Transcranial direct current stimulation

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see also Transcranial alternating current stimulation.

Transcranial direct current stimulation (tDCS) is a form of neurostimulation that uses constant, low direct current delivered via electrodes on the head; it can be contrasted with cranial electrotherapy stimulation which generally uses alternating current the same way.

It was originally developed to help patients with brain injuries or psychiatric conditions like major depressive disorder. tDCS appears to have some potential for treating depression.

Surfeit locus protein 4 (SURF4) functions as a cargo receptor that is capable of transporting newly formed proteins from the lumen of the endoplasmic reticulum into vesicles and Golgi apparatus. However, the role of SURF4 in the central nervous system remains unclear. Hu et al. investigated the role of SURF4 and its underlying mechanisms in cerebral ischemia-reperfusion injury in rats, and whether it can be used effectively for novel therapeutic intervention. They also examined whether transcranial direct current stimulation (tDCS) can exert a neuroprotective effect via SURF4-dependent signaling. Following cerebral I/R injury in rats, a significant increase was observed in the expression of SURF4. In both I/R injury and oxygen-glucose deprivation (OGD) insult, suppressing the expression of SURF4 demonstrated a neuroprotective effect, while overexpression of SURF4 resulted in increased neuronal death. They further showed that the levels of nerve growth factor precursor (proNGF), p75 neurotrophin receptor (p75NTR), sortilin, and PTEN were increased following cerebral I/R injury and that SURF4 acted through the PTEN/proNGF signal pathway to regulate neuronal viability. They demonstrated that tDCS treatment reduced SURF4 expression and decreased the infarct volume after cerebral I/R injury. Together, this study indicates that SURF4 plays a critical role in ischemic neuronal injury and may serve as a molecular target for the development of therapeutic strategies in acute ischemic stroke [1)]

There is no good evidence that it is useful for cognitive enhancement in healthy people, memory deficits in Parkinson's disease and Alzheimer's disease, schizophrenia, non-neuropathic pain, nor improving upper limb function after stroke.

The basic idea of TES is that the application of weak currents can interact with neural processing, modify plasticity and entrain brain networks, and that this in turn can modify behaviour. The technique is now widely employed in basic and translational research, and increasingly is also used privately in sport, the military and recreation. The proposed capacity to augment recovery of brain function, by promoting learning and facilitating plasticity, has motivated a burgeoning number of clinical trials in a wide range of disorders of the nervous system [2)].

Rising threshold level during monitoring of motor evoked potentials (MEP) using transcranial Electrostimulation (TES) has been described without damage to the motor pathway in the cranial surgery, suggesting the need for monitoring of affected and unaffected hemisphere

Redondo-Castro et al have applied transcranial Electrostimulation to rats with spinal cord injury and selectively tested the motor evoked potentials (MEPs) conveyed by descending motor pathways with cortical and subcortical origin. MEPs were elicited by Electrostimulation to the brain and recorded on the tibialis anterior muscles. Stimulation parameters were characterized and changes in MEP responses tested in uninjured rats, in rats with mild or moderate contusion, and in animals with complete transection of the spinal cord. All injuries were located at the T8 vertebral level. Two peaks, termed N1 and N2, were obtained when changing from single pulse stimulation to trains of 9 pulses at 9 Hz. Selective injuries to the brain or spinal cord funiculi evidenced the subcortical origin of N1 and the cortical origin of N2. Animals with mild contusion showed small behavioral deficits and abolished N1 but maintained small amplitude N2 MEPs. Substantial motor deficits developed in rats with moderate contusion, and these rats had completely eliminated N1 and N2 MEPs. Animals with complete cord transection had abolished N1 and N2 and showed severe impairment of locomotion. The results indicate the reliability of MEP testing to longitudinally evaluate over time the degree of impairment of cortical and subcortical spinal pathways after spinal cord injuries of different severity [3)].

A group of European experts was commissioned by the European Chapter of the International Federation of Clinical Neurophysiology to gather knowledge about the state of the art of the therapeutic use of transcranial direct current stimulation (tDCS) from studies published up until September 2016, regarding pain, Parkinson's disease, other movement disorders, motor stroke, poststroke aphasia, multiple sclerosis, epilepsy, consciousness disorders, Alzheimer's disease, tinnitus, depression, schizophrenia, and craving/addiction. The evidence-based analysis included only studies based on repeated tDCS sessions with sham tDCS control procedure; 25 patients or more having received active treatment was required for Class I, while a lower number of 10-24 patients was accepted for Class II studies. Current evidence does not allow making any recommendation of Level A (definite efficacy) for any indication. Level B recommendation (probable efficacy) is proposed for: (i) anodal tDCS of the left primary motor cortex (M1) (with right orbitofrontal cathode) in fibromyalgia; (ii) anodal tDCS of the left dorsolateral prefrontal cortex (DLPFC) (with right orbitofrontal cathode) in major depressive episode without drug resistance; (iii) anodal tDCS of the right DLPFC (with left DLPFC cathode) in addiction/craving. Level C recommendation (possible efficacy) is proposed for anodal tDCS of the left M1 (or contralateral to pain side, with right orbitofrontal cathode) in chronic lower limb neuropathic pain secondary to spinal cord lesion. Conversely, Level B recommendation

(probable inefficacy) is conferred on the absence of clinical effects of: (i) anodal tDCS of the left temporal cortex (with right orbitofrontal cathode) in tinnitus; (ii) anodal tDCS of the left DLPFC (with right orbitofrontal cathode) in drug-resistant major depressive episode. It remains to be clarified whether the probable or possible therapeutic effects of tDCS are clinically meaningful and how to optimally perform tDCS in a therapeutic setting. In addition, the easy management and low cost of tDCS devices allow at home use by the patient, but this might raise ethical and legal concerns with regard to potential misuse or overuse. We must be careful to avoid inappropriate applications of this technique by ensuring rigorous training of the professionals and education of the patients [4].

Case series

The aim of a study of Abboud et al. was to compare sensitivity and specificity between the novel threshold and amplitude criteria for motor evoked potentials (MEPs) monitoring after transcranial Electrostimulation (TES) during surgery for supratentorial lesions in the same patient cohort.

One hundred twenty-six patients were included. All procedures were performed under general anesthesia. Craniotomy did not expose motor cortex, so that direct mapping was less suitable. After TES, MEPs were recorded bilaterally from abductor pollicis brevis (APB), from orbicularis oris (OO), and/or from tibialis anterior (TA). The percentage increase in the threshold level was assessed and considered significant if it exceeded by more than 20% on the affected side the percentage increase on the unaffected side. Amplitude on the affected side was measured with a stimulus intensity of 150% of the threshold level set for each muscle.

Eighteen of 126 patients showed a significant change in the threshold level as well as an amplitude reduction of more than 50% in MEPs recorded from APB, and 15 of the patients had postoperative deterioration of motor function of the arm (temporary in 8 cases and permanent in 7 [true-positive and false-negative results]). Recording from TA was performed in 66 patients; 4 developed postoperative deterioration of motor function of the leg (temporary in 3 cases and permanent in 1), and showed a significant change in the threshold level, and an amplitude reduction of more than 50% occurred in 1 patient. An amplitude reduction of more than 50% occurred in another 10 patients, without a significant change in the threshold level or postoperative deterioration. Recording from OO was performed in 61 patients; 3 developed postoperative deterioration of motor function of facial muscles (temporary in 2 cases and permanent in 1) and had a significant change in the threshold level, and 2 of the patients had an amplitude reduction of more than 50%. Another 6 patients had an amplitude reduction of more than 50% but no significant change in the threshold level or postoperative deterioration. Sensitivity of the threshold criterion was 100% when MEPs were recorded from APB, OO, or TA, and its specificity was 97%, 100%, and 100%, respectively. Sensitivity of the amplitude criterion was 100%, 67%, and 25%, with a specificity of 97%, 90%, and 84%, respectively.

The threshold criterion was comparable to the amplitude criterion with a stimulus intensity set at 150% of the threshold level regarding sensitivity and specificity when recording MEPs from APB, and superior to it when recording from TA or OO [5].

2016

Between October 2014 and October 2015, TES-MEP were performed in 143 patients during surgery for unilateral supratentorial lesions in motor-eloquent brain areas. All procedures were performed under general anesthesia using a strict protocol to maintain stable blood pressure. MEP were evaluated

bilaterally to assess the percentage increase in threshold level, which was considered significant if it exceeded 20% on the contralateral side beyond the percentage increase on the ipsilateral side. Patients who developed a postoperative motor deficit were excluded. Volume of subdural air was measured on postoperative magnetic resonance imaging. Logistic regression was performed to identify factors associated with the intraoperative recorded changes in threshold level.

A total of 123 patients were included in the study. On the affected side, 82 patients (66.7%) showed an increase in threshold level, which ranged from 2% to 48% and 41 patients (33.3%) did not show any change. The difference to the unaffected side was under 20% in all patients. The recorded range of changes in the systolic and mean pressure did not exceed 20 mm Hg in any of the patients. Pneumocephalus was detected on postoperative magnetic resonance imaging scans in 87 patients (70.7%) and 81 of them (93.1%) had an intraoperative increase in threshold level on either sides. Pneumocephalus was the only factor associated with an increase in threshold level on the affected side ($P<0.001$), while each of pneumocephalus and length of the procedure correlated with a change in threshold level on the unaffected side ($P<0.001$ and 0.032, respectively).

Pneumocephalus was the only factor associated with increase in threshold level during MEP monitoring without damaging motor pathway. Threshold level on the affected side can rise up to 48% without being predictive of postoperative paresis, as long as the difference between the increased threshold of the affected and unaffected side is within 20%. Changes in systolic or mean blood pressure within a range of 20 mm Hg do not seem to influence intraoperative MEP [6)].

Warning criteria for monitoring of motor evoked potentials (MEP) after direct cortical stimulation during surgery for supratentorial tumors have been well described. However, little is known about the value of MEP after transcranial Electrostimulation (TES) in predicting postoperative motor deficit when monitoring threshold level. The authors aimed to evaluate the feasibility and value of this method in glioma surgery by using a new approach for interpreting changes in threshold level involving contra- and ipsilateral MEP.

Between November 2013 and December 2014, 93 patients underwent TES-MEP monitoring during resection of gliomas located close to central motor pathways but not involving the primary motor cortex. The MEP were elicited by transcranial repetitive anodal train stimulation. Bilateral MEP were continuously evaluated to assess percentage increase of threshold level (minimum voltage needed to evoke a stable motor response from each of the muscles being monitored) from the baseline set before dural opening. An increase in threshold level on the contralateral side (facial, arm, or leg muscles contralateral to the affected hemisphere) of more than 20% beyond the percentage increase on the ipsilateral side (facial, arm, or leg muscles ipsilateral to the affected hemisphere) was considered a significant alteration. Recorded alterations were subsequently correlated with postoperative neurological deterioration and MRI findings.

TES-MEP could be elicited in all patients, including those with recurrent glioma (31 patients) and preoperative paresis (20 patients). Five of 73 patients without preoperative paresis showed a significant increase in threshold level, and all of them developed new paresis postoperatively (transient in 4 patients and permanent in 1 patient). Eight of 20 patients with preoperative paresis showed a significant increase in threshold level, and all of them developed postoperative neurological deterioration (transient in 4 patients and permanent in 4 patients). In 80 patients no significant change in threshold level was detected, and none of them showed postoperative neurological deterioration. The specificity and sensitivity in this series were estimated at 100%. Postoperative MRI

revealed gross-total tumor resection in 56 of 82 patients (68%) in whom complete tumor resection was attainable; territorial ischemia was detected in 4 patients.

The novel threshold criterion has made TES-MEP a useful method for predicting postoperative motor deficit in patients who undergo glioma surgery, and has been feasible in patients with preoperative paresis as well as in patients with recurrent glioma. Including contra- and ipsilateral changes in threshold level has led to a high sensitivity and specificity [7)].

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Hu W, Kong X, Cui Y, Wang H, Gao J, Wang X, Chen S, Li X, Li S, Che F, Wan Q. Surfeit Locus Protein 4 as a Novel Target for Therapeutic Intervention in Cereb

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Skill increase in motor performance can be defined as explicitly measuring task success but also via more implicit measures of movement kinematics. Even though these measures are often related, there is evidence that they represent distinct concepts of learning. In a study, the effect of multiple tDCS-sessions on both explicit and implicit measures of learning is investigated in a pointing task in 30 young adults (YA) between 27.07 ± 3.8 years and 30 old adults (OA) between 67.97 years ± 5.3 years. We hypothesized, that OA would show slower explicit skill learning indicated by higher movement times/lower accuracy and slower implicit learning indicated by higher spatial variability but profit more from anodal tDCS compared with YA. We found age-related differences in movement time but not in the accuracy or spatial variability. TDCS skilled learning facilitates learning neither explicit nor implicit parameters. However, contrary to our hypotheses, we found tDCS-associated higher accuracy only in YA but not in spatial variability. Taken together, our data show limited overlapping of tDCS effects in explicit and implicit skill parameters. Furthermore, it supports the assumption that tDCS is capable of producing a performance-enhancing brain state at least for explicit skill acquisition ((Kaminski E, Engelhardt M, Hoff M, Steele C, A Villringer, Ragert P. TDCS effects on pointing task learning in young and old adults. Sci Rep. 2021 Feb 9;11(1):3421. doi: 10.1038/s41598-021-82275-4. Erratum in: Sci Rep. 2021 May 4;11(1):9871. PMID: 33564052; PMCID: PMC7873227.

2)

Bestmann S, Walsh V. Transcranial Electrostimulation. Curr Biol. 2017 Dec 4;27(23):R1258-R1262. doi: 10.1016/j.cub.2017.11.001. PubMed PMID: 29207262.

3)

Redondo-Castro E, Navarro X, García-Alías G. Longitudinal Evaluation of Residual Cortical and Subcortical Motor Evoked Potentials in Spinal Cord Injured Rats. J Neurotrauma. 2016 May 15;33(10):907-16. doi: 10.1089/neu.2015.4140. Epub 2016 Jan 28. PubMed PMID: 26560177.

4)

Lefaucheur JP, Antal A, Ayache SS, Benninger DH, Brunelin J, Cogiamanian F, Cotelli M, De Ridder D, Ferrucci R, Langguth B, Marangolo P, Mylius V, Nitsche MA, Padberg F, Palm U, Poulet E, Priori A, Rossi S, Schecklmann M, Vanneste S, Ziemann U, Garcia-Larrea L, Paulus W. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Clin Neurophysiol. 2016 Oct 29;128(1):56-92. doi: 10.1016/j.clinph.2016.10.087. [Epub ahead of print] Review. PubMed PMID: 27866120.

5)

Abboud T, Schwarz C, Westphal M, Martens T. A comparison between threshold criterion and amplitude criterion in transcranial motor evoked potentials during surgery for supratentorial lesions. J Neurosurg. 2018 Sep 7:1-10. doi: 10.3171/2018.4.JNS172468. [Epub ahead of print] PubMed PMID: 30192199.

6)

Abboud T, Huckhagel T, Stork JH, Hamel W, Schwarz C, Vettorazzi E, Westphal M, Martens T. Why Does Threshold Level Change in Transcranial Motor-evoked Potentials During Surgery for Supratentorial Lesions? J Neurosurg Anesthesiol. 2016 Aug 1. [Epub ahead of print] PubMed PMID: 27482981.

7)

Abboud T, Schaper M, Dührsen L, Schwarz C, Schmidt NO, Westphal M, Martens T. A novel threshold criterion in transcranial motor evoked potentials during surgery for gliomas close to the motor pathway. J Neurosurg. 2016 Jan 22:1-8. [Epub ahead of print] PubMed PMID: 26799297.