## Transcranial electric stimulation with multiple electrodes can reach deep brain areas

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**Introduction:** To reach a deep target in the brain with transcranial electric stimulation (TES), currents have to pass through the cortical surface. Thus, it is generally thought that TES cannot achieve focal deep brain stimulation. Recent efforts with interfering waveforms (Grossman et al.,2017) and pulsed stimulation (Voroslakos et al, 2018) have argued that one can achieve a focal hot spot at some depth in the brain. However, here we show that conventional transcranial stimulation with multiple current sources can also achieve deep brain stimulation by using optimized multi-electrode approach.

**Methods:** The multi-electrode TES can be numerically optimized to maximize intensity or focality at a desired target location (Dmochowskiet al., 2011). We performed this numerical optimization across all the brain locations in a 0.5 mm resolution head model (Huang et al, 2016) to see if TES can reach focal or intense stimulation in deep brain areas. To prove the pulsed stimulation protocol is equivalent to multi-electrode TES in terms of targeted stimulation, the max-intensity optimization was also computed for each brain location following the electrode placement setup in Voroslakos et al, 2018. Mathematical derivation was performed, with further modeling evidences, to prove that temporal interfering stimulation (Grossman et al.,2017) achieves no gains in depth of stimulation compared to conventional TES with amplitude-modulated waveform.

**Results:** Deep brain areas may in fact be strongly stimulated (achieve an electric field of up to 1.5 V/m with 2 mA injected current) under optimized multi-electrode TES. Increasing injected current to 6 mA delivered through 6 anodes (following Voroslakos et al, 2018) gives almost the same electric field distribution as the TES case, with field

intensity at the target achieving 3 V/m. The modulation depth of the interfering sinusoidal waveform (Grossman et al.,2017) is mathematically shown to be equal or smaller than what can be achieved with conventional TES with the same two pairs of electrodes.

**Conclusion:** Recently proposed new approaches do not show any significant advantages compared to multi-electrode TES in reaching deep brain areas.