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Language recovery following stroke

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Abstract

Objective: To review the research literature pertaining to poststroke language recovery, and to discuss neurocognitive assessment in patients in the context of aphasia, time course of language recovery, factors associated with language recovery, and therapeutic techniques designed to facilitate language recovery.

Method: Articles were identified through PubMed, MEDLINE, PsychINFO, and Google Scholar searches. Examples of utilized keywords include "post-stroke aphasia," "post-stroke language recovery," "post-stroke neurocognitive assessment," and "neuropsychology and aphasia."

Results: Most language recovery occurs in the first few weeks following stroke, but residual recovery may occur for many years. Although initial aphasia severity is the single largest determinant of post-stroke language recovery, a number of other variables also contribute. Several techniques have been developed to aid in the recovery process including speech-language therapy and noninvasive brain stimulation, although the effectiveness of acute and subacute treatment remains unclear. Some degree of valid neurocognitive assessment is possible in patients with aphasia, and the information gained from such an evaluation can aid the rehabilitative process

Conclusions: Significant recovery of language function is possible following a stroke, but prediction of level of recovery in an individual patient is difficult. Information about initial aphasia severity and the integrity of cognitive domains other than language can help guide the rehabilitation team, as well as manage expectations for recovery.

Keywords

Stroke; aphasia; language recovery; post-stroke neurocognitive assessment

Aphasia and stroke: an overview

In this review paper, we provide a general overview of post-stroke language recovery, with focus given to information and previous studies that are relevant to clinical

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neuropsychologists and other clinicians working in a rehabilitative setting. The review will begin with an introduction to the different types of aphasia syndromes. Next, we will discuss how aphasia can complicate obtaining a valid neuropsychological assessment. Discussion will then turn to research on the time course of language recovery following stroke.

Language is the most prominent of the many forms of human communication. Among its properties, language includes aspects that are not only expressed but also understood. Examples of language properties include semantics (elements of meaning) and structure (syntax and phonology), with examples of meaningful elements including sounds, print, gestural signs, and ideographs. The disordered language production characteristic of aphasia can be differentiated from other components of oral communication. For example, speech dysfunction also can be attributed to dysarthria, which arises from abnormality of the articulatory apparatus (pharynx, palate, tongue and lip), or the motor pathways controlling it (Darley, Aronson, & Brown, 1975). For the sake of this discussion, aphasias will refer to acquired disorders of language, in contrast to those of developmental origin.

The causes of aphasia are numerous, including traumatic brain injury, neurodegenerative disease, brain tumor, and brain infection. The most common cause of aphasia, however, is stroke. According to the American Heart Association, almost 800,000 people suffer a stroke yearly in the US, which equates to one new stroke occurring approximately every 40 seconds (Benjamin et al., 2017). Most strokes do not result in aphasia, but aphasia after stroke is a prevalent phenomenon, occurring in 21%–38% of cases (Berthier, 2005). Aphasia is a complicating factor for post-stroke recovery and is associated with increased length of stay and complications during acute stroke admission (Lazar & Boehme, 2017), as well as greater mortality, morbidity, and cost expenditures (Berthier, 2005).

Three types of aphasia were described in early writings relating to cerebral localization, including Wernicke's (fluent or receptive) aphasia (Wernicke, 1874), Broca's (expressive) aphasia (Broca, 1861), and global aphasia (Lazar & Mohr, 2011). But as recognition increased that aphasia represented an independent clinical syndrome localized in the left hemisphere, deficits were better classified, and types of aphasia were expanded to include anomic aphasia, transcortical aphasia, conduction aphasia, and isolation aphasia (Godefroy, Dubois, Debachy, Leclerc, & Kreisler, 2002; Lazar & Antoniello, 2008; Pashek & Holland, 1988; Pedersen, Vinter, & Olsen, 2004). Using neurocognitive tests to assess for patterns of deficits in aphasia, the frequencies of subtypes of aphasia have been listed as 25%–40% for global aphasia, 10%–14% for Broca's aphasia, 14%–29% for Wernicke's aphasia, 3%–25% for anomic aphasia, and 9%–15% for transcortical, conduction, and isolation/mixed transcortical aphasias (Godefroy et al., 2002; Lazar & Antoniello, 2008; Pashek & Holland, 1988; Pedersen et al., 2004). Studies that do not use strict Western Aphasia Battery (WAB) (Kertesz, 1982) criteria also allow for an "unclassified" aphasia subtype. Estimates of the unclassified subtype range from 12% to 26% and account for the wide variation seen in estimates of anomic aphasia (Godefroy et al., 2002; Lazar & Antoniello, 2008; Pashek & Holland, 1988). Aphasia resulting from stroke is a dynamic process, however, and approximately 30%–60% of patients presenting with one aphasia type will exhibit characteristics of another aphasia type during the recovery period (Lazar & Antoniello, 2008). For example, a very large lesion in the upper division of the left middle cerebral

artery (see below) can produce a global aphasia at the time of acute stroke onset, and evolve over the course of admission to a Broca's aphasia (Mohr, Lazar, & Marshall, 2011).

Aphasia is most commonly associated with brain injury in the left perisylvian network (i.e. inferior frontal gyrus [IFG], middle frontal gyrus [MFG], angular gyrus [AG], supramarginal gyrus [SMG], superior temporal gyrus [STG], middle temporal gyrus [MTG], inferior temporal gyrus [ITG], and supplementary motor area [SMA]), with lesion location being a determining factor in aphasia subtype (Kiran, 2012). With the advent of CT and MR imaging, it has also come to be recognized that subcortical injury, including the thalamus, also results in aphasic syndromes (Damasio, Damasio, Rizzo, Varney, & Gersh, 1982; Graff-Radford, Damasio, Yamada, Eslinger, & Damasio, 1985). Wernicke's aphasia is characterized by impairment of comprehension and impaired language production characterized variously by anomia, circumlocution, semantic and phonemic paraphasias, neologisms, and in some cases, neologistic jargon. In Broca's aphasia, brain damage occurs from very large lesions encompassing much of the frontal and anterior temporal convexity cortex, and extending variously to the post-central cortex, manifested by relatively intact comprehension of speech but impaired ability of oral and written language. In practice, Broca's aphasia typically emerges during the course of recovery from global aphasia. In global aphasia, left perisylvian network damage is more widespread and affects both the ability to produce and comprehend language. Anomic aphasia is associated with damage to the left parietal or temporal lobes, and is characterized by mild word-finding deficits and circumlocution, and is most often seen late during the evolution of earlier, more severe syndromes. Transcortical aphasia can be either sensory or motor. Transcortical sensory aphasia is most often associated with damage in the temporal-parietal-occipital borderzone between the middle and posterior cerebral arteries and is characterized by impaired comprehension and expression but intact repetition and speech fluency. In transcortical motor aphasia, damage is usually located in the frontal lobe of the dominant (usual left) hemisphere and is characterized by marked loss of fluency and simplification of syntax. Conduction aphasia encompasses two subtypes. Reproduction conduction aphasia is characterized by phonemic paraphasias and anomia, has been well reported with small lesions of posterior perisylvian cortex, and may be related, at least in part, to damage to the arcuate fasciculus. Repetition conduction aphasia is characterized by intact repetition by the semantic route (hence inability to repeat non-words) and occurs in the context of large posterior perisylvian lesions. In isolation (or mixed transcortical) aphasia, brain damage results in functional isolation of language areas from other areas of the brain, often by more than one lesion, and is characterized by impaired comprehension and language production, but with good repetition. It is uncommon, however, in the setting of stroke.

Aphasia: post-stroke recovery of language function

Hillis and colleagues (2006) suggested three phases in post-stroke language recovery, defined according to time from stroke onset. The acute phase occurs in the first few hours to days following a stroke and is marked by reperfusion of the damaged brain area. In this phase, a combination of neural plasticity, reduction in edema and metabolic disturbances, and restoration of tissue function underlies functional language gains. It has been found, for example, that large vessel occlusion resulting in both infarcted and ischemic, but not

yet permanently infarcted tissue, produces an aphasic syndrome that matches the entire affected volume. If reperfusion either spontaneously or deliberately rescues the ischemic tissue, aphasia severity lessens to that affected only by the residual infarction (Hillis et al., 2004). In the next few weeks following a stroke, the subacute recovery phase occurs during which functional language gains are driven by neural reorganization such as establishment of alternative networks, synaptic remodeling, and axonal sprouting. In the initial weeks following stroke, an important factor in language recovery is the resolution of diaschisis. During this process, undamaged areas of the brain that have nevertheless lost connectively with damaged areas gradually regain normal synaptic connection strength and background activity. The most important outcome of resolution of diaschisis is recovery of function of previously intact but dysfunctional neurons. Finally, the chronic phase of language recovery begins months to years following stroke and may continue for the duration of the patient's life. Functional language improvement in this phase is marked by compensatory reorganization of cognition, even in the absence of further neural recovery.

Neurocognitive assessment and aphasia

The focus of this review is the recovery of language function following stroke, with emphasis on the analysis of behavior using cognitive measures. In the literature on post-stroke language recovery, most studies only report data about language function, and attention is less commonly given to other cognitive domains. While much of the limited focus given to nonlanguage domains is driven by the nature of the research (i.e. recovery of language function), some of the limited attention is also due to challenges inherent when assessing the cognition of a patient with an acquired language disorder. Nevertheless, we argue that much can be gained from knowledge about a patient's overall cognitive function for neuropsychologists and other practitioners who work in post-stroke rehabilitation. For instance, virtually all aphasia therapies utilize learning and memory, and require visuospatial processing of images, gestures, and written material (Fonseca, Ferreira Joaquim, & Pavão Martins, 2017). Thus, information about the integrity of cognitive domains other than language may help guide the rehabilitation team, as well as manage expectations for recovery.

Although deficits arising from stroke are highly associated with lesion location, it is widely recognized that general cognitive dysfunction is a common post-stroke condition, regardless of the presence or absence of language deficit. In a seminal study by Tatemichi and colleagues, a comprehensive cognitive test battery was administered to 227 patients three months following ischemic stroke (Tatemichi et al., 1994). In comparison to a control group of 240 healthy controls, the stroke group exhibited significantly poorer performance on all administered cognitive measures. After adjusting for demographic variables, impairment (i.e. performance falling below the fifth percentile) estimates ranged from 10.2% to 38.5% on individual tests, with highest rates of impairment occurring in the cognitive domains of auditory spatial attention, language (particularly verbal fluency), memory, and visuospatial ability.

Despite the study by Tatemichi et al. being among the first to describe cognitive deficits in a large sample of patients following stroke, focus was not given to executive function. In a

later study, multiple measures designed to assess executive functions were administered to a group of 256 patients three-to-four months following ischemic stroke (Pohjasvaara et al., 2002). In total, 40.6% of the sample showed at least some level of executive dysfunction, with cognitive deficits being worse for lesions in the anterior (middle and anterior cerebral arteries) circulation. The authors noted that 75 patients were not able to complete the test battery due to fatigue and that visual hemi-neglect and/or visual agnosia made difficult the assessment of executive function in another six patients. Another 32 patients were not assessed due to the presence of severe aphasia. Thus, true rates of executive dysfunction in a general stroke population were likely underestimated.

The above study illustrates well a dilemma in neurocognitive assessment. In the Pohjasvaara and colleagues' study, patients with severe aphasia were excluded because the language deficit could potentially confound performance on the study measures. Fonseca, Ferreira and Martins noted that many traditional cognitive tests require linguistic understanding and/or production that may not be present in a patient with aphasia (Fonseca et al., 2017). Thus, when assessing the cognition of an aphasic patient, priority should be given to initially assessing the actual degree of language competence. Then, the battery should be constructed as to avoid a strong language component, recognizing that some elements of cognition cannot be addressed.

Fonseca and colleagues reviewed cognitive studies in samples of patients with aphasia (Fonseca et al., 2017) and found that although there are many tests designed to measure nonverbal abilities, even these presumably visually-based measures require at least some level of auditory comprehension to understand instructions. Nevertheless, the authors concluded that there exists an "applicability of several nonverbal tests to people with language disorders, which suggests that this evaluation is feasible and therefore that patients with aphasia should not be excluded from studies of vascular or other dementia on the basis of their language impairment alone" (pg. 136) (Fonseca et al., 2017). The authors acknowledge, however, that more standardization of nonverbal test batteries is needed, especially given the relationship between language/speech rehabilitation and cognitive abilities such as attention and nonverbal memory.

Among the 38 studies included in the review by Fonseca and colleagues, the most commonly utilized cognitive measures included memory for figures (i.e. Rey-Osterrieth Complex Figure Test) (Osterrieth, 1944)—which has also been shown to be associated with executive function (Luria & Tsvetkova, 1964; Pillon, 1981)—tests of visual memory span, varying versions of progressive matrices tests, the Wisconsin Card Sorting Test (Heaton, Chelune, Talley, Kay, & Curtiss, 1993), and some measures from the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). Although variable results were found across many reports, most studies showed that patients with aphasia also exhibit impairment on many nonverbal cognitive tests. Yet, only 29% of studies noted poorer performance of aphasia patients on nonverbal cognitive measures when compared to patients who had sustained neurologic injury without a corresponding aphasia syndrome. Fonseca and colleagues concluded that patients with aphasia likely have cognitive deficits that are independent from an underlying language disorder.

Time course of post-stroke language recovery

Early studies investigating the course of language recovery following stroke took place prior to the development of the stroke unit and often did not include patients in the acute phase. As studies began to include more acute stroke patients, however, evidence started to emerge that much of post-stroke language recovery occurred relatively quickly following the initial neurologic insult. In a widely cited article by Pedersen and colleagues, the majority of language recovery occurred within two weeks for patients with mild aphasia, within six weeks for patients with moderate aphasia, and within ten weeks for patients with severe aphasia (Pedersen et al., 2004). In a study that classified aphasia type using the WAB, patients with the following syndromes were followed for up to 24 weeks: 19 Broca's aphasia, 9 Wernicke's aphasia, 14 Global aphasia, 15 anomic aphasia, and 4 conduction aphasia (Bakheit, Shaw, Carrington, & Griffiths, 2007). Of the different aphasia types, patients with Broca's aphasia showed more language recovery than patients with anomic or conduction aphasia at all follow-up testing sessions, and patients with Wernicke's aphasia exhibited more language recovery than patients with anomic, conduction, or global aphasia by week 24. With respect to overall recovery, all aphasia groups showed progressive increases in WAB scores over the course of the study. Rates of improvement peaked at week four but language recovery was seen throughout the duration of the study.

After 3–6 months, rates of post-stroke language recovery appear to be slower, but there is some evidence that residual recovery may occur over the remainder of life. In a study of multiple aspects of language recovery following stroke, 147 patients with aphasia were followed for one year (El Hachioui et al., 2013). Study assessment measures assessed linguistic components (i.e. semantics, phonology, and syntax), verbal communication, and receptive disturbance. Different rates of recovery were observed across study measures. For measures of semantics and syntax, significant improvement did not continue past six weeks. Phonology and receptive language ability improved for up to six months, and verbal communication recovery plateaued at six-month follow-up. Although the rate of recovery significantly flattened after six months in the study by El Hachioui and colleagues, evidence exists that longstanding language recovery is possible in some stroke patients. For instance, visual confrontation naming and phrase length in nonfluent speech has been shown to improve up to 5–12 years following stroke (Naeser et al., 1998). In the same sample, the ability of patients with chronic aphasia to name pictures improved for up to 5–15 years following stroke (Fitzpatrick, Glosser, & Helm-Estabrooks, 1988). The improvement in picture naming endured even after improvement of other language abilities such as single-word auditory comprehension and repetition had stopped.

Factors associated with Post-Stroke recovery of language function

Initial severity of aphasia

Although a great deal of inter-individual variability exists in post-stroke language recovery (Lazar & Antoniello, 2008), it has been shown that the best predictor of recovery is initial aphasia severity (Kertesz & McCabe, 1977; Pedersen et al., 2004; Wade, Hewer, David, & Enderby, 1986). Two studies by Lazar and colleagues illustrate this relationship. In one study, measures of naming, repetition, and comprehension were administered to 22

patients with aphasia 24–72 hours post-stroke and at 90-day follow-up (Lazar, Speizer, Festa, Krakauer, & Marshall, 2008). Those language skills were chosen because they are commonly assessed in clinical settings, have excellent inter-rater reliability, and are well tolerated by patients with language deficits. At baseline testing, naming was the most commonly affected language function, with 15 patients (68%) exhibiting post-stroke decline. Most patients showed deficits in at least two language areas. Overall, language function significantly improved from baseline to follow-up testing. Initial language score was found to be predictive of recovery at 90-day follow-up and accounted for 41% of shared variance. Thus, although much of the variance was accounted for by initial performance, some variance was left to be accounted for by other variables. In a later study, Lazar and colleagues administered subtests of the WAB to 21 patients with aphasia 24–72 hours post-stroke and at 90-day follow-up (Lazar et al., 2010). Patients with severely impaired comprehension were excluded. Similar to the initial study, baseline scores on an abbreviated version of the WAB were found to be highly predictive of performance at 90-day follow-up, accounting for 81% of shared variance. Although the exact reason between the differences in the amount of shared variance reported in the two studies is not able to be determined, it is likely that differences in the measures utilized had some effect.

Lesion size and location

Although initial severity of aphasia well predicts post-stroke language recovery, a number of other factors have also been shown to contribute. One factor is the brain area affected by infarction. Not surprisingly, previous studies have shown that lesions located in sensitive language areas led to a more severe aphasia syndrome and a slower recovery of language function following stroke. In most studies, lesions in the superior temporal gyrus and, in particular, the posterior superior temporal gyrus, are associated with a more pervasive aphasia syndrome and slower language recovery (Alexander, Naeser, & Palumbo, 1990; Demeurisse & Capon, 1987; Hanlon, Lux, & Dromerick, 1999; Kang et al., 2010; Kertesz, Lau, & Polk, 1993; Naeser, Helm-Estabrooks, Haas, Auerbach, & Srinivasan, 1987; Parkinson, Raymer, Chang, Fitzgerald, & Crosson, 2009; Selnes, Knopman, Niccum, Rubens, & Larson, 1983; Watila & Balarabe, 2015). However, novel findings were reported in a study by Parkinson and colleagues, which examined object and action naming in 15 patients with left hemisphere stroke and a corresponding aphasia who completed one of two language treatment programs (Parkinson et al., 2009). Two main findings were noted. First, after controlling for basal ganglia lesion size, patients with greater anterior lesion load performed better on language measures at baseline. Second, when controlling for anterior lesion load, basal ganglia lesion size was predictive of worse naming at baseline and less improvement during treatment. The authors concluded that patients with large anterior cortical lesions but intact basal ganglia may show greater cortical reorganization and corresponding behavioral improvement in post-stroke language function. These authors postulated two mechanisms for the unexpected findings, with both mechanisms involving suppression of frontal activity. However, they noted that the study contained a small number of subjects, was correlational, and was composed of patients with chronic aphasias with substantial naming impairments who did not show good initial language recovery. Moreover, major lesions of the basal ganglia are a sign of occlusion of the middle cerebral artery prior to the birfurcation into the upper and lower divisions. The most obvious direct result of this

occlusion is striatocapsular infarction, often extending into the periventricular white matter. However, the entire cerebral cortical mantel is rendered ischemic to some degree, depending upon the adequacy of collateral circulation supplied in the borderzones by the anterior and posterior cerebral arteries. If the basal ganglia are relatively spared in an MCA stroke, this is evidence that embolism traveled further to the insula cortex or beyond leading to less extensive cortical ischemia (Nadeau & Crosson, 1997).

There appears to be a complex relationship between lesion size and post-stroke language recovery, and varying results are found in the research literature. For example, both Lazar et al. and Laska et al. found that lesion size at stroke onset was not predictive of either aphasia severity or language recovery, nor was able to differentiate between patients who did and did not completely recover language function (Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001; Lazar et al., 2008). However, other studies have noted a significant relationship between lesion size and post-stroke recovery of language function (Heiss, Thiel, Kessler, & Herholz, 2003; Henseler, Regenbrecht, & Obrig, 2014; Kertesz, Harlock, & Coates, 1979; Pedersen, Jorgensen, Nakayama, Raaschou, & Olsen, 1995; Watila & Balarabe, 2015). Nevertheless, lesions located in sensitive brain areas produce more profound aphasia and slower language recovery. Thus, in general, a small lesion in a brain area critical for language function will lead to more initial language deficits and a slower overall recovery of language function than a large lesion in an area less strongly associated with language ability.

Sex

Brain activation during language tasks was investigated in men and women in a seminal article by Shaywitz and colleagues that supported a long-held belief that sex differences existed in language processing (Shaywitz et al., 1995). In males, brain activation was largely lateralized to the left inferior frontal gyrus. In females, brain activation was more diffuse and involved both the left and right inferior frontal gyrus. The differential patterns of brain activation during language tasks between males and females has led to the notion that brain reorganization and compensation following aphasia would be greater in females and lead to a quicker recovery of language function. Evidence supporting this theory, however, has been found to be weak and inconclusive (Watila & Balarabe, 2015). Although some studies have noted better recovery of oral expression (Basso, Capitani, & Moraschini, 1982) and language comprehension (Pizzamiglio, Mammucari, & Razzano, 1985) in female than in male patients with aphasia, most studies have noted no differences in language recovery between the sexes (Godefroy et al., 2002; Inatomi et al., 2008; Lazar et al., 2008; Lendrem & Lincoln, 1985; Pedersen et al., 1995; Seniów, Litwin, & Leśniak, 2009), and one study even noted a moderately increased recovery in males compared to females (Holland, Greenhouse, Fromm, & Swindell, 1989). In addition, as previously noted by Lazar and Antoniello (Lazar & Antoniello, 2008), the lack of greater language impairment in females than in males with right hemisphere stroke (Kertesz & Sheppard, 1981) adds another layer of evidence against the theory that bilateral language representation in females contributes to increased rates of language recovery following stroke.

Handedness

Similar to that of sex, lateralization is central to theories of differences in language recovery in right- handed vs. left-handed patients. Left-handed children show more bilateral representation of language function than do right-handed children (15%–33% compared to 7%–9%, respectively) (Szaflarski et al., 2012), with rates of lateralization being only slightly greater in adults (Szaflarski et al., 2002, 2012; Szaflarski, Holland, Schmithorst, & Byars, 2006). As was shown in relation to sex, the hypothesis that the increased bilateral representation of language function seen in left-handers will lead to increased recovery of language function following stroke has not been well supported (Lazar et al., 2008; Pedersen et al., 1995; Watila & Balarabe, 2015).

Cognitive ability at time of stroke

Cognitive decline and impairment after stroke have been shown in numerous population-based and clinical studies (Dhamoon et al., 2018; Sun, Tan, & Yu, 2014). Yet, the risk posed by cognitive impairment for stroke and the prevalence of cognitive impairment prior to stroke have not been well studied, which is surprising since associations exist between factors that increase stroke risk as well as risk for cognitive decline (e.g. hypertension, microvascular disease, intracranial arterial microatheroma, large vessel atheromatous disease with silent infarction). As part of the Chicago Heath and Aging Project, 7217 older adults (aged ≥65 years old) without a history of stroke underwent neurocognitive assessment at three-year intervals (Rajan, Aggarwal, Wilson, Everson-Rose, & Evans, 2014). Of the sample, 1187 had incident stroke during follow-up. When analyzing the data for markers of risk for subsequent stroke, results showed that lower prestroke cognition was associated with a 61% higher risk of incident stroke. In a later study by Banerjee and colleagues, the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Jorm, 1994) was used to evaluate baseline cognitive impairment in 166 patients with imaging-confirmed intracerebral hemorrhage (Banerjee et al., 2017). Among this group, 41 (24.7%) met the IQCODE threshold for baseline cognitive impairment, which was highly associated with the Boston criteria for probable cerebral amyloid angiopathy (Greenberg et al., 1996). These two studies suggest that the presence of cognitive impairment is likely common prior to stroke, and may pose a significant risk for incident ischemic or hemorrhagic events.

Little seems to be known about the impact of preexisting cognitive impairment on post-stroke language recovery. Some of this knowledge gap is likely due to difficulty obtaining reliable estimates of prestroke cognitive function. Ideally, studies examining the impact of preexisting cognitive decline on post-stroke outcomes would evaluate patients using a comprehensive neurocognitive test battery in close proximity to stroke. However, this would require that neurocognitive assessments be administered at regular intervals for a number of years to a large group of community-dwelling adults. The amount of resources required for such study would be vast and, to our knowledge, only a limited number of these types of studies exist. Nevertheless, methods of retroactively obtaining estimates of cognitive decline are available. In the study by Banerjee and colleagues (Banerjee et al., 2017), informant responses were used to establish the presence or absence of pre-existing cognitive decline via the IQCODE. However, as noted in a Cochrane review by Quinn and colleagues, “although IQCODE test accuracy is in a range that many would consider

"reasonable", in the context of community or population settings the use of the IQCODE alone would result in substantial misdiagnosis and false reassurance" (pg. 1) (Quinn et al., 2014). Nevertheless, even though studies using instruments such as the IQCODE to establish estimates of preinsult cognitive decline have limitations, testable hypotheses could be generated, which could possibly enhance the literature.

Education

Conflicting results have been reported in studies that analyze the effect of education on post-stroke language recovery. In a retrospective study, Connor and colleagues noted that education was associated with aphasia severity but did not affect rate of recovery of language function (Connor, Obler, Tocco, Fitzpatrick, & Albert, 2001). The finding that years of education did not affect post-stroke language recovery was supported by a later prospective study by Lazar and colleagues (Lazar et al., 2008). In contrast to the Connor and colleagues' study, however, Lazar et al. did not find an association between years of education and aphasia severity.

More recent findings by Hillis and Tippet have noted an association between post-stroke language recovery and level of education (Hillis & Tippett, 2014). In a sample of 45 patients with acute left hemisphere ischemic stroke, the WAB was administered on average 35 months after onset of stroke (this contrasts to the 90-day follow-up in the Lazar et al. study). Results showed that WAB quartile was significantly predicted by a model that included education, age, volume of infarct, and antidepressant use, with education showing the strongest effect. From these results, Hillis and Tippet concluded that better recovery from chronic aphasia is associated with higher education.

Hillis and Tippet reported being surprised by their findings and set out to determine if education might also be associated with better recovery of other cognitive abilities. The authors chose to evaluate spatial attention (i.e. hemispatial neglect) after right hemisphere stroke. Baseline testing took place approximately one day following stroke and at a mean of 32 weeks following initial testing. The extent of recovery in stimulus-centered neglect was associated with education and initial neglect severity. Results also showed that degree of recovery in viewer-centered neglect was associated with education and initial severity of neglect. There was a significant correlation between education and accuracy in stimulus detection at follow-up, but not at baseline.

Premorbid intelligence

For purposes of exposition, premorbid intelligence refers here to estimated intelligence prior to neurologic compromise (e.g. stroke). Similar to establishing the presence of prestroke cognitive decline and impairment, obtaining an estimate of premorbid intelligence prior to stroke is difficult. Under ideal conditions, establishing an estimate of premorbid intelligence would involve obtaining the results of a cognitive evaluation administered to the patient prior to stroke, which is rarely performed in the absence of other pathology.

Other methods have been devised to obtain estimates of premorbid intelligence. For example, reading ability does not significantly differ in relation to healthy controls even in older adults diagnosed with mild dementia (McGurn et al., 2004), and measures such as the

National Adult Reading Test (NART) (Nelson, 1982) have been designed to help researchers and clinicians estimate premorbid intelligence. The NART contains low-frequency/irregular English words that the patient is instructed to read aloud. The number of words pronounced correctly comprise a total score. Normative data correcting for age, gender, and education are available (Kiely et al., 2011). Post-stroke aphasia can affect oral reading, however, rendering this method of obtaining premorbid intelligence less useful. In addition, reading in the setting of left-hemisphere stroke can also be affected by a visual field defect resulting from infarction in the optic pathways (supplied by the inferior division of the left middle cerebral artery). Thus, methods of obtaining premorbid intelligence estimates in the context of aphasia not reliant on reading estimates would appear to be more valid. Statistical models have been designed to estimate premorbid intelligence from demographic variables that have been shown to be superior to clinical judgment, and statistically associated with results of intelligence testing (Crawford, Millar, & Milne, 2001). To our knowledge, studies utilizing these types of statistical models to establish premorbid intelligence to determine its impact on post-stroke language recovery have yet to be conducted.

A note on conflicting results in aphasia studies

It should be noted that the available research literature on aphasia is replete with studies that yielded conflicting conclusions because the sample sizes were small and, thus, not representative of the general population.

Techniques designed to improve or accelerate Post-Stroke language recovery

Speech therapy

In a 1999 Cochrane analysis, Greener and colleagues examined 12 randomized controlled trials in speech therapy and noted inconclusive results about overall effectiveness (Greener, Enderby, & Whurr, 1999). Since that review, however, evidence began to accumulate that speech therapy is an effective method of enhancing post-stroke language recovery. In a later Cochrane review by Brady and colleagues, 57 randomized controlled trials involving 3002 participants were analyzed. (Brady, Kelly, Godwin, Enderby, & Campbell, 2016). In contrast to the earlier review by Greener et al., Brady et al. noted a number of aspects in which speech therapy appeared effective. For instance, speech therapy resulted in clinically and statistically significant benefits in “functional communication” in reading, writing, and expressive language. Although benefits were not evident at long-term follow-up, follow-up studies were fewer in number. In studies comparing different methods of delivering speech therapy (38 studies involving 1242 patients), high-intensity speech therapy (many hours of therapy over a short time span) was found to aid in functional language use and to reduce aphasia severity compared to low-intensity speech therapy. Attrition rates, however, were higher in the high-intensity groups.

Another question about the effectiveness of post-stroke speech therapy relates to generalizability. As noted in a chapter by Nadeau (2014), most speech therapy is designed to treat anomia and more than 160 trials for the treatment of anomia following stroke have been conducted. Nadeau noted that results of a meta-analysis of word-finding treatments

for aphasia showed that although strong gains were found for words used during the course of treatment (treated words), only a small-to-medium effect size was found for words encountered outside of the therapeutic setting, regardless of the presence or absence of a semantic or phonologic similarity with the treated words (Wisenburn & Mahoney, 2009). Gains made for treated words remained fairly stable over the course of three months. However, a sharp decline in gain for untreated words was seen. Nadeau concluded, “thus, we have strong empirical evidence that currently used therapies do not yield enduring generalization to untrained stimuli,” and that “only broadly generalizing treatments can enhance the ability of the patient to flexibly communicate verbally regardless of context—the true measure of rehabilitative success” (pg. 67). Nadeau further suggests alternatives to conventional speech-therapy that have potential to achieve broad generalization. For instance, phonologic sequence therapy and semantic therapy may lead to increased generalization because treated and untreated material share common features (Edmonds, Mammino, & Ojeda, 2014; Kendall, Oelke, Brookshire, & Nadeau, 2015).

Transcranial magnetic stimulation

In transcranial magnetic stimulation (TMS), magnetic fields are used to generate a small electrical current in the brain. A number of factors influence the effectiveness of TMS including stimulus intensity, pulse frequency, coil configuration, and distance between the coil and the cortex (Coslett, 2016). TMS is most useful for stimulating cortex that is close to the skull and may be administered as a single pulse or as a series of pulses (repetitive TMS [rTMS]) (Coslett, 2016). In contrast to single-pulse TMS, the effects of rTMS are longer lasting but rarely last more than an hour when conducted in a single session (Coslett, 2016). When administered in a series of sessions, however, rTMS effects may extend far longer (Coslett, 2016; Pascual-Leone et al., 1998).

Coslett reviewed TMS studies designed to ameliorate aphasia (Coslett, 2016). In total, 22 studies with over 200 patients with post-stroke aphasia were included. Since 2011, nine of these studies have included both a control group and a group blinded to treatment condition. Only 10 of the studies included more than 10 patients. The rTMS paradigm pioneered by Naeser and colleagues (1-Hz stimulation at 90% of motor threshold to the right IFG) (Naeser et al., 2005, 2012) was employed in addition to speech therapy over the course of several weeks in three of these studies (Barwood et al., 2012; Medina et al., 2012; Thiel et al., 2013). Results showed 20%–30% improvement from baseline on verbal tasks (e.g. naming, picture description) over the course of 6–10 months. In the review, Coslett calculated effect sizes for studies that reported data on picture naming. The average effect size was 0.379, with a range of 0.181 to 0.889. When effect sizes were only calculated for studies that used inhibitory right IFG stimulation, a mean effect size of 0.584 was found.

Coslett went on to review variables that may impact the effectiveness of rTMS as a therapy for aphasia. With respect to other rTMS paradigms, Coslett noted that although most studies have used the approach designed by Naeser and colleagues, a number of other designs have been tested. However, evaluation of the effectiveness of TMS therapy for aphasia is complicated by the high variability seen in the research literature (e.g. aphasia type, aphasia chronicity, site of stimulation, TMS stimulation parameters, and the use of speech therapy in

conjunction with TMS). rTMS was noted to be more effective for nonfluent (anterior) versus fluent (posterior) aphasia, but it was reported that the available studies have not classified aphasia type well enough for definite conclusions to be made. Inhibitory stimulation to the right inferior frontal gyrus seemed to produce reliable benefits but the extent of variations in study design made it difficult to derive optimal therapeutic doses. In general, rTMS appeared to be more beneficial in patients with severe aphasia. It remains unclear the extent to which patients with mild or profound aphasia may receive benefit.

Transcranial direct current stimulation

In transcranial direct current stimulation (tDCS), electrodes are used to deliver a small electrical current to the brain. As with TMS, Anodal tDCS is most often used to increase excitability in left hemisphere language areas (Coslett, 2016; Sebastian, Tsapkini, & Tippett, 2016). tDCS has several practical advantages over rTMS, including being less expensive, allowing for easier administration, and being more conducive for study blinding (Sebastian et al., 2016). tDCS as an aphasia therapy has been examined in two reviews (Coslett, 2016; Sebastian et al., 2016). Due to significant variation in methods, effectiveness was evaluated across a number of variables in both reviews. With regard to electrode placement/stimulation area, two paradigms have largely been used (i.e. facilitating activity in the lesioned/perilesional areas and downregulating activity in the right hemisphere) but superiority of effectiveness of either paradigm is currently not established (Coslett, 2016; Sebastian et al., 2016). Stimulation intensity and duration are fairly consistent in the available literature (between 1 mA and 2 mA), but tDCS applied for 20 minutes appears to be superior to tDCS applied for 10 minutes (Sebastian et al., 2016). Both reviews noted that a major limitation is the lack of studies with long-term follow-up. Finally, in terms of overall outcome, as noted by Coslett, 2016, almost all studies have reported effectiveness, but significant variability exists about the level of effectiveness. In addition, Coslett noted that effect sizes are typically not reported in tDCS studies, but that effect sizes were able to be calculated from studies that provided information about changes in accuracy. Effect sizes in these studies ranged from 0.175 to 1.064, with a mean of 0.489. However, Coslett cautioned that effect size data should be considered preliminary and that any conclusions about tDCS must be tempered by the lack of long-term follow-up data showing positive gains in patients with subacute aphasia.

The timing of speech-language therapy

There is evidence for the efficacy of rehabilitation for post-stroke hemiparesis when it begins within two weeks after stroke onset, especially for upper-extremity weakness treated with constraint of the unaffected limb and forced used of the affected limb (Kwakkel et al., 2016). Motor Rehabilitation within the first 24-hours, may be harmful, at least for mobilization (ATC, 2015).

There are mixed data, however, for beginning language therapy during the acute (within 1 week) and subacute (within 2 – 4 weeks) periods after stroke. One small/pilot randomized control trial in which intensive therapy was implemented 3.4 days after stroke onset showed benefit (Godecke, Hird, Lalor, Rai, & Phillips, 2012). In the largest trial to date (Nouwens et al., 2017), however, patients were enrolled two weeks after first-time stoke in intensive

language therapy vs no therapy. At the four-week primary outcome point, there was no benefit for the intervention group.

It should also be noted that timing of intervention may be a factor in studies of aphasia therapy. For instance, if treatments were conducted less than six months after stroke, gains due to spontaneous recovery may be misinterpreted as gains derived from therapy.

Conclusion

Stroke remains the most common cause of aphasia. Although virtually all cognitive measures contain some level of language processing, some level of valid cognitive data can nevertheless be obtained from a patient with aphasia and potentially used to help guide the rehabilitative process and manage expectations. The majority of language recovery seems to occur in the weeks following stroke, but residual recovery may occur over the duration of a patient's life, albeit from compensatory rather than restorative mechanisms. Several variables have been shown to affect post-stroke language recovery, but initial aphasia severity has been identified as the single largest contributing factor. Speech therapy has long been used in rehabilitative settings to aid in post-stroke language recovery. Although initial evidence of its effectiveness was seen as inconclusive, more recent studies have identified speech-language therapy as an effective method of enhancing post-stroke recovery. Research about the ability of noninvasive brain stimulation to aid in the language recovery process is ongoing but estimates of effectiveness are variable and influenced by a number of factors.

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