Transcranial Direct Current Stimulation Modifies Automatic and Controlled Verbal Fluency

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Background and Objectives

Overt human behaviors are generally acknowledged to be the result of a variable admixture of automatic and controlled mental processes [Kahnemann & Frederick, 2005]. The production of words on verbal fluency tests shows a pattern of production over time that has been felt to represent such an admixture of automatic and controlled retrieval – rapid production of clusters of related words, alternating with slower, apparent switches to clusters representing different relational criteria [Troyer et al., 1997; Fernaeus & Almkvist, 1998]. Evidence from behavioral, imaging, and lesion studies suggests that, in individuals who are left-hemisphere dominant for speech, automatic functions in this task rely upon left posterior temporal-parietal regions and controlled functions upon left prefrontal regions, although this evidence is far from completely consistent [e.g., Vilkki & Holst, 1994]. Transcranial direct current stimulation (tDCS), which involves passing a weak, direct electrical current through the cortex, may enhance or inhibit functions that underlie cerebral tissues, depending upon the polarity of the applied current [Wasserman & Grafman, 2005; Nitsche et al., 2008]. Iyer and colleagues [2005] found that anodal tDCS at 2.0 mA to the left frontal region significantly increased the total number of words produced in a letter fluency task, although stimulation at 1.0 mA did not. We sought to replicate and extend these results. In particular, we hypothesized that different phases of task performance might be differentially susceptible to tDCS over the left prefrontal region. Because initial production is dominated by more automatic retrieval, and later production by more controlled searching, the influence of left frontal tDCS on cognitive control might be most apparent in the first part of the task.

Methods

Statistical Design. The basic design was a single-blind group comparison of active stimulation (anodal or cathodal) against sham stimulation.

Subjects. Adults (n=66; ages 18-63, mean 32.9) were recruited from the community. All were healthy and right handed (as assessed by the Edinburgh Inventory), with education ranging from 12-20 years (mean 14.7 years).

Tasks. Critical tasks were a letter fluency task and a category fluency task. For the letter fluency task, the subject was instructed to name as many words as possible that began with a given letter of the alphabet (S or P) in 60 sec, without naming words that begin with capital letters, names of numbers, or different forms of the same word. For the category fluency task, subjects were asked to name as many members of a particular category (animals or supermarket items) in two-60 sec. trials. If an error was made, the subject was reminded that words of that type (e.g., non-animals) were not allowed. If the subject did not say anything for 15 sec, the instructor repeated, “Tell me some other animals/supermarket items.”

Procedures and tDCS Stimulation. Subjects were randomly assigned to one of 8 test sequence conditions in counterbalanced order; assigned groups did not significantly differ in age or education. Stimulation electrodes were in place during all conditions, from the start of the sessions. For what we are considering ‘active’ stimulation, current was ramped up to 1.0 mA for a total duration of 30 min. For what we term ‘sham’ stimulation, current was ramped up to 1.0 mA and then ramped down over a 1-min period with the stimulator off for the remainder of the session. (1.0 mA was used to maintain blinding, since in this and prior studies in our lab, subjects could often reliably detect tDCS applied at 2.0 mA.) Stimulation was applied with a constant current stimulator (Iomed Phoresor II Model PM850) through 7.6x7.6-cm sponge electrodes. The ‘active’ electrode was placed over the left prefrontal region (F3), the ‘indifferent’ electrode over the vertex or right supraorbital region.

During Session 1, there were practice trials of verbal fluency tasks. During the last 6 min of stimulation, the critical tasks were administered. Responses were audio recorded using a studio-quality microphone and the Audacity program (version 1.2.6) on a PC. The Experimenter wrote down any homophones or irregular/unclear pronunciations and asked the participants for clarification of their word choices (spelling/meaning) at the end of the trial.

A 90-min washout period followed Session 1. At 80 min into the washout period, the experimenter re-attached the stimulator to the electrodes.

Session 2 (30 min total) was started and was essentially a repeat of the Session 1 protocol, but with alternative practice and test sets. At the end of Session 2, the tDCS equipment was removed.

Analyses. Audio recordings were transcribed after the experimental sessions by an RA. Productions were scored as to the number of words generated, switches, number of clusters, and percent words in clusters, using a scoring system developed by members of our group [Ledoux et al., 2009] from one proposed by Troyer et al. [1997].

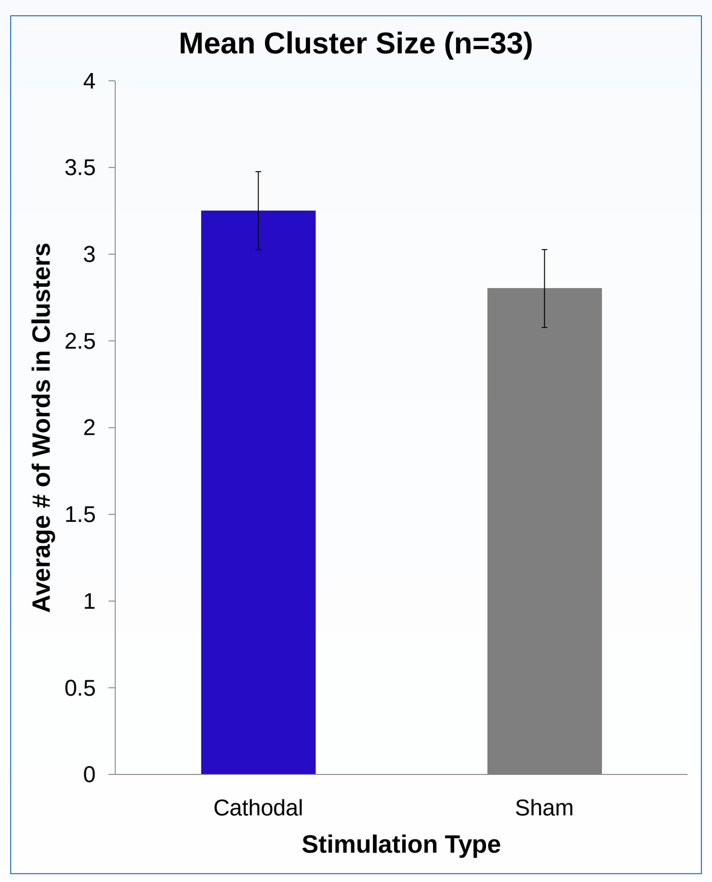

Chart 1. Mean number of words in clusters during the category-cued fluency tasks.

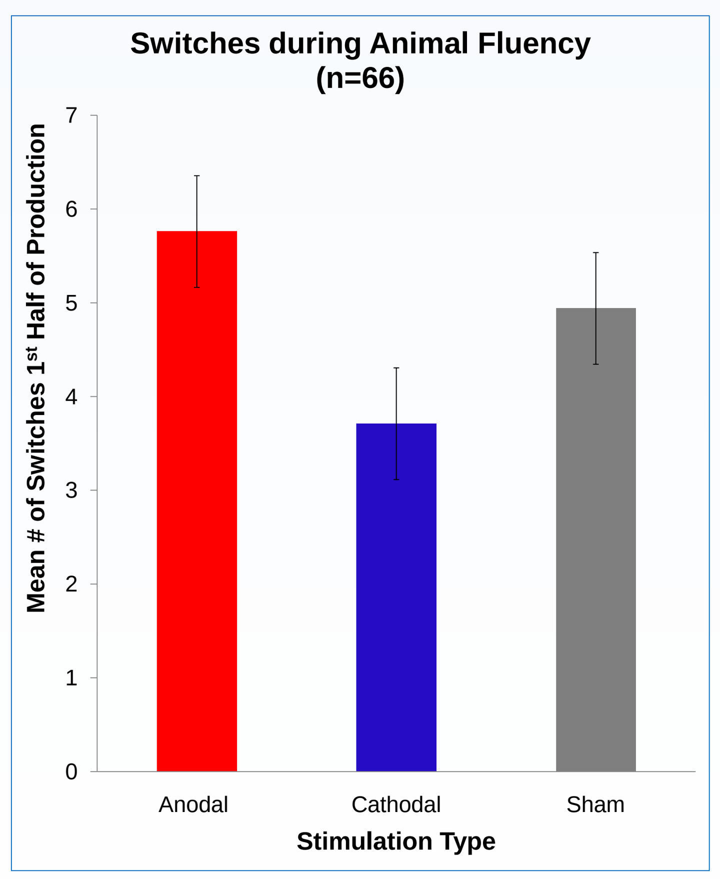

Chart 2. The mean number of switches made during the first half of production in the category animal fluency task.

Results

There was no difference in total number of words produced on either the letter fluency or the category fluency tasks with different polarities of active stimulation. However, on the letter fluency task, anodal stimulation was associated with a trend towards the production of more clusters (p=0.06) and a greater percentage of words within clusters (p=.08). For the category fluency task, cathodal stimulation yielded a greater average number of words in clusters (p<.01) compared to sham stimulation (Chart 1). Subjects who had completed fewer years of education (in our group, males and older adults) tended to show larger tDCS-related alterations in productivity.

Collectively, as expected, our participants produced more multi-word clusters during the first half of animal fluency tasks (first half [M=2.54, SD=1.0], second half [M=2.0, SD=0.7]; p<.01), and more switches during the second half (first half [M=4.83, SD=2.0], second half [M=5.5, SD=1.7]; p=.02). Accordingly, the data were split such that the total number of words produced was halved, and the number of switches was tallied for each participant. Between-groups analyses revealed that, compared to cathodal stimulation, anodal stimulation was associated with more switches on the category animal fluency task (M=3.71, and 5.76, respectively, $t_{(32)}$=3.386, p<.01), such that anodal stimulation to the left prefrontal cortex increased controlled mental processes. No differences were observed in switching behavior in the sham conditions (Chart 2).

In a *post hoc* analysis, participants were separated based on their preferred style of response (clustering or switching). ‘Clusterers’ were defined as individuals who produced a total number of clusters that was less than half of the total number of words produced (e.g., 30 words with <15 clusters). Among participants who met the definition of a clusterer (n=10; 4 cathodal, 6 anodal) in both category fluency tasks, the total number of switches (Animals + Supermarket) was significantly greater among participants who received anodal stimulation (M=12) compared to sham (M=9.83), $t_{(8)}$=2.735, p<.05, such that anodal stimulation increased switching. Additionally, the change in switching (active stimulation – sham) was compared for the category fluency tasks. The change in total number of switches from sham was greater in the anodal condition (M=2.167) compared to cathodal (M=-3), $t_{(8)}$=2.43, p<.05. Analysis of the letter fluency tasks demonstrated a greater increase in the mean run size (average size of multiple word clusters) in the cathodal condition (M=0.725) compared to anodal (M=0.16), $t_{(8)}$=2.29, p=.051. Among people whose preferred response style was switching, anodal stimulation did not improve clustering (as expected), nor did anodal stimulation improve switching in a sample of individuals already at ceiling.

Conclusions and Significance

Iyer et al. [2005] only found an improvement in letter fluency with left frontal tDCS at 2 mA, not 1 mA. Our study, done with 1 mA current to ensure blinding, also did not show a benefit of stimulation in terms of overall performance. However, with a finer grain of analysis, we did find evidence for the effects of tDCS over the left frontal region, some expected, some perhaps not. Left frontal anodal stimulation appeared to facilitate switching (controlled word retrieval), and cathodal stimulation appeared to facilitate clustering (automatic word retrieval). Individuals who might be expected to show less-efficient verbal productivity, namely those with lower education, appeared to be the most responsive to the tDCS intervention.

The processes involved in lexical selection and retrieval are undoubtedly far more complex, both behaviorally and neuroanatomically, than the simplified working model we adopted as the basis for this study (for example, see Badre and colleagues [2005, 2009]) and attempted interpretation of its results. In ongoing tDCS experiments, we are seeking to overcome some of the limitations of the work reported here and exploit the more detailed knowledge that is now available about the organization of cognitive control systems. Nonetheless, we believe that these preliminary findings help provide an empirical foundation for future studies of investigational and therapeutic uses of tDCS in disorders of language production.

References

Badre D et al. (2005) Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. Neuron 47:907-18.

Badre D, D'Esposito M (2009) Is the rostro-caudal axis of the frontal lobe hierarchical? Nat Rev Neurosci 10:659-69.

Fernaeus SE, Almkvist O (1998) Word production: dissociation of two retrieval modes of semantic memory across time. J Clin Exp Neuropsychol 20:137-43.

Iyer MB, Mattu U et al (2005) Safety and cognitive effect of frontal DC brain polarization in healthy individuals. Neurology 64:872-5.

Kahneman D, Frederick S (2005) A model of heuristic judgment. In: The Cambridge Handbook of Thinking and Reasoning (Holyoak KJ, Morrison RG, eds), pp 267-93; NY: Cambridge University Press.

Ledoux K, Vannorsdall TD et al (2009) Development, reliability, and construct validity of a new approach to analyzing qualitative aspects of speeded lexical retrieval. J Int Neuropsychol Soc 15:121.

Nitsche MA, Cohen LG et al (2008) Transcranial direct current stimulation: state of the art 2008. Brain Stimulat 1:206-23.

Troyer AK, Moscovitch M, Winocur G (1997) Clustering and switching as two components of verbal fluency: evidence from younger and older healthy adults. Neuropsychology 11:138-46.

Vilkki J, Holst P (1994) Speed and flexibility on word fluency tasks after focal brain lesions. Neuropsychologia 32:1257-62.

Wassermann EM, Grafman J (2005) Recharging cognition with DC brain polarization. Trends Cogn Sci 9:503-5.

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