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Toward comprehensive tDCS safety standards

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We thank Chhatbar and colleagues for the editorial commentary (Chhatbar et al., 2017) on the original paper “Safety parameter considerations of anodal transcranial Direct Current Stimulation in rats” (Jackson et al., 2017). Chhatbar et al. argue that charge density at the electrode is a more “comprehensive” measure than electrode current density because electrode charge density factors in both current density and the duration of stimulation. We are not aware of any studies that systematically investigated this assumption – which would require varying both electrode current density and time while maintaining electrode charge density. For example, relying simply on charge density would mean that for a given brain injury, across any animal model or human intervention, altering the stimulation parameters by both increasing the stimulation duration 100-fold and decreasing the current density 100-fold would result in an identical brain injury. Rather, Jackson et al. demonstrate and make explicit throughout the manuscript that the electrode current density threshold for injury, and so the derivative metric of charge density, varies with electrode montage (animal model) and *possibly* polarity. Any analysis (figure or table) that relies on summary metrics without recognizing the critical particulars of each animal model can be misrepresentative.

Safety guidelines should consider the totality of evidence and modeling support, which is in agreement with a recent consensus on a conservative rationale for tDCS safety (Bikson et al., 2016). Predictions on human safety thresholds should not be based on any single metric no matter how “comprehensive”, nor should the canonical study by Liebetanz et al. (Liebetanz et al., 2009) be saddled with implications beyond those intended by the authors. For example, Liebetanz shows applying high charge densities ($>52.4 \text{ kC/m}^2$) by increasing stimulation duration rather than current density does not result in brain injury below 142.9 A/m^2 . Liebetanz et al. are also careful to qualify the use of charge density as an applicable

lesion metric only at a specific current density range, showing current and charge density are both relevant measures but not independently comprehensive for predicting brain injury.

Human tDCS protocols circa 1970 used relatively low current intensities but with smaller electrodes and longer durations than are common today, with cases of electrode charge density $>100 \text{ kC/m}^2$; only mild side effects were reported (Esmaeilpour et al., 2017), further limiting the simple reliance on electrode charge density to predict brain injury thresholds. Regardless, given the limitations of animal models and unknowns about injurious mechanisms and dynamics, we do not agree that data from Jackson et al. on reduced current density thresholds for injury during anodal tDCS can be dismissed as “incorrect”. Disproportionate reliance on any single dose metric (e.g. electrode charge density) can set unscientific standards for safety, both restricting worthwhile dose-response studies and endorsing unjustified interventions.

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