do you do talk therapy with someone who can't talk? Perspectives from mental health providers on delivering services to individuals with aphasia. Am J Speech Lang Pathol. 2021;30(6):2681–92.