Neuroscience Letters 719 (2020) 133329

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Review article

The potential effects of transcranial direct current stimulation (tDCS) on language functioning: Combining neuromodulation and behavioral intervention in aphasia

Paola Marangolo

Università Federico II, Napoli & IRCCS Fondazione Santa Lucia, Roma, Italy

ARTICLE INFO

Keywords:
Aphasia
Language rehabilitation
tDCS and aphasia
Neuromodulation and aphasia

ABSTRACT

Aphasia is a highly disabling language disorder usually caused by a left stroke brain damage. Even if traditional language therapies have been proved to induce an adequate clinical recovery, a large percentage of patients are left with chronic deficits at 6 months post-stroke. Therefore, new strategies to common speech therapies are urgently needed in order to maximize the recovery from aphasia. The recent application of transcranial direct current stimulation (tDCS) to language rehabilitation has already provided promising results. This brief review gives an overview of the most important results achieved using this approach and discusses how the application of this treatment might potentiate aphasia recovery.

1. Introduction

Aphasia is an acquired language disorder occuring in about 30% of left stroke survivors [1]. Due to its drammatic impact on the patient's ability to verbally communicate, it represents one of the most devastating consequence of stroke [2]. In order to accomplish to the language and communication deficits that persons with aphasia encounter, increasing support for the efficacy of Speech and Language Therapy (SLT) has been proposed [3]. However, given that even specific- and deficit-oriented therapy delivered with high intensity may result in moderate treatment effect sizes [4], over the years, the need to explore new strategies to optimize the effect of aphasia therapy has been suggested. The application of non invasive stimulation techniques, such as transcranial magnetic stimulation (TMS) and tDCS, has already considered a promising new approach to enhance the effect of regular SLT in the context of aphasia rehabilitation [5].

2. TMS vs. tDCS and the treatment of aphasic disorders

To date, two approaches have primarily been used in the application of non invasive brain stimulation for language recovery: TMS and tDCS [6,7]. Both approaches rely to the hypothesis that neuromodulation may have a role in rebalancing the activity of both hemispheres after a stroke. Indeed, it has been proposed that in patients with left hemispheric damage, the homotopic contralateral right hemispheric areas may be in a state of abnormally high activation and may exert an inhibitory effect over the left damaged hemisphere [8,9]. Thus, language recovery may be enhanced either by increasing the output of the perilesional left hemisphere through excitatory stimulation [10–28] or decreasing the inhibition from the intact right hemisphere over the left hemispheric areas by applying inhibitory current over the contralesional cortex [29–39]. Accordingly, during aphasia recovery, it has been shown that, while in the acute stage there is a recruitment of right hemisphere structures for language tasks, over time, for a number of chronic patients at least, a redistribution of language processing back to the left hemispheric perilesional areas is observed [40,41]. Inhibitory stimulation of intact contralesional cortical areas may, thus, facilitate increased recruitment of perilesional regions of the left hemisphere into reorganized language networks by diminishing the impact of transcallosal inhibitory inputs to those areas [5]. Indeed, TMS studies have already employed inhibitory stimulation of the right homologous language areas with the goal of inhibiting the underlying neural activity in order to potentiate the recovery process in the perilesional left language areas [29,32–35]; while some others have investigated beneficial TMS excitatory effects through stimulation over the perilesional left cortex [10–13]. However, although it has not yet been clarified what form of stimulation is the most effective and clinically appropriate, there are some aspects which should be considered when employing TMS in brain-damaged patients. Indeed, it has been observed that TMS might induce seizures, especially in patients who are seizure prone [42], it requires an expensive special equipment not easy to apply concurrently with behavioral tasks and needs trained health professionals. Thus, more recently, a growing body of evidence has suggested that tDCS might be a reliable alternative to TMS, since it is quite safe with mild

E-mail address: paola.marangolo@unina.it.

https://doi.org/10.1016/j.neulet.2017.12.057
Received 19 September 2017; Received in revised form 22 December 2017; Accepted 27 December 2017
Available online 28 December 2017

Table 1
Aphasia studies on tDCS combined with language treatments.

Articles	Number and type of patients	Target	Control condition	Stimulation polarity and intensity	Duration and number of sessions		Results
Norise et al. [52]	9 (chronic stroke/non-fluent aphasics: 8–116 months after stroke)	Anodal over the LIFG in 3 patients and Cathodal over LIFG in 3 patients; Anodal over the RIFG 1 patient and Cathodal over the RIFG in 1 patient	sham	Anodal, Cathodal, 2 mA		20 min, 10 sessions (during picture naming task)	Improvement in fluency after real tDCS at 2 weeks follow up only for patients with severe baseline
Marangolo et al. [65]	12 (chronic stroke/non-fluent-aphasics: 14–37 months after stroke)	Right cerebellar cortex (1 cm under and 4 cm lateral to the inion)	sham	Cathodal, 2 mA		20 min, 5 sessions (during verb generation and verb naming)	Improvement in verb generation accuracy after C-tDCS at post-treatment and at 1 week follow-up.
Marangolo et al. [66]	14 (chronic stroke/non-fluent-aphasics: 18–103 months after stroke)	9th-10th thoracic spinal vertebrae	sham	Anodal, Cathodal, 2 mA		20 min, 5 sessions (during verb and noun naming)	Improvement in verb naming after A-tsDCS at post treatment and at 1 week follow up.
Meinzer et al. [64]	26 (chronic stroke/non-fluent-aphasics: 15–108 months after stroke)	Left primary motor cortex (M1)	sham	Anodal, 1 mA		20 min, 8 sessions (2 × 1.5 h/day of computer-assisted naming treatment)	Improvement in noun naming for trained and untrained items after A-tDCS at post treatment and at 6 months follow up.
Marangolo et al. [51]	9 (chronic stroke/non-fluent aphasics: 7–96 months after stroke)	Bihemispheric tDCS: Anodal tDCS over LIFG and Cathodal tDCS over RIFG	sham	Anodal and Cathodal, 2 mA		20 min, 15 sessions (during syllables and words repetition)	Improvement in repetition accuracy on trained and untrained stimuli after bihemispheric tDCS at post-treatment and at 1 week follow-up. rs-fMRI results showed an increase of functional connectivity after real stimulation in the left hemisphere.
Wu et al. [28]	12 (post-subacute stroke/8 non-fluent aphasics, 2 fluent aphasics and 2 mixed aphasics: 3–6 months after stroke)	Left posterior perisylvian region (PPR), including Wernicke's area	sham	Anodal, 1.2 mA		20 min, 20 sessions (during picture naming and auditory word-picture identification tasks)	Improvement in picture naming and in auditory word-picture identification after A-tDCS over PPR at post-treatment. No follow up
Shah-Basak et al. [27]	5 (chronic stroke/non fluent aphasics: 7–101months after stroke)	Left DLPFC, Right DLPFC	sham	Anodal, Cathodal, 2 mA		20 min, 10 sessions (during picture naming task based on CILT)	Trend toward improvement in WAB-AQ after C-tDCS over the left DLPFC at 2-weeks and a significant improvement at 2-months
Galletta & Vogel-Eyny [19]	1 (chronic stroke/fluent-anomic aphasic: 20 months after stroke)	LIFG	sham	Anodal, 1 mA		20 min, 10 sessions (during noun and verb production in sentence context).	Improvement of verb retrieval after A-tDCS at post treatment
de Aguiar et al. [50]	9 (chronic stroke/3 fluent aphasics and 6 non fluent aphasics: 8 −92 months after stroke)	Bihemispheric, tDCS: stimulation site was determined individually, based on MRI scans.	sham	Anodal and Cathodal, 1 mA		20 min, 10 sessions ("ACTION" therapy)	Improvement in verbs production (on treated and untreated items) after bihemispheric tDCS. No follow up
Cipollari et al. [31]	6 (chronic stroke/non-fluent aphasics: 10–79 months after stroke)	RIFG	sham	Anodal, 2 mA		20 min, 15 sessions (during Melodic Intonation Therapy)	Improvement in repetition accuracy for words and sentences (on trained and untrained stimuli) after A-tDCS at post-treatment and at 1 week follow-up.
Campana et al. [15]	20 (chronic stroke/non-fluent aphasics: 6–84 months after stroke)	LIFG	sham	Anodal, 2 mA		20 min, 10 sessions (during conversational therapy)	Improvement in picture description, noun and verb naming after A-tDCS at post-treatment. No follow up
Vestito et al. [53]	3 (chronic stroke/2 non-fluent aphasics, 1 fluent anomic aphasic: 20–64 months after stroke)	LIFG	sham	Anodal, 1.5 mA		20 min, 10 sessions (during picture naming)	Improvement of naming performance after A-tDCS at post treatment and at 16 weeks follow up.
Marangolo et al. [23]	7 (chronic stroke/non-fluent aphasics: 10 −72 months after stroke)	Bihemispheric, tDCS: Anodal tDCS over LIFG and Cathodal tDCS over RIFG	sham	Anodal and Cathodal, 2 mA		20 min, 10 sessions (during conversational therapy)	Improvement in picture description, noun and verb naming after bihemispheric tDCS at post-treatment and at 1 week follow-up
Marangolo et al. [24]	8 (chronic stroke/non-fluent-aphasics: 6–84 months after stroke)	Left IFG, Left Wernicke's area	sham	Anodal, 1 mA		20 min, 10 sessions (during conversational therapy)	Improvement in cohesive devices (pronouns, ellipses, word repetitions, conjunctions) (on treated and untreated stimuli) after A-tDCS over LIFG. No follow-up
Manenti et al. [49]	1 (chronic stroke/non-fluent aphasic: 8 months after stroke)	Bihemispheric, tDCS: Anodal tDCS over LDLPFC and Cathodal tDCS over RDLPFC	no	Anodal and Cathodal, 2 mA		25 min, 20 sessions (followed by 25 min of verb naming task)	Improvement in verb naming accuracy (on treated and untreated items) at post-treatment and at 48 months follow-up.

(*continued on next page*)

Table 1 (*continued*)

Articles	Number and type of patients	Target	Control condition	Stimulation polarity and intensity	Duration and number of sessions		Results
Polanowska et al. [25]	24 (post-acute stroke/non-fluent aphasics: 2–24 weeks after stroke)	LIFG	sham	Anodal 1 mA		10 min, 15 sessions (followed by 45 min of picture naming task)	Improvement in naming accuracy and naming response time in both groups (A-tDCS and Sham).
Polanowska et al. [26]	37 (post-acute stroke/non-fluent aphasics: 2–24 weeks after stroke)	LIFG	sham	Anodal 1 mA		10 min, 15 sessions (followed by 45 min of picture naming task)	Improvement in the BDAE in both groups (A-tDCS and Sham) both at post-treatment and at 3 months follow-up.
Marangolo et al. [20]	12 (chronic stroke/non-fluent aphasics: 5–84 months after stroke)	LIFG Left Wernicke's area	sham	Anodal, 1 mA		20 min, 10 sessions (during conversational therapy)	Improvement in content units, verbs and sentences production after tDCS over LIFG at post- treatment and at 1 month follow-up.
Marangolo et al. [21]	12 (chronic stroke/non-fluent aphasics: 6–74 months after stroke)	Bihemispheric, tDCS: Anodal tDCS over LIFG and Cathodal tDCS over RIFG	sham	Anodal and Cathodal, 2 mA		20 min, 10 sessions (during repetition task)	Improvement in repetition accuracy and response time for syllables, words and sentences (on trained and untrained stimuli) after bihemispheric tDCS at post-treatment and at 1 week follow-up.
Marangolo et al. [22]	8 (chronic stroke/non-fluent aphasics: 12–84 months after stroke)	LIFG Left Wernicke's area	sham	Anodal, 1 mA		20 min, 5 sessions (during verb naming)	Improvement in verb naming after A- tDCS over the LIFG at post-treatment and at 1 month follow-up.
Lee et al. [48]	11 (chronic stroke/6 non-fluent and 5 fluent aphasics: 8–180 months after stroke)	Bihemispheric, tDCS: Anodal tDCS over LIFG and Cathodal tDCS over RIFG Single tDCS, LIFG	no no	Anodal and Cathodal, 2 mA Anodal, 2 mA		30 min, 1 session (during picture naming task)	Improvement in naming response time in the BNT after bihemispheric tDCS, no significant improvement after single tDCS. Improvement in naming accuracy after bihemispheric and single tDCS. No follow-up
Fiori et al. [17]	7 (chronic stroke/non-fluent aphasics: 9–84 months after stroke)	LIFG, Left Wernicke's area	sham	Anodal, 1 mA		20 min, 5 sessions (during noun and verb naming)	Improvement in noun naming after A-tDCS over left Wernicke's and in verb naming after A-tDCS over LIFG at post-treatment and at 1 and 4 weeks follow-up.
Cherney et al. [30]	1 (chronic stroke/non-fluent aphasic: 204 months after stroke)	Right Wernicke area	no	Cathodal, 1 mA		13 min, 30 sessions (during SLT)	Improvement in WAB AQ and in auditory comprehension at post- treatment.
You et al. [37]	21 (post-acute stroke/non-fluent aphasics: 16–38 days after stroke)	Left or right Wernicke's area	sham	Anodal over left Wernicke's area or cathodal right Wernicke's area, 2 mA		30 min, 10 sessions (during SLT)	Improvement in auditory verbal comprehension after C-tDCS at post-treatment. No follow-up.
Vines et al. [39]	6 (chronic stroke/non-fluent aphasics: 15–120 months after stroke)	RIFG	sham	Anodal, 1.2 mA		20 min, 3 sessions (during MIT)	Improvement in verbal fluency after A-tDCS at post-treatment. No follow-up
Marangolo et al. [58]	3 (chronic stroke/non-fluent aphasics: 7–48 months after stroke)	LIFG	sham	Anodal, 1 mA		20 min, 5 sessions (during repetition task)	Improvement in syllables and words repetition after A- tDCS at post-treatment and at 2 months follow-up Improvement in different language subtests.
Jung et al. [38]	37 (post-acute/chronic stroke: average 221 days after stroke)	RIFG	no	Cathodal, 1 mA		30 min, 10 sessions (during SLT)	Improvement in the WAB AQ. No follow-up.
Kang et al. [36]	10 (chronic stroke/8 non-fluent and 2 fluent aphasics: 6 −181 months after stroke)	RIFG	sham	Cathodal, 2 mA		20 min, 5 session (during word-retrieval training)	Improvement in naming accuracy in the BNT at 1 h following the last C-tDCS session, no changes after sham. No follow-up.
Fridriksson et al. [18]	8 (chronic stroke/fluent aphasics: 10–150 months after stroke)	Left posterior cortex	sham	Anodal, 1 mA		20 min, 5 sessions (during picture naming)	Improvement in naming accuracy after A-tDCS at post-treatment and at 3 weeks follow-up.
Floel et al. [67]	12 (chronic stroke/9 non-fluent aphasics and 3 fluent aphasics: 14–260 months after stroke)	Right temporo-parietal cortex	sham	Anodal, Cathodal, 1 mA		20 min, 3 sessions (2 × 1 h/day of computer-assisted naming)	Improvement in naming accuracy after A-tDCS at post-treatment and at 2 weeks follow-up.
Fiori et al. [16]	3 (chronic stroke/non-fluent aphasics: 21–71 months after stroke)	Left Wernicke's area	sham	Anodal, 1 mA		20 min, 5 sessions (during SLT)	Improvement in naming accuracy and response time after A-tDCS at post-treatment and at 3 weeks follow-up.

(*continued on next page*)

Table 1 (*continued*)

Articles	Number and type of patients	Target	Control condition	Stimulation polarity and intensity	Duration and number of sessions		Results
Baker et al. [14]	10 (chronic stroke/6 fluent and 4 non-fluent aphasics: 10–242 months after stroke)	Left frontal cortex	sham	Anodal, 1 mA		20 min, 5 session (during SLT)	Improvement in naming accuracy (on treated and untreated items) at post-treatment and at 1 week follow-up.

LIFG: Left inferior frontal gyrus.
RIFG: Right inferior frontal gyrus.
AAT: Aachen Aphasia Test.
BDAE: Boston Diagnostic Aphasia Examination.
BNT: Boston Naming Test.
CILT: Constraint-Induced Language Therapy.
DLPFC: Dorsolateral Prefrontal Cortex.
WAB AQ: Western Aphasia Battery Aphasia Quotient.
SLT: Speech Language Therapy.

and transient side effects [7,43], easy to use and less expensive. Therefore, although the employment of large electrodes (typically 5 × 7 or 5 × 5 cm) with tDCS makes it difficult to precisely identify which brain area or areas are being targeted, because tDCS electrodes are simply secured to the scalp and leave the patient free to move, tDCS is considered more suitable to deliver during rehabilitation (online stimulation) compared to TMS. In the next paragraphs, a brief overview of the most important tDCS aphasia treatment findings published in these last years is reported together with some suggestions for challenges and future directions on the use of tDCS for language recovery.

3. tDCS and the treatment of aphasic disorders

tDCS involves the application of small electrical currents (typically 1–2 mA) to the scalp through a pair of surface electrodes over a long period, usually in minutes (5–30 min), to achieve changes in cortical excitability by influencing spontaneous neural activity. An active electrode is placed on the site overlying the cortical target and a reference electrode is usually placed over the contralateral supraorbital area or in a non-cephalic region (i.e. the shoulder). tDCS induces long-lasting changes in the brain and it can be used to manipulate brain excitability via membrane polarisation: generally, the anode increases cortical excitability when applied over the region of interest, whereas the cathode decreases it, whereby the induced after-effects depend on polarity, duration and intensity of the stimulation [44,45]. In line with the model of interhemispheric competition outlined before, most tDCS studies have promoted left perilesional recruitment through excitatory current (anodal tDCS) [14–28] or inhibition of the right areas through cathodal tDCS [29–39] with the reference electrode placed over the contralateral supra-orbital region (see Table 1). Since the left inferior frontal gyrus (IFG) has long been considered to play a key role for the recovery of different language units (i.e. content words, verbs, sentences, [46,47]) and can be easily and comfortably targeted with tDCS, a large amount of studies has applied excitatory tDCS over this region [14–24,27]**;** while some other studies have applied inhibitory current over its right homologue [27,36–39]

More recently, dual stimulation where both the left and the right IFG are simultaneously targeted with anodal and cathodal tDCS respectively, has been also utilized to improve language function in patients with post-stroke aphasia [21,23,49–51] (see Table 1).

In general, the experimental protocols in tDCS aphasia studies published through 2017 used a crossover design whereby each participant received at a minimum two different stimulation conditions: an active condition which allowed researchers to explore the effect of stimulation over the targeted area (e.g., IFG) and a placebo control condition (the sham condition) in which the tDCS stimulator is turned off after a few seconds. In both conditions, the participant and the clinician are blind as to whether the participant is receiving real tDCS. This design was implemented to ensure that the patient's behavioral changes are attributable to stimulation [5].

The fact that word-finding difficulty is the most common phenomenon observed in aphasia has influenced the literature on tDCS and aphasia treatment. Indeed, predominantly, most of the studies choose word-finding therapy as the behavioral treatment component to be paired with tDCS [14,16–18,22,25–28,48,52,53]. The first use of tDCS for anomia in aphasia was reported by Monti et al. [54] who explored the immediate effects of a single tDCS session in eight chronic aphasic patients on a picture-naming task immediately prior to and after completion of stimulation but with no additional language training prior to or during the task. Since Monti et al.'s study [54], there has been an increase in the number of published papers combining tDCS with behavioral anomia therapy [14,16–18,22,25–28,48,52,53]. Those studies have suggested that lasting effects might be more easily obtained with multiple stimulations sessions and coupling the stimulation with concurrent language treatments [14,16–18,22,25–28,48,52,53]. The hypothesis underlying multiple-session studies is that the short-lasting

effects from a single session will accumulate with repeated sessions and eventually lead to a permanent improvement in the treated function [55]. Although is not yet clear how this approach might determine an improvement of language over time, the hypothesis has been advanced that multiple tDCS stimulation sessions induce a more effective relearning of language than with single session [55]. Indeed, irrespective of electrode configurations (uni vs. bihemispheric), site of stimulation (left anodal tDCS vs. right cathodal tDCS) and stimulation intensity (1 mA vs. 2 mA), all studies have pointed to an additional effect of tDCS on word recovery, when combined with SLT in a multiple session paradigm [see review 56]. However, these studies have some important methodological limitations, among which the fact that the word retrieval training mainly employed a computerized naming task of a large set of nouns and/or verbs [14,16–18,22], which has been considered an ineffective training in the aphasia rehabilitation literature [57].

Since the aphasic symptoms are heterogeneous and differently affect the language system, more recently, the application of tDCS to behavioral treatment for aphasia has been extended beyond remediation of word-finding difficulties, such as to the recovery of articulatory deficits [21,51,58] and speech production [20,23,24][e.g., 20,23,24]. In a preliminary study on a small sample of chronic patients, Marangolo et al. [58] showed that repetitive anodal tDCS over the left IFG coupled with language training helped patients to recover from their articulatory disturbances [58]. More recently, the same authors wondered if similar results would be achieved using bihemispheric tDCS delivered over the left and right IFG [21,51]. Results showed that only after the real stimulation condition the number of correct syllables, words and sentences significantly improved and significant changes persisted at one week after the end of treatment. Moreover, the improvement generalized also to other oral language tasks (picture description, noun and verb naming, word repetition and reading) and it was still present at one week after the therapy [21].

With regard to speech production, the Conversational Approach, a well-known established method in the aphasia treatment literature [59], was chosen in order to consider the relevance of combining a pragmatic treatment approach with tDCS [15,20,23,24]. The underlying theoretical motivation in choosing this approach is that having a verbal exchange in a natural context more easily prompts, in nonfluent aphasics, the use of informative speech and, therefore, communication, even if not always formally correct. The authors found that compared with the placebo condition (the sham condition), the combined effects of tDCS with conversational therapy led to the production of more informative speech, which persisted at 1 month after the end of treatment and generalized to materials that had been administered only at the beginning and at the end of the therapy sessions [15,20,23,24].

In summary, all of the above studies indicate the possibility to determine a wide spectrum of linguistic outcomes through short-term but intensive treatment programms which make use of tDCS. Therefore, this technique might be used as a supplementary treatment approach for different language deficits in patients with chronic aphasia.

4. Future research

Although the tDCS results reported above are promising and have already shown significant improvement in different language domains, many aspects remain unclear and require further investigations. Crucial elements to be considered in future studies are: 1) the necessity to include large randomized clinical controlled trials, 2) to monitor over time the benefits obtained during the treatment (i.e. not all the above cited studies included follow-ups) and 3) the inclusion of different outcome measures, such as standardized tests of everyday communication abilities [60], to be administered before and after the treatment. This in order to demonstrate that the results obtained are reliable as replicable in larger sample sizes, are not temporary and they reflect significant changes on the partecipants' ability to use language in daily-life situations. The inclusion of large sample size is important for planning and interpreting treatment findings since the larger the reference population the more representative the results limiting the influence of outliers and the risk of reporting false-negative findings. In general, researchers agree on the fact that a sample size of 30 respondents would provide a reasonable starting point [61]. Although, it should be noted that it is not always easy to find such a large homogeneous sample of subjects in the aphasia population. This is the reason why most of the already published studies have included small sample sizes. It should also be observed that, most of the tDCS studies were aimed at improving oral production [56,57], thus, we still don't know if the positive results already found might be extended to other aspects of the aphasia syndrome, such as the improvement of comprehension deficits and/or reading and writing disorders. Most importantly, when choosing the behavioral treatment to be paired with tDCS, we must verify if this treatment has already been proved to be useful in aphasia rehabilitation and which patients are the most suitable for this type of intervention [see 56 for review]. It has not also been yet established which area of the brain (non-lesioned left language dominant or right non dominant) and/or which type of stimulation (excitatory vs. inhibitory) and electrode configurations (uni vs. bihemispheric) are the most suitable to be combined with the language therapy. Previous evidence have suggested that targeting the left IFG through excitatory tDCS leads to the recovery of different language deficits (i.e. articulation disorders, non fluent speech, verb retrieval deficits) [5,56]. These results have been further supported by studies with functional magnetic resonance imaging (fMRI) [51] and computer modeling [62] which showed that the application of anodal tDCS over the left IFG primarily recruits the left perilesional regions [51] and focused the current path into the left perilesional cortex [62]; structures which are considered to be associate with the best recovery from language [40,41]. One interesting growing area of research which should be promoted in the near future for optimizing the electrode configuration (with respect to the electric field magnitude over the target region) and, therefore, in reliably assessing the efficacy of tDCS in language rehabilitation, is the use of small "high- definition" electrodes which allows to increase the electric field strengths in the targeted cortex and, thus, to identify precisely which brain area or areas are being affected [63]. Another very recent new approach to the use of tDCS for aphasia treatment relies to the hypothesis of modulating "less classical" language areas, such as the motor cortex [64], the spinal cord [65] and the cerebellum [66]. Indeed, it has been suggested that these structures, through their connections to the sensory-motor system, might work as vicarious systems in language recovery and, in particular, for those words made up of sensory-motor semantic properties, such as action verbs [65,66]. Accordingly, tDCS over the spinal cord [65] or the cerebellum [66] enhanced verb retrieval in different groups of post-stroke aphasics. Since verbs are essential for sentence construction and speech fluency, these findings, if replicated, would be extremely important for treatment outcomes in persons with aphasia.

5. Conclusion

In conclusion, although for future approaches we need to address several methodological issues outlined in this review (i.e.lack of large sample sizes, the inclusion of evidence-based language treatments to be paired with tDCS), overall the literature seems to suggest that tDCS is a viable tool for language recovery in chronic stroke patients which can be used in daily practice as an additional treatment option. Indeed, since it is considered to be quite safe with mild and transient side effects, it could be even self-administered in the patient's own home resulting in an additional economical and practical treatment for language rehabilitation.

References

[1] S.T. Engelter, M. Gostynski, S. Papa, et al., Epidemiology of aphasia attributable to

first ischemic stroke: incidence, severity, fluency, etiology, and thrombolysis, Stroke 37 (2006) 1379–1384.
[2] H. El Hachioui, H.F. Lingsma, M.E. van de Sandt-Koenderman, D.W. Dippel, P.J. Koudstaal, E.G. Visch-Brink, Recovery of aphasia after stroke: a 1-year follow-up study, J. Neurol. 260 (2013) 166–171.
[3] M.C. Brady, H. Kelly, J. Godwin, P. Enderby, Speech and language therapy for aphasia following stroke, Cochrane Database Syst. Rev. 5 (2012).
[4] H. Kelly, M.C. Brady, P. Enderby, Speech and language therapy for aphasia following stroke, Cochrane Database Syst. Rev. 5 (2010).
[5] P. Marangolo, C. Caltagirone, Options to enhance recovery of aphasia by means of non-invasive brain stimulation and action observation therapy, Expert Rev. Neurother. 14 (2014) 75–91.
[6] J.P. Lefaucher, N. André-Obadia, A. Antal, et al., Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (TMS), Clin. Neurophysiol. 125 (2014) 2150–2206.
[7] J.P. Lefaucher, A. Antal, S.S. Ayache, et al., Evidence-based guidelines on the therapeutic use of transcranial direct curent stimulation (tDCS), Clin. Neurophysiol. 128 (2017) 56–92.
[8] P. Belin, P. Van Eeckhout, M. Zilbovicius, et al., Recovery from nonfluent aphasia after melodic intonation therapy: a PET study, Neurology 47 (1996) 1504–1511.
[9] N. Murase, J. Duque, R. Mazzocchio, L.G. Cohen, Influence of interhemispheric interactions on motor function in chronic stroke, Ann. Neurol. 55 (2004) 400–409.
[10] W. Kakuda, M. Abo, G. Uruma, N. Kaito, M. Watanabe, Low-frequency rTMS with language therapy over a 3-month period for sensory-dominant aphasia: case series of two post-stroke Japanese patients, Brain Inj. 24 (2010) 113–117.
[11] W. Kakuda, M. Abo, G. Uruma, N. Kaito, M. Watanabe, A. Senoo, Functional MRI based therapeutic rTMS strategy for aphasic stroke patients: a case series pilot study, Int. J. Neurosci. 120 (2010) 60–66.
[12] M. Cotelli, A. Fertonani, A. Miozzo, et al., Anomia training and brain stimulation in chronic aphasia, Neuropsychol. Rehabil. 21 (2011) 717–741.
[13] J.P. Szaflarsky, J. Vannest, S.W. Wu, M.W. Di Francesco, C. Banks, D.L. Gilbert, Excitatory repetitive transcranial magnetic stimulation induces improvements in chronic post-stroke aphasia, Med. Sci. Monit. 25 (2011) 132–139.
[14] J.M. Baker, C. Rorden, J. Fridriksson, Using transcranial direct-current stimulation to treat stroke patients with aphasia, Stroke 41 (2010) 1229–1236.
[15] S. Campana, C. Caltagirone, P. Marangolo, Combining voxel-based lesion-symptom mapping (VLSM) with A-tDCS language treatment: predicting outcome of recovery in nonfluent chronic aphasia, Brain Stimul. 8 (2015) 769–776.
[16] V. Fiori, M. Coccia, C.V. Marinelli, et al., Transcranial direct current stimulation (tDCS) improves word retrieval in healthy and nonfluent aphasic subjects, J. Cogn. Neurosci. 23 (2011) 2309–2323.
[17] V. Fiori, S. Cipollari, M. Di Paola, C. Razzano, C. Caltagirone, P. Marangolo, tDCS segregates words in the brain, Front. Hum. Neurosci. 7 (2013) 32–40.
[18] J. Fridriksson, J.D. Richardson, J.M. Baker, C. Rorden, Transcranial direct current stimulation improves naming reaction time in fluent aphasia, Stroke 42 (2011) 819–821.
[19] E.E. Galletta, A. Vogel-Eyn, Translational treatment of aphasia combining neuromodulation and behavioral intervention for lexical retrieval: implications from a single case study, Front. Hum. Neurosci. 9 (2015) 3–7.
[20] P. Marangolo, V. Fiori, M.A. Calpagnano, S. Campana, C. Razzano, C. Caltagirone, A. Marini, tDCS over the left inferior frontal cortex improves speech production in aphasia, Front. Hum. Neurosci. 7 (2013) 53–59.
[21] P. Marangolo, V. Fiori, S. Cipollari, S. Campana, C. Razzano, M. Di Paola, C. Caltagirone, Bihemispheric stimulation over left and right inferior frontal region enhances recovery from apraxia of speech in chronic aphasia, Eur. J. Neurosci. 38 (2013) 3370–3377.
[22] P. Marangolo, V. Fiori, M. Di Paola, et al., Differential processing of the left frontal and temporal regions in verb naming: a tDCS treatment study, Restor. Neurol. Neurosci. 31 (2013) 63–72.
[23] P. Marangolo, V. Fiori, F. Gelfo, J. Shofany, C. Razzano, C. Caltagirone, F. Angelucci, Bihemispheric tDCS enhances language recovery but does not alter BDNF levels in chronic aphasic patients, Restor. Neurol Neurosci. 32 (2014) 367–379.
[24] P. Marangolo, V. Fiori, S. Campana, M.A. Calpagnano, C. Razzano, C. Caltagirone, A. Marini, Something to talk about: enhancement of linguistic cohesion through tDCS in chronic nonfluent aphasia, Neuropsychologia 53 (2014) 246–256.
[25] K.E. Polanowska, M.M. Leśniak, J.B. Seniów, W. Czepiel, A. Członkowska, Anodal transcranial direct current stimulation in early rehabilitation of patients with post-stroke non-fluent aphasia: a randomized, double-blind, sham-controlled pilot study, Restor. Neurol. Neurosci. 31 (2013) 761–771.
[26] K.E. Polanowska, M. Leśniak, J.B. Seniów, A. Członkowska, No effects of anodal transcranial direct stimulation on language abilities in early rehabilitation of post-stroke aphasic patients, Neurol. Neurochir. Pol. 47 (2013) 414–422.
[27] P.P. Shah-Basak, C. Norise, G. Garcia, J. Torres, O. Faseyitan, R.H. Hamilton, Individualized treatment with transcranial direct current stimulation in patients with chronic non-fluent aphasia due to stroke, Front. Hum. Neurosci. 9 (2015) 56–60.
[28] D. Wu, J. Wang, Y. Yuan, Effects of transcranial direct current stimulation on naming and cortical excitability in stroke patients with aphasia, Neurosci. Lett. 589 (2015) 115–120.
[29] C.H. Barwood, B.E. Murdoch, B.M. Whelan, et al., The effects of low frequency Repetitive Transcranial Magnetic Stimulation (rTMS) and sham condition rTMS on behavioural learning in chronic non-fluent aphasia: short term outcomes, Neurorehabilitation 28 (2011) 113–128.
[30] L.R. Cherney, E.M. Babbitt, R. Hurwitz, L.M. Rogers, J. Stinear, X. Wang, T. Parrish, Transcranial direct current stimulation and aphasia: the case of Mr C, Topics Stroke Rehab. 20 (2013) 5–21.
[31] S. Cipollari, D. Veniero, C. Razzano, C. Caltagirone, G. Koch, P. Marangolo, Combining TMS-EEG with transcranial direct current stimulation language treatment in aphasia, Expert Rev. Neurother. 15 (7) (2015) 833–845.
[32] M.A. Naeser, P.I. Martin, N. Marjoire, et al., Improved picture naming in chronic aphasia after TMS to part of right Broca's area: an open-protocol study, Brain Lang. 93 (2005) 95–105.
[33] M.A. Naeser, P.I. Martin, K. Lungren, et al., Improved language in a chronic non-fluent aphasia patient after treatment with CPAP and TMS, Cogn. Behv. Neurol. 23 (2010) 29–38.
[34] N. Weiduschat, A. Thiel, I. Rubi-Fessen, et al., Effects of repetitive transcranial magnetic stimulation in aphasic stroke: a randomized controlled pilot study, Stroke 42 (2011) 409–415.
[35] L. Winhuisen, A. Thiel, B. Schumacher, et al., Role of the contralateral inferior frontal gyrus in recovery of language function in poststroke aphasia: a combined repetitive transcranial magnetic stimulation and positron emission tomography study, Stroke 36 (2005) 1759–1763.
[36] E.K. Kang, Y.K. Kim, H.M. Sohn, L.G. Cohen, N.J. Paik, Improved picture naming in aphasia patients treated with cathodal tDCS to inhibit the right Broca's homologue area, Restor. Neurol. Neurosci. 29 (2011) 141–152.
[37] D.S. You, D.Y. Kim, M.H. Chun, et al., Cathodal transcranial direct current stimulation of the right Wernicke's area improves comprehension in subacute stroke patients, Brain Lang. 119 (2011) 1–5.
[38] I.Y. Jung, J.Y. Lim, E.K. Kang, et al., The factors associated with good responses to speech therapy combined with transcranial direct current stimulation in post-stroke aphasic patients, Ann. Rehabil. Med. 35 (2011) 460–469.
[39] B.W. Vines, A.C. Norton, G. Schlaug, Non-invasive brain stimulation enhances the effects of melodic intonation therapy, Front. Psych. 2 (2011) 5–9.
[40] S.F. Cappa, The neural basis of aphasia rehabilitation: evidence form neuroimaging and neurostimulation, Neuropsychol. Rehabil. 21 (2011) 742–754.
[41] D. Saur, G. Hartwigsen, Neurobiology of language recovery after stroke: lessons from neuroimaging studies, Arch Phys Med Rehab 93 (2012) 15–25.
[42] J. Reis, F. Rosenow, B. Fritsch, S. Knake, W.H. Oertel, H.M. Hamer, Possible transcallosal seizures induction by paired pulse transcranial magnetic stimulation in a patient with frontal lobe epilepsy, J. Neurol. Neurosurg. Psychiatry 76 (2005) 454–455.
[43] C. Poreisz, K. Boros, A. Antal, W. Paulus, Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients, Brain Res. Bull. 72 (2007) 208–214.
[44] M.A. Nitsche, W. Paulus, Transcranial direct current stimulation—update 2011, Restor. Neurol. Neurosci. 29 (2011) 463–492.
[45] M.P. Jackson, M. Bikson, M. Nitsche, Toward comprehensive tDCS safety standards, Brain Behav. Immun. 66 (2017) (Epub ahead of print.).
[46] M.F. Burns, J. Fahy, Broca's area: rethinking classical concepts from a neuroscience perspective, Top. Stroke Rehabil. 17 (2010) 401–410.
[47] A. Marini, C. Urgesi, Please get to the point! A cortical correlate of linguistic informativeness, J. Cogn. Neurosci. 24 (2012) 2211–2222.
[48] S.Y. Lee, H.J. Cheon, K.J. Yoon, W.H. Chang, Y.H. Kim, Effects of dual transcranial direct current stimulation for aphasia in chronic stroke patients, Ann. Rehab. Med. 37 (2013) 603–610.
[49] R. Manenti, M. Petesi, M. Brambilla, S. Rosini, A. Miozzo, A. Padovani, M. Cotelli, Efficacy of semantic-phonological treatment combined with tDCS for verb retrieval in a patient with aphasia, Neurocase 4794 (2014) 37–41.
[50] V. de Aguiar, R. Bastiaanse, R. Capasso, M. Gandolfi, N. Smania, G. Rossi, G. Miceli, Can tDCS enhance item-specific effects and generalization after linguistically motivated aphasia therapy for verbs, Front. Behav. Neurosci 9 (2015) 45–50.
[51] P. Marangolo, V. Fiori, U. Sabatini, et al., Bilateral transcranial direct current stimulation language treatment enhances functional connectivity in the left hemisphere: preliminary data form aphasia, J. Cog. Neurosci. 28 (2016) 724–738.
[52] C. Norise, D. Sacchetti, R. Hamilton, Transcranial direct current stimulation in post-stroke chronic aphasia: the impact of baseline severity and task specificity in a pilot sample, Front. Hum. Neurosci. 11 (2017) 34–38.
[53] L. Vestito, S. Rosellini, M. Mantero, F. Bandini, Long-term effects of transcranial direct-current stimulation in chronic post-stroke aphasia: a pilot study, Front. Hum. Neurosci. 8 (2014) 78–82.
[54] A. Monti, F. Cogiamanian, S. Marceglia, et al., Improved naming after transcranial direct current stimulation in aphasia, J. Neurol. Neurosurg. Psychiatry. 79 (2013) 451–453.
[55] K. Monte-Silva, M.F. Kuo, S. Hessenthaler, et al., Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation, Brain Stimul. 6 (2013) 424–432.
[56] E. Galletta, P. Conner, A. Vogel-Eyny, P. Marangolo, Use of tDCS in aphasia rehabilitation: a systematic review of the behavioral interventions implemented with noninvasive brain stimulation for language recovery, Am. J. Speech Lang. Pathol. 25 (2016) S854–S867.
[57] M.C. Brady, H. Kelly, G. Godwin, P. Enderby, Speech and language therapy for aphasia following stroke (review), Cochrane Database Syst. Rev. 5 (2012) 1–45.
[58] P. Marangolo, C.V. Marinelli, S. Bonifazi, 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. 225 (2011) 498–504.
[59] P. Marangolo, V. Fiori, C. Caltagirone, A. Marini, How conversational therapy influences language recovery in chronic non-fluent aphasia, Neuropsychol. Rehabil. 23 (2013) 715–731.
[60] M.B. Ruiter, H.H.J. Kolk, T.C.M. Rietveld, et al., Towards a quantitative measure of verbal effectiveness and efficiency in the Amsterdam-Nijmegen Everyday Language Test (ANELT), Aphasiology 25 (2011) 961–975.

[61] K.S. Button, J.P.A. Ioannidis, C. Mokrysz, B.A. Nosek, J.F. Flint, E.S.J. Robinson, M.R. Munafò, Power failure: whay small sample size undermines the reliability of neuroscience, Nature Rev. Neurosci. 14 (2013) 365–376.
[62] E. Galletta, A. Cancelli, C. Cottone, I. Simonelli, F. Tecchio, M. Bikson, P. Marangolo, Use of computational modeling to inform tDCS electrode montages for the promotion of language recovery in post-stroke aphasia, Brain Stimul. 8 (2015) 1108–1115.
[63] J.P. Dmochowski, A. Datta, Y. Huang, et al., Targeted transcranial direct current stimulation for rehabilitation after stroke, Neuroimage 75 (2013) 12–19.
[64] M. Meinzer, R. Darkow, R. Lindenberg, A. Flöel, Electrical stimulation of the motor cortex enhances treatment outcome in post-stroke aphasia, Brain 139 (2016) 1152–1163.
[65] P. Marangolo, V. Fiori, J. Shofany, T. Gili, C. Caltagirone, G. Cucuzza, A. Priori, Moving beyond the brain: transcutaneous spinal direct current stimulation in post-stroke aphasia, Front. Neurol. 8 (2017) 400.
[66] P. Marangolo, V. Fiori, C. Caltagirone, F. Pisano, A. Priori, Transcranial cerebellar direct current stimulation enhances verb generation but not verb naming in post-stroke, Aphasia. J. Cog. Neurosci (2017) 1–12 (Epub ahead of print).
[67] A. Floel, M. Meinzer, R. Kirstein, S. Nijhof, M. Deppe, S. Knecht, C. Breitenstein, Short-term anomia training and electrical brain stimulation, Stroke 42 (2011) 2065–2067.