

DOI: 10.21767/2471-9854.100030

# Transcranial Direct Current Stimulation as a Potential Tool for Cognitive Rehabilitation on Alzheimer's Disease

Sergio Machado<sup>1-3\*</sup><sup>1</sup>Laboratory of Panic and Respiration, Institute of Psychiatry, Federal University of Rio de Janeiro (IPUB/UFRJ), Rio de Janeiro, Brazil<sup>2</sup>Physical Activity Neuroscience Laboratory, Physical Activity Sciences, Postgraduate Program-Salgado de Oliveira University (UNIVERSO), Niterói, Brazil<sup>3</sup>School of Psychology and Administration, Santa Ursula University, Rio de Janeiro, Brazil**\*Corresponding author:** Sergio Machado, PhD, Laboratory of Panic and Respiration, Institute of Psychiatry, Federal University of Rio de Janeiro (IPUB/UFRJ), Rio de Janeiro, Brazil, Tel: +2121384964; E-mail: secm80@gmail.com**Received date:** Sep 26, 2016; **Accepted date:** Sep 27, 2016; **Published date:** Sep 30, 2016**Copyright:** © 2016 Machado S. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.**Citation:** Machado S. Transcranial Direct Current Stimulation as A Potential Tool for Cognitive Rehabilitation on Alzheimer's Disease. Clin Psychiatry. 2016, 2:3.

## Alzheimer's Disease

In recent years, non-invasive brain stimulation techniques have rapidly become an important approach as potential therapeutic tools to improve the outcome of cognitive rehabilitation of patients affected by neurodegenerative or neuropsychiatric disorders, such as Alzheimer's disease (AD) [1]. One of the new techniques most commonly used is the transcranial direct current stimulation (tDCS) [2].

tDCS acts modulating the excitability of a targeted brain area by altering neuronal membrane potentials, consequently modifying the brain circuitries related to the targeted areas [3,4]. tDCS has been recently considered as a potential non-invasive tool for neuromodulation due to its ability to promote cortical changes, reflecting on changes in cognitive functions [3-7]. tDCS applies a small electrical current across a particular area of the brain. This is usually done non-invasively via two small electrodes placed on the scalp [4,6,8]. tDCS could be used to treat patients who had suffered some type of neurodegeneration, such as Alzheimer's disease [9]. Thus, tDCS has gained public attention due its reported capability to improve cognitive abilities for these patients [10,11].

In previous studies, tDCS was combined to transcranial magnetic stimulation (TMS) to investigate changes in cortical excitability on the primary motor cortex (M1) [5,12]. The mechanisms are still unclear, but presumably, the current induces changes in the resting membrane potential of neurons. These changes seems to be specific to anodal polarity, cathodal depolarization and hyperpolarization of resting membrane potential [5,6].

Some studies have been conducted in order to understand the physiological mechanism and it seems that posterior neuroplastic effects are N-methyl-D-aspartate (NMDA) receptor dependent [13]. In fact, it was shown that the effects can be modified, extended or even reversed by drugs that act on the central nervous system (CNS) [14]. It is noteworthy that

NMDA receptors have been reported as having a critical role in synaptic plasticity, long-term potentiation (LTP) that affect learning and memory. However, these studies are motor domain and are not yet clear to what extent these results are transferable to other areas of the brain. However, during the last decade a growing body of experimental work has extensively explored the effects of tDCS in brain areas than M1. These studies demonstrated significant effects from tDCS on cognitive processes assessed by a variety of cognitive tasks not only in healthy subjects but also in AD. As a result, there has been a growing interest in using tDCS as a safe technique and relatively low cost to neuropsychological rehabilitation as shown by recent studies [15,16].

In the study Khedr, et al. [16], 34 patients (mean age 69.7 years, mean MMSE=18.1, range=12-23) were treated and followed for two months. Ten sessions of anodal tDCS or cathodal tDCS on the left DLPFC, vs sham-ETCC, were given randomly among the study subjects. The global cognitive functioning (MMSE) and intelligence (WAIS-III) were assessed at four time points (baseline, end of 10 sessions, 1 and 2 months after the end). Furthermore, the cortical motor excitability and the event-related potential (P300) were assessed at baseline and after the last tDCS session. The authors found that 10 sessions of either anodal tDCS or cathodal tDCS on the left DLPFC improved the MMSE compared with sham, with an increase in 1 and 2 months of follow-up. In addition, cathodal tDCS showed low positive effects on WAIS-III.

Suemoto, et al. [17] investigated the effectiveness of anodal tDCS in 40 AD patients and moderate cognitive impairment (MMSE 10-20) on apathy and overall cognitive functioning. Six sessions of anodal tDCS on the left DLPFC vs sham-tDCS were administered in a randomized cross-over design. Patients were evaluated at baseline, after the first and second weeks of stimulation, and 1 week after the end of the intervention. The authors found that anodal tDCS had no effect on apathy or global cognitive performance, or the sub-item ADAS-Cog. This

study shows that applying anodal tDCS on the left DLPFC in patients with a relatively advanced state of deterioration is not able to improve their cognitive deficits and apathy.

In a study combining tDCS with cognitive training, Cotelli, et al. [18] evaluated the first time the impact of tDCS combined with individualized training of associative memory on specific tests of learning and associative memory, attention, language and perceptual-motor. Ten consecutive sessions of anodal tDCS on the left DLPFC during memory training or anodal tDCS on the left DLPFC during motor training or sham-tDCS during memory training were administered randomly among 36 patients, divided into 12 per group [19]. Neuropsychological evaluation was performed in 4 different times (before, 2 weeks, 3 and 6 months later). An improvement, only in stimuli selectively trained and induced by memory training was observed, regardless of location for both anodal tDCS and sham-tDCS. In other words, anodal tDCS on the left DLPFC did not generate an additional effect on memory training. Moreover, the improvement was to specific stimuli to the task and does not generalized to other domains.

The use of tDCS in the field of neurocognitive rehabilitation of AD patients seems to be promising. However, this new approach should be tested in large clinical trials to determine if they offer significant clinical effects.

## References

- Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, et al. (2015) Non-invasive electrical and magnetic stimulation of the brain, spinal cord, root and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. *Clin Neurophysiol* 126: 1071-1107.
- Peterchev AV, Wagner TA, Miranda PC, Nitsche MA, Paulus W, et al. (2012) Fundamentals of transcranial electric and magnetic stimulation dose: definition, selection, and reporting practices. *Brain Stimul* 5: 435-453.
- Levasseur-Moreau J, Brunelin J, Fecteau S (2013) Non-invasive brain stimulation can induce paradoxical facilitation. Are these neuro enhancements transferable and meaningful to security services? *Front Hum Neurosci* 7: 449.
- Nitsche MA, Paulus W (2011) Transcranial direct current stimulation: update 2011. *Restor Neurol Neurosci* 29: 463-492.
- Nitsche MA, Paulus W (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol* 3: 633-639.
- Nitsche MA, Fricke K, Henschke U, Schlitterlau A, Liebetanz D, et al. (2003) Pharmacological modulation of cortical excitability shifts induced by transcranial direct current stimulation in humans. *J Physiol* 553: 293-301.
- Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, et al. (2003) Modulation of cortical excitability by weak direct current stimulation-technical, safety and functional aspects. *Suppl Clin Neurophysiol* 56: 255-276.
- Guleyupoglu B, Schestatsky P, Edwards D, Fregni F, Bikson M (2013) Classification of methods in transcranial electrical stimulation (tES) and evolving strategy from historical approaches to contemporary innovations. *J Neurosci Methods* 219: 297-311.
- Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N, et al. (2008) Transcranial direct current stimulation: State of the art 2008. *Brain Stimul* 1: 206-223.
- Kuo MF, Paulus W, Nitsche MA (2014) Therapeutic effects of non-invasive brain stimulation with direct currents (tDCS) in neuropsychiatric diseases. *Neuroimage* 3: 948-960.
- Miniussi C, Cappa SF, Cohen LG, Floel A, Fregni F, et al. (2008) Efficacy of repetitive transcranial magnetic stimulation/transcranial direct current stimulation in cognitive neurorehabilitation. *Brain Stimul* 1: 326-36.
- Priori A, Berardelli A, Rona S, Accornero N, Manfredi M (1998) Polarization of the human motor cortex through the scalp. *Neuroreport* 9: 2257-2260.
- Nitsche MA, Jaussi W, Liebetanz D, Lang N, Tergau F, et al. (2004). Consolidation of human motor cortical neuroplasticity by D-cycloserine. *Neuropsychopharmacology* 29: 1573-1578.
- Stagg CJ, Nitsche MA (2011) Physiological basis of transcranial direct current stimulation. *Neuroscientist* 17: 37-53.
- Elder GJ, Taylor JP (2014) Transcranial magnetic stimulation and transcranial direct current stimulation: treatments for cognitive and neuropsychiatric symptoms in the neurodegenerative dementias? *Alzheimers Res Ther* 6: 74.
- Khedr EM, Gamal NF, El El-Fetoh NA, Khalifa H, Ahmed EM, et al. (2014) A double-blind randomized clinical Trial on the efficacy of cortical direct current stimulation for the treatment of Alzheimer's disease. *Front Aging Neurosci* 6: 275.
- Suemoto CK, Apolinario D, Nakamura-Palacios EM, Lopes L, Paraizo Leite RE, et al. (2014) Effects of a non-focal plasticity protocol on apathy in moderate Alzheimer's Disease: a randomized, double-blind, sham-controlled trial. *Brain Stimul* 7: 308-313.
- Cotelli M, Manenti R, Brambilla M, Petesi M, Rosini S, et al. (2014) Anodal tDCS during face-name associations memory training in Alzheimer's patients. *Front. Aging Neurosci* 6: 38.
- Flöel A (2014) tDCS-enhanced motor and cognitive function in neurological diseases. *Neuroimage* 3: 934-947.