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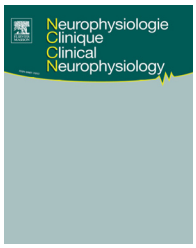

COMPREHENSIVE REVIEW/REVUE GÉNÉRALE

A comprehensive database of published tDCS clinical trials (2005—2016)

Une base de données complète des études cliniques utilisant la tDCS (2005—2016)

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Treatment

Summary Transcranial direct current stimulation (tDCS) is a technique of noninvasive cortical stimulation allowing significant modification of brain functions. Clinical application of this technique was reported for the first time in March 2005. This paper presents a detailed list of the 340 articles (excluding single case reports) which have assessed the clinical effect of tDCS in patients, at least when delivered to cortical targets. The reviewed conditions were: pain syndromes, Parkinson's disease, dystonia, cerebral palsy, post-stroke limb motor impairment, post-stroke neglect, post-stroke dysphagia, post-stroke aphasia, primary progressive aphasia, multiple sclerosis, epilepsy, consciousness disorders, Alzheimer's disease and other types of dementia, tinnitus, depression, auditory hallucinations and negative symptoms of schizophrenia, addiction and craving, autism, and attention disorders. The following data were collected: (i) clinical condition; (ii) study design; (iii) sample size; (iv) anode and cathode locations; (v) stimulation intensity and electrode area; (vi) number and duration of sessions; (vii) clinical outcome measures and results. This article does not include any meta-analysis and aims simply at providing a comprehensive overview of the raw data reported in this field to date, as an aid to researchers.

MOTS CLÉS
Cortex ;
Neurologie ;

Résumé La stimulation transcrânienne à courant continu (*transcranial direct current stimulation* [tDCS]) est une technique de stimulation corticale non invasive capable de modifier de manière significative les fonctions cérébrales. L'application clinique de cette technique a été rapportée pour la première fois en mars 2005. Ce document présente une liste détaillée des quelques 340 articles (à l'exclusion des rapports de cas individuels) qui ont évalué l'effet

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clinique de la tDCS chez des patients, au moins lorsque la cible était corticale. Les situations cliniques suivantes ont été examinées : les syndromes douloureux, la maladie de Parkinson, les dystonies, la paralysie cérébrale, les troubles moteurs des membres, la négligence, et les troubles de déglutition ou de la parole suivant un accident vasculaire cérébral, l'aphasie primaire progressive, la sclérose en plaques, l'épilepsie, les troubles de la conscience, la maladie d'Alzheimer et autres types de démence, les acouphènes, la dépression, les hallucinations auditives et les symptômes négatifs de la schizophrénie, la toxicomanie ou les conduites addictives, l'autisme et les troubles de l'attention. Les données suivantes ont été recueillies : (i) le contexte clinique ; (ii) la conception du protocole d'étude ; (iii) la taille de l'échantillon et du nombre de patients stimulés ; (iv) la localisation des électrodes de stimulation, anodes et cathodes ; (v) l'intensité de la stimulation et la taille des électrodes ; (vi) le nombre et la durée des séances de stimulation ; (vii) les paramètres d'évaluation utilisés et les effets cliniques obtenus. Cet article ne comprend pas d'analyse ou de méta-analyse des résultats publiés, mais vise simplement à aider les chercheurs pour leur donner une vue d'ensemble et la plus exhaustive possible des données brutes de la littérature rapportées dans ce domaine à ce jour.

Transcranial direct current stimulation (tDCS) has received renewed clinical interest since the end of the 1990s [284,313] as a technique of noninvasive cortical stimulation able to significantly modify brain functions. Low-intensity current is delivered transcranially (1—2 mA) using relatively large electrodes generally placed on the scalp according to a bipolar montage (one anode and one cathode). Other montages can be used, such as Laplacian ones (one cathode or anode surrounded by four equally distant electrodes with reversed polarity) [96]. The value of the electric field induced by tDCS into the brain varies between studies, ranging from 0.3 to 1.6 V/m, according to head models or in vivo measurements and influenced by individual anatomical and montage characteristics [30,97,262—264,291,292,299—301]. There is controversy regarding whether these values of electric field and the corresponding peak current density (in mA/m^2) are sufficient to modulate neuronal network activity. However, there are convincing experimental data to suggest that neurons are sensitive to such weak electric fields, resulting in action potential firing changes, synaptic plasticity triggering, or neurogenesis promotion [6,49,135,199,305,329], not to mention subtle effects on glial cells [154,182,265,330]. On the other hand, it is certain that the effect of tDCS cannot be considered as similar to that of other methods of cortical stimulation, such as repetitive transcranial magnetic stimulation (rTMS) or implanted epidural cortical stimulation, which are able to induce sufficient current intensity to directly elicit action potentials at the membrane level of cortical axons [218—220]. Conversely, tDCS is able to modulate the resting membrane potential of cortical axons in the direction of depolarisation or hyperpolarisation, according to the polarity of the electrodes (anode vs. cathode) and the orientation of the axons in the induced electric field.

Whatever the underlying mechanisms of action, the first tDCS studies largely demonstrated that this technique was able to significantly modulate cortical excitability, possibly via N-methyl-D-aspartate (NMDA) receptor-dependent glutamatergic neuroplasticity [228,285]. The first tDCS studies were 'physiological' studies conducted in healthy subjects, and it took several years for 'clinical' studies considering the therapeutic potential of this technique to be published. In fact, the first clinical tDCS study was published on March 2005 [178]. In this sham-controlled crossover study, the authors showed in 6 patients with chronic motor stroke that a single session of tDCS delivered at 1 mA with the anode placed over the motor cortex of the lesioned hemisphere and the cathode over the opposite supraorbital region could significantly improve motor hand function after active stimulation compared to sham. Following this pioneering study, about 340 other papers (excluding single case reports) have been published, reporting the assessment of clinical effects of tDCS in patients with various types of diseases. The present review presents a comprehensive and detailed list of these papers. The reviewed conditions were pain syndromes (Table 1), Parkinson's disease (Table 2), dystonia and cerebral palsy (Table 3), post-stroke limb motor impairment (Table 4), post-stroke neglect (Table 5), post-stroke dysphagia (Table 6), post-stroke aphasia (Table 7), primary progressive aphasia (Table 8), multiple sclerosis (Table 9), epilepsy (Table 10), consciousness disorders (Table 11), Alzheimer's disease and dementia (Table 12), tinnitus (Table 13), depression (Table 14), auditory hallucinations and negative symptoms of schizophrenia (Table 15), addiction and craving (Table 16), autism (Table 17), and attention disorders (Table 18).

The following data were collected from all the published studies and reported in these Tables:

- clinical condition;
- study design (crossover, parallel-arm, or open-label design);
- sample size (detailing the number of patients in each experimental group in case of parallel-arm study);
- anode and cathode locations;
- stimulation intensity (in mA) and electrode area (in cm^2), allowing calculation of current density;
- total number of sessions and duration of each session (in min);
- clinical outcome measures and main results, comparing active to sham condition in controlled studies.