Cortical Neuromodulation Modifies Cerebral Vasomotor Reactivity

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Background and Purpose—Cerebral vasomotor reactivity (VMR) is a capability of cerebral vessels to dilate in response to hypercapnia. Transcranial direct current stimulation (tDCS) effects on cerebral hemodynamics have been poorly studied.

Methods and Results—Ten healthy subjects underwent anodal/cathodal tDCS on the left motor cortex. Before and after tDCS, VMR assessment by transcranial Doppler and an electrocardiogram were performed. Normalized low-frequency band power of heart rate variability and its reactivity from basal to VMR condition (LFNreact) were estimated as relative markers of sympathetic activation. tDCS exerted a polarity-specific effect on both VMR (P=0.0001) and LFNreact (P=0.001). Anodal tDCS decreased VMR by 3.4%/mm Hg CO2 bilaterally and increased LFNreact whereas cathodal tDCS increased VMR by 0.8%/mm Hg CO2 bilaterally and reduced LFNreact.

Conclusions—Cerebral VMR is modified by tDCS. Based on the consensual changes with heart rate variability, we can hypothesize that the sympathetic nervous system could modulate the bihemispheric modification of VMR. Further studies are needed to confirm this hypothesis. (Stroke. 2010;41:2087-2090.)

Key Words: cerebral hemodynamics  ■ heart rate variability  ■ stroke  ■ transcranial direct current stimulation  ■ transcranial Doppler
0.15–0.4); and total frequency (TOTbasal, TOTCO2; <0.4 Hz). Vagal nerve is the major contributor to the high-frequency component. Although the significance of low-frequency power component is controversial, normalized low-frequency power (LFN=[LF/\text{TOT}/VLF]*100) is a reliable measure of sympathetic response to autonomic fibers activation. We estimated the reactivity of LFN (LFNreact=LFNCO2–LFNbasal) during CO2 compared with basal condition as a measure of sympathetic responsiveness during VMR assessment.

**tDCS**
A 15-minute 1-mA tDCS was delivered through an active 35-cm² sponge electrode positioned over the left M1 (C3 scalp position of the International EEG 10/20 System). The reference was placed above the ipsilateral arm.

**Post-tDCS Evaluation**
Pre-tDCS evaluation procedures were repeated.

**Statistical Analysis**
Stimulation (before vs after tDCS), polarity (A-tDCS vs C-tDCS), and hemisphere (stimulated vs contralateral) effects and their interactions were assessed for basal MFV and VMR (repeated-measures general linear model). The same analysis was applied on behavioral scales and HRV for stimulation*polarity. An effect of VMR evaluation on HRV (CO2 effect, repeated measures general linear model) was explored.

**Results**
Basal MFV was not different between stimulation, hemisphere, and polarity. No interaction was significant.

A tDCS stimulation*polarity effect (P=0.0001) on bihemispheric VMR (stimulation*hemisphere; P=0.307) was found: A-tDCS reduced VMR ≈3.4%/mm Hg CO2, whereas C-tDCS provided a VMR increase of ≈0.8%/mm Hg CO2
tDCS was not found to affect either sleepiness/alertness visual analogic scale or Stanford Sleepiness Scale. Mean heart rate did not show a stimulation*polarity effect. Among HRV parameters, neither single stimulation nor polarity effects were found. LF_{basal}, LF_{CO2}, LFN, LF_{NCO2}, and LFN_{react} showed a stimulation*polarity effect (P = 0.031; P = 0.033; P = 0.008; P = 0.032; P = 0.001). Mean values analysis demonstrated that LF_{basal} and LFN_{basal} decreased after A-tDCS and increased after C-tDCS. Opposite modifications were found for LF_{CO2}, LFN_{CO2}, and LFN_{react}, thus supporting the hypothesis that tDCS can affect the sympathetic system with polarity specificity (Figure 3A, B). A constant normalized low-frequency reduction from basal to VMR recording was found, even if CO2 effect was not significant for all the conditions (Figure 3B; before A-tDCS, P = 0.001; before C-tDCS, P = 0.355; after A-tDCS, P = 0.427; after C-tDCS, P = 0.029). No correlations were found between HRV parameters and VMR changes.

Discussion

The present study demonstrated a polarity-specific effect of tDCS on cerebral VMR in a healthy population. A-tDCS produced a bilateral reduction of VMR, whereas C-tDCS produced its increase.

Cerebral VMR is orchestrated by nervous, myogenic, and metabolic factors. The nervous control is determined mainly through sympathetic efferents regulating arteriolo-capillary caliber. Sympathetic system is not supposed to influence cerebral blood flow under normal conditions, but it plays a key role when the autoregulation limits are overcome. Although a reduction of sympathetic activity lowers the inferior limit, its increase allows maintenance of functional compliance above the superior. Accordingly, an increasing sympathetic activity, as we observed after A-tDCS, could reduce the potential capability of further dilating vessels after a hypercapnic stimulus, as reflected in VMR measurements. The
opposite could be true for a reduced sympathetic tone and C-tDCS effects. Because tDCS effect on cortical excitability is unilateral, its bihemispheric impact on VMR supports the hypothesis of a systemic effect.

An interaction between cortical excitability and the autonomic system is in line with recent findings demonstrating a correlation between the sympathetic activity and M1,9 and a neuronal connection between the peripheral sympathetic nervous system and M1.10 Neurophysiological observations also support this assumption.11

tDCS could also affect extracellular pH and \([\text{Ca}^{2+}]_\text{j}\);12 therefore, its influence on the myogenic and the metabolic control of cerebral circulation cannot be excluded. However, these effects might be topographically limited under the electrode,12 contrasting with bihemispheric effects we observed. Our study has some methodological limitations: autonomic activity was estimated only by HRV and may have been influenced by hypercapnia.

Conclusion

In conclusion, tDCS on M1 induced a bilateral modification of cerebral VMR in a polarity-specific manner. Based on consensual changes with HRV, we can speculate that these effects are modulated by the sympathetic nervous system. Further studies are needed to confirm this hypothesis before launching therapeutic trials for stroke with tDCS.

Disclosures

None.

References

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