2020-10-26

Targeted multielectrode tDCS increases functional connectivity within the arcuate fasciculus network: An exploratory study and analysis

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Et al.

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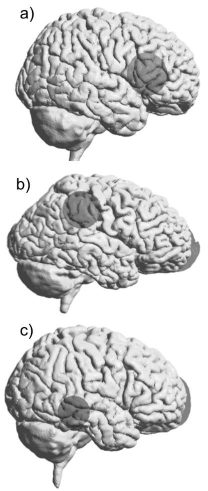


Figure 1. Three single-electrode montages that were tested: IFG (a), SMG (b), and STG (c).

Introduction. tDCS is an important tool in stroke recovery and other types of patient care. Stroke and other problems can lead to dysfunction of the arcuate fasciculus network (AF-network), a gray matter tract in both hemispheres that connects STG, SMG, and IFG regions. Stimulation of those network nodes can lead to increased functional connectivity and behavioral outcomes, but a single electrode is typically used. Stimulation of multiple nodes of the network simultaneously may hasten behavioral outcomes, particularly in aphasic stroke recovery in the hemisphere contralateral to the lesion. Here we test two multielectrode tDCS montages for the effects on functional connectivity between SMG and IFG, and contrast that with single-electrode montages. We find that a triangular multielectrode montage significantly increases functional connectivity compared to single-electrode montages, and that finite-element modeling confirms that functional connectivity should be increased, particularly with the doses we selected for each anodal electrode.

Methods. 27 subjects were recruited to undergo simultaneous tDCS and resting state fMRI (rs-fMRI) to record the BOLD signal and analyze functional connectivity using SPM and CONN free software. 4 sessions of each of 3 single-electrode montages were run (Fig. 1), and 3 sessions for each of 2 multielectrode montages were run. For comparison, 6 sessions without any tDCS stimulation were also run (no-stim). If any montage led to an increase in functional connectivity compared to a threshold established with the no-stim sessions, 3 more sessions were run. The triangular multielectrode montage did pass this threshold, so a total of 6 were run for that montage (Fig. 2b). The electric field in the brain induced by the tDCS was also modeled with SimNIBS. The current density tangential to the cortical surface (J tangent) was analyzed for homogeneity between SMG and IFG to correlate with functional connectivity.

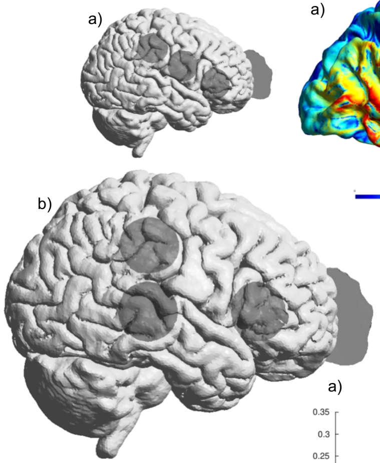


Figure 2. Two multielectrode montages that were tested: Linear (a), and triangular (b), the latter of which having shown good results.

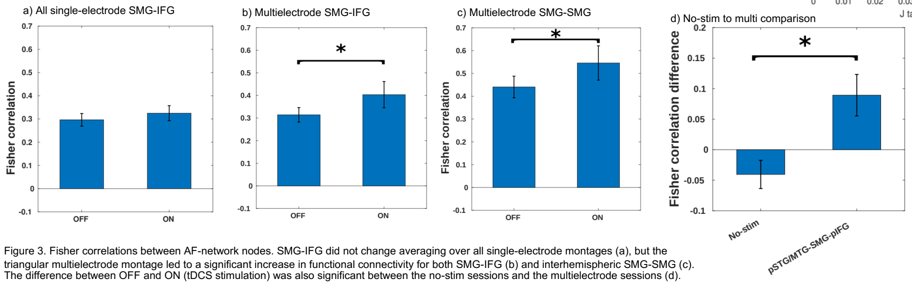


Figure 3. Fisher correlations between AF-network nodes. SMG-IFG did not change averaging over all single-electrode montages (a), but the triangular multielectrode montage led to a significant increase in functional connectivity for both SMG-IFG (b) and interhemispheric SMG-SMG (c). The difference between OFF and ON (tDCS stimulation) was also significant between the no-stim sessions and the multielectrode sessions (d).

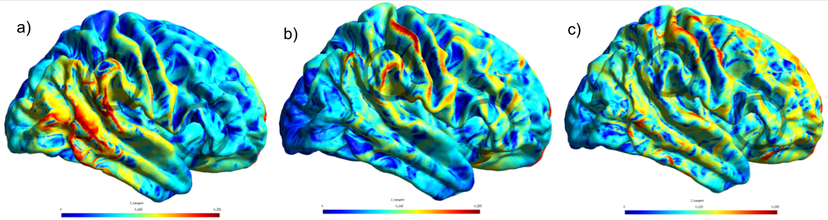
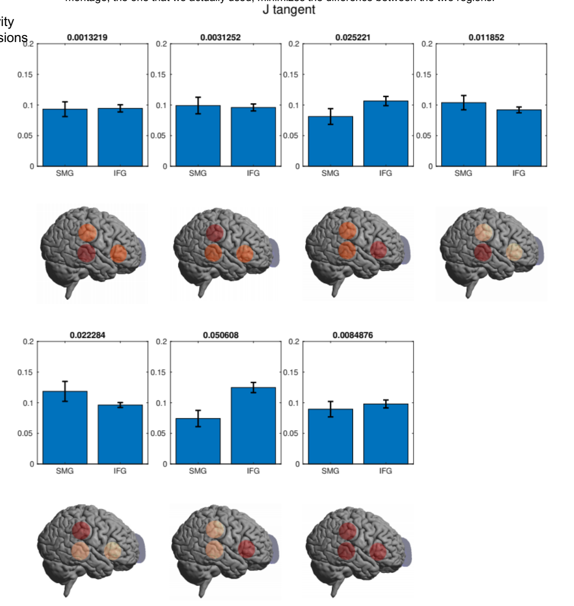


Figure 5. SimNIBS models of J tangent for three different electrode montages: Single-electrode STG (a), single-electrode SMG (b), and the triangular multielectrode montage that led to significant functional connectivity increases (c). SMG and IFG regions are highlighted with translucent circles. It is evident that current density is more homogeneous for the latter of the three montages.

BOLD first-level contrasts were obtained, as well as functional connectivity measures from several pairs of ROIs chosen for their proximity to nodal cortical points of the AF network, consisting of specific cortical regions and a prominent subcortical white matter tract, the AF. Considering the anatomy and course of AF fibers, five ROIs for AF functional connectivity analysis were selected: anterior SMG, posterior SMG, IFG pars opercularis, IFG pars triangularis, and IFG pars orbitalis. With two SMG and three IFG ROIs, six total functional connectivity values of SMG-IFG ROI pairs were extracted, and these values were averaged to obtain the approximation of overall SMG-IFG functional connectivity.

Results. No single-electrode montage significantly changed functional connectivity (Fig. 3a), and neither did the linear multielectrode montage. However the triangular multielectrode montage (Fig. 2b) significantly increased SMG-IFG functional connectivity (Fig. 3b). Upon further analysis, this montage also significantly changed functional connectivity between interhemispheric SMG regions. A comparison of the 6 triangular montage sessions with the 6 no-stim sessions revealed a significant difference as well (Fig. 3d). BOLD contrast images for ON vs. OFF (tDCS stimulation) were also obtained to compare with functional connectivity and modeling. A significant negative correlation was found between J tangent SMG-IFG difference and functional connectivity change. Therefore the reciprocal of J tangent difference, homogeneity between the regions, became our modeling proxy for functional connectivity. A significant positive correlation was found between SMG-IFG BOLD sum and J tangent difference (Fig. 4b), the reciprocal of our proxy for functional connectivity, homogeneity of J tangent. We also modeled 6 current ratio setups in addition to the one we actually used (Fig. 6). In addition to 2-1-1 mA, we modeled 1-2-1, 1-1-2, 3-0.5-0.5, 0.5-3-0.5, 0.5-0.5-3, and 1.33-1.33-1.34, to test whether there is a better current ratio setup, judging with J tangent homogeneity. As is evident in Fig. 6, the current doses that we actually used turn out to be the best for functional connectivity increase.

Figure 6. SimNIBS models for several different current setups were also run. Darker colors of the electrodes indicated greater share of the stimulating current. In the order STG-SMG-IFG, the current setups of 2-1-1, 1-2-1, 1-1-2, 3-0.5-0.5, 0.5-3-0.5, 0.5-0.5-3, and 1.33-1.33-1.34 were tested, in this order below. J tangent difference is on top of each plot. It can be seen that the 2-1-1 montage, the one that we actually used, minimizes the difference between the two regions.



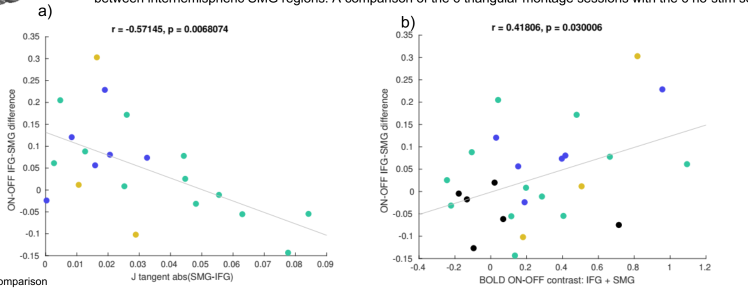


Figure 4. Functional connectivity correlates with both homogeneity of modeled J tangent current density in SMG and IFG (a) and a BOLD ON-OFF contrast image summing both SMG and IFG regions. Single-electrode montages are in green, triangular in blue, linear in yellow, and no-stim in black.

Discussion. A novel design was devised to determine whether a multielectrode tDCS montage targeting nodal cortical regions of an established network, the right AF-network, could differentially increase functional connectivity between nodes of this network. One particular montage that was designed to target these nodes was found to significantly increase functional connectivity between two prominent cortical nodes, the right SMG and IFG, compared to single electrode stimulation. No increase in functional connectivity was found with single-electrode stimulation targeting single regions of the network, while a different multielectrode montage that targeted cortical regions in a more linear fashion showed a trend of a functional connectivity increase, but only on the order of single-electrode montages. The multielectrode montage that had an effect, triangular, also targeted both anterior and posterior/inferior nodes of the AF-network, which could be a reason for its ability to drive functional connectivity. All single-electrode montages, either separately or in combination, did not have a significant effect on functional connectivity between nodes of the AF-network in the targeted right hemisphere. A clear path toward answering the interesting questions on this topic more directly has thus been laid through the combinations explored in this study.