

Perception and Pain Thresholds of tDCS and tACS

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Summary

Transcranial electric stimulation (tES) protocols strictly need to keep the safety of stimulations and to avoid the unpleasant feelings of stimulated subjects. Following that, the aim of the paper was to find out both the perception and the pain thresholds of different tES modalities. The perception thresholds and the pain thresholds at AF7 and AF8 electrodes with transcranial direct and alternating current stimulation (tDCS and tACS) were performed. Average perception and pain thresholds did not differ significantly inter-individually but intra-individually. With gradually increasing intensity the analysis of thresholds showed that 1) an average participant perceived as first 20 Hz and 40 Hz tACS, then 10 Hz tACS and cathodal tDCS and then anodal tDCS, and 2) the pain was felt first for anodal tDCS, then for 6, 10 and 20 Hz tACS, then for cathodal tDCS and finally for 40 Hz tACS. Besides that, intensity-dependent regularities in feelings of different tES modalities were found. Perception thresholds for 2 types of tDCS (anodal and cathodal) and 4 types of tACS (6-40 Hz) are arranged in sequence of gradually increased values (threshold current): anodal tDCS – cathodal tDCS – 6 – 10 – 20 – 40 Hz tACS. whereas pain thresholds are arranged with decreased threshold values.

Key words

Perception • Pain • Threshold • Transcranial electrical stimulation

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Introduction

Transcranial electrical stimulation with direct and alternating current (tDCS and tACS) are non-invasive

methods used in experiments focused on therapeutic purposes (e.g. pain treatment, neurological and psychiatric diseases, etc.) as well as cognitive effects (working memory, attention, language skills, numerical skills etc.). Since the first reports of tDCS (Lippold and Redfearn 1964, Priori *et al.* 1998, Nitsche and Paulus 2000 and 2001, Nitsche *et al.* 2003) and similarly tACS (Antal *et al.* 2008, Antal and Herrmann 2016) there are ongoing efforts of tuning-up the stimulation protocols, including thresholds of both the perception and the pain, as for clinical therapy as for research. In both, tDCS and tACS, are studies (Nitsche *et al.* 2003, Iyer *et al.* 2005, Lagopoulos and Degabriele 2008, Bikson *et al.* 2009, Dell'Osso *et al.* 2011, Brunoni *et al.* 2011, Antal *et al.* 2016) reporting also some adverse effects which are usually mild and disappear soon after stimulation. Preparation of all kinds of application protocols follows, besides desired stimulation effects, also the aim of keeping safety and avoiding unpleasant feelings caused by electric stimulation. Thus, there is a need of knowing the thresholds of the perception and pain as well as the relationship among threshold values for individual participant.

Methods

Experiments were performed with 60 healthy participants (age 18-23, average age 19) without both the history of epilepsy and the wounds on frontal skull area. Participants were exposed to stimulation set which consists from random order of anodal tDCS, cathodal tDCS, 6 Hz tACS, 10 Hz tACS, 20 Hz tACS and 40 Hz tACS. Stimuli were generated by Starstim (Neuroelectronics Ltd, Spain) with intensity from range 0.2-2.0 mA (increment 0.1 mA) via circular sponge electrodes

(diameter 5 cm) placed at AF7 and AF8 sites (10-20 system). Each stimulus lasted 10 sec (RAMP 1 sec) followed by 6 sec inter-stimuli pause. Participants were instructed to write down both perception threshold and pain threshold. The experiments were approved by the Ethics Committee of Third Faculty of Medicine, Charles University in Prague and they have been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Results

Perception

According to the participant's reporting, the average perception thresholds did not differ significantly (Table 1). The minimum threshold of perception for all 6 kinds of stimulations (anodal-tDCS, cathodal-tDCS, tACS on 6, 10, 20 and 40 Hz) was in average 0.2 mA, whereas the maximum perception thresholds ranged from

0.13 for cathodal tDCS and 40 Hz tACS, to 0.17 mA for anodal tDCS and 20 Hz tACS.

Although the average thresholds for 6 different stimulations did not differ significantly, the regularities in intra-individual relationships of perception thresholds of different stimulation modalities were found (Fig. 1). Based on intra-individual comparison of thresholds for different stimulations, the perception threshold for anodal tDCS and 6 Hz tACS were usually the same and higher than thresholds for cathodal tDCS and for 10 Hz tDCS by 15 %. Thresholds for cathodal tDCS and for 10 Hz tDCS were higher than thresholds for 20 Hz tACS by 26 %. Threshold for 20 Hz was usually higher than threshold for 40 Hz tACS by 5 %.

Describing perception thresholds of tES with gradually increasing intensity, we can say that an average participant sense first 40 Hz tACS, then 20 Hz tACS, then 10 Hz tACS together with cathodal tDCS and then the last (with highest threshold) anodal tDCS together with 6 Hz tACS.

Table 1: Average perception thresholds

Stimulation	Average Threshold	STD	Minimum	Maximum	Thresholds < 2 mA
Anodal tDCS	0.60	0.34	0.20	1.70	95 %
Cathodal tDCS	0.54	0.26	0.20	1.30	97 %
6 Hz tACS	0.62	0.37	0.20	1.60	98 %
10 Hz tACS	0.57	0.30	0.20	1.60	98 %
20 Hz tACS	0.53	0.34	0.20	1.70	98 %
40 Hz tACS	0.56	0.29	0.20	1.30	97 %

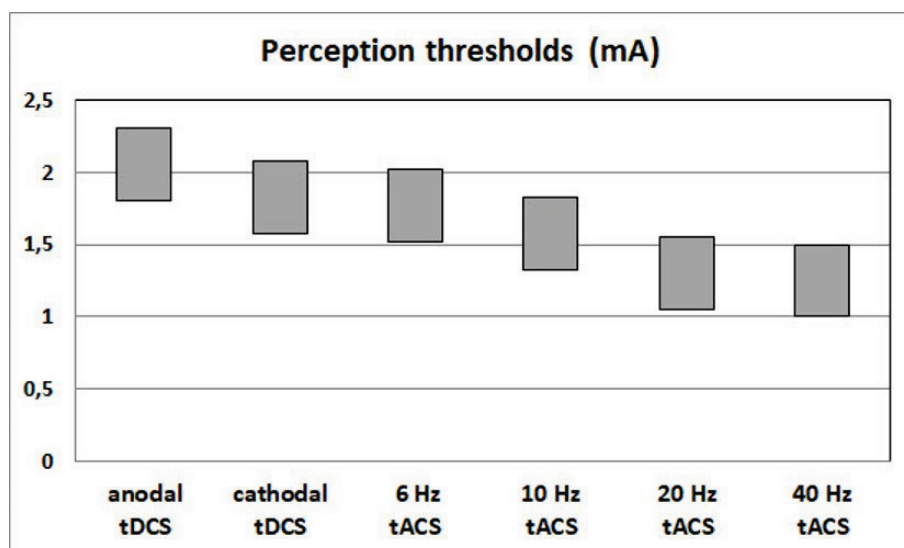


Fig. 1. Relative relationships among perception thresholds of different transcranial electrical stimulation modalities.

Pain

Average pain thresholds for stimuli we applied did not differ significantly (Table 2). For anodal tDCS was the average pain threshold 1.14 mA, for cathodal tDCS 1.34 mA, for 6 Hz, 10 Hz and 20 Hz tACS threshold was 1.39 whereas for 40 Hz tACS the average pain threshold was 1.52 mA. The minimum pain threshold in average was 0.30 mA for anodal tDCS and 0.40 for other 5 kinds of stimulations. For each stimulation modality, the pain threshold was higher than 2.00 mA for half of participants (Table 2).

Analysis of intra-individual relationships among the pain threshold of different stimulations showed that the situation is the opposite of that for perception

thresholds (Fig. 2). Individual pain threshold for anodal tDCS was usually lower than pain threshold for cathodal tDCS by 23 %. Threshold for 6 Hz tACS was higher than threshold for cathodal tDCS by 11 %. Threshold for 10 Hz tACS was higher than threshold for 6 Hz tACS by 9 %. Threshold for 20 Hz tACS was higher than threshold for 10 Hz tACS by 9 %. Threshold for 40 Hz tACS was higher than threshold for 20 Hz tACS by 17 %.

Pain thresholds (for an average participant) of different tES modalities were found in following sequence: pain was first felt for anodal tDCS, then for cathodal tDCS, then for 6 Hz, then for 10 Hz, then for 20 Hz tACS and then for 40 Hz tACS.

Table 2. Average pain thresholds

Stimulation	Average Threshold	STD	Minimum	Maximum	Thresholds < 2 mA
Anodal tDCS	1.14	0.45	0.30	2.00	47 %
Cathodal tDCS	1.34	0.50	0.40	2.00	57 %
6 Hz tACS	1.39	0.51	0.40	2.00	47 %
10 Hz tACS	1.40	0.45	0.40	2.00	52 %
20 Hz tACS	1.39	0.48	0.40	2.00	57 %
40 Hz tACS	1.52	0.46	0.40	2.00	55 %

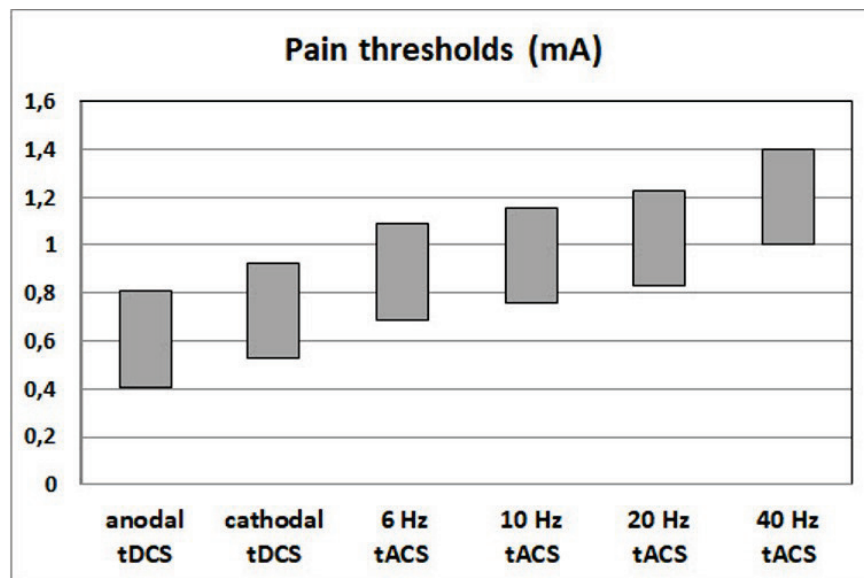


Fig. 2. Relative relationships among pain thresholds of different transcranial electrical stimulation modalities.

Discussion

Our experimental results showed that the perception and the pain threshold for anodal tDCS,

cathodal tDCS and tACS on 4 different frequencies (6 Hz, 10 Hz, 20 Hz and 40 Hz) did not differ in average significantly. On the other hand, they differed inter-individually. This phenomenon can be plausible

explained by different individual sensitivity to transcranial stimulation as described elsewhere. Most important outcome of our results is general relationship among intra-individual thresholds for different types of stimulations.

Different perception and discomfort (sometimes referred as a pain) during transcutaneous electrical stimulation could be explained by the excitation of peripheral nerves; electrochemical processes (Minhas *et al.* 2011), facilitated by sweat, skin wounds etc. (Nitsche *et al.* 2003, Datta *et al.* 2008). Our finding of adverse effects occurrence corresponds with some other studies (Brunoni *et al.* 2011, Minhas *et al.* 2011) reporting about tingling, headache, discomfort and burning perception but should be pointed out our study did not evaluate after effects of electrical stimulation unlike some other studies (Nitsche *et al.* 2008, Palm *et al.* 2008, Palm *et al.* 2008, Fertoni *et al.* 2015). Like some studies (Turi *et al.* 2013, Ambrus *et al.* 2010, Raco *et al.* 2014) our healthy subjects felt often cutaneous perceptions during tACS; we did not record any dizziness, probably because of very short stimulation time. On the other hand, some studies (Chaieb *et al.* 2014, Naro *et al.* 2016) stimulating frontally with 2 mA for 5 min tACS at 10, 50, 300, 5000 Hz found no adverse events at all. Congruently with our findings, all reported adverse events of tACS have been transient rather than persistent (Raco *et al.* 2014, Naro *et al.* 2016). Summarizing, whereas in average the perception and pain thresholds of tDCS and tACS at 6, 10, 20 and 40 Hz

seems to be equal, there are intra-individual regularities among thresholds for 6 different stimulation modalities.

As regarding sensitivity to different transcranial electrical stimulation types, we report here, the average participant sensed at lowest intensity 20 and 40 Hz tACS then cathodal tDCS, and then on 20 % lower intensities than anodal tDCS or 6 Hz tACS. Participants usually started to sense 20 Hz or 40 Hz tACS at intensities by 20-28 % lower than they sensed 10 Hz tACS. Average participant started to perceive 6 Hz tACS at intensity 22 % higher than he/she started to perceive 10 Hz tACS and 50 % higher than he/she started to perceive 20 Hz tACS.

From intra-individual relationships point of view, the relationships between pain thresholds values for different types of stimulation are the opposite of those for perception thresholds values (Table 4). Individual pain threshold for anodal tDCS was usually lower than pain threshold for cathodal tDCS by 28 % and lower than threshold for 6 Hz tACS by 18 %. Individual pain thresholds for 6 Hz, 10 Hz and 20 Hz did not differ significantly. Individual threshold for 40 Hz was usually higher by 14-20 % than for three other tACS stimulations.

Conflict of Interest

There is no conflict of interest.

Acknowledgements

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