Aphasia following a stroke: recovery and recommendations for rehabilitation

Monica Koenig-Bruhin[a], Beate Kolonko[b], Ayse At[c], Jean-Marie Annoni[d], Erika Hunziker[b]
[a] Spitalzentrum Biel, Switzerland
[b] Studiengang Logopädie, Interkantonale Hochschule für Heilpädagogik Zürich, Switzerland
[c] Service de Neuropsychologie et Neuroréhabilitation, Centre hospitalier universitaire vaudois, Lausanne, Switzerland
[d] Neurology, Department of Medecine, Fribourg University and Hospital, Switzerland

Funding / potential competing interests: Partly supported by the Swiss National Science Foundation 325130-118362 to Jean-Marie Annoni.

Summary

Aphasia, an acquired language disorder, affects some 5,000 patients each year in Switzerland. Recovery from and therapy for aphasia are challenging areas of study for neurorehabilitation because they concern one neurological domain (language) but different functions, such as verbal communication and activities involving daily life and self-organisation. The vast majority of aphasia patients have the potential to recover, if they do not suffer from dementia. Studies on therapy efficacy suggest that different types of therapy have their merits, including group therapies or treatment involving families, but they: (1.) must be adapted to the type of aphasia; (2.) must be adapted to the patient; and (3.) often require a minimum of intensity (between three sessions per week and once a day during the acute phase) and of duration (at least three months). Focused interventions in the chronic phase have also demonstrated their effectiveness. Moreover, in about half of the cases, therapy in one language can be generalised to another language spoken by the patient.

Key words: aphasia following stroke; recovery; rehabilitation; therapy; language therapy

Introduction

Aphasia is a language disorder caused by an acquired lesion of the central nervous system. Phenotypes of aphasia are supposed to be simple, since they refer to one cognitive domain, but are in fact complex because they can alter phonological, semantic, syntactic, pragmatic (the capacity to integrate language into the context) levels, and even discourse and executive aspects of language. This is why aphasic syndromes can be so heterogeneous. Classical Broca and Wernicke aphasias represent only 26% of the selected population. In terms of lesions, aphasia occurs after focal brain lesions in the perisylvian area of the left hemisphere in 99% of right- and 70% of left-handed people, particularly in the cortical temporoparietal, insular and frontal regions, but also in the subcortical and thalamic areas (following the borders of the "quadrilatère de Pierre Marie"). The aetiology of aphasia is vascular in 80% of cases; other aetiologies include tumours, brain injury, hypoxia, neuroinflammatory disorders, and, with increasing age, language-specific neurodegenerative processes such as primary progressive aphasia. The incidence of aphasia due to first strokes is 0.43 per 1,000 each year, which means 3,440 new aphasics in Switzerland per year after a first stroke [1]. The prevalence of aphasia is evaluated at 30% in all cases of strokes, and one can evaluate the present number of aphasics in Switzerland at around 5,000, of whom 4,000 are vascular in origin.

Correspondence:
Monica Koenig-Bruhin
Spitalzentrum Biel
Chante-Merle 84
CH-2501 Biel
Switzerland
monica.koenig[at]szb-chb.ch

Outcome of aphasia

In a cohort of initial aphasic patients following strokes, 44% of survivors have no more aphasia after six months. In fact, speech features normalise in about one-third of patients with initial aphasia after one month, then the recovery curve flattens [2]. However, severe chronic aphasia is not rare, since one year on 19% of stroke patients still suffer from persistent communication disorders [3]. The most important prognostic factors for recovery are the initial severity of aphasia, the size of the lesion and (probably) the functional activation patterns during the acute phase (86% correct prediction) [4].

Other negative predictors include ischaemia-induced lesions which exceed a volume of 100 cm^3, prior strokes and other linguistic or non-aphasic cognitive disorders. The extent of recovery is independent of education and/or profession. The influence of factors such as handedness, age, and sociocultural background seems low. Aphasia affects the possibility of returning to work, since after three years only 20% of patients with acute post-stroke aphasia have returned to their job even partially, whereas 40% have done so if they did not have aphasia [5].

Recovery mechanisms

Recovery mechanisms for moderate to severe aphasia include functional and neural elements. On the functional side, language recovery often starts with an improvement of comprehension capacities, with production abilities improving in a second phase [6]. Improvement of comprehension in the first two weeks is a positive sign of general language recovery. Like all motor and cognitive processes, the recovery of language necessitates a process of explicit re-learning. This point is conceptually important: although oral language is generally learned in an implicit incidental way, relearning and speech therapy

is based on explicit strategies, and this may influence neural processes of recovery. On the neural side, three mechanisms appear to play important roles:

1. In the first week functional imaging studies show initially a reduced activation of the remaining left language areas, followed by an upregulation of the homologue (right hemispheric) language zones. This improvement correlates with an improvement in language during the first month. In the third phase (4–12 months), a normalisation of activation has been observed, and it has been suggested that this reflects the consolidation of the language system [7]. Therefore, the right homologue area plays a role in language recovery, but the efficient restoration of language is usually only achieved if the left temporal areas can be reintegrated into the functional network [6].
2. Recovery is favoured by the integrity of the hippocampal structures [8], suggesting the important role of explicit learning in language recovery.
3. Subcortical and frontal lesions are often associated with earlier reactivations of the left superior temporal gyrus (STG) during language tasks and consequently with better outcomes; and also during simple language tasks such as word repetition.

Principles of language therapy

Indication

Losing the ability to express and understand language after a stroke (or brain damage) has painful consequences and impacts the quality of life of the affected people and of their families. Communication is essential in daily life, and for social activities and participation [9]. After a stroke, people with aphasia (or suspected aphasia) should be referred to an appropriately qualified and specialised speech and language therapist for detailed language assessment; that is, for the evaluation of the presence, nature and severity of the language impairment. This should be followed by a targeted specific language and communication training [10]. In Switzerland, it is the physicians' responsibility to prescribe the assessment and therapy for aphasics. To participate in language treatment, patients need attention, concentration and motivation [11].

Assessment of aphasia

Assessment of aphasia is a target-oriented evaluation of language impacts. It is performed at any stage of treatment: at the beginning, during and at the end of therapy. At the beginning, a specific and detailed assessment is necessary to identify and describe the patients' language abilities. Later it is essential to include the impairment in communication interactions, as well as the impact on daily life and the patients' restriction in participation [12]. The assessment has the following goals:

- designation of aetiological factors: presence or absence of aphasia and associated problems;
- determination of (neuro)linguistic skills: verbal expression, auditory comprehension, reading and writing;
- analysis of language in everyday life: pragmatic abilities and communication in different social situations;
- establishing of intervention goals: treatment prognosis and specification of intervention goals from which appropriate intervention and procedures are established.

A crucial issue in the assessment is the stage of the disorder. In particular, aphasia screenings are performed in the acute stage, whereas batteries/tests are used later in the chronic stage [13]. Evidence-based practice suggests the use of psychometrically-controlled tools. Helpful screening tools in German are the *Kurze Aphasieprüfung*, the *Aphasie-Check-List* or the *Language Screening Test* in French [14–16]. For further assessments, speech therapists use assessment tools which help to determine the severity and which help to analyse and to understand the complexity and patterns of the patient's language. These instruments provide information about the strengths and weakness in different modalities of their spoken and written languages.

According to the World Health Organisation (WHO) framework (International Classification of Functioning), the specific assessment should also incorporate highly or moderately structured observations such as, for instance, retelling a story, describing pictures, nonstandard spontaneous language analysis or the fluency in different semantic naming tasks [17]. Dialogue situations support the examination of comprehension in communication interactions and elicit production of spontaneous language, including compensatory strategies (verbal and nonverbal) in everyday situations. Assessment of reading and writing must also take into consideration the individual's ability and performance in everyday life [18]. The patient's attitude to his or her language disorder is also an important aspect. Finally, the specific assessment should also make use of observations from clinical professionals, family and friends, who can often provide valuable information about the patient's current language skills, activities and participation in life [13]. Tools for collecting this type of information are the *Fragebogen zu den Auswirkungen der Sprachstörungen auf die Alltagskommunikation*, the *Communication Effectiveness Index CETI* and the *Echelle de Communication Verbale de Bordeaux ECVB* [19–21]. The *Therapieindikatoren Aphasie* helps speech and language therapists to summarise the nature and degree of patients' language impairments, as well as the impact on personal activities and social participation [22]. In the future, it would be desirable if new theoretically well-founded tests and assessment tools could be developed, with the aim of identifying the functional and social consequences of aphasia [13].

Goals of therapy

Aphasia is a chronic disorder with long-term consequences. In line with the International Classification of Functioning, Disability and Health of the WHO, the improvement of communication and social participation is the ultimate goal of therapy [23, 24]. The restoration of the linguistic processing is essential for communication and participation. The improvement of verbal expression and comprehension in spo-

ken and written language is a fundamental aim of aphasia intervention.

Despite linguistic progress, many people with aphasia have residual communication problems. Achieving an optimal level of communication, given these linguistic deficits, is fundamental for social participation. In the eyes of people with aphasia and their families, the recovery of their communicative functions is a most important goal [25].

The optimisation of communicative strategies and effectiveness involve both the client and their communication partner [26, 27]. There are goals relating to the patients' psychological factors, such as reducing frustration and increasing their acceptance of aphasia, their confidence and independence. Information about aphasia, stroke, rehabilitation or support groups serves to empower the patient and leads to greater independence [28].

In practice, the treatment goals are set individually and should be negotiated directly with the patient and/or their relatives.

Treatment of language impairment

Aphasia is a heterogeneous disorder and the severity and type of aphasia change over time. The initial severity and type of aphasia influence language recovery [29]. Recovery from aphasia varies widely between individuals, aphasia types and its initial severity. Further improvement, even in the chronic stage, is possible [30].

There is a broad range of treatments for aphasia which are currently in use, although there is no universally established intervention that is valid for every individual [31]. At the start of the treatment, the therapists establish the goals and the methods to be used, taking into account the various key factors [23]. Normally the therapist chooses from a diversity of therapeutic methods or applies an individually adapted method/programme when appropriate [31].

Acute phase

Cognitive therapies. Cognitive- or neuro-linguistic oriented treatment concentrates on language-specific impairment and the treatment involves specific tasks such as naming, semantic or phonological training, sentence production, writing and reading. Other approaches include multimodal treatment or computer-based aphasia treatment. These interventions are based on psycholinguistic or cognitive neuropsychological models.

Functional therapies. The functional treatment approach aims at achieving a level of communication with interactive focused-intervention such as PACE (Promoting Aphasia Communication Effectiveness) or therapeutic role-playing, dialogue training, the use of strategies and alternative and augmentative training such as gestural cueing [32–34]. People with severe aphasia in particular may benefit from augmentative and alternative communication strategies used in functional activities [34]. The information and training of communication partners and the reduction of communication barriers in the external environment are complementary approaches used in cases of severe aphasia [12]. All the above-mentioned approaches are useful for enhancing social activity and participation and help to increase the individual's quality of life [10, 12].

Chronic phase

At the chronic phase of aphasia, the following methods are established, based (at least partly) on the evidence to date:

- linguistic task-specific therapy (semantic, phonological or syntactic treatment);
- computer-based treatments;
- Constraint-Induced Aphasia Therapy (CIAT), where the use of nonverbal communication strategies is not allowed;
- group language therapy;
- training conversation/communication partners in community-based aphasia programs [30].

Treatment-specific effects are linked to the type of impairment; for example, task-specific semantic therapy improves semantic skills and phonological training improves phonological processing. Both methods may improve verbal communication [33, 35]. Participation in group therapy results in communicative and linguistic improvements [33, 35]. Constraint-induced aphasia therapy may result in improved language function and everyday communication. Combined with additional training in everyday communication, this therapy leads to a greater improvement in communication effectiveness [30, 35, 36].

Interventions are, in general, individually tailored and used in conjunction with additional group therapy. Treatment should also involve communication partners. To maximise functional communication, speech and language, therapists working with aphasia patients should also involve the patients' families and carers [31]. Aphasia therapy should be led by an appropriately qualified speech and language therapist [10]. As mentioned earlier, language therapy is most effective when provided intensively. Therefore, patients' language therapy provided by the speech and language therapist can be complemented by including trained and supervised family members or care persons (e.g., to help with additional self-managed computer treatment) [33, 37, 38].

Principles of a participation-orientated aphasia intervention

Aphasia rehabilitation involves more than simply treating speech and language. Chapey et al. have considered a change in the treatment of aphasia which has led to a growing interest in treatments that produce meaningful real-life outcomes [39]. Although a social approach to aphasia is relatively new and further research is needed, there is evidence that social communication, communication opportunities and well-being benefit from this form of intervention [40, 41].

People with aphasia have to learn to cope with activity limitation due to their communication problems. They need support to improve their participation in everyday life [42]. Chapey et al. argue for a "Life Participation Approach to

Aphasia" (LPAA), which focuses on reengagement in life from the beginning to the end of the therapy [39]. The everyday concerns of individuals with aphasia and others affected by it are at the centre of all decision making. A participation-oriented treatment emphasises competence and inclusion in daily life, focusing as much on the consequences of the disorder as on the language difficulty.

Communication, increasing participation, providing support systems and increasing confidence are specific objectives in social approaches to aphasia interventions [40]. Outcome evaluation involves documenting the quality of life and participation changes [13, 23]. Discharge from therapy should be discussed with the patients and their relatives [43], as the consequences of aphasia change over time. The patients can decide whether to discontinue the treatment and re-enter later should they wish to continue working on an existing goal or to attain a new life goal.

Environmental factors

One of the determining factors in the effectiveness of therapeutic intervention is the amount of environmental support given to people with aphasia. A highly supportive environment can lessen the consequences of aphasia [39, 44]. Communication training of both the patients and their spouses can help to improve everyday communication and support the "hidden victims" of aphasia. Partner or family training enhances communication and also potentially expands the opportunities for satisfying interactions [27, 40, 45]. To facilitate participation in social life, other communication partners such as friends, service providers, work colleagues et cetera should be informed about aphasia and helpful strategies for communication.

Aphasia therapy in bilinguals

Bilingual aphasic patients show different patterns of recovery after a stroke, ranging from parallel recovery in most (60%) of the cases (i.e., when both impaired languages improve to a similar extent and concurrently) to selective recovery of a given language (i.e., one language remains impaired while the other recovers, whether it is L1 or L2), or, in rarer cases, a pathological mixing of two languages (i.e., the elements of the two languages are involuntarily mixed during language production) [46]. Factors such as proficiency, immersion, emotional and social relationship with the other language play important roles.

The few studies that have addressed the subject of interlanguage transfer from language therapy [47] suggest that: (1.) simultaneous therapy in both languages may delay language recovery; (2.) therapy in one language does formally transfer to the other language in around 50% of cases; (3.) this transfer seems more consistent from L2 to L1 than inversely; and (4.) transfer is easier when both languages have common roots.

Effectiveness of language therapy

The effectiveness of language therapy in poststroke aphasia has been extensively studied since the 1950s. There is good evidence that frequency (intensity) and amount(duration), as well as starting time have an impact on the effectiveness of language therapy [48]. Recent reviews and guidelines considered not only Randomised Controlled Trials(RCT), but also rigorous single case studies [49, 50]. Single case studies are now considered as a source of acceptable evidence in this specific field, in which the application of the RCT methodology remains difficult for several reasons: the lack of consensus on the treatment's target, the methodology of the intervention and the assessment of the outcomes. A fundamental difficulty of this approach lies in the highly heterogeneous nature of cognitive deficits.

The 2012 Cochrane review concluded that there is some evidence of the effectiveness of language therapy regarding improved functional communication, receptive and expressive language. Some indication of the benefits of intensive over low frequency language therapy was observed, but no difference in functional communication outcome was found. The potential benefits of intensive over conventional language therapy were lessened by a significantly higher drop-out from intensive therapy. In the comparisons of language therapy versus no language therapy, therapy resulted in significant gains in functional communication, comprehension and expressive language [31].

According to the guidelines on cognitive rehabilitation of the European Federation of Neurological Societies, there exists considerable evidence for a probable effectiveness for language therapy in poststroke aphasia (grade B recommendation) [49].

In the updated review of the American Congress of Rehabilitation Medicine, cognitive-linguistic therapies are recommended as a practice standard during the acute and postacute rehabilitation for language deficits secondary to left hemisphere stroke. Cognitive interventions for specific language impairments, such as language formulation or reading comprehension, are recommended as practice guidelines after left hemisphere strokes [35].

Dosage and timing for starting language therapy

The interaction between timing, treatment intensity, outcomes and other variables that impact the therapeutic process seems to be complex [48]. Currently, there is no agreement on an operational definition of low and high frequency language therapy.

Recently, Basso et al., (2011) in a systematic review, searched the literature from 1950 to 2007 for neuropsychological (cognitive) treatments for vascular aphasic disorders, including meta-analyses, systematic reviews, group studies and single case studies [50]. All included meta-analyses confirmed the efficacy of aphasia rehabilitation. When groups of treated and untreated patients were compared, improvement was always significantly greater in the treated patients, unless treatment was short or of low frequency. The amount of therapy seems to be a key factor.

Group studies which failed to demonstrate effects of language therapy tended to have shorter duration (two to three months) or low intensity of therapy (usually two hours weekly or less) [50–52].

In the Constraint-Induced Language Therapy approach (CILT), oral production exercises are administered for several hours a day over a relatively short period of time (two weeks). CILT has often been successful in chronic patients [53, 54]. But other approaches, such as model-oriented therapy or PACE, have also provided positive results in chronic patients when administered with an intensity equal to CILT [55, 56].

Early-starting interventions

Therapies which start early are necessary in order to reduce non-use and maladaptive compensatory strategies as well as to reduce the psychological strain caused by aphasia. Currently, two studies have investigated language therapy starting within two or three days after onset of a stroke. Laska (2011) found significant communication benefits in some, but not all, patients. Starting within two days after the stroke onset, patients were given 45 minutes of therapy, five times a week over three weeks. A *post-hoc* analysis showed that a group of patients with fluent aphasia improved significantly [2]. In the Australian trial [11], the treated patients received 30–80 minutes of language therapy, five times a week over one month, starting within three days after onset. Communication outcomes were better in the daily treatment group compared with a group of patients who received only the usual care (spontaneous recovery alone) at three weeks poststroke [11]. Remission effects due to spontaneous recovery can almost be doubled by starting language therapy intervention in the first weeks after a stroke [57].

Interventions in the chronic phase

There is a potential for recovery through language therapy even years after the onset of aphasia [30,58]. A strong relationship between intensity and positive outcomes has been established in the chronic phase [48]. Basso and Macis (2011) report on a retrospective study where patients with chronic aphasia received weekly sessions of language therapy and in addition completed two to three hours of homework with the help of a family member, supervised by a professional therapist. Therapy lasted as long as improvements were evident. Only four of the 23 enrolled patients showed no improvements. The authors explained the late recovery as a result of the intensity of the work done [37].

Future research should systematically investigate the effects of treatment intensity both independently and in combination with influencing factors. Outcomes should be measured on the impairment and the participation levels.

Other therapies

Other options that have been "scientifically studied" include pharmacotherapy and magnetic or electric stimulations.

Three types of molecules have been studied in controlled or open trials: cognitive enhancers, dopaminergic and serotoninergic substances. The theoretical background is not very clear, but the main purpose seems to be to globally stimulate brain processes for the first two classes and to increase neural functional reorganisation for the third class. A certain consensus is that dopaminergic drugs given in conjunction with therapy do improve the effects of therapy, particularly in patients with frontal cortical or subcortical lesions. The strongest effect has been seen on the speed of language production [59]. Other effects of cognitive enhancers have included piracetam 4.8 mg/day [60], memantine, anticholinesterase inhibitors and dextroamphetamine [61]. However, none of these therapies are currently reimbursed for aphasia therapy, except in some exceptional situations. Reimbursement can sometimes be requested, particularly if the aphasia is of traumatic origin, the patient is young and it can be demonstrated that the therapy can change the functional level of the patient.

The first studies using Transcranial Magnetic Stimulation (TMS) on aphasia were performed by Martin et al. (2004) and Naeser et al. (2005) [62, 63]. Since then, several studies have revealed that TMS and transcranial Direct Current Stimulation (tDCS), which are noninvasive brain stimulation techniques, are useful tools for enhancing recovery in aphasia. These noninvasive brain stimulation tools allow areas of interest in the brain to be focally stimulated by increasing or decreasing the excitability in targeted cortical areas. Most stimulation studies on aphasia are based on the assumption that right hemispheric overactivation may impair language recovery and thus apply inhibitory repetitive TMS to right-sided homologues. For a review of TMS studies in aphasia, see Medina et al. (2012) and for a review of tDCS studies in aphasia, see Torres et al. (2013) [64, 65].

Most studies with repetitive TMS stimulate the pars triangularis homologue of Broca's area and observe improvements in the Boston Naming Test and picture naming, spontaneous speech improvements and improvements of auditory comprehension [66–68]. All these studies showed that patients with moderate symptoms demonstrated the greatest improvements compared to mild or severe cases. Cotelli et al. (2012) observed improvements when stimulating the dorsolateral prefrontal cortices [69].

One week of intensive language treatment for apraxia in aphasic patients associated with tDCS anodal stimulation (which increases excitability) of perilesional areas improved naming accuracy and reaction times in aphasic patients [70]. The beneficial effects persisted for up to two months after treatment [70]. Vines et al. (2011) observed a beneficial effect of melodic intonation therapy, which was increased with anodal stimulation over the right posterior inferior frontal gyrus [71]. Kang et al. (2011) showed improvements in picture naming with cathodal stimulation (which decreases excitability) of the homologue of Broca's area [72].

A very recent study by Marangolo et al. (2013) demonstrated that bihemispheric tDCS stimulation of left (excitatory stimulation) and right frontal (inhibitory stimulation) areas significantly increased the accuracy and the speed in articulating and could be generalised to many other language tasks like word repetition, word reading, picture

description, noun and verb naming, reduction in phonological errors and improvement in speech praxis. These effects were still observable one week later [73].

From the foregoing clinical evidence, it can be concluded that both rTMS and tDCS have beneficial effects on both fluent and nonfluent aphasia. The action of these noninvasive methods seems to involve the reversion of the imbalance of interhemispheric inhibition after a stroke. Several studies stress the importance of combining anodic tDCS stimulation over the perilesional areas with classical language therapy to obtain the most beneficial effects [73].

Recommendations

Following a stroke, patients with suspected aphasia should be referred to an appropriately qualified language therapist for detailed assessment of language deficits and their impact on communication and also their participation in social life.

Language therapy should start within the first days after the stroke, as soon as the patient is able to cope [11, 24]. Inpatients should be given daily sessions (five times a week for up to 45 minutes). Treatment protocols should be adapted to the individual patient's condition. Very intensive therapies may provoke high dropout rates, especially in the first four weeks [74]. Usually outpatients should attend at least three times a week in the postacute phase.

In the chronic phase, intervals with intensive language therapy are recommended [24]. Maintenance of the ability to communicate is now also considered as an indication for treatment. Language therapy later than twelve months after the onset of aphasia should also address the transfer of reacquired communication skills. Low frequency language therapy (one to two times a week) is recommended for supporting the transfer and/or maintenance of reacquired communications skills.

The duration of language therapy is an important factor in recovery. The length of intervention in the postacute and chronic stage should be at least three months [10].

The patient's family and carers should be involved in the therapy.

Language therapy provided by the therapist can be intensified by doing additional homework or self-managed computer therapy eventually with the help of carers [37].

Acknowledgement: Thanks to Ann Travis for the editing.

References

1 Engelter S, Gostynski M, Papa S, Frei M, Born C, Ajdacic-Gross V, et al. Epidemiology of Aphasia Attributable to First Ischemic Stroke: Incidence, Severity, Fluency, Etiology, and Thrombolysis. Stroke. 2006;37:1379–84.
2 Laska AC, Kahan T, Hellblom A, Murray V, von Arbin M. A randomized controlled trial on very early speech and language therapy in acute stroke patients with aphasia. Cerebrovasc Dis Extra. 2011;1(1):66–74.
3 Dijkerman HC, Wood VA, Hewer RL. Long-term outcome after discharge from a stroke rehabilitation unit. J R Coll Physicians Lond. 1996;30(6):538–46. Epub 1996/11/01. PubMed PMID: 8961209.
4 Saur D, Lange R, Baumgaertner A, Schraknepper V, Willmes K, Rijntjes M, et al. Dynamics of language reorganization after stroke. Brain. 2006; 129(Pt 6):1371–84. Epub 2006/04/28. doi: 10.1093/brain/awl090. PubMed PMID: 16638796.
5 Wozniak MA, Kittner SJ, Price TR, Hebel JR, Sloan MA, Gardner JF. Stroke location is not associated with return to work after first ischemic stroke. Stroke. 1999;30(12):2568–73. Epub 1999/12/03. PubMed PMID: 10582979.
6 Heiss WD. WSO Leadership in Stroke Medicine Award Lecture Vienna, September 26, 2008: functional imaging correlates to disturbance and recovery of language function. Int J Stroke. 2009;4(2):129–36.
7 Saur D, Ronneberger O, Kummerer D, Mader I, Weiller C, Kloppel S. Early functional magnetic resonance imaging activations predict language outcome after stroke. Brain : a journal of neurology. 2010;133(Pt 4): 1252–64. Epub 2010/03/20. doi: 10.1093/brain/awq021. PubMed PMID: 20299389.
8 Meinzer M, Mohammadi S, Kugel H, Schiffbauer H, Floel A, Albers J, et al. Integrity of the hippocampus and surrounding white matter is correlated with language training success in aphasia. NeuroImage. 2010;53(1):283–90. Epub 2010/06/15. doi: 10.1016/j.neuroimage.2010.06.004. PubMed PMID: 20541018.
9 Nouwens F, Dippel DWJ, de Jong-Hagelstein M, Visch-Brink EG, Koudstaal PJ, de Lau LML, et al. Rotterdam Aphasia Therapy Study (RATS) – 3: "The efficacy of intensive cognitive-linguistic therapy in the acute stage of aphasia"; design of a randomised controlled trial2013 18.7.2013.
10 National Institute for Health and Clinical Excellence. Stroke rehabilitation: the rehabilitation and support of stroke patients: NICE guideline. Draft for Consultation. 2011 [updated August, 2011]. Available from: http://www.nice.org.uk/nicemedia/live/11950/56130/56130.pdf.
11 Godecke E, Hird K, Lalor EE, Rai T, Phillips MR. Very early poststroke aphasia therapy: a pilot randominized controlles efficacy trial International Journal of Stroke. 2012;7:635–44.
12 Simmons-Mackie N, Kagan A. Application of the ICF in Aphasia Seminars in Speech and Language. 2007;28(4):244–53.
13 Patterson JP, Roberta C. Assessment of Language Disorders in Adults In: Roberta C, ed. Language Intervention Strategies and Related Neurogenic Communication Disorders 5th ed. Baltimore: Lippincott Williams & Wilkins; 2008. p. 64–160.
14 Lang C, Dehm A, Dehm B, Leuschner T. Kurze Aphasieprüfung. Frankfurt: Swets; 1999. German.
15 Kalbe E, Reinhold, N., Ender, U., Kessler, J. Aphasie Check Liste. Köln: Prolog; 2002. German
16 Flamand-Roze C, Falissard B, Roze E, Maintigneux L, Beziz J, Chacon A, et al. Validation of a new language screening tool for patients with acute stroke: the Language Screening Test (LAST). Stroke. 2011;42(5):1224–9.
17 WHO. ICF Internationale Klassifikation der Funktionsfähigkeit, Behinderung und Gesundheit. Organization WH, ed. Genf; DIMDI; 2005. German.
18 Royal Collegue of Speech and Language Therapists; Departement of health (UK); National Institute for Clinical Excellence (NICE). EBP Compendium: Summary of Clinical Practice Guideline RCSLT Cliniclal Guidelines: 5.12 Aphasia 2005 [cited 2013 July 15]. Available from: http://www.asha.org/Members/ebp/compendium/guidelines/Clinical-Guidelines-for-Stroke-Rehabilitation-and-Recovery.htm.
19 Bongartz R. Kommunikationstherapie mit Aphasikern und Angehörigen. 1st ed. Springer L, Schrey-Dern D, eds. Stuttgart New York: Thieme; 1998. German.
20 Lomas J, Pickard L, Bester S, Elbard H, Finlayson A, Zoghaib C. The Communicative Effectiveness Index: Development und psychometric evaluation of a functional communication measure for adult aphasia. Speech Hearing Disorders. 1989;54:113–24.
21 Darrigrand B, Mazaux J-M. Evaluer la communication de la personne aphasique dans la vie quotidienne - proposition d'une Échelle de Communication Verbale. Rééducation Orthophonique. 1999;198:137–44. French.
22 Kolonko B, Hunziker E. Therapieindikatoren Aphasie TInA. Idstein: Schulz-Kirchner; 2013. German.
23 van de Sandt-Koenderman ME, van der Meulen I, Ribbers GM. Aphasia rehabilitation: more than treating the language disorder. Arch Phys Med Rehabil. 2012;93:1–3
24 aphasie suisse. Guidelines zur Behandlung von Aphasien. Schweizerische Ärztezeitung 2005;86(40):2290–7. German.
25 Worall L, Sherrat S, Rogers P, Howe T, Hersh D. What people with aphasia want: Their goals according to the ICF. Aphasiology. 2011;25(3): 309–22.
26 Bauer A, de Langen-Müller U, Glindemann R, Schlenck C, Schlenck K-J, Huber W. Qualitätskriterien und Standarts für die Therapie von Patienten mit erworbenen neurogenen Störungen der Sprache (Aphasie) und des Sprechens (Dysarthrie): Leitlinien 2001. Sprache Stimme Gehör. 2001;25:148–61. German.
27 Bauer A, Kulke F. Language exercises for dinner: Aspects of aphasia management in family settings. Aphasiology. 2004;18(12):1135–60.
28 Sherrat D, Worall L, Pearson C, Howe T, Hersh D, Davidson B. "Well it has to be language-related": Speech-language pathologists goals for people with aphasia and their families. International Journal of Speech and Language Pathology. 2011;13(4):317–28.
29 Lazar R, Minzer B, Antoniello D, Festa JR, Krakauer JW, Marshall RS. Improvement in Aphasia Scores After Stroke Is Well Predicted by Initial Severity.[Article]. Stroke. 2010;41(7):1485–8.
30 Allen L, Metha S, McClure JA, R. T. Therapeutic Interventions for Aphasia Initiated More then Six Months Post Stroke: A Rewiew of the Evidence. TTop Stroke Rehabil. 2012. 19(6):523–33.
31 Brady MC, Kelly H, Godwin J, Enderby P. Speech and language therapy for aphasia following stroke: Cochrane Stroke Group; 2012.

32 Davis GA, Wilcox MJ. Incorporating parameters of natural conversation in aphasia treatment. In: Chapey, editor. Language Intervention Strategies in Adults Baltimore: Williams und Wilkins; 1981. p. 169–83
33 Salter K, Teasell R., Bhogal S, Zettler L., N. F. Evidence-Based Review of Stroke Rehabilitation 2005–2013: Aphasia 2012 [cited 2013 July 15]. 15 [Available from: http://www.ebrsr.com/uploads/Aphasia-SREBR-SREBR-15_1.pdf.
34 Ziegler W, Ackermann H, Goldenberg G, Huber W, Sedlmeier C, Schupp W, et al. Rehabilitation aphasischer Störungen nach Schlaganfall. In: Diener H-C, editor. Leitlinien für Diagnostik und Therapie in der Neurologie. Stuttgart: Thieme 2008. German.
35 Cicerone KD, Langenbahn DM, Braden C, Malec JF, Kalmar K, Fraas M, et al. Evidence-Based Cognitive Rehabilitation: Updated Review of the Literature From 2003 Through 2008. Archives of Physical Medicine and Rehabilitation. 2011;92(4):519–30. doi: http://dx.doi.org/10.1016/j.apmr.2010.11.015.
36 Cherney LR, Patterson JP, Raymer A, Frymark t, Schooling T. Evidence-Based Systematic Review: Effects of Intensity of Treatment and Contraint-Induced Language Therapy for Individuals With Stroke-induced Aphasia. J Speech Lang Hear Res. 2008;51:1282–99.
37 Basso A, Macis M. Therapy efficacy in chronic aphasia. Behav Neurol. 2011;24:317–5.
38 Palmer R, Enderby P, Cooper C, Latimer N, Julious S, Paterson G, et al. Computer therapy compared with usual care for people with long-standing aphasia poststroke: a pilot randomized controlled trial. Stroke. 2012;43(7): 1904–11.
39 Chapey R, Duchan JF, Elman RJ, Garcia LJ, Kagan A, Lyon JG, et al. Life-participation Approach to Aphasia: A Statement of Values for the Future. In: Roberta C, editor. Language Intervention Strategies and Related Neurogenic Communication Disorders 5th ed. Baltimore: Lippincott Williams & Wilkins; 2008. p. 279–84.
40 Simmons-Mackie N. Social Approaches to Aphasia In: Roberta C, ed. Language Intervention Strategies and Related Neurogenic Communication Disorders 5th ed. Baltimore: Lippincott Williams & Wilkins 2008. p. 290–313.
41 Wilkinson R, Wielaert S. Rehabilitation Targeted at Everyday Communication: Can We Change the Talk of People With Aphasia and Their Significant Others Within Conversation?. Arch Phys Med Rehabil. 2012;93(1, Suppl):70–6.
42 Sjörqvist-Nätterlund B. A new life with aphasia: everyday activities and social support. Scand J Occup The. 2010;17(2):117–29.
43 Hersh D, Cruice M. Beginning to teach the end: the importance of including discharge from aphasia therapy in the curriculum. Int J Lang Commun Disord. 2010;45(3):263–74.
44 Threats T. The ICF framework and Third Party Disability: Application to the Spouses of Persons With Aphasia. Top Stroke Rehabl. 2010;17(6):451–7.
45 Bauer A, Auer P. Aphasie im Alltag. Luise S, Schrey-Dern D, eds. Stuttgart: Thieme; 2009. German.
46 Paradis M. Aphasies chez les bilingues et les multilingues. In: Seron JRaX, editor. Troubles du Langage: Bases théoriques, diagnostic et rééducation. Bruxelles: Mardaga; 1999. p. 529–49. French.
47 Faroqi-Shah Y, Frymark T, Mullen R, Wang B. Effect of treatment for bilingual individuals with aphasia: a systematic review of the evidence. Journal of Neurolinguistics. 2010;23(4):319–34.
48 Cherney LR, Patterson JP, Raymer AM. Intensity of aphasia therapy: evidence and efficacy. Curr Neurol Neurosci Rep. 2011;11(6):560–9.
49 Cappa SF, Benke T, Clarke S, Rossi B, Stemmer B, van Heugten CM, et al. EFNS guidelines on cognitive rehabilitation: report of an EFNS task force. Eur J Neurol. 2005;12(9):665–80.
50 Basso A, Cattaneo S, Girelli L, Luzzatti C, Miozzo A, Modena L, et al. Treatment efficacy of language and calculation disorders and speech apraxia: a review of the literature. Eur J Phys Rehabil Med. 2011;47(1):101–21.
51 Bhogal SK, Teasell R, Speechley M. Intensity of aphasia therapy, impact on recovery. Stroke. 2003;34(4):987–93.
52 Bowen A, Hesketh A, Patchick E, Young A, Davies L, Vail A, et al. Effectiveness of enhanced communication therapy in the first four months after stroke for aphasia and dysarthria: a randomised controlled trial. Brit Med J. 2012;345: e4407
53 Meinzer M, Elbert T, Djundja D, Taub E, Rockstroh B. Extending the Constraint-Induced Movement Therapy (CIMT) approach to cognitive functions: Constraint-Induced Aphasia Therapy (CIAT) of chronic aphasia. NeuroRehabilitation. 2007;22(4):311–8.
54 Pulvermüller F, Neininger B, Elbert T, Mohr B, Rockstroh B, Koebbel P, et al. Constraint-induced therapy of chronic aphasia after stroke. Stroke. 2001;32(7):1621–6.
55 Maher LM, Kendall D, Swearengin JA, Rodriguez A, Leon SA, Pingel K, et al. A pilot study of use-dependent learning in the context of Constraint Induced Language Therapy. J Int Neuropsychol Soc. 2006;12(6):843–52.
56 Barthel G, Meinzer M, Djundja D, Rockstroh B. Intensive language therapy in chronic aphasia: Which aspects contribute most? Aphasiology. 2008;22(4): 408–21.
57 Robey RR. A meta-analysis of clinical outcomes in the treatment of aphasia. J Speech Lang Hear Res. 1998;41(1):172–87.
58 Moss A, Nicholas M. Language rehabilitation in chronic aphasia and time postonset: a review of single-subject data. Stroke. 2006;37(12):3043–51.
59 Seniów J, Litwin M, Litwin T, Leśniak M, Członkowska A. New approach to the rehabilitation of post-stroke focal cognitive syndrome: effect of levodopa combined with speech and language therapy on functional recovery from aphasia. J Neurol Sci. 2009;283(1-2):214–8.
60 Greener J, Enderby P, Whurr R. Pharmacological treatment for aphasia following stroke. Cochrane Database Syst Rev. 2001;4.
61 Walker-Batson D, Curtis S, Natarajan R, Ford J, Dronkers N, Salmeron E, et al. A double-blind, placebo-controlled study of the use of amphetamine in the treatment of aphasia. Stroke. 2001;32:2093–8.
62 Martin PI, Naeser M, Theoret H, Tormos JM, Nicholas M, Kurland J, et al. Transcranial magnetic stimulation as a complementary treatment for aphasia. Semin Speech Lang. 2004;25:181–92
63 Naeser MA, Martin PI, Nicholas M, Baker EH, Seekins H, Kobayashi M, et al. Improved picture naming in chronic aphasia after TMS to part of the right Broca' area: an open-protocol study. Brain Lang. 2005;93:95–105.
64 Medina J, Norise C, Faseyitan O, Coslett H, Turkeltaub P, Hamilton R. Finding the right words:Transcranial magnetic stimulation improves discourse productivity in non-fluent aphasia after stroke. Aphasiology. 2012;26(9): 1153–68.
65 Torres J, Drebing D, Hamilton R. TMS and tDCS in post-stroke aphasia: integrating novel treatment approaches with mechanisms of plasticity. RestorativeNeurology and Neuroscience. 2013;31:501–15.
66 Naeser MA, Martin PI, Lundgren K, Klein R, Kaplan J, Treglia E, et al. Improved language in a chronic nonfluent aphasia patient after treatment with CPAP and TMS. Cogn Behav Neurol. 2010;23(1):29–38.
67 Barwood CH, Murdoch BE, Whelan BM, Lloyd D, Riek S, O'Sullivan JD, et al. Improved receptive and expressive language abilities in nonfluent aphasic stroke patients after application of rTMS: an open protocol case series. Brain Stimul. 2012;5(3):274–86.
68 Abo M, Kakuda W, Watanabe M, Morooka A, Kawakami K, Senoo A. Effectiveness of low-frequency rTMS and intensive speech therapy in poststroke patients with aphasia: a pilot study based on evaluation by fMRI in relation to type of aphasia. Eur Neurol. 2012;68(4):199–208.
69 Cotelli M, Manenti R, Alberici A, Brambilla M, Cosseddu M, Zanetti O, et al. Prefrontal cortex rTMS enhances action naming in progressive non-fluent aphasia. Eur J Neurol. 2012;19(11):1404–12.
70 Marangolo P, Marinelli CV, Bonifazi S, Fiori V, Ceravolo MG, Provinciali L, et al. Electrical stimulation over the left inferior frontal gyrus (IFG) determines long-term effects in the recovery of speech apraxia in three chronic aphasics. Behav Brain Res. 2011;225(2):498–504.
71 Vines BW, Norton AC, Schlaug G. Noninvasive brain stimulation enhances the effects of melodic intonation therapy. Front Psychol. 2011;2:230–40.
72 Kang EK, Kim YK, Sohn HM, Cohen LG, Paik NJ. Improved picture naming in aphasia patients treated with cathodal tDCS to inhibit the right Broca's homologue area. Restor Neurol Neurosci. 2011;29(3):141-52.
73 Marangolo P, Fiori V, Cipollari S, Campana S, Razzano C, Di Paola M, et al. Bihemispheric stimulation over left and right inferior frontal region enhances recovery from apraxia of speech in chronic aphasia. Eur J Neurosci. 2013; 38(9):3370–7. doi: 10.1111/ejn.12332. PubMed PMID: 23930827.
74 Bakheit AM, Shaw S, Barrett L, Wood J, Carrington S, Griffiths S, et al. A prospective, randomized, parallel group, controlled study of the effect of intensity of speech and language therapy on early recovery from poststroke aphasia. Clin Rehabil. 2007;21(10):885–94.