

# On the Use of the Terms Anodal and Cathodal in High-Definition Transcranial Direct Current Stimulation: A Technical Note

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**Background:** The terms “anodal” and “cathodal” are widely used to describe transcranial direct current stimulation (tDCS) of opposing polarities, often interpreted as excitatory and inhibitory, respectively. However, high-definition tDCS allows for complex electrode configurations that may not be characterized accurately as “anodal” and “cathodal.”

**Method:** To illustrate challenges to data interpretation that may result from unclarity about the neuromodulatory effects of different field orientations, we present two high-definition tDCS experiments in the language domain, with different electrode configurations. We also present the modeled electric fields for a traditional tDCS setup, showing how brain stimulation may far exceed target regions.

**Conclusions:** More research is warranted on the hypothesized inhibitory or excitatory effects of different electrode configurations. Moreover, conventional bicephalic  $1 \times 1$  configurations using sponges or HD electrodes may not be accurately described by the terms “anodal” and “cathodal” either, as these terms only pertain to the desired effects over an area of interest, but not any other areas affected. Therefore, design and interpretation of (HD-)tDCS and conventional tDCS research studies should not be constrained by the anodal/cathodal dichotomy.

**Keywords:** Anodal, brain stimulation, cathodal, polarity, tDCS

**Conflict of Interest:** Dr. Datta has equity in Soterix Medical, Inc., a startup company that aims to commercialize HD-tDCS. Dr. Datta also has patent rights to HD-tDCS technology.

## INTRODUCTION

Transcranial direct current stimulation (tDCS) can be applied using two electrodes embedded in large sponges (conventional tDCS) or with high-definition silver chloride electrode placement in holders filled with conductive gel (“High Definition,” HD-tDCS). Both methods allow for stimulation at the level of the cortex by acting on the resting membrane potential, affecting sodium and calcium channels, as well as NMDA receptors (1). Traditional tDCS uses two sponge electrodes (typically  $5 \times 5$  cm or larger; (2)) of opposite polarity with current flowing from the positive electrode (anode) to the negative electrode (cathode). Typically, anodal tDCS lowers the activation threshold (excitation) through depolarization, while cathodal tDCS results in inhibition through hyperpolarization, increasing the threshold for neuronal firing (3), though see Jacobson et al. (4). However, many factors in addition to the anodal/cathodal polarity modulate the excitatory/inhibitory effect of stimulation, including positioning of the electrodes, orientation of the neurons and axons in the brain, degree of current conduction or impedance, duration and intensity of stimulation, initial neural activation state of affected areas, and individual differences in skull thickness, gyral structure, and other anatomical features (5–11).

This technical report does not address directly the related issue concerning the behavioral effects of neural excitation/inhibition, which is commonly acknowledged to be complex (4). The inhibition of neurons that themselves inhibit the action potentials of other

neurons may in fact paradoxically lead to increases in functional behavior. In addition, the role that neurons may play in neural circuitry, i.e., as part of neural networks that support particular functions, will also affect the behavioral effects of their focal excitation or inhibition. Neural network architecture cannot be assumed to remain functionally stable when parts of the network are changed; functional connectivity may well adapt in response to partial network modulation (as suggested, for example, by visual “Sprague

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effects" in animals and humans (12,13)). We focus here, however, on the presumed direct physiological effects of tDCS on target areas.

It is important to emphasize that the term anodal refers to the injection of positive charge from the anode electrode while cathodal refers to the removal of it from the cathode electrode. Any net effect manifest is due to the combined effect of the induced cortical electric field vector on neuronal structures, with radial and tangential components affecting somatic and axon terminals differently (14). More relevant than "anodal" vs. "cathodal" stimulation, then, is the accurate description of the local direction (orientation) of the electric fields generated by different setups, i.e., the orientation at which they supposedly "hit" the affected neurons. This applies to conventional tDCS setups, but perhaps even more to HD-tDCS, with its expanded range of configuration options through the use of multiple HD electrodes. One common HD-tDCS configuration is a  $4 \times 1$  ring configuration, in which the active electrode is placed in the center and four return electrodes are placed in a concentric circle around it (15). A configuration with a positively charged active electrode is a counterpart of anodal stimulation, whereas a configuration with a negatively charged active electrode is a counterpart of cathodal stimulation (16). However, more flexible electrode placements are often better suited to achieve optimal target focality or intensity of stimulation.

Modeling software (for example, HD-Targets and HD-Explore; (17)) allows researchers to obtain the optimal electrode configuration by specifying the number of current sources (4,8,16), a preference for maximum focality or intensity, and field orientation (radial in/out, posterior/anterior, left/right). Electrode configurations other than a  $4 \times 1$  ring may be yielded as the optimal setup, including configurations that have more than one "anode" or "cathode." In the context of optimizing for the electric field over a desired brain target, consideration of electric field orientation is more relevant than the polarity of the electrodes themselves. An additional issue is whether using the opposite field orientation (basically, reversing current polarities) should necessarily yield the opposite (inhibitory/excitatory) type of behavioral effect, if neurons are hit laterally with either current direction.

As an illustration of the problem we address here, we briefly present methodological issues in two studies using HD-tDCS, accentuating the point that the terms "anodal" and "cathodal" may not be optimal for describing electrode setups. Different current directions or field orientations may have effects that vary with the cortical area that is targeted using focal HD-tDCS. Even in conventional bicephalic tDCS, areas potentially affected by stimulation stretch beyond the immediate regions over which electrodes are placed.

## MATERIALS AND METHODS

We used HD-Targets™ (Soterix Medical Inc., New York, NY, USA) software to model electrode configurations for stimulation over target brain areas delivered with the M x N HD-tDCS Stimulator (Soterix Medical Inc., New York, NY, USA) in two experiments. Electrodes were Ag/AgCl sintered ring electrodes, which have inner and outer periphery diameters of 6 mm and 12 mm, respectively. This results in a  $140 \pm 5$  mm<sup>2</sup> contact area, including side surfaces (18). To select these configurations, we examined all possible combinations of parameters and selected those that optimally resulted in high field intensities at target coordinates while affecting other brain areas as little as possible. The Institutional Review Board at the University of South Carolina approved both experiments, and written consent was obtained from the participants prior to their participation. Data analysis was completed using SPSS (19).

**Table 1.** Electrode Locations (10-10 EEG System) and Current Strengths (in mA) in the Left Posterior Field Orientation (LPFO) and Right Anterior Field Orientation (RAFO), for Target Area Left Posterior Superior Temporal Gyrus (#442 in HD-Targets) Modeled With Four Current Sources and Maximum Focality (Experiment 1).

	FT9	TP7	CP5	Pz	FT7
LPFO	0.32	-1.21	-0.79	0.31	1.37
RAFO	-0.32	1.21	0.79	-0.31	-1.37
Current density	2.3	8.6	5.6	2.2	9.8
Current density (in A/m <sup>2</sup> ) under each electrode appears in the bottom row.					

### Experiment 1: Configuration 2 x 3

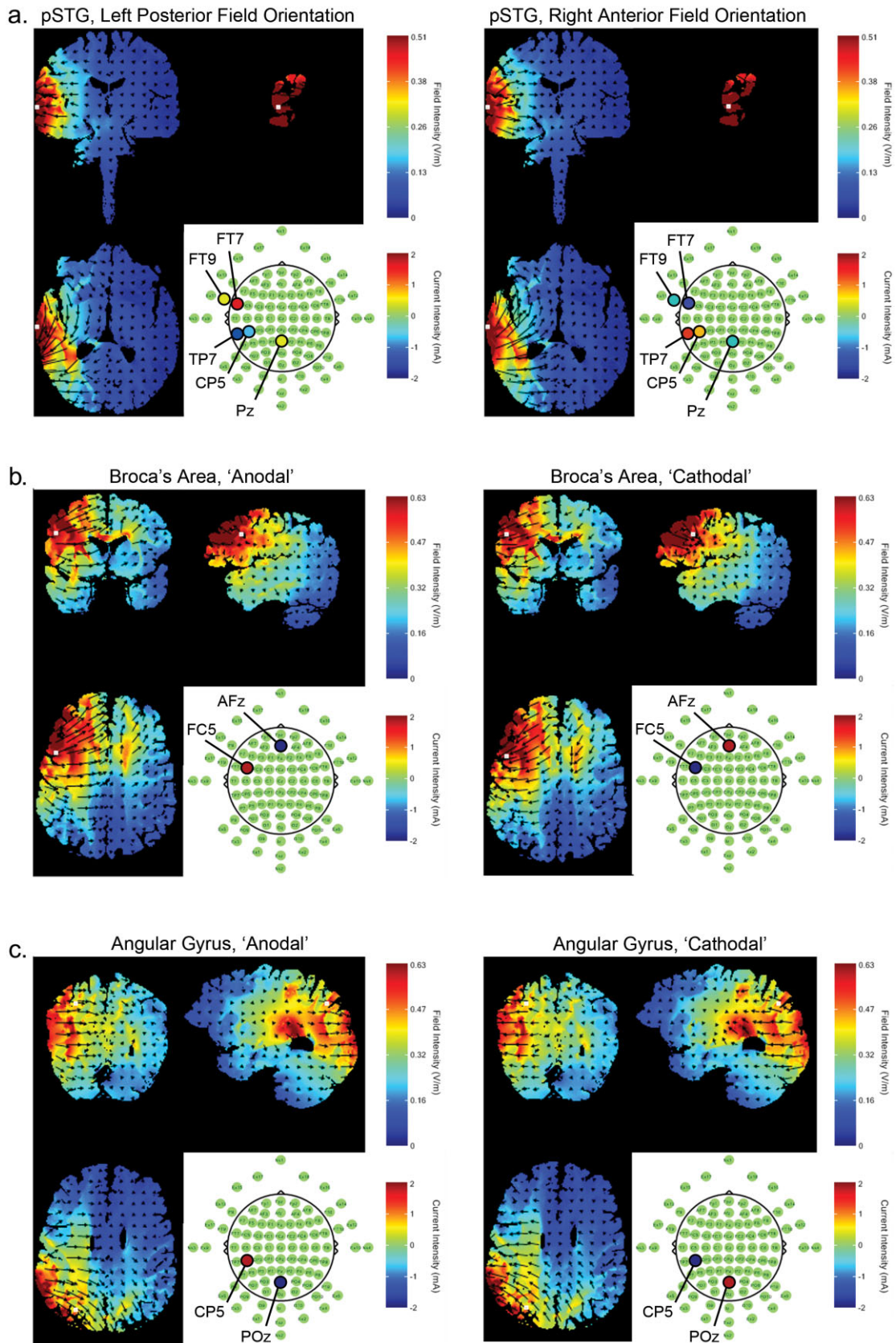
The target area in our first study was left posterior superior temporal gyrus (pSTG); specifically, in the parcellation used by HD-Targets (<http://www.talairach.org/labels.txt>), we selected label 442, designated as left cerebrum, temporal lobe, superior temporal gyrus, gray matter, Brodmann area 22. The configuration that we judged as optimal (Fig. 1, panel a, left, and Table 1) used the following parameters: four current sources, maximum focality, and left posterior field orientation, resulting in modeled field intensity of 0.63 V/m at target coordinates. The resulting electrode montage was different from a  $4 \times 1$  ring: the five electrodes were placed further from each other and their current strengths, polarities, and location did not correspond to a "central" electrode with four "return" electrodes spaced at 90 degree angles outward from the central electrode. Rather, four of the electrodes were located close together on the left temporal area, with the fifth electrode located over the posterior parietal area, in the midline. Reversing the field orientation parameter in the software from left-posterior to right-anterior (Fig. 1, panel a, right) reverses the polarity for each electrode, resulting in what could be considered an opposite direction of stimulation.

A continuous-stimulation sham condition used the same electrode positions, but with current flowing directly between the two pairs of adjacent electrodes (FT9-FT7 and TP7-CP5, at 1 mA in each pair). Current was thus modeled to pass the cortex only minimally (20) without participants sensing the difference between sham and cortical stimulation (21).

The experimental design was within-subjects, with the order of the three session types (sham plus the two field orientations) counterbalanced across subjects and a minimum of 24 hours between sessions. Twenty participants received stimulation (or sham) for 20 min, after which they performed a phoneme monitoring task, responding by button press to the presence of phonemic targets in lexical items presented as pictures, as a measure of phonological encoding and covert speech monitoring abilities.

### Experiment 2: 1 x 1 configurations

In our second study, we targeted left Broca's area (BA) in one participant group and left angular gyrus (AG) in the other group. The configuration that we judged as optimal for BA stimulation (Fig. 1, panel b, left, and Table 2) targeted label 812 (middle frontal gyrus) designated by the software, and used maximum intensity, four current sources, and left field orientation, resulting in modeled field intensity of 0.61 V/m at target coordinates. The configuration that we judged as optimal for AG stimulation (Fig. 2, panel c, left, and Table 3) targeted label 927 (left cerebrum, parietal lobe, supramarginal gyrus, gray matter, Brodmann area 40) and used maximum



**Figure 1.** a. Experiment 1, modeled field potentials in an adult male brain, when using left posterior field orientation (left) and right anterior field orientation (right) for target area left posterior superior temporal gyrus (#442 in HD-Targets). Arrows indicate field orientation and intensity. b and c. Experiment 2, modeled field potentials in an adult male brain, when targeting Broca's area (#912 in HD-Targets) using right field orientation (b, left) and left field orientation (b, right) and targeting left angular gyrus (#927 in HD-Targets) using right posterior field orientation (c, left) and left anterior field orientation (c, right).

**Table 2.** Electrode Locations (10-10 EEG System) and Current Strengths (in mA) in the Right Field Orientation (RFO) and Left Field Orientation (LFO), for Target Area Left Broca's Area (#812 in HD-Targets) Modeled With Four Current Sources and Maximum Intensity (Experiment 2).

	FC5	AFz
RFO	+2.00	-2.00
LFO	-2.00	+2.00
Current density	14.3	14.3
Current density (in A/m <sup>2</sup> ) under each electrode appears in the bottom row.		

**Table 3.** Electrode Locations (10-10 EEG System) and Current Strengths (in mA) in the Right Posterior Field Orientation (RPFO) and Left Anterior Field Orientation (LAFO), for Target Area Left Angular Gyrus (#927 in HD-Targets) Modeled With Four Current Sources and Maximum Intensity (Experiment 2).

	CP5	POz
RPFO	+2.00	-2.00
LAFO	-2.00	+2.00
Current density	14.3	14.3
Current density (in A/m <sup>2</sup> ) under each electrode appears in the bottom row.		

intensity, four current sources, and left-anterior field orientation, resulting in modeled field intensity of 0.52 V/m at target coordinates. Both were 1 × 1 configurations that may be characterized as “anodal” because the electrode over the target area has positive polarity. For both configurations, reversing field orientation (from left to right and from left-anterior to right-posterior) yielded the opposite current polarities and thus “cathodal” stimulation (Fig. 1, panels b,c, right, and Tables 2 and 3).

As in Experiment 1, we used continuous stimulation for the sham condition. Two extra electrodes were placed adjacent to the two electrode sites used for anodal and cathodal stimulation, so that current flowed in and out at adjacent electrodes (at 1 mA per pair), only minimally affecting the cortex (20,21). To better mask the sham condition by having equal numbers of electrodes on the participant's scalp across stimulation types, these two additional electrodes were also added to the cap in the anodal and cathodal stimulation conditions, but without administering current.

In a between-subjects design, 14 participants received BA stimulation in the two configurations described above (as well as sham) and 13 participants received AG stimulation in the two configurations described above (as well as sham) on separate days. After 20 min of cortical/sham stimulation, participants performed a picture-naming task, with nouns and verbs as lexical targets.

For comparison purposes, we also modeled montages where current was applied over approximately the same areas of the scalp as in the above montages but with the current sources modeled as 5 × 5 cm sponge pads rather than HD-electrodes, using the same HD-Targets software and selecting the pad configuration option (Fig. 2).

### Experimental Results

The topic of this technical note is not the actual research questions behind these experiments, nor their detailed results, but rather

the issues associated with data interpretation in light of the uncertainty regarding the effects of field orientation on tDCS. Therefore, we only briefly summarize the relevant results here.

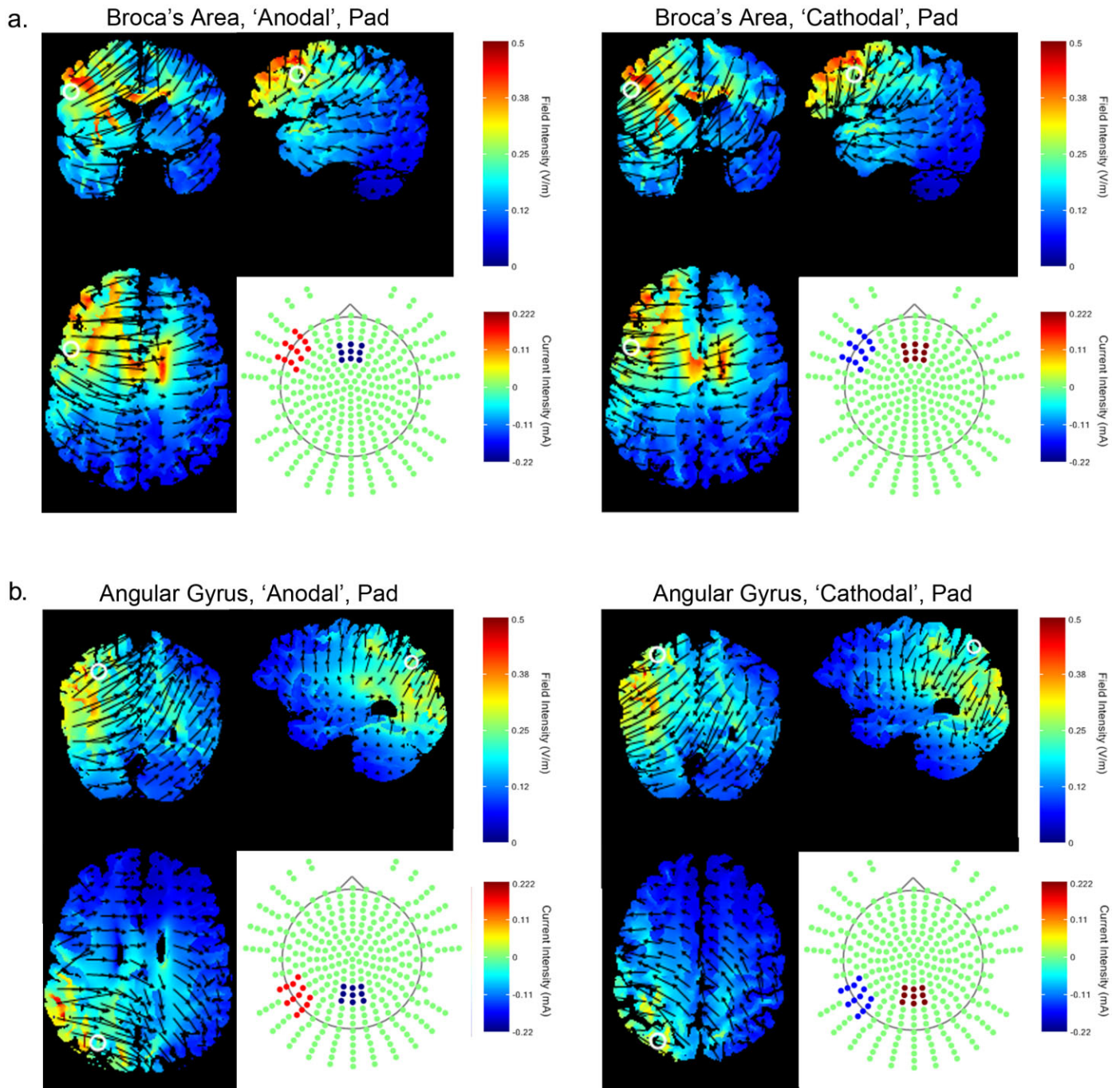
The first (2 × 3 configuration) experiment was part of a study into effects of stimulation on phoneme monitoring, i.e., scanning the word form of a lexical stimulus, presented as an object picture, for the presence of specific sounds (phonemes) in its phonological representation. pSTG was targeted for its role in phonological processing and encoding (22), and the outcome measures were reaction time and accuracy of participants' responses. Stimulation with neither of our two opposite field orientations was associated with modulation of behavior relative to the sham condition for reaction time ( $F(2, 38) = 0.246$ ;  $p = 0.783$ ) or accuracy ( $F(2,38) = 0.644$ ,  $p = 0.531$ ).

The second (1 × 1 configuration) experiment investigated effects of stimulation of left-hemisphere BA vs. AG on picture-naming latency. Both of these regions are commonly associated with different levels of speech and language planning and execution. Naming in general has been shown to be positively modulated by stimulation of Broca's area (23–25), and access to verbs in particular, relative to nouns, has been associated with left inferior frontal regions (26). By contrast, lexical-syntactic complexity of verbs has also been associated with increased left inferior parietal activation (27). Besides results that lie beyond the scope of the present paper, there was a main effect of stimulation type on naming latencies ( $F(2, 128.96) = 6.04$ ,  $p = 0.003$ ), with the “cathodal” stimulation over both stimulation regions yielding significantly *faster* naming times than “anodal” and sham stimulation, for both nouns and verbs.

## DISCUSSION

In both of the experiments provided here as illustrations, interpretation of results, including null effects (exp. 1), is complicated by uncertainty about the basic effects that stimulation over a given brain area with different field orientations may be expected to have, neurophysiologically and, therefore, behaviorally. Naturally, null results may occur for a number of reasons, not least of which are an erroneous  $H_1$  or a faulty study design, but the problem here is that we know too little about the fundamentals of the stimulation effects to start addressing such issues with confidence. Likewise, in experiment 2, we did not find the expected facilitation of naming following anodal stimulation over Broca's area (23–25); instead, we found positive behavioral effects after cathodal stimulation over the left angular gyrus and Broca's area that run counter to what might have been expected from earlier reports on effects of cathodal stimulation over language-related areas. Even though there is in fact some previous research that shows evidence of increased performance after cathodal stimulation over task-related areas (28,29), whether one interprets such results as variants of the Sprague effect or as evidence that cathodal stimulation may lead to excitation of underlying neurons is dependent on our understanding of the neurophysiological effect of the particular stimulation setting and electrode configuration used in different experiments.

In fact, in cognitive studies with traditional sponge tDCS, particularly language studies, effects of cathodal stimulation over brain areas associated with a measured task are far less homogeneous than in studies in the motor domain, with fewer reported inhibitory effects (4). As suggested in Jacobson et al. (4), this may well be related to the greater complexity and compensatory opportunities of brain networks supporting higher cognitive functions. In our view, the inhomogeneity of reported cognitive effects may also be partially due to



**Figure 2.** a. Modeled field potentials in an adult male brain, when targeting Broca's area with an anodal electrode pad (left) and a cathodal electrode pad (right). Arrows indicate field orientation and intensity. b. Modeled field potentials in the brain, when targeting left angular gyrus with an anodal electrode pad (left) and a cathodal electrode pad (right).

a wider variety of brain areas stimulated across cognitive studies compared to motor research. Because any behavioral modulations result from a combination of effects across the brain, configurations that aim to affect the target brain area anodally or cathodally may yield different effects depending on the total exposure to stimulation of target as well as nontarget brain areas (see a further illustration of this point below in the discussion of the reference electrode positioning in our experiment 2). Thus, without a better understanding of the basic effects of stimulation by means of different configurations and field orientations over target brain areas, findings such as

those in our illustration experiment 2 will continue to raise questions about the generalizability of the method and the predictability of its neurophysiological effects. The latter is important for the formulation of directional *a priori* hypotheses for studies using (HD-)tDCS.

We selected model-based optimal HD-tDCS configurations for stimulation of left pSTG, BA, and AG. The selected configuration for pSTG stimulation had five electrodes placed at a distance from each other without a clearly defined "central" electrode. While this configuration seems to provide the optimal targeting of the desired area, it cannot be characterized straightforwardly as anodal or cath-

odal and consequently it remains unclear whether one should hypothesize excitatory or inhibitory effects on neural polarization. Indeed, the predictions from HD-Targets are purely focused on optimizing the electric field along a limited number of prespecified directions, even though it remains unclear which field orientation is most effective in eliciting the desired neuromodulation (17). Meanwhile, though the concept of polarity may be critical to achieve desired neuromodulation at the level of individual neurons, reference to neuromodulation effects are made on a macro scale (for example, motor cortex excitability reverses in opposite polarity (30)).

More basic research is therefore warranted on possible patterns of inhibitory/excitatory effects of such complex HD configurations. This is not a trivial exercise, as the ability to formulate *a priori* directional hypotheses about brain-behavior relations is an important constraining factor in the design and interpretation of brain stimulation studies and may be vital in the validation of the new methods used in the emerging field of human neuromodulation. For superficial cortical targets, preferred orientation is presumably straightforward to define, with pyramidal neurons oriented normally to the surface, and the aim might consequently be to direct current flow in a radial direction. The interaction between gyral convolutions and current flow, however, even complicates this most basic situation, as in our illustrations here. In the absence of dominant cell orientation in subcortical targets, the situation is much less clear and one may opt to select montages that maximize current magnitude among all possible orientations.

The selected  $1 \times 1$  configurations for AG and BA stimulation were similar to bicephalic (or bipolar) setups in conventional tDCS, in which the reference electrode is placed on the scalp rather than on another part of the body. However, in both these cases the terms “anodal” and “cathodal” still do not capture the whole picture, as anodal stimulation of the target brain area, whether administered through HD-electrodes or sponge pads, necessarily corresponds to cathodal stimulation of the area under the “reference” electrode, and vice versa. For example, “anodal” and “cathodal” stimulation of AG in our Experiment 1 also differed in the direction of the current flowing in and out of the occipital cortex. Any behavioral modulations may therefore result from a combination of effects across the brain, i.e., over all cortical and subcortical areas affected, as well as cranial nerves (31,32). The point that not only targeted but also distant brain areas are affected has also been made for transcranial magnetic stimulation (33). This precludes the drawing of generalized conclusions about the effects of “anodal” and “cathodal” stimulation on the target area. One way to meet this challenge may be to use an experimental design in which the position of the reference cathode is systematically varied, with the main “target” electrode remaining in place. If results between these setups are consistent, any behavioral modification may be more readily attributed to the stable factor, i.e., the position and polarity of the target electrode.

### Ways Forward

For the time being, we recommend that researchers provide maximum details about their electrode configurations (in terms of target brain area, electrode number and positioning with corresponding current values, intensity at target and “control” brain areas, field orientation, etc., to the extent that this information is available from modeling) both in the reporting of results and, importantly, in their discussion, avoiding generalized conclusions about the effects of “anodal” and “cathodal” stimulation. Detailed descriptions of

modeled current flow direction and intensity through target regions may ultimately become more informative than the mere use of “anodal” vs. “cathodal” stimulation as descriptive terms, though not before a greater understanding is attained about what neurophysiological and functional effects may be expected from which stimulation settings.

To achieve this understanding, development of modeling approaches is crucial. They provide critical insight into current flow patterns, can challenge simplified assumptions (for example, about the current flow increase directly “under” anodes and cathodes (15) and about the role of the reference electrode’s position and size (34)), and can be used to interpret findings (35). If tDCS treatment success is predicated by plasticity in a certain cortical region, it is rational to plan stimulation montages to enhance stimulation in that specific cortical region while sparing other regions. However, this technical note highlights the point that while conventional tDCS montages are planned based on anodal and cathodal current flow, HD-tDCS montage planning is based on optimizing the electric field along prespecified directions. It is important to note that while the concept of polarity (anodal and cathodal) is critical at the level of individual neurons, reference to neuromodulation effects continues to be made on a macro scale in conventional tDCS literature. This is presumably due to the fact that on a macro level, the anodal electrode does in fact inject positive charge into the head while the cathodal electrode removes it. However, when current traverses through the skin, skull, and cerebrospinal fluid (CSF), and ultimately reaches the cortex, the direction of its local flow (inward vs. outward) may change significantly across opposite walls of the sulci, owing to the convoluted and tortuous topography of the cortex (36).

For more complex HD configurations, the only way forward seems to be experimentation to test montages that reveal maximal electric field magnitude among all possible directions. In the past decade, computational models have advanced from using simplified geometries (concentric spheres) to proliferation of high-resolution magnetic resonance imaging (MRI)-derived modeling publications. Indeed, the forward analysis software used in the experiments above is based on a single individual, but efforts are currently under way to first include a database of heads and then to incorporate trial-specific heads. The challenge to including subject-specific heads on a more regular basis currently consists of MRI scanning cost (the model is MRI derived), manual intervention cost, postautomatic segmentation routines (for instance, ensuring continuity of the CSF layer; (37)), and the computational workload of computing finite element models that incorporate millions of elements. While our team has already embarked on the process (6,38) and similar advances are being made for other types of brain stimulation such as transcranial magnetic stimulation (39), further automation is needed for economical and broad dissemination. Ultimately, neural activation is predicted by coupling the electric field data to multicompartiment biophysical models for individual neurons. While it becomes intractable to incorporate neuron models of the entire cortex, it is clear that model-based approaches should continue to be leveraged to inform montage design and interpretation of results.

Naturally, future research will have to adjudicate if current flow modeling and optimization is critical for tDCS outcome or if the unoptimized approach of placing the active sponge electrode “over” the region of interest would suffice. Even independently from other factors that may affect the functional effects of focal neurostimulation (neural circuitry, inhibition of inhibitors, Sprague effects, etc.), we suggest that it will not.

## CONCLUSIONS

In HD-tDCS stimulation, electrode setups other than  $1 \times 1$  or  $4 \times 1$  ring configurations may be optimal to achieve maximum focality or intensity of stimulation, largely depending on the cortical target site. More research is warranted on the inhibitory vs. excitatory effects of such configurations, as they do not correspond to the traditional dichotomy between “anodal” and “cathodal” stimulation used in conventional tDCS studies. Moreover, even in traditional bicephalic  $1 \times 1$  configurations, using either HD electrodes or sponge pads, the terms “anodal” and “cathodal” do not fully determine expected behavioral effects, as these terms only pertain to the desired type of stimulation over the brain area of interest, but not to other areas that are potentially affected, such as those that lie immediately under the reference electrode.

Descriptions that use the terms “anodal” and “cathodal” should not merely specify the target area, but include specifics regarding the area over which the reference electrode is placed (15,40). On top of that, other stimulation variables such as duration and intensity also affect behavioral outcomes in terms of excitation vs. inhibition of performance, even if the polarity of configurations is kept constant (9). Therefore, (HD-)tDCS research would benefit from not constraining its conclusions or methods by the anodal/cathodal dichotomy, and more basic methodological research is warranted into the modulatory effects of different field orientations on neuronal excitability.

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## Authorship Statements

Ms. Garnett and Dr. den Ouden designed experiment 1 and Ms. Garnett conducted the experiment, including participant recruitment, data collection, and data analysis. Ms. Malyutina and Dr. den Ouden designed experiment 2 and Ms. Malyutina conducted the experiment, including participant recruitment, data collection, and data analysis. Ms. Garnett and Ms. Malyutina prepared the manuscript draft, with equal contribution. Drs. den Ouden and Datta edited and finalized the manuscript. All authors approved the final manuscript.

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