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The rehabilitative effects on written language of a combined language and parietal dual-tDCS treatment in a stroke case

Barbara De Tommaso[1], Alessandro Piedimonte[2], Marcella M Caglio[3], Federico D'Agata[3*], Marcello Campagnoli[4], Laura Orsi[3], Simona Raimondo[1], Sergio Vighetti[3], Paolo Mortara[3], Giuseppe Massazza[4], Lorenzo Pinessi[3]

[1] Speech Therapy, AOU Città della Salute e della Scienza (Presidio Molinette)

[2] Psychology Department, University of Turin

[3] Neuroscience Department, University of Turin

[4] Physical Medicine and Rehabilitation, University of Turin

* Corresponding Author: Federico D'Agata, Via Cherasco, 15 - 10126, Turin, Italy

Tel: 0039 011 633 6298/5426, Fax: 0039 011 696 3487

Mail: federico.dagata@unito.it

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Abstract:

In this paper we reported the effect of a combined tDCS and Speech Language Therapy on linguistic deficits following left brain damage in a stroke case. We showed that simultaneous electrical excitatory stimulation to the left and inhibitory stimulation to the right parietal regions (dual-tDCS) affected writing and reading rehabilitation, enhancing speech therapy outcomes. The results of a comparison with healthy controls showed that application of dual-tDCS could improve particularly the sub-lexical transcoding and specifically the reading of non-words with increasing length and complexity. Positive repercussions on patient's quality of functional communication was also ascertained. Significant changes were found out also in other language and cognitive tasks not directly treated (comprehension and constructive apraxia).

Keywords: Speech Language Therapy, tDCS, reading and writing rehabilitation, stroke

Introduction

Transcranial Direct Current Stimulation (tDCS) is a non-invasive neuromodulation technique that induces brain excitability changes and promotes cerebral plasticity. Recent research suggests that it may be a viable approach to improve the effectiveness of Speech Language Therapy (SLT) in the treatment of post-stroke aphasia (Fridriksson, Richardson, Baker, & Rorden, 2011; Holland & Crinion, 2012; Monti et al., 2013). Thanks to its simplicity, low cost and suitability for online use, tDCS holds great promise in the field of aphasia rehabilitation. Furthermore, it is also noninvasive and relatively painless.

tDCS modulates neuronal activity through a weak direct current delivered on the scalp, inducing prolonged functional after-effects in the brain. Small currents (typically 1-2 mA) are applied to the scalp during a restricted time window (usually between 10 and 30 minutes) through two surface electrodes (usually 5×5 cm^2, or 5×7 cm^2 in size) soaked in isotonic saline solution (Nitsche & Paulus, 2000; Nitsche et al., 2003). tDCS is considered safe and induces no major adverse effects (Nitsche et al., 2003; Poreisz, Boros, Antal, & Paulus, 2007).

Commonly tDCS has been used placing the stimulating (anodal) electrode over the target area while the reference (cathodal) electrode can be placed on the scalp (‘bipolar tDCS’) or on a different body part, usually the right shoulder, (‘monopolar tDCS’). Different electrode configurations are believed to affect the focality of stimulation and the path of current flow (Borckardt et al., 2012).

The mechanisms of tDCS are classified as synaptic: changes by altering the strength of synaptic transmission and non-synaptic: shifts in resting membrane potential of pre- and post-synaptic neurons (Brunoni et al., 2012; Stagg & Nitsche, 2011). Although the exact mechanisms of tDCS action still need to be clarified, it is generally accepted that different effects on brain excitability can be obtained by varying the current polarity, intensity and duration of the stimulation. Normally anodal stimulation is supposed to depolarize neurons leading to an increase in excitability, whereas cathodal stimulation has the opposite effect.

While anodal tDCS applied over the perilesional areas has been shown to improve linguistic skills after brain damage (Baker, Rorden, & Fridriksson, 2010; Fiori et al., 2011; Fridriksson et al., 2011; Marangolo et al., 2011), cathodal tDCS seems to be effective when applied over the lesioned cortex (Monti et al., 2008) or on the contralateral hemisphere (Jung, Lim, Kang, Sohn, & Paik, 2011; Kang, Kim, Sohn, Cohen, & Paik, 2011; You, Kim, Chun, Jung, & Park, 2011). Therefore, placing the anodal electrode over the perilesional area with the cathodal over the contralateral hemisphere could, theoretically, boost tDCS-induced language improvement (Fridriksson et al., 2011; Monti et al., 2013), but most tDCS studies have investigated the effects of monohemispheric stimulation. To our knowledge only a few reports have examined the role of bihemispheric tDCS (dual-tDCS) on aphasia recovery (Lee, Cheon, Yoon, Chang, & Kim, 2013; Marangolo et al., 2013).

Among post-stroke aphasic patients, impairments affecting the written language abilities are quite frequent, and typically reading and writing are more impaired than spoken language (Sinanović, Mrkonjić, Zukić, Vidović, & Imamović, 2011). However, Monti's review on tDCS studies on language functions in patients with aphasia, reveals that, to date, no study directly assesses the effects of tDCS on written language disorders (Monti et al., 2013).

Furthermore, the 2013 Cochrane review (Elsner, Kugler, Pohl, & Mehrholz, 2013) found no study using any formal outcome measure for measuring aphasia in a real-life communicative setting.

Based on these three considerations, we report the case of a patient with a left parietal brain lesion, diagnosed with post-stroke aphasia, characterized by moderate impairment in the written language domain that presented a significant improvement after a combined SLT and dual-tDCS treatment.

Turkeltaub et al., (2012a) used a similar dual temporo-parietal tDCS montage that demonstrated a greater than sham effect in word reading efficiency only in in below-average readers. The authors suggested that the enhancing could potentially be optimized by pairing stimulation with behaviors that engage specific cognitive processes.

Literature findings also suggested that frontal lobe stimulation could be most useful for patients with frontal lobe lesions whereas posterior stimulation may be more useful for patients who also present with primarily posterior lesions (Baker, Rorden, & Fridriksson, 2010).

Costanzo et al. (2012) used high frequency rTMS to evaluate the contribution of left and right inferior parietal lobe (IPL) and left and right superior temporal gyrus (STG) to reading aloud in normal subjects. The authors demonstrated that high frequency rTMS (stimulating) over the left IPL improves non-word reading accuracy whereas over the right STG increased text reading errors probably by enhancing inhibition over the left homologous area. The effects were target specific as STG is associated with the auditory representation of spoken words, IPL operates in phonological computation (Costanzo et al., 2012). Similar effects were also found in dyslexic patients (Costanzo et al., 2013) with an improvement of non-word reading after the stimulation of left IPL.

In view of all the above considerations, the rationale of left IPL anodic stimulation paired with SLT was of promoting the recovering of perilesional areas functioning during the relearning of skills during the STL rehabilitation.

We included in the test battery the ASHA-FACS (Functional Assessment of Communication skills for Adults, Frattali, Holland, Thompson, Wohl, & Ferketic, 2004). ASHA-FACS is a tool to monitor through quantitative measures the improvements in functional communication skills. This aspect was particularly relevant as the difficulties in reading and writing were recognized by the patient himself as the most detrimental on the efficacy of his functional communication and on his social participation and few works examined these aspects in the evaluation of the effectiveness of a rehabilitation protocol.

The principal aim of this preliminary study was to discuss the outcomes of the combined behavioral and neurostimulation approach, comparing it to a simple behavioural approach. Furthermore, we wanted to investigate tolerability, feasibility and efficacy of a bihemispheric parietal stimulation montage on a stroke patient with written language deficits.

Methods

Participants

We enrolled for the study a 58 years old male FC patient (8 years of education), with a left-parietal ischemic infarction causing aphasic disorders mainly in the written language domain and oral narrative abilities, with significant deficits in the pragmatic abilities of daily communication. The stroke event (see the acute post-stroke CT scan in Fig. 1) occurred 6 months before the study and affected many parietal areas including parts of IPL, angular and supramarginal gyrus (Brodmann Area 40). On clinical observation no cognitive impairment or unilateral neglect syndrome were noted. The MMSE (score = 24.74) was normal (cut-off >23.4), but evidenced working memory, reading, writing and praxic deficits.

Eight participants (mean age ± standard deviation = 60 ± 3 years; mean education ± standard deviation = 8 ± 2 years) were recruited as control group for the evaluation of unstandardized cognitive-behavioral and linguistic-communicative tests. All participants agreed and signed the informed consent form and the experimental procedure was approved by the Hospital ethics board in accordance with Helsinki declaration.

Experimental design

FC underwent the rehabilitation sessions in the AOU Città della Salute e della Scienza, Turin. Speech therapy rehabilitation and tDCS were administered in a room of the Speech Therapy ward in the Otorhinolaryngology 2 U department of the hospital.

The patient underwent SLT twice in two different conditions:

1. during bihemispheric stimulation (anodic ipsilesional stimulation over the left parietal area and cathodic contralesional stimulation over the right homologue area);
2. without stimulation.

Both SLT lasted 12 sessions (3 consecutive days per week for a month) and a 30-days intersession interval period between the conditions 1 and 2 was planned (in order to minimize carry-over effects). Each day, electrodes were placed on the scalp of the participant before the starting of SLT.

Each complete session of SLT lasted one hour, while tDCS stimulation lasted only 20 minutes. While the stimulation ended before the conclusion of the session, that there is strong evidence that direct current effects have long lasting effects, at least accounting for the first half hour after the stimulation (Schlaug & Renga, 2008).

Direct current stimulation

Direct current was administrated using a Newronika device via two 5 x 5 cm^2 pads soaked with saline solution. The anode, known to facilitate neuronal activity, was placed in the area on the left hemisphere damaged by the stroke (corresponding to P3 position in the 10-20 EEG system) while the cathode, known to inhibit neural activity, was placed to the analogue position on the right hemisphere (P4 position). The intensity of the stimulation was set at 1.5 mA and the duration of the tDCS was set at 20 minutes: both parameters are in line with safety limits established in animal and human studies (Poreisz et al., 2007).

The technique used was not focal, but spread over a large area (see Fig. 1). As the effect resulted from the interaction of the neural activity (language relearning focused on reading/writing) and of the enhanced neuroplasticity, we put the electrode in proximity of the intended perilesional target positioning the electrodes over the Brodmann Area 40 (Herwig, 2003).

Speech Language Therapy

The SLT approach was based on an integrated and multi-level intervention and focused on the cognitive and communicative profile emerging from the assessment. Thus a specific intervention on the reading/writing domains was integrated with the training of the skills in functional communication, to enhance a higher independence and competence in different conversational contexts.

The Semantic-Lexical Model (Caramazza, 1988) and the associated *two-ways diagram* (Coltheart, Patterson, & Marshall, 1990) for the reading and writing systems (Dual Route Cascade model, DRC), was adopted as reference model to orient our SLT for the recovery of the patient specific deficits.

The DRC model is a computational model of reading which is intended to explain how skilled readers perform certain basic reading tasks. The acronym emphasizes the two fundamental properties of the model: it is a Dual Route model, and within the model information processing occurs in a Cascaded fashion.

The DRC model computes pronunciation from print via two-ways, a lexical procedure and a nonlexical procedure. The lexical procedure involves accessing a representation in the model's orthographic lexicon of real words and from there activating the word's node in the model's phonological lexicon of real words, which in turn activates the word's phonemes at the phoneme level of the model. The nonlexical procedure of the DRC model applies grapheme-phoneme correspondence rules to the input string to convert letters to phonemes (see supplementary materials to read a more extended description of DRC).

The pragmatic aspects were approached with attention to enhance informativity and a correct organization of the oral telling ability. At this aim different materials were selected in accordance with patient's main interests and needs. The training of the skills in functional communication was carried out through applying the rules of the pragmatic and pragmalinguistic approach into a conversational setting, aimed at enhance a correct and proficient message exchange. Thus, higher and better informativity, congruence and coherence within the communication exchange were gained through continuous feedbacks and remodeling actions provided by the trainer in response to the adequacy of the patient contribute.

The main areas of interventions (selected on the basis of the results of the assessment) were:

- sublexical mechanisms (at the basis of grapheme-to-phoneme conversion and vice versa), mainly involved in non-word reading and writing,
- lexical procedures, which sustain the ability in reading aloud and writing words (within a dictation task).

In order to compare the results of the two treatment cycles, SLT was carried out with similar modalities and homogeneous material in both blocks. Thirty minutes of each session were dedicated to treat reading and writing deficits (with a longer time employed for the reading skills rather than the writing ones). The final part of each session was dedicated at enhancing the textual and pragmatic abilities. The therapeutic intervention was organized within a rigorous setting (materials and modalities) during the direct treatment of the written language domain, and a more flexible approach during the training dedicated to the pragmatic aspects.

Reading deficits: a specific training focused on the segmental conversion functions was proposed, because they offer a rapid generalization of the acquired learning and a highly probable transfer from reading to writing skills (Carlomagno, & Luzzatti, 1997). Syllabic segments were employed in order to stimulate the sublexical mechanisms of the phonological-orthographical conversion (in the Italian language system the contextual rules of conversion occur at the syllabic level). We excluded the use of lexical strategies which could guarantee exclusively an item-specific learning. During treatment, lists of mono/bi/tri-syllabic elements (non-words), with different patterns, were presented for a short (and controlled) time on a monitor. The patient had to read aloud the stimulus and write it after its disappearance. Lists of words with different levels of difficulties (representative of all the semantic and grammatical categories) were also presented. Lists of syntagms and complete phrases were also included in the treatment material.

Writing deficits, treatment was analogous to the one for reading deficits: the patient had to write lists of syllables, non-words, words and short phrases which were dictated by the therapist (with different patterns of length and complexity). He was encouraged at a correct segmentation of the stimulus into its syllabic units.

All the *sublexical* lists were balanced in the occurrence of phonemes and consonant groups; the *lexical* lists were balanced with respect of the frequency of use and the grammatical categories of the Italian language. The lists presented in each block of treatment include different stimuli, but a homogeneous distribution of them was guaranteed so to avoid learning effect.

Speech and neuropsychological testing

We evaluated FC with standardized tests for neuropsychological and communication/language assessment and with an unstandardized protocol containing tasks from the BADA battery (Batteria per l'Analisi dei Deficit Afasici, Battery for the Analysis of Aphasic Deficit, Miceli, Laudanna, Burani, & Capasso, 1994).

FC was tested four times: at T0 a day before SLT, at T1 a day after SLT, at T2 a day before SLT/dual-tDCS and at T3 a day after SLT/dual-tDCS.

The neuropsychological assessment consisted of a battery of cognitive tests assessing: attention, verbal and spatial short-term memory, verbal long-term memory, visuospatial skills, language production and comprehension. The battery included: Attentional Matrices, Digit Span, Corsi Block-Tapping Test, Rey Auditory Verbal Learning Test (RAVLT), Copy of Figure, Line Bisection Test, Phonemic Fluency, Token Test. The Hamilton self-report questionnaire (HAM-D) was used to quantify depression.

The language assessment consisted in 4 subtests of AAT (Aachener Aphasia Test, Luzzatti, Willmes, & De Bleser, 1996): repetition, reading and writing, naming, speech comprehension; and 4 qualitative communication dimensions of the ASHA-FACS (Frattali et al., 2004): social communication, communication needs, reading/writing/number concepts, daily planning. We used the Italian normative data of these test to evaluate if the subject performance was impaired.

The unstandardized protocol included: non-words reading task, non-words writing task, lexical decision task (visual and auditory), words reading task (with words in sentences and words isolated), words writing task, sentence repetition task, generation task (oral phonemic criterion, oral grammatical criterion and written). We included the BADA tasks to obtain an evaluation with more trials compared to standardized subtests in order to be more accurate and statistically sound.

Parallel and equivalent forms were used for all testing, along the evaluations, where necessary.

See supplementary materials to read a more extended description of the tests.

Statistical analysis

In this single case study, we adopted the matched control sample approach, adopting the statistical procedures developed by Crawford and collaborators (Crawford, Garthwaite, & Porter, 2010; Crawford & Garthwaite, 2007). For each variable, we computed an effect size estimation called z_{cc} (z case-controls) and the probability that a member of the control population would obtain a lower score than the single case. Cutoff of normality was computed from normal group data as mean + 2 standard deviations for errors and mean -2 standard deviations for word generation.

To compare the patient FC performance in the different linguistic domains through the different time points of the study (T0 = baseline, T1 = after SLT, T2 = after 1 month pause, T3 = after SLT/dual-tDCS) we applied non parametric Cochran Q test. When T3 and T1 differed, as a post-hoc analysis to exclude that the result at T3 represents a combination of sustained gain from the first round of SLT and the second round with dual-tDCS, we directly compared also the effects of the treatments: T1-T0 vs. T3-T2.

Results

We had no adverse effects and the patient tolerated well all the tDCS sessions.

AAT and ASHA-FACS

At T0 the AAT evidenced moderate problems in comprehension, writing and reading while the repetition and naming were spared (Table I). The comprehension became normal at T1 after SLT and lasted along all the time points (T2, T3). The writing and reading performances were below threshold at all the time points (T0, T1, T2, T3) but showed a tendency to improve, especially between T2 and T3 (11 points gain).

The ASHA-FACS evidenced a good functional qualitative profile in all areas except reading and writing (Table I). Nevertheless, the impairment in ASHA-FACS reading/writing/number concepts subscale disappeared only after SLT/dual-tDCS treatment. The final score of 4/5 takes the patient performance over the cut-off expected for the Italian normative sample.

Neuropsychological

FC showed a conserved short-term spatial and visual memory (Corsi and Digit Span). The tests did not show neglect or depression (HAM-D), but a stable attentional deficit was evident (Table I). The rehabilitation increased verbal memory (RAVLT) and fluency either for SLT alone or with dual-tDCS, while only dual-tDCS treatment could bring the scores in the Copy of Figure and Token Test (comprehension) to normal range (Table I).

Modified BADA

In the *non-words reading* task (Fig. 2), the analysis showed a reduction of the errors from T0 to T1, after the first SLT rehabilitation ($p<0.01$), and from T2 to T3, after the SLT/dual-tDCS combined rehabilitation ($p<0.01$). The analysis showed a worsening from T1 to T2, when no rehabilitation program was delivered ($p<0.01$). Finally, we found a reduction of errors between T1 (SLT) and T3 (SLT/dual-tDCS, $p<0.01$) showing that the combined rehabilitation had better results in comparison to the simple SLT (post-hoc T3-T2>T1-T0, $p<0.01$). The percentage of errors of patient FC was significantly higher than the percentage in the control group at T0, T1 and T2, but at T3, after the combined rehabilitation sessions, it became normal. The effect was particularly evident for disyllabic and trisyllabic reading (Fig. 2).

In *non-words writing* (Fig. 2), the analysis showed an error reduction after both treatments ($p<0.01$) and an error increase during the pause ($p<0.01$). However, no difference between treatments was evident. There was a difference between patient and controls' performances at T0 and T2, but no differences were found in T1 and T3 after treatments, especially for monosyllabic and trysillabic writing (Fig. 2).

In the *word reading* task (Fig. 2), when the patient was reading isolated words, we found a significant error reduction between T0 and T1 ($p<0.01$) and this change lasted between T1 and T2 where no difference was found ($p>0.05$). We found an error reduction between T2 and T3 ($p<0.01$) and, furthermore, the analysis found a reduction of errors between T1 (SLT) and T3 (SLT/dual-tDCS, $p<0.01$, post-hoc T3-T2>T1-T0, $p<0.01$). When the patient was reading words in sentences, we found a reduction of errors between T0 and T1 ($p<0.01$), an error increase between T1 and T2

($p<0.01$) and an error reduction between T2 and T3 ($p<0.01$) but no difference between rehabilitation conditions T1 and T3 ($p>0.05$).

In the *words writing* task (Fig. 2) patient performance presented a reduction of errors between T0 and T1 ($p<0.01$), an increase of errors between T1 and T2 ($p<0.01$) and a reduction of errors between T2 and T3 ($p<0.01$). Finally, the analysis found a slightly significant reduction of errors between T1 (SLT) and T3 (SLT/tDCS) ($p<0.05$, but post-hoc T3-T2>T1-T0, $p>0.05$).

In the word reading and word writing task patient performances were characterized by a significantly higher percentage of errors in respect to controls' performance; even though the patient improved drastically from T0 to T3 he was still deficitary compared to control group (Fig 2).

In the *visual lexical decision* task (Fig. 2), we found a significant error reduction between T0 and T1 ($p<0.01$), an increase in errors between T1 and T2 ($p<0.01$) and a significant error reduction between T2 and T3 ($p<0.01$). Also, the analysis found a reduction of errors between T1 (SLT) and T3 (SLT/tDCS) ($p<0.01$, post-hoc T3-T2>T1-T0, $p<0.01$).

In the *auditory lexical decision* task (Fig. 2), the analysis showed a significant error reduction between T0 and T1 ($p<0.05$), a worsening of the errors between T1 and T2 ($p<0.01$) and a highly significant error reduction between T2 and T3 ($p<0.01$). However no difference between T1 and T3 was found ($p>0.05$).

In the auditory lexical decision task (Fig. 2) both the treatments were effective (T1 and T3) and normalized the performance of the patient. On the contrary, in the visual lexical decision task, patient errors stayed significantly higher than the controls in all time points.

In the *sentence repetition* task, patient presented no error reduction between T0 and T1 ($p>0.05$) but a significant error reduction between T1 and T2 ($p<0.01$) and the errors were nullified between T2 and T3 ($p<0.01$). This result was confirmed by a reduction of errors between T1 (SLT) and T3 (SLT/dual-tDCS) ($p<0.01$, post-hoc T3-T2>T1-T0, $p<0.01$). Only after dual-tDCS the patient performance was similar to normal controls (Fig. 2).

In the *oral generation* (Fig. 2), using the phonemic criterion, patient production presented the only increase between T2 and T3, after the SLT/tDCS ($p<0.05$). Following the grammatical criterion, patient production presented an increase between T0 and T1 ($p<0.01$), a decrease between T1 and T2 ($p<0.01$) and an increase between T2 and T3 ($p<0.01$). However no difference was found between rehabilitation conditions T1 and T3 ($p>0.05$).

In the *written generation* the analysis did not find any difference in patient production in the different time points (T0, T1, T2, T3). Only in the oral generation with the grammatical criterion the performance reached a normal level after both treatments (Fig. 2).

See supplementary results for the detailed statistical values of the statistical analyses.

Discussion

In this paper we reported the effect of a combined tDCS and SLT therapy on linguistic deficits following left brain damage. We adopted a dual-tDCS approach, based on the idea that after a vascular stroke, an hyper-activation of the right hemisphere can be observed as a way to compensate for the left stroke, and on the evidence that stimulation of the left hemisphere while simultaneously down-regulating the activity of the right hemisphere proved to be effective in stroke recovery in motor rehabilitation (Lindenberg, Renga, Zhu, Nair, & Schlaug, 2010) and in aphasia (Marangolo et al., 2013). This neurostimolation paradigm was well tolerated in our patient and can be considered safe and applicable for future studies.

The analysis of the case described here suggested that simultaneous excitatory (anodic) stimulation to the left ipsilesional hemisphere and inhibitory (cathodic) stimulation to the right contralesional regions, in a sub-acute aphasia patient, may affect the treated functions enhancing SLT outcomes.

Results in Costanzo et al. (2012) confirmed the prevalent role of the left IPL in grapheme-to-phoneme: the non-word reading improvement after left IPL stimulation provide a direct link between left IPL activation and advantages in sublexical procedures, mainly involved in non-word reading. This work on healthy subjects could explain the neural correlates between the deficits of our patient and its lesion.

As to the linguistic functions of the right hemisphere, there are mixed evidences in literature. The right hemisphere could have either adaptive or maladaptive functions. It has an inhibitory role on the left hemisphere, and in stroke it could interfere with the reacquiring of linguistic skills, but it could also have a substitute role for some linguistic function. This could be appreciated even in a single patient (as reported by Turkeltaub et al., 2012b).

We decided to apply cathodic inhibition over right IPL to diminish maladaptive interference of this right area over the left homologue, promoting the left activation. The possibility of limiting a hypothetic right replacement function was controlled by the choice of the application of tDCS online: in fact, the behavior output (language) is congruent with the suppression of the maladaptive inhibition of the right hemisphere and the contrary is true for its substitute function.

Our results (Fig. 2) can be summarized as follow: time alone (without rehabilitation - the difference between T1 and T2) did not ameliorate patient performance, as after the pause the patient performance worsened in 14 out of 17 tasks. We found that both SLT (T0 vs. T1) and SLT/dual-tDCS (T2 vs. T3) increased patient performances on almost all the linguistic tasks proposed (14 out of 17 for SLT and 16 out of 17 for dual-tDCS) and, more interestingly, these increases reached healthy participant performance in 6 out of 14 tasks for SLT and in 9 out of 16 tasks for dual-tDCS. The combined rehabilitation approach (i.e. SLT/dual-tDCS) proved to be more useful than the sole SLT in 7 tasks out of 17 tasks: non-words reading, visual lexical decision, isolated words reading, word writing and sentence repetition, but in 2 of these 7 tasks a combination of sustained gain from the two rounds of treatments could a probable alternative explanation: trisyllabic non-words reading and word writing. The application of parietal dual-tDCS could improve writing and reading rehabilitation, particularly on sub-lexical transcoding and specifically the reading of complex phonemes (di- and trisyllabic) in agreement with the postulated grapheme-to-phoneme function sustained by IPL. Positive repercussions on patient’s quality of functional communication, in everyday life situations, were also ascertained. The score changing from 7 to 11 at the AAT test (Table I), attests a good measure of recovery within the reading/writing domain, so that the severity of aphasia passed from a mid to a slight level. All therapies (SLT and combined SLT/dual-tDCS) led to a significant increase in reading, writing and speech abilities. Application of dual-tDCS significantly enhanced the rehabilitation outcome, especially in respect to the reading ability, whereas the tDCS role in the recovery from the writing deficits seemed to be much less decisive. Interestingly, significant changes were found out also in other language and cognitive tasks not directly treated (comprehension and constructive apraxia). The positive impact on different untreated language and cognitive tasks can be explained with the tDCS feature of being a non-focal stimulation technique.

In spite of the sub-acute phase of the pathology, a spontaneous recovery seemed to be unlikely, considered that the subject's behavior returned to (or approached) the baseline level when the intervention was withdrawn in many tests.

Some tasks showed an improved rehabilitation effects when SLT was paired with dual-tDCS over IPL, we can hypothesize a specific correlation of these results in relation to the literature findings. In healthy subjects reading is associated with at least 3 systems: an anterior, mainly located in the inferior frontal gyrus, and two posterior, one ventral (occipito-temporal) and one in the dorsal (parieto-temporal). The dorsal system is important for converting the visual stimuli into sounds (phonology), left IPL and STG are essential for the application of phonological rules: L-ILP has been involved in mapping from sublexical phonological to grapheme representations (Taylor, J.S., Rastle, K., & Davis, M.H. , 2013), L-STG in lexical phonology particularly in sentences and text.

In dyslexia, functional alterations of the left temporo-parieto-occipital brain regions have been consistently found and cognitive rehabilitation improving reading ability usually increases activation in these same brain areas. The key role of the left IPL in sequential computations and grapheme transduction has been underlined in dyslexics (Costanzo et al., 2013).

Our results confirm the prevalent role of the left IPL in grapheme-to-phoneme conversion also in our aphasic patient.

Summarizing the main strength of the case:

1. we used a multi-factorial evaluation, including a tool to monitor improvement in functional communication skills (ASHA-FACS), demonstrating that the traditional assessment could be may be insufficient to capture all the complex changes induced by a rehabilitation
2. parietal dual-tDCS was shown to be as a new, tolerable and effective montage on stroke patients with written language deficits, especially for reading tasks
3. the results were perfectly matched with IPL postulated functions
4. previous studies that reported a beneficial effect of combining tDCS with language treatment, generally used the same stimuli both during training and assessment, thus the outcome seemed to strictly depend on the *trained* item. Here, SLT was carried-out on different items from those included in the baseline, thus avoiding a learning effect and pointing out possible generalizations.

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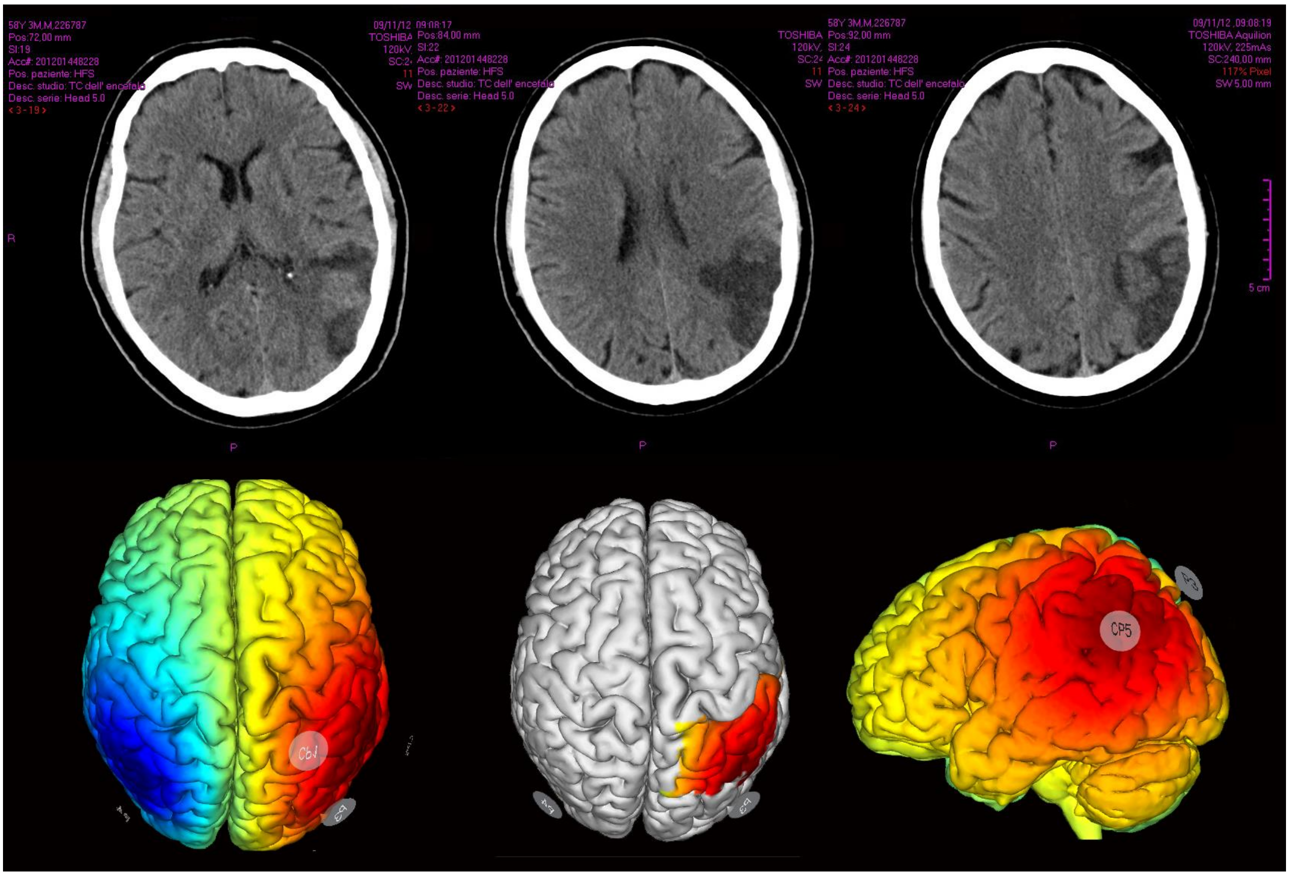
Table I. Speech and neuropsychological tests scores

Test	T0	T1	T2	T3
AAT repetition /150	136	140	141	143
AAT read-write /90	**48***	**55***	**62***	**73***
AAT naming /120	73	77	77	77
AAT comprehension /120	**89***	104	100	99
ASHA-FACS social com /5	4	4	4	5
ASHA-FACS com needs /5	5	5	5	5
ASHA-FACS read-write /5	**3***	**3***	**3***	4
ASHA-FACS planning /5	5	5	5	5
Attentional Matrices	**17.25***	**33.25***	**31.25***	**30.25***
Digit Span	4.5	6.5	5.5	4.5
Corsi Block-Tapping Test	4.25	5.25	4.25	3.75
RAVLT	**31.4***	32.4	**28.8***	34.4
Copy of Figure	**1***	**1***	**1***	2
Line Bisection Test	-0.60	-0.56	-0.55	-0.50
Phonemic Fluency	**13.3***	17.3	**14.8***	21.3
Token Test	**22.25***	**25.75***	**22.75***	29.25
HAM-D	3	2	1	2

Com = communication, HAM-D = Hamilton Rating Scale for Depression, AAT = Aachener Aphasia test, RAVLT = Rey Auditory Verbal Learning Test. The neuropsychological scores are corrected for age and education. In **bold** with * scores under cut-off compared to an Italian normative sample.

Figure Caption

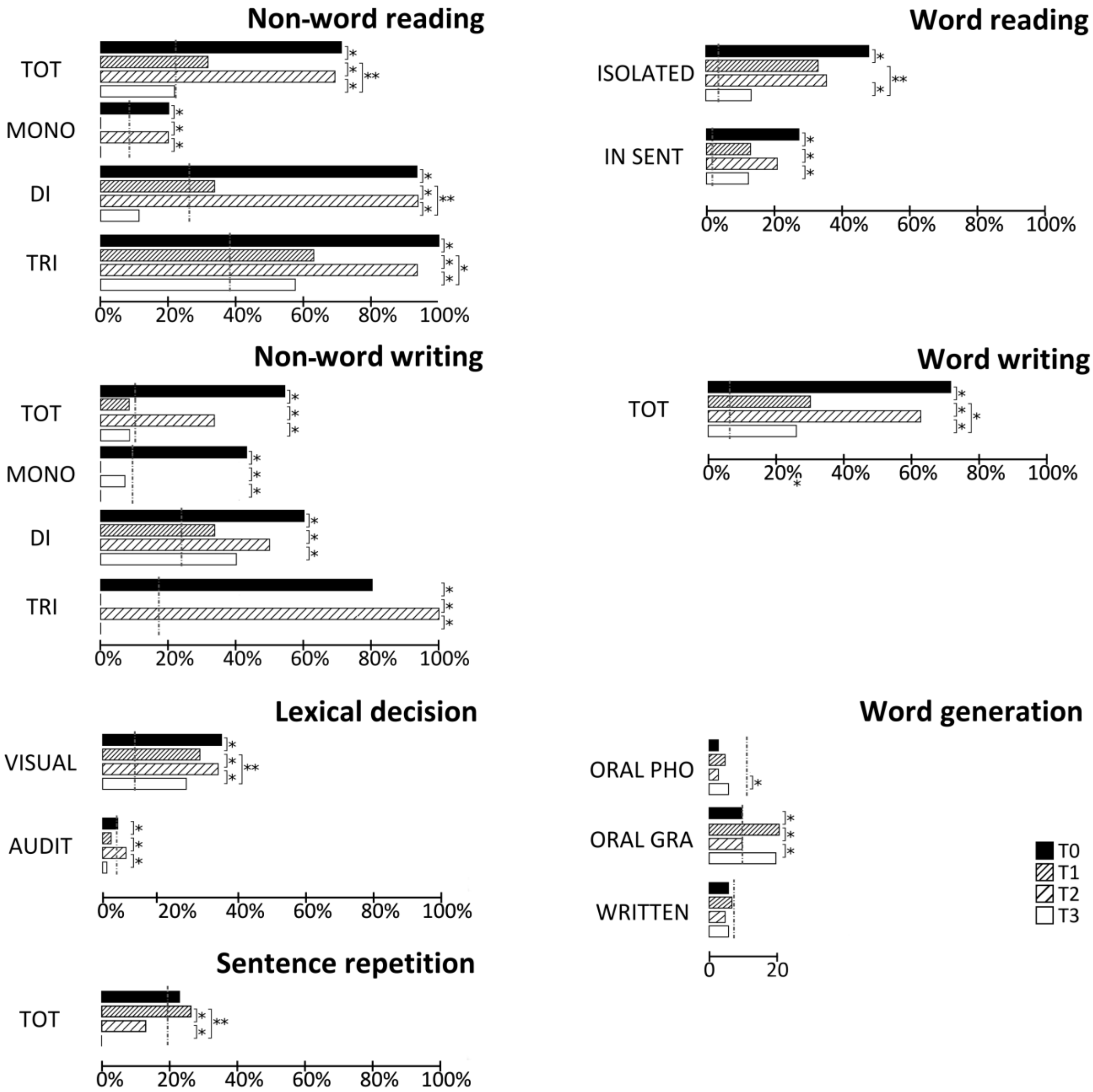
Figure 1. Brain lesion and induced electrical potential field by dual-tDCS



Upper row, CT scan post stroke of FC patient, an hypodense lesion is visible in the left parietal area including inferior parietal lobule, angular and supramarginal gyrus.

Low row, simulation of the electric potential field induced by P3, P4 dual-tDCS (10-20 EEG system) over the cortex of a mean normal subject, in red positive field, in blue negative. The simulation was carried out with the Stimviewer component of the Neuroelectrics Instrument Controller software (wiki.neuroelectrics.com). On the left top view, in the middle top view evidencing inferior parietal lobule, angular and supramarginal gyrus, on the right left view.

Figure 2. Results of patient FC language rehabilitation



Scores registered from patient FC are depicted during the four different time points: T0 = baseline in black, T1 = after SLT in dense diagonal pattern, T2 = after 1 month pause in diagonal pattern, T3 = after SLT/dual-tDCS in white.

There were 17 tasks in 7 main domains: non-words reading and writing, words reading and writing, lexical decision, word generation. All the tasks scores were given as percentage of errors with the exception of word generation that was in number of words produced.

The first star (between T0 and T1) showed a SLT significant effect, the second (between T1 and T2) a worsening during the pause and the third (between T2 and T3) a dual-tDCS significant effect. The lateral star (between T1 and T3) a superiority of dual-tDCS over the SLT treatment, the lateral double star a greater effect of dual-tDCS compared to SLT (T3-T2 > T1-T0).

The level of normal performance was represented with a single line traced over a cutoff computed from normal group data as mean + 2 standard deviations for errors and mean -2 standard deviations for word generation: the normal range was on the left of the lines for errors and on the right for word generation.

For the abbreviations: TOT = total, MONO = monosyllabic, DI = disyllabic, TRI = trisyllabic, AUDIT = auditory, SENT = sentence, PHO = phonemic, GRA = grammatical.