Post-Stroke Aphasia Therapies

Subjects: Neurosciences

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Aphasia is an acquired language disorder (derived from the Greek word “afaˈsia”) that affects spoken and/or written language resulting from brain injury (e.g., stroke). Four categories of aphasia interventions, either in isolation or combined, have been explored over the years: (1) pharmacological therapies (i.e., growth factors, monoclonal antibodies, cell-based therapies, and drugs); (2) behavioral (SALT); (3) additional therapeutic approaches (e.g., technological aids); and (4) non-invasive brain stimulation-based therapies (NIBST) (i.e., Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (tDCS)).

aphasia post-stroke therapies

1. Introduction

Aphasia is an acquired language disorder (derived from the Greek word “afaˈsia”) that affects spoken and/or written language resulting from brain injury (e.g., stroke). Apart from having devastating consequences on communication, aphasia also undermines the individual’s sense of identity with serious effects on family life and social participation. Loss of independence, limitations in activities of daily living, decreases in social networks [1] (poor quality of life (QoL) [2], and long-term disability [3] are some of the major repercussions of aphasia.

The etymology of the word aphasia implies that people that experience it are characterized by a complete absence of language; that is, they have global aphasia. Nevertheless, in clinical practice, the global aphasia phenotype is uncommon and even though people that exhibit it often show late recovery [4], they more typically evolve to have Broca’s aphasia [5]. Thus, although the term “dysphasia” would sound more appropriate for all aphasia syndromes except global aphasia, in speech and language therapy (SALT), the convention is to use the term “aphasia” in all cases of acquired language disorders resulting from brain injury, irrespective of their type, severity, and stage of characterization. In brief, aphasias are classified into non-fluent (global, mixed transcortical, Broca’s, transcortical motor, and aphemia/pure word mutism) and fluent (Wernicke’s, transcortical sensory, conduction, and anomic) [6]. Non-fluent aphasias share a common speech deficit, that is, non-fluent speech. Fluent aphasias reflect (almost) intact verbal fluency.

2. Post-Stroke Aphasia Therapies

Globally, there are over 13.7 million new strokes each year [7]. Aphasia, being a significant consequence of stroke, affects more than a third of all stroke survivors [8]. Considering those figures on an annual basis and global scale, the need for effective aphasia treatments is imperative.

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2.1. Pharmacological Therapies

Several promising pharmacological agents have been explored either in isolation or together with other forms of treatments (e.g., SALT) to promote improvements in aphasia symptoms. Drugs that show moderately positive outcomes include acetylcholinesterase inhibitors and dextroamphetamine sulfate [9], while selective serotonin reuptake inhibitors may also help aphasia recovery [10]. Piracetam, a well-explored agent, is a nootropic drug that enhances cognitive functions by facilitating vascular microcirculation. In a systematic review and meta-analysis, it was found that piracetam enhances written language skills but plays a limited role in the recovery of overall language deficits, and its short-lived benefits represent a major drawback of this agent [11]. On the other hand, memantine—a N-methyl-D-aspartate receptor antagonist—has shown potential for sustained language improvement in chronic post-stroke aphasia especially when it is combined with Constraint-Induced Aphasia Therapy (CIAT) [12]. The main limitation of most studies is that many are open label or cross-sectional trials with small numbers of participants. The lack of sham (control) conditions leaves the trials open to likely placebo effects (i.e., believing that a procedure/treatment will work leading to symptom modulation by the brain) and makes it impossible to explore whether the observed language gains are due to (i) placebo effects or (ii) pharmacotherapy alone or (iii) a combination of drugs and other forms of treatment.

In sum, the effect sizes of most trialed pharmacological treatments for aphasia are small and the functional and structural correlates of the possible positive effects are mostly unknown [13]. There is one notable exception though. Berthier et al. [14] conducted a randomized controlled trial with 26 participants and found that the administration of 10 mg of donepezil (a cholinesterase inhibitor) in combination with two hours of SALT per week improved picture naming (Cohen's d = 0.92) and the severity of aphasia (Cohen's d = 0.87). Such promising findings highlight the potential synergistic effect of donepezil and SALT on language gains in chronic post-stroke aphasia. Nonetheless, this was a study with a small sample size and therefore further research is needed to confirm such findings, and to fully understand the potential benefits and limitations of using donepezil in aphasia rehabilitation.

Unfortunately, there is also evidence supporting the detrimental effects of several drugs on post-stroke recovery (e.g., a-blockers [15]; dopamine antagonists [16]; carbamates [17]). Overall, currently no pharmacological interventions for aphasia are approved by the United States Food and Drug Administration (FDA) [18], and, according to a large-scale study, behavioral language activities strongly remain the gold standard for aphasia treatment [19].

2.2. Behavioral Therapies

SALT protocols are continuously being explored, and, as a result, several different types of aphasia therapy approaches have been implemented over the years. Following the International Classification System (ICF) of the World Health Organization (WHO) [20], several aphasia interventions focus on one or more of the following: speech and language deficits, personal and activity limitations, and environmental barriers. Aphasia interventions can be also divided into those targeting speech and language deficits (i.e., didactic, behavioral modification, stimulating) and those emphasizing functional communication rather than language recovery (i.e., pragmatics school) [21]. Findings from two systematic reviews indicate that therapies that target language impairment are effective [22][23]. Even though for several approaches there is robust evidence supporting their efficacy (while for others the evidence is emerging), there are limitations concerning the maintenance and generalization of gains beyond trained items for at least some PWA. Also, the expectation of transfer of skills from one domain to another (e.g., from speaking to reading) is currently unexplored territory.

Up until now, there has been limited understanding around the standardization of aphasia therapy protocols, resulting in a vast collection of behavioral treatments for PWA. For example, in the systematic review of Husak et al. [24] in which the effects of SALT initiated within four months of stroke-induced aphasia onset were explored, it was reported that there is still a need for high-quality research to define which types of therapy are most effective during this period. Despite notable progress, as evidenced by the publication of five clinically meaningful studies [19][25][26][27][28], each with a substantial sample size and rigorous methodology, disparities in findings persist among these studies, highlighting the ongoing need for further research to achieve the desired standardization of aphasia treatments. The COMPARE trial by Rose and colleagues [25] found that constraint-induced or multimodality aphasia treatment is better than usual care in terms of language gains for chronic aphasia post-stroke. The Big CACTUS trial [26] demonstrated the superiority of self-managed, computerized SALT over usual care or attention control for chronic aphasia post-stroke. Breitenstein et al. [19] reported that 3 weeks of intensive SALT resulted in significant improvements in verbal communication for people with chronic aphasia post-stroke. The VERSE study by Godecke and colleagues [27] revealed that early, intensive aphasia therapy did not improve communication recovery within 12 weeks post-stroke compared to usual care. Also, in their exploration of early cognitive–linguistic treatment for post-stroke aphasia, the researchers of the Rotterdam Aphasia Therapy Study-3 [28] demonstrated results that do not show a clinically relevant effect of very early cognitive–linguistic treatment on everyday language.

An overview of important and commonly used aphasia treatment approaches is presented below. The list that follows is not comprehensive, and it should be noted that in the different phases of aphasia (acute versus chronic), a different therapeutic approach may be suitable due to the different neurophysiological mechanisms underpinning each phase.

2.2.1. Phonomotor Treatment

Phonomotor Treatment (PMT) aims to boost word retrieval through the training of phonological skills based on the assumption that phonology is fundamental for all language functions [29][30]. It is believed that, as in any language, the number of phonemes and their respective sequences are limited, and by cultivating phonological skills in PWA, gains in trained and untrained words are feasible [31]. For phonological training purposes, a multimodal approach is adopted (i.e., mirrors, mouth pictures, written representations, kinesthetic feedback, etc.). Training starts with single phonemes and gradually progresses to phoneme sequences in nonwords and real words. Crucially, Socratic maieutics, a form of argumentative dialogue between people, is used to urge PWA to reflect on their own attempts. Recent evidence shows that PMT has the potential to enhance the confrontation naming of trained items with some generalization to and maintenance of untrained words [32]. PMT has also the potential to lead to improvements in discourse production [33], revealing a transfer effect from phonology to discourse.

2.2.2. Semantic Feature Analysis

Semantic Feature Analysis (SFA) also facilitates word retrieval and relies on theoretical models suggesting that the human semantic system is organized into concept networks [34]. When a person attempts to retrieve a word, all characteristics of the target concept together with features for other associated concepts are activated. The feature(s) that are activated the most are selected first and then the respective phonological representation(s) and motor program execution(s) are activated. PWA may activate the wrong concepts, and, as a result, they articulate incorrect, but semantically related, words in place of the target word. During treatment, PWA are prompted to use feature analysis charts that provide information regarding use, location, physical properties, and association concepts to generate semantic features of target concepts. Successful attempts strengthen semantic networks and help with lexical retrieval. Several studies suggest that SFA leads to word-finding improvements in trained items e.g., [35][36], and there is also evidence that a positive treatment response is linked to the number of semantic characteristics PWA generate during treatment [37].

2.2.3. Verb Network Strengthening Treatment

Verb Network Strengthening Treatment (VNeST) also aims to facilitate lexical retrieval and is based on the theoretical model that highlights the central role of verbs in semantics and syntax (see [38]). During treatment, PWA are prompted to generate thematic roles (i.e., agent and patient) for trained verbs. A single verb can generate many thematic role pairs that all reinforce the target verb. In addition, PWA are asked WH-questions (e.g., why, where, when) about explicit thematic roles for each trained verb. This way, treatment gradually targets the facilitation of sentence production and discourse. Several studies support the potential of VNeST to aid the lexical retrieval of single words, sentences, and discourse in PWA with different types and severities of language deficits e.g., [39][40]. However, collectively, the number of participants investigated in this type of treatment remains low and further research is needed to support VNeST efficacy and effectiveness.

2.2.4. Sound Production Treatment

Sound Production Treatment (SPT) is a type of articulatory–kinematic treatment [41] whereby incorrectly produced sounds (i.e., monosyllabic and polysyllabic words, phrases, sentences) are practiced hierarchically through modeling, repetition, minimal pair contrast, orthographic cuing, integral stimulation (i.e., “watch me, listen to me, say it with me”), and articulatory placement instructions. This treatment is not a therapeutic approach to aphasia per se, but more so for apraxia of speech (AoS). However, AoS appears alongside post-stroke aphasia subtypes as well as several aphasia etiologies (e.g., non-fluent progressive aphasia), and, for that reason, SPT is widely used in aphasia rehabilitation. There is evidence that SPT leads to language gains in trained and untrained word production, phrases, and sentences [41].

2.2.5. Treatment of Underlying Forms

Treatment of Underlying Forms (TUF) is based on generative syntax [42] and targets deficits exhibited at the sentence level in people with agrammatic aphasia by training the production of grammatically complex sentences [43]. PWA are provided with written cards that have the components of simple active declarative sentences (e.g., subject, verb) and a picture illustrating the action. After identifying the verb, PWA are trained to reorder sentence components to produce more complex sentences. There is evidence supporting TUF-related improvements in complex sentence production [44] and generalization for untrained and less complex sentences [45].

2.2.6. Constraint-Induced Language Therapy

Constraint-Induced Language Therapy (CILT) is a treatment approach for expressive language difficulties. The key component of CILT is the forced use of spoken language and the restraint of all other communication modalities (e.g., hand gesturing). Shaping (i.e., modification of linguistic requirements) is another feature of CILT which requires more difficult language goals as treatment progresses. CILT is known for its intensive approach necessitating massed practice [46]. The central activity of CILT is the “Go Fish” game in which a person asks another for a card that matches one of their own. If the other individual possesses the requested card, it is given to the requestor. If not, then the requestor must “go fish” (i.e., draw a card from the deck). When one of the players no longer holds any unmatched cards, the game is over. Pulvermüller et al. [47] conducted the first CILT study with favorable results. Several studies support CILT-related language gains in PWA e.g., [48][49]. More recently, it was found that CILT delivered in both intensive and distributed dosages had beneficial effects on both standardized and discourse measures [50].

2.2.7. Melodic Intonation Therapy

Melodic Intonation Therapy (MIT) was first developed to recruit right hemispheric brain regions related to the awareness of melody and rhythm to improve expressive language in individuals with non-fluent aphasia [51]. The two main components of MIT are (i) rhythmic tapping of the left hand that accompanies the production of syllables, and (ii) exaggeration of the natural prosody of speech [52]. There is emerging evidence favoring the efficacy of MIT [53][54], and, for that reason, several modified MIT protocols have been evaluated by different research centers and clinical settings e.g., [55].

2.3. Additional Therapy Approaches

There are several other therapeutic approaches that are used in aphasia rehabilitation. For example, “Response Elaboration Training (RET)” is a treatment strategy that aims to improve the informational load and length of an individual’s utterances, focusing on spontaneous responses to action pictures [56]. “Promoting Aphasics’ Communicative Effectiveness (PACE)” takes advantage of natural conversation and allows multiple communication strategies (e.g., speaking, writing) [57]. “Oral Reading for Language in Aphasia (ORLA)” aims to enhance reading comprehension in PWA [58].

There is robust evidence supporting the benefits of computerized aphasia therapies [59] derived via computers, smartphones, or tablets without the physical help of a clinician. The use of technology for PWA allows for long-term and low-cost therapy options, and is especially suitable for PWA that live in remote areas and do not have access to SALT services. During the COVID-19 pandemic, technology-supported aphasia therapy was highly valued by PWA and their caregivers, as therapy interruption and fragmentation were prevented. The “EVA PARK” online virtual environment, which simulates a fantasy island context that contains several locations (e.g., houses, coffee shops, a disco) is one software that has been studied [60]. PWA are represented by personalized avatars and communicate with others via speech or written language in various virtual settings. The virtual island offers various scenarios and situations that simulate real-life communication contexts that address specific language goals, promoting active participation and learning. The “EVA PARK” technology is considered accessible, acceptable, and engaging to PWA, and has the potential to drive language gains [61]. In addition, it has been found that by using this virtual platform, PWA feel comfortable and safe and appreciate the opportunity to interact with other PWA [62].

Importantly, technology in aphasia rehabilitation is also used in the form of alternative and augmentative communication (AAC) systems to compensate for, temporarily or permanently, the loss of speech. Low-tech AAC systems include the use of objects, pictures, written keywords, and communication books, whereas high-tech ACC systems can include speech-generating devices. Even though there is a variety of ACC systems, many PWA abandon them for several reasons (e.g., cognitive barriers, system complexity) over time [63]. The barriers leading to abandonment need to be evaluated and addressed to make AAC accessible, user-friendly, and acceptable for PWA, their families, and their immediate community.

Finally, two general therapeutic approaches (i.e., “Communication Partner Training (CPT)” and “Aphasia Communication Groups” (ACGs)) are adopted in aphasia rehabilitation. “Communication Partner Training (CPT)” trains communication partners (e.g., caregivers, friends) on how to best support interaction and communication for PWA [64]. In ACGs, PWA together with their communication partners interact all together on a regular basis. Interestingly, there is increasing evidence supporting the multifaceted benefits of ACGs for PWA (see [65]). For instance, improvements in conversational skills and communication strategies [66]; psychological well-being [67]); psychosocial adjustment [68]; and social connectedness [69] have all been reported.

2.4. Non-Invasive Brain-Stimulation-Based Therapies

Overall, even though the evidence indicates that behavioral aphasia rehabilitation leads to significant improvements in communication, the effect sizes of behavioral aphasia treatment studies are somewhat small (=0.28 when comparing SALT with no SALT [22]), and this may lead to only moderate improvements in most cases. This observation has urged aphasiologists to explore complimentary aphasia rehabilitation pathways, such as NIBST.

Over the last two decades, two NIBST (i.e., Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS)) have been investigated in post-stroke aphasia research for their potential to enhance neural plasticity and facilitate language recovery. Seizures and other adverse effects are minimal when NIBST are administered within the specified stimulation guidelines [70].

To induce language gains in aphasia, both rTMS and tDCS aim to either downregulate neural activity in contralesional brain regions through inhibitory stimulation protocols (i.e., low frequency (LF) rTMS or cathodal tDCS) or upregulate neural activity in perilesional brain areas of the affected hemisphere through excitatory stimulation protocols (i.e., high frequency (HF) rTMS or anodal tDCS). Both approaches are based on two proposed theoretical models of reorganization of language networks post-stroke. The first is the "interhemispheric competition model" [71], according to which there exists a mutual and balanced inhibition between the brain hemispheres. Stroke-induced damage to one hemisphere disrupts this balance leading to reduced inhibition from the affected to the unaffected hemisphere. The unaffected hemisphere, in turn, increases its inhibitory signals to the affected hemisphere. Eventually, activity is decreased in the affected and increased in the unaffected hemisphere. Over the years, it has been reported that the observed activation in unaffected language brain regions of the right hemisphere is deleterious to recovery e.g., [72][73]. Based on this assumption, by downregulating contralesional homologous brain regions via inhibitory stimulation NIBST protocols, language recovery can be induced. The second model suggests that perilesional regions of the left hemisphere are recruited to subserve the reorganization of language networks [74]. This means that, by upregulating perilesional brain regions via excitatory stimulation NIBST protocols, language gains can be achieved.

Regarding TMS aphasia research, studies have explored the effectiveness of TMS on language gains in all stages of recovery: post-acute e.g., [75][76], subacute e.g., [77][78], and chronic e.g., [79]. Most trials have investigated the effects of LF TMS over the contralesional inferior frontal gyrus (IFG) followed by SALT. The therapeutic potential of LF rTMS has also been reported as a standalone treatment e.g., [80][81][82]. Studies using HF rTMS on perilesional tissue in the left frontal regions [83][84][85] or the left dorsolateral prefrontal cortex (DLPFC) [86] are also promising for language and cognitive gains post-stroke. Regarding the evidence from tDCS studies, cathodal tDCS over the right hemisphere e.g., [87], anodal tDCS over perilesional areas e.g., [88], and simultaneous cathodal and anodal tDCS e.g., [89][90] can induce favorable language effects in PWA. In current NIBST aphasia-related studies, especially tDCS trials, NIBST are used concurrently with behavioral therapy to maximize language gains in PWA.

Findings suggest that NIBST may drive language improvement in PWA post-stroke. Nevertheless, a recent review of systematic reviews reported that the evidence of LF rTMS for aphasia rehabilitation is inconclusive [91]. In addition, a recent meta-analysis indicated that even though tDCS has the potential to enhance the naming of nouns, it does not appear to improve functional communication in PWA post-stroke [92]. Overall, even though NIBST are promising tools for boosting aphasia recovery, larger-scale, long-term studies are needed (i) to test different protocols tailored to individual needs, (ii) to clarify the precise mechanisms of rTMS and tDCS underlying language recovery, and (iii) to determine which PWA are good responders to those treatment modalities and why others are not.

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