Editorial

Electrode montages for tDCS and weak transcranial electrical stimulation: Role of "return" electrode's position and size

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In this issue, Moliadze and colleagues investigate the role of electrode montage in the induction of acute lasting excitability changes by transcranial Direction Current Stimulation (tDCS) and transcranial Random Noise Stimulation (tRNS); specifically they demonstrate that during weak transcranial electrical stimulation, the position of the "return" electrode affects neuro-modulation under the "active" electrode. Moliadze and colleagues introduce the development of modern tDCS protocols at the turn of the decade (Priori et al., 1998; Nitsche and Paulus, 2000, 2001; Terney et al., 2008). Despite wide-spread subsequent dissemination of tDCS, there remain significant unknowns about the mechanisms of tDCS and the design of electrode montages, including electrode size and placement. Moliadze and colleagues address the role of "return" electrode's position (and distance) in the induction of Transcranial Magnetic Stimulation (TMS) evoked excitability changes under an "active" electrode over motor cortex (Moliadze et al., in this issue).

Understanding and controlling electrotherapy dose is evidently critical in determining behavioral and clinical outcome. The position of stimulating electrodes governs current flow through the body, and hence the distribution of induced electric fields in the brain. These induced cortical currents/electric fields modulate neuronal excitability for DC stimulation and, in turn, determine behavioral and clinical outcomes (Bikson et al., 2008).

The most simplistic dose design schemes for tDCS assume a region of "increased excitability" in the cortex directly under the anode electrode, and a region of "decreased excitability' under the cathode, with intermediary regions largely spared (unaffected). Several studies have suggested limitations in this simplified approach including the need to consider: (1) increased current density at the electrode edges (Nitsche et al., 2007; Miranda et al., 2006, 2009); (2) individual differences (Madhavan and Stinear, 2010); (3) significant current flow in intermediary regions, including the potential for current clustering (Datta et al., 2009); (4) montages for unidirectional modulation (Rossini et al., 1985; Saypol et al., 1991; Datta et al., 2008); and (5) relative electrode position, including inter-electrode distance (Stecker, 2005; Datta et al., 2008) and the use of extra-cephalic electrodes (Accornero et al., 2007; Ferrucci et al., 2008; Baker et al., 2010). Generally, increasing electrode separation on the head is expected to increase cortical modulation by increased relative amount of current entering the brain rather than "shunted" across the scalp.

The report by Moliadze and colleagues provides some of the strongest clinical evidence to-date that the relative position of stimulation electrodes can affect neuro-modulation under each electrode – namely that in determining electrotherapy dose the two stimulating electrodes *cannot* be considered separately and independently, even for relatively distant electrode positions. Moreover, increasing electrode distance may *decrease* the magnitude of neuro-modulation, depending on the specific montage and physiological measure.

The current flow through the body is strongly influenced by anatomical details, because of the different electrical conductivities of tissues such as scalp, skull/vertebrae, muscle, CSF, and brain – as a result the induced current profile in the brain may be detailed and complex. Given this, it is thus not surprising that the position of *both* electrodes determines the resulting current flow distribution through the cortex. Simultaneously, the complexity of current flow indicates that determining electrode montages dose by simplified assumptions may not be prudent, as highlighted by the results of Moliadze et al., in this issue.

One solution to addressing this complexity in the design of rational stimulation protocols is the prediction of current flow patterns through the brain using computer models. The sophistication of computer models using finite-element-methods (FEM) for this purpose (Butson et al., 2007; De Lucia et al., 2007) has increased to allow high-resolution (e.g. 1 mm; Datta et al., 2009) and individualized modeling (Wagner et al., 2007; Datta et al., 2010). Fig. 1 illustrates the resulting brain current flow for three electrode montages – in all cases, the size and position of the "active" electrode over motor cortex is fixed, while the position or size of the "return" electrode is varied. The position and size of the "return" electrode affects the electric field distribution across the entire cortex. In addition, changing the position of the "return" electrode affects the electric field distribution in cortex directly under the "active" electrode.

Our modeling results support the clinical finding by Moliadze and colleagues that even if the direct actions of the "return" electrode are mitigated by its position (e.g. extracephalic) or size (Nitsche et al., 2007); the "return" electrode will still influence the current path through the brain from the "active" electrode. For example, the re-positioning of the return pad from the contralateral forehead to the contralateral upper arm may have shifted the preferential flow of current from across the frontal regions to across the posterior regions of the brain (see Montages A and C versus Montage B in Fig. 1). More generally, the regions of brain modulation may *not* be simply under the "active" electrode (Lang et al., 2005; Datta et al., 2009; Sadleir et al., 2010), such that some
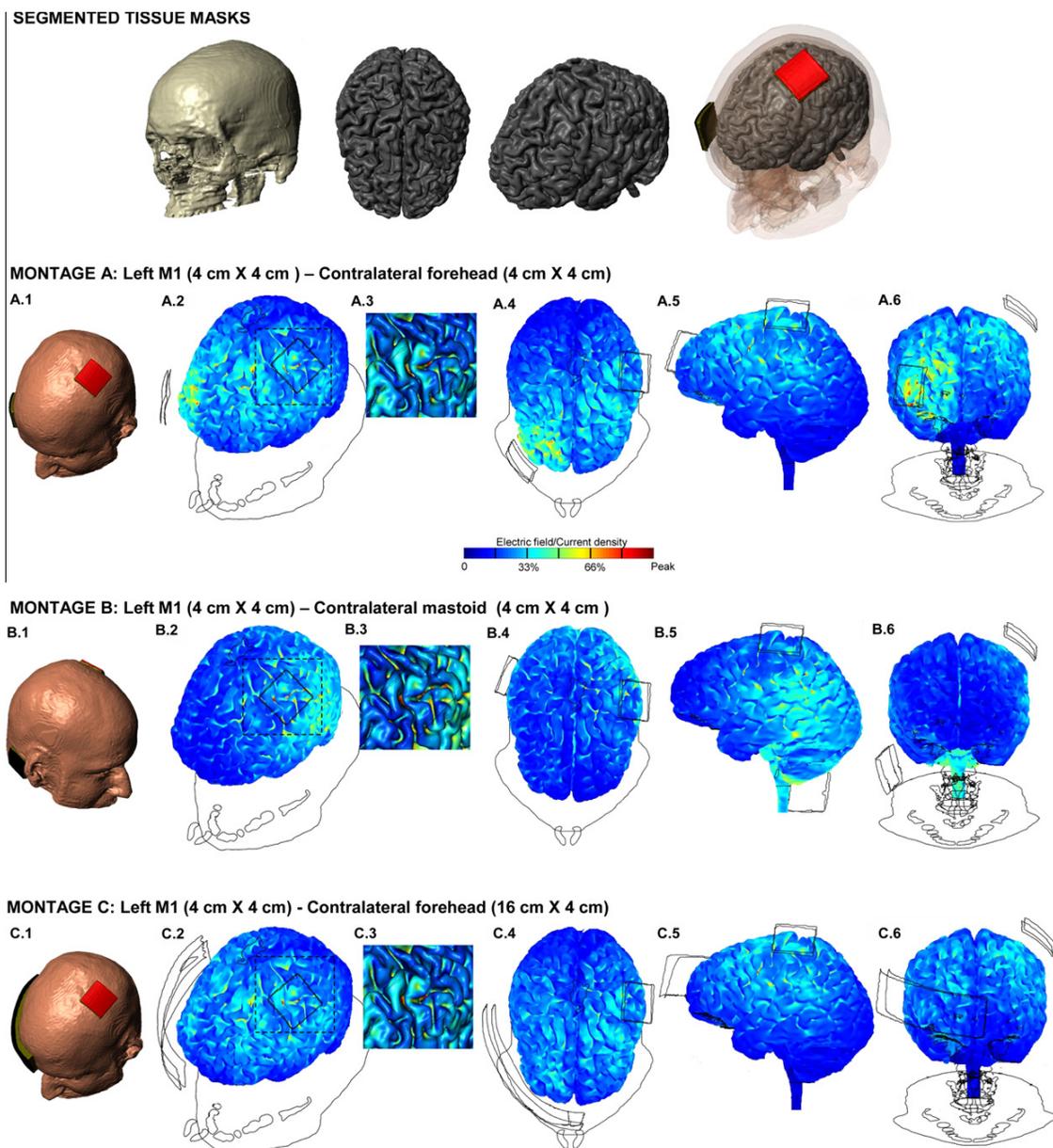
Fig. 1. Effect of "return" electrode's *position* and *size* on cortical electric fields induced by a 4×4 cm "active" electrode over the left primary motor cortex. An individualized FEM head model was created from MRI scans of an adult male at $1 \times 1 \times 1$ mm resolution (Soterix LLC, NY, USA). The head was segmented into compartments representing the brain, CSF, skull, scalp, muscle, eyes, and air. The Laplace equation was solved and current densities corresponding to 1 mA total current was applied. Induced cortical electric field (EF) magnitude maps for the different electrode montages were determined. All false color maps were generated between 0 and 0.44 V/m; the *peak* cortical EF magnitude induced in Montage A. Top row: Sample segmentation masks. (A) Stimulation with a 4×4 cm return electrode over the contralateral forehead (Montage A) results in significant cortical activation in the right frontal lobe, as well as diffuse and clustered activation between the electrodes. (B) Stimulation with a 4×4 cm return electrode on the contralateral mastoid (approximating an extra-cephalic electrode; Montage B) results in cortical electric field on the left hemisphere as current preferentially flows down the posterior regions of the brain and through the brain stem. (C) Stimulation with a 16×4 cm electrode wrapped around the contralateral forehead (Montage C) results in diffuse and clustered cortical electric fields. The insets (A.3, B.3, C.3) highlight gyri/sulci modulation directly under the pad (with the "lighting on" feature). For montages with different placements of return electrode (Montages A and B), the pattern of cortical electric fields directly *under* the "active' electrode (inset) was distinct.

"surprising" clinical findings, including by Moliadze and colleagues may be understood by considering the concurrent neuro-modulation of multiple cortical and sub-cortical regions. Additional experimental studies investigating the specific role of electrode placements and intensity, and careful consideration of electrode montage in designing therapeutic protocols, is warranted.

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