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Research Project Brief

Effects of transcranial direct current stimulation in primary progressive aphasia (2013 – 2015)

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Research Question: Can transcranial direct current stimulation (tDCS) augment the effects of re-learning language (and in particular spelling) in primary progressive aphasia (PPA), an early neurodegenerative disease? If so how this happens in the brain and in particular how brain connectivity and certain brain metabolites change as a result of re-learning through spelling and spelling plus tDCS interventions.

Interdisciplinary Approach: This work bridged both basic and clinical research to study how spelling interventions coupled with or without electrophysiological stimulation affect brain connectivity and physiology. To answer this question we compared behavioral (language) changes and changes in brain networks and metabolites between two language interventions: one coupled with electrical stimulation of the brain and another by itself.

Potential Implications of Research: Research on developing better and more effective language interventions in neurodegenerative diseases and understanding how these interventions work at the neuronal level is particularly important since it may inform us on how to develop better interventions to prevent or postpone the development of these diseases. In the long term, this research may help reduce the cost of care for people with neurodegenerative diseases and help people stay more functional and for longer time in their work, family, community and society in general.

Language and spelling interventions in particular have been shown to significantly improve the course of post-stroke language rehabilitation. The little existing evidence from neurodegenerative diseases is encouraging but not lasting. Even less is known about how language interventions in neurodegenerative diseases (such as Alzheimer's disease or Fronto-temporal dementia) affect the brain. This project investigated whether tDCS, a brain stimulation technique in which a weak electrical current is applied to the scalp, coupled with spelling therapy is more beneficial than spelling therapy alone and if so, how this changes the way different brain regions work together. The primary aim was to evaluate the effects of intervention and determine the neural correlates of electrical stimulation with and without spelling interventions that may lead to improved language outcomes.

Method: Eighteen patients diagnosed with PPA underwent 10-15, 45-min daily sessions of spelling intervention with and without tDCS (the electrostimulation session lasted only 20 min each time). Resting-state fMRI data were obtained on the first treatment condition from 13 participants who underwent written language intervention at 3 time-points: before, after, and 2-months post-intervention. Several neuropeptides were also measured at the same time-points: GABA, NAA, Glx etc. The left inferior frontal gyrus (IFG), known as Broca's area was chosen as the site of electrical stimulation since it is implicated in all spelling networks.

Results: All participants' spelling performance on trained items improved in both tDCS+ spelling therapy and spelling therapy alone. Generalization of treatment on untrained items was significant only in tDCS condition (see Figure 1). Therapy gains lasted longer in the tDCS condition as well, at least up to 2 months. Therefore, tDCS coupled with spelling therapy resulted in longer lasting and more generalizable gains of language interventions than language interventions alone. Second, analyses of brain connectivity data (resting-state fMRI) revealed that tDCS increased the correlation between left and the homologous right inferior frontal gyrus (IFG). Higher connectivity between these

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areas is associated with improvement in therapy outcomes for both trained and untrained items. This change was significant even at 2-months post intervention and this effect was stronger for participants with larger baseline volumes in the right IFG, i.e., with better-preserved brain tissue in general. The investigation on the role of neuropeptides is still underway and data from more participants are needed to conduct any meaningful analyses.

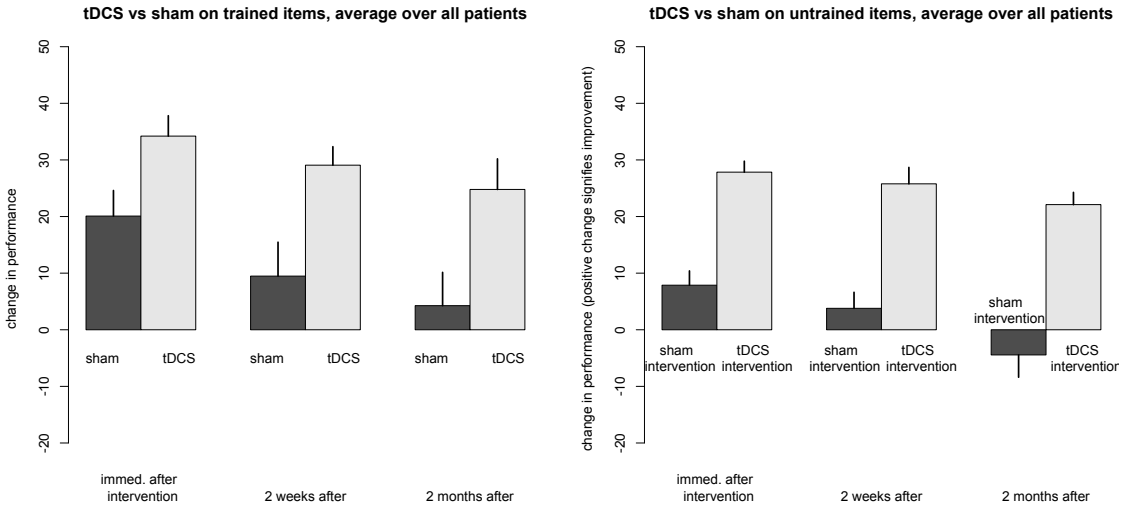

Figure 1. Overall performance of 8 participants on trained and untrained items (tDCS+language therapy effects are shown in grey, language therapy effects only are shown in black. Immediately after treatment, gains are 35% for tDCS+language therapy and 20% for language therapy alone on trained items.

Conclusions: tDCS represents an increasingly valuable treatment option in language rehabilitation even in neurodegeneration. Late intervention is as beneficial as early intervention but improvement seems more dramatic in early cases. Different possibilities are discussed: tDCS may indeed change the course of the disease, i.e., it may slow down the rate of decline or, language improvement due to tDCS may hold the spread of decline to other cognitive functions, thus, early interventions appear more beneficial. The correlation between functional connectivity and language production outcomes is expected to shed light on how tDCS works in the brains of people with a neurodegenerative disease. Implications of functional connectivity changes between language areas involved in the targeted language function will inform further interventions. The goals of this investigation are now further pursued through a R01 grant to study the effects of tDCS in written and oral production in PPA.