Neurodegenerative language impairments and transcranial stimulation

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Abstract

The mental lexicon is the stock of words, in long-term memory, as an association of syntactic, semantic and phonological/orthographic structures. Being able to access word meaning rapidly and flexibly is essential for efficient communication and it involves highly specialized brain networks. Its breakdown is present in different neurodegenerative diseases, as Primary Progressive Aphasia (PPA), Frontotemporal dementia (FTD) and Progressive Supranuclear Palsy (PSP). Transcranial direct current stimulation can help improve language deficits in these diseases. We compared the language deficits of these patients with controls and look for the effects of tDCS in such deficits.

Introduction

Language defines humans, and words are a distinctive language-specific part of human knowledge (Jackendoff 2002). Words are an association, in the long-term memory, of syntactic, semantic and phonological/orthographic structures, which is known as the mental lexicon (Jackendoff 2002). Research in the domain of language is often pursued at the word level because words are relatively well defined minimal units that carry many codes of analysis and processing distinctions (automatic vs. attentional). The access to the mental lexicon involves several mental representations that recruit temporal, parietal and frontal areas (Minicucci et al. 2013). The breakdown of critical nodes within this intricate system is present in different neurodegenerative diseases and at different levels.

Semantic and logopenic Primary Progressive Aphasia (svPPA, lvPPA) affect, respectively, the left anterior temporal lobe (ATL) and the left temporoparietal junction (TPJ) and impair conceptual knowledge (svPPA) and single-word retrieval (lvPPA) (Gorno-Tempini et al., 2011). The behavioral variant of Frontotemporal dementia (bvFTD) damages the prefrontal cortex (Rascovsky et al. 2011) and Progressive Supranuclear Palsy (PSP) affects subcortical structures but also the dorsolateral prefrontal cortex (DLPFC) (Paviour et al. 2006). Both impair language initiation and research mechanisms in the mental lexicon (Paviour et al. 2006).

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique able to modulate cortical activity and promote neuroplasticity and has been employed in the language domain with encouraging results (e.g. Cotelli et al. 2014). It operates by delivering a very weak constant current (1-2 mA) between at least two electrodes (an anode and a cathode) placed on separated scalp locations of the head. Single sessions of tDCS induce short lasting reversible modulations of cortical activity, whereas the accrual of periodical sessions enables longer lasting impacts by engaging neuroplasticity.

In this study we applied single sessions of tDCS to groups of patients with different neurodegenerative diseases to evaluate its ability to modulate language and its therapeutic potential. We also expected to contribute to a better characterization of the extent of the language deficits and the anatomical systems subtending them in such diseases.

Materials and methods

Four groups of neurodegenerative patients: svPPA, lvPPA, bvFTD, PSP (n=12 for each) were recruited at the Pitié-Salpêtrière Hospital, Paris. Patients underwent 3 tDCS sessions (20 minutes, 1.59 mA, 0.06 mA/cm^2) and immediately before and after each session they performed a series of language tasks. Each group was stimulated over a left cortical damaged region (anodal tDCS), over its right homologue (cathodal tDCS): ATL for svPPA, TPJ for lvPPA and DLPFC for bvFTD and PSP, and with sham tDCS. Four experimental tasks were used to characterize language impairments and to check for the effects of stimulation: *Letter fluency (LF)*, *Category decision (CD)*, *Semantic association* (SA) and *Picture naming (PN)*. Two versions for each task were designed and the order of application was counterbalanced between each group of patients, as well as the order of the three stimulation sessions. Fifteen healthy controls (HC) were also recruited to have normative values for each task. Healthy controls were not stimulated.

Results

To characterize language impairments for each group, ANOVAs were performed for each task, with 'group' as the independent variable and 'performance' (before stimulation) as the dependent variable, with Tukey posthoc tests. Results are summarized in Figure 1.

Biophysically inspired computational models, using a template head, to predict tDCS current magnitude and distribution in the brain for each group can be seen in Figure 2.

To check for the effects of tDCS, ANOVAs contrasted pre- and post-stimulation performances by comparing left-anodal and right-cathodal with sham stimulation. Results can be found in Figure 3.

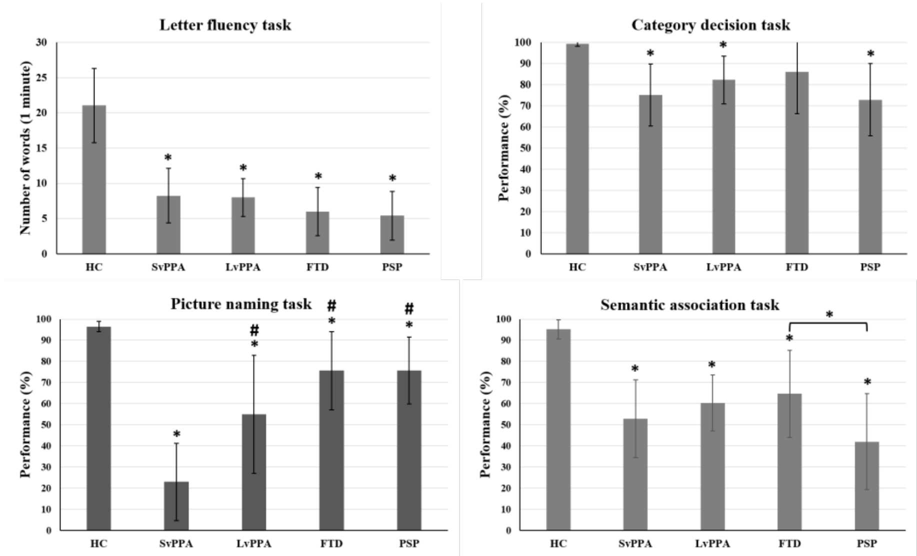

Figure 1. Group performance outcomes at baseline. * significantly different from HC (p<0.001); # significantly different from svPPA (p<0.05); * *with a claudator:* significantly different between them (p<0.05).

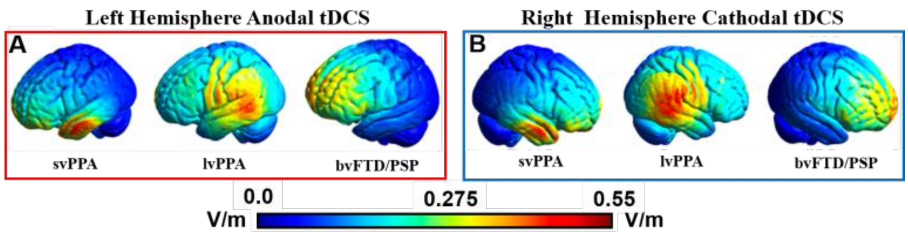

Figure 2. Computational models of current magnitude and distribution in the cortex. A) Anodal stimulation, left hemisphere view: current flows in, promotes neuron activity by reducing resting membrane potential (depolarization). B) Cathodal stimulation, right hemisphere view: current flows out, inhibits neuron activity by increasing resting membrane potential (hyperpolarization). Colour bar: signals the norm of the electric field at the cortical surface (V/m).

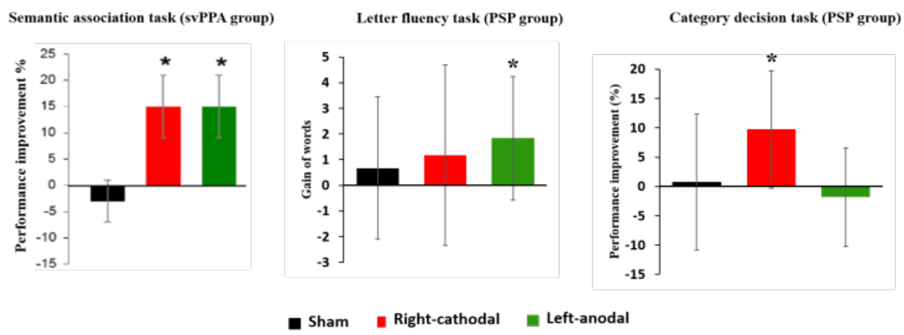

Figure 3. A) Improvements after both types of stimulation in the SA task for the svPPA group. B) Improvements after left-anodal stimulation in the LF task for the PSP group. C) Improvements after right-cathodal stimulation in the CD task for the PSP group. No other effects were found.

Conclusion

All patients present language deficits in all different tasks, showing that language deficits extend beyond the expected ones for each group according to the localization of anatomical damage. TDCS induced currents in the brain that encompass the intended targeted region, however, with different behavioral effects for each group. We conclude that tDCS can prove beneficial in helping to contain deficits in neurodegenerative diseases such as those presented here.

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