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Reply to the letter to the editor

Reply to Dr. Paulus

Nitsche and Paulus (2000) asserted that "The current intensity and duration we used did not exceed the safety limits stated by Agnew and McCreery (1987)". Agnew and McCreery (1987) on page 144, right-hand column, lines 6–8, stated that "…charge/phase…must be considered as a factor in stimulation induced neural damage", and in their final Recommendations on page 145, right-hand column, lines 5–6, "The charge density at the stimulating electrode should not exceed 40 μC/cm^2 per phase". Hence readers reasonably argue that Nitsche and Paulus (not specifying any limit) referred to the main safety limit (i.e. μC/cm^2) proposed by Agnew and McCreery (1987). In a previous study Yuen et al. (1981) stated that "Specifically…neural damage is more strongly correlated with charge density per phase of the stimulus pulse than with either the pulse duration or the pulse amplitude". Yet, because a tDCS pulse is assimilable to a single phase in a train of stimuli, the charge density at the stimulating electrode is potentially applicable also to tDCS. The charge density values calculated for the protocol used by Nitsche and Paulus (2000) nevertheless exceed the value proposed by Agnew and McCreery (1987). Hence, although the other stimulus variables indicating tissue damage that Nitsche and Paulus (2000) used might not have exceeded the safety limits, the main limit indicated by Agnew and McCreery (1987) was clearly exceeded. The Nitsche and Paulus's assertion (2000) therefore is somewhat imprecise. I am happy to see that Nitsche et al. in their letter agree with me about the need for further experiments on the safety of tDCS. Given the potential importance of the methodology and considering the well-known dangers of direct currents (DC), readers should be aware that the protocol proposed by Nitsche et al.'s letter is uncontrolled, has not been validated and is based—at least partly—on unpublished observations. Though the letter reports some technical and methodological considerations, the lack of validated and published safety criteria for tDCS still remains. The currently available safety criteria for transcranial brain stimulation with short (<1 ms) magnetic or electric pulses are not immediately applicable to tDCS lasting some minutes and delivered with large electrodes even because "It is uncertain how neural damage thresholds would be affected by the activation of a much larger population of neurons, as would occur with the use of much larger scalp electrodes" (Agnew and McCreery, 1987). Finally, a theoretically possible mechanism of tDCS-induced tissue damage that Nitsche et al. do not consider but could be especially relevant for long tDCS pulses is the displacement and migration of charged molecules, as it happens for protein electrophoresis.

Since our early report (Priori et al., 1998) we have increasingly realized the potential importance of tDCS. I now therefore share Nitsche et al.'s optimism (Priori, 2003). Even so, the absolute safety of the technique must be scientifically guaranteed before large scale application of tDCS, always keeping in mind the medical aphorism *primum non nocere*. For a delicate issue such as the consensus on the safety of a potential therapeutic technique, tDCS, I would suggest instituting an ad hoc committee of the World Federation for Clinical Neurophysiology.

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