Final Report

Author: Assoc/Prof. Marcus Meinzer
Qualification: PhD
Institution: The University of Queensland
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Title of Project:

Neural mechanisms underlying language facilitation by transcranial direct current stimulation in post-stroke aphasia.

Simplified Title:

How does brain stimulation impact on language functions in patients with stroke?

Summary:

Non-invasive transcranial direct current stimulation (tDCS) has shown promise in improving impaired language function after stroke (aphasia; Meinzer et al., 2015). However, the neural mechanisms underpinning language facilitation by this new approach are not known. In the present studies we (1) exploited recent developments in brain stimulation paired with neuroimaging technology, to assess how tDCS modulates brain function in post-stroke aphasia and (2) conducted a clinical trial that investigated whether tDCS can enhance the effectiveness of intensive language therapy.

Study 1: In a first study, we aimed to target specific regions of the residual language cortex with tDCS during simultaneous functional magnetic resonance imaging (fMRI) to assess how the stimulation modulates brain function. This study demonstrated that it is feasible to precisely target individually determined brain regions in patients with aphasia (**Figure 1, left panel**), but also that active (anodal-tDCS) vs. placebo (sham-tDCS) stimulation facilitated neural processing at the stimulation site (**Figure 1 right panel**, **red box**, Ulm et al., 2015).

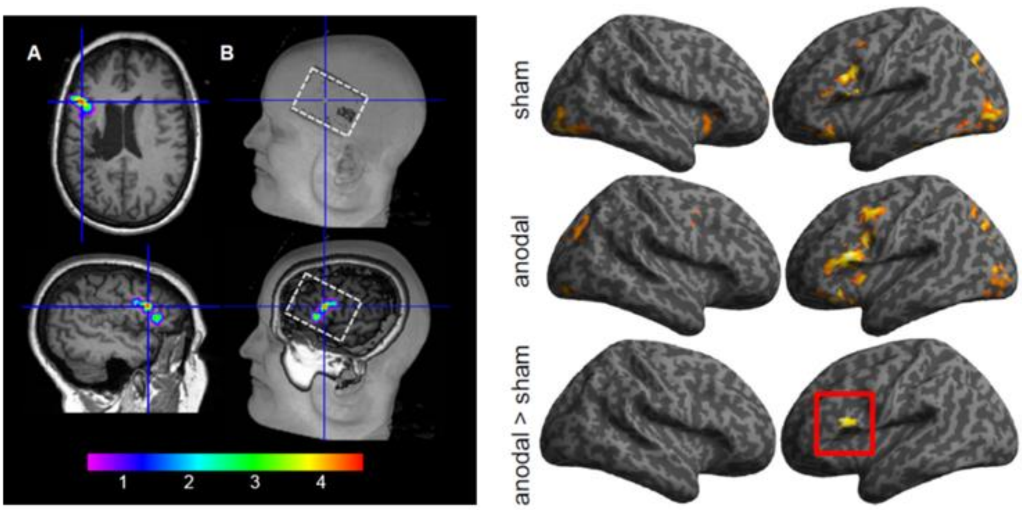

Figure 1: Left part of image: The left column illustrates the location of peak activity in the left inferior frontal gyrus as determined by a baseline fMRI session (crosshair on axial and sagittal slices). The right column shows the location of the electrode on the scalp on the co-registered structural image of the patient acquired during anodal-tDCS (upper right image, white box). The lower right panel shows a more medial view of the same image with peak activity during the baseline scan overlaid. This illustrates that the stimulation was precisely administered to the target region. **Right part of image**: Illustrates activity patterns associated with two fMRI sessions (anodal- and sham-tDCS) as surface rendering overlaid on an inflated standard brain for sham-tDCS and anodal-tDCS sessions. The bottom panel illustrates the location of increased task-related activity during anodal- vs. sham-tDCS.

<u>Study 2:</u> In follow-up study, 16 patients with aphasia were recruited and scanned during simultaneous active- or placebo-tDCS (Darkow, Martin, Flöel, & Meinzer, in preparation). Across the group, the comparison of data acquired with or without tDCS revealed: (1) More efficient task-related brain activity during a picture naming task across the patient group, indicated by reduced activity in domain general brain regions like the anterior cingulate cortex. (2) A functional network analysis showed that excitatory anodal-tDCS selectively enhanced overall activity in the language network, but not in the motor or visual networks. (3) A spectral frequency analysis of the data demonstrated increased power in lower frequency bands in the language network, which suggests that tDCS improved communication between spared language-related regions.

<u>Study 3:</u> In a third study, we conducted a randomised, placebo-tDCS controlled clinical trial that assessed whether anodal-tDCS can enhance language therapy outcome in patients with chronic aphasia (Meinzer et al., in press). The results demonstrated that active vs. placebo-tDCS resulted in superior treatment outcome for trained and untrained materials **(Figure 2)** and also more pronounced generalization to everyday communication – all with medium to large effect sizes. Superior treatment effects due to tDCS were maintained six month months after the end of the intervention period. This is the first clinical trial that demonstrated beneficial effects of tDCS on impairment measures and also everyday communication. Importantly, those effects were maintained for several months after the end of the intervention.

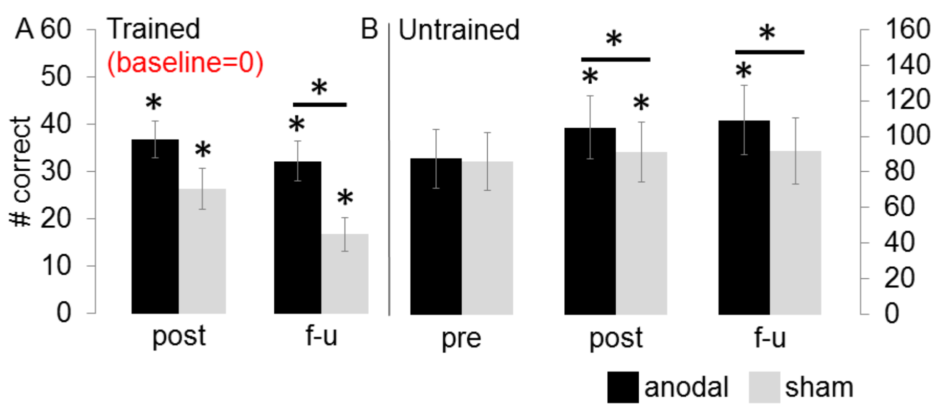

Figure 2: Details of outcome measures for impairment measures (A) trained (N=60) and (B) untrained items (N=284) that were assessed immediately before (pre) and after the end of the treatment (post) and six months later (follow-up, f-u). Trained items could not be named correctly during repeated baseline assessments. Patients treated with active-tDCS (anodal)

showed superior treatment outcome for trained and untrained items. Only in the active-tDCS group treatment effects for untrained materials were maintained 6 months after the training. * indicates significant improvement compared to baseline assessments and interactions (TIME x STIMULATION).

References:

Meinzer M., Darkow R., Lindenberg R., Flöel A. (in press, accepted 12/2015) Electrical stimulation of the motor cortex enhances treatment outcome in post-stroke aphasia. **Brain**

Meinzer M. Ulm L., Lindenberg R. (2015) Biological markers of aphasia recovery (**Oxford Handbook of Aphasia and Language Disorders**, eds. S. Raymer & L. Rothi-Gonzales, Oxford University Press, p. 1-17)

Ulm L., Copland D., McMahon K., Meinzer, M. (2015) Neural mechanisms underlying perilesional transcranial direct current stimulation in aphasia: A feasibility study. **Frontiers in Human Neuroscience** 9:e55