Novel cognitive ageing rehabilitation with transcranial direct current stimulation

Abstract
Impairment of cognitive function and mobility are commonly found in ageing. The transcranial Direct Current Stimulation (tDCS), has increasingly purposive treatments for cognitive rehabilitation. It is inexpensive, easy to administer after well trained, portable, and home used design considered as the most cost-effective and good compliance therapy. The local effect of calcium-dependent synaptic plasticity of glutamatergic neurons, locally reduce gamma-aminobutyric acid (GABA) neurotransmission, remote effect of the interference with functional connectivity, synchronization, and oscillatory activities in various cortical and subcortical networks, involve in transmembrane ion conductance, membrane structure, cytoskeleton, or axonal transport, degradation of the beta-amyloid and other pathological proteins. In addition, tDCS can enhance axonal regeneration and neurite outgrowth and therefore hypothetically improve functional neuron recovery, produce brain-derived neurotrophic factor (BDNF) that increases synaptogenesis and neurogenesis in the long term, increases glucose metabolism and also be useful to limit the vicious circle of auto-destructive events due to the increased Ca²⁺ influx resulting from excessive membrane depolarization or intra-axonal Na⁺ overload in the context of ischemia or energetic resource failure. The review of several studies of tDCS for cognitive rehabilitation in normal elderly with mild cognitive impairment (MCI) and Alzheimer’s disease (AD) are included. More evidences are upcoming in cognitive rehabilitation with tDCS. In conclusion, tDCS is cost-effective and safety for cognitive ageing rehabilitation.

Keywords: transcranial direct current stimulation (tDCS), ageing, cognitive rehabilitation

How tDCS works on cognitive function
The effect of tDCS on neurons are as the followings; (1) A subthreshold shift of resting membrane potentials towards depolarization or hyperpolarization at the synaptic level, depending on current flow direction relative to axonal orientation. (2) Reduce gamma-aminobutyric acid (GABA) neurotransmission, regardless of stimulation polarity and impact on glutamatergic plasticity. (3) The interference with functional connectivity, synchronization, and oscillatory activities in various cortical and subcortical networks. (4) The modulation of resting membrane potential more generally along the whole axons resulting in non-synaptic effects which made long-
lasting after-effects. (5) The changes of conformation and function of various axonal molecules, involved in transmembrane ion conductance, membrane structure, cytoskeleton, or axonal transport. (6) the changes in non-neuronal tissues in the brain, including endothelial cells, lymphocytes, or glial cells, influencing on the inflammatory response. (7) The beta-amyloid and other pathological proteins can be modified to slower the process of AD. (8) The enhancement of axonal regeneration and neurite outgrowth will improve functional recovery. (9) The production of brain-derived neurotrophic factor (BDNF) that increases synaptogenesis and neurogenesis in long term effects. (10) The increasing of cerebral glucose metabolism induced by increasing neuronal activity. (11) Limit the vicious circle of autodestructive events due to the increased Ca^{2+} influx resulting from excessive membrane depolarization or intra-axonal Na^{+} overload in the context of ischemia or energetic resource failure.6–22

Evidences of tDCS for cognitive aging rehabilitation

tDCS is safe to use and has shown potential for enhancing cognition in several studies as the followings; In 2008, Ferrucci et al. studied the cognitive effect of tDCS over the temporoparietal areas in 10 patients with AD with anodal tDCS, cathodal tDCS and sham tDCS in 3 sessions for 30 minutes. This study revealed that anodal tDCS over the temporoparietal areas can specifically affect the recognition memory performance in AD.23

In 2012, Boggio et al.24 studied cognitive functions in 15 AD patients. 2 mA tDCS for 30 minutes, 5 consecutive days. The tDCS current was delivered bilaterally through two scalp anodal electrodes placed over the temporal regions and a reference electrode over the right deltoid muscle. This study revealed that bilateral anodal tDCS over the bilateral temporal regions improve visual recognition memory for at least 4 weeks after therapy.24

In 2013, Park et al. randomized 40 elderly to receive sham or active tDCS during computer-assisted cognitive training 10 sessions (5 days/per week for 2 weeks) for 30 min a day. The active 2 mA tDCS current and sham tDCS using two stimulators or two anodes were placed over F3 and F4 (bilateral prefrontal cortex) and two cathodes were placed on the non-dominant arm for 30 min a day. There are significant improvements in digit span forward tests in both groups. The effect on verbal working memory accuracy improvement lasted for 28 days after tDCS. This study revealed that bilateral anodal tDCS over bilateral prefrontal cortex enhance cognitive function in healthy elderly and lasted over the stimulation period.25

In 2013, Meinerz et al.26 used a task-based fMRI study with tDCS examined the effects of tDCS on language function in 20 healthy elderly (age 60–76) and healthy adults (aged 19–31). Active tDCS with 1 mA for 17 min followed by a semantic word generation task. The anode was placed over the left inferior frontal gyrus (IFG) (10–20 EEG system corresponding to the intersection of T3-F3 and F7-C3 and the midpoint between F7-F3) and the cathode on the contralateral supraorbital region. During Sham tDCS, there are lower semantic word-generation tasks ability in healthy elderly associated with enhanced task-related activity in bilateral IFG activation. The active tDCS in elderly produced significantly higher performance compared to the young adults, and significantly reduced task-related hyperactivity in the bilateral prefrontal cortex (PFC). Increased connectivity was also observed between the left IFG and the language related cortical areas during the resting state in active tDCS. This study revealed that tDCS enhance cognitive function in elderly with direct impact on underlying neural response patterns.25

In 2014, Hartly et al.27 studied the effects of tDCS on error awareness in 96 healthy elderly, divided into 4 groups with 24 healthy elderly per group. The study tested the influence of current polarity and electrode location (anode over F3 or F4, and cathode over Cz), on error monitoring. During 1 mA tDCS application, the elderly performed a computerized test of error awareness (5 blocks, each 7.5 min and 1-min resting time within each block), a Go/No-go response inhibition task that required constant monitoring to detect errors. The group with anode stimulation over the right DLPFC (F4) was the only group to experience improved error detection during the task. This study revealed that the right DLPFC tDCS have a larger role on error awareness.27

In 2015, Meinerz et al.28 performed a double-blind, cross-over, sham-controlled study. Anodal-tDCS 1 mA, for 20 minutes stimulated at the left inferior frontal cortex during task-related and resting-state functional magnetic resonance imaging (fMRI) to assess its impact on cognition and brain functions in MCI. During sham stimulation, patients produced fewer correct semantic-word-retrieval responses than matched healthy controls, which was correlated with hyperactivity in bilateral prefrontal regions. Anodal-tDCS significantly improved performance to the level of controls, reduced task-related prefrontal hyperactivity and resulted in “normalization” of abnormal network configuration during resting-state fMRI. This study revealed that anodal-tDCS exerts beneficial effects on cognition and brain functions in MCI and repeated stimulation sessions can produce the sustained improvement of cognition.28

In 2016, Menenti et al.29 studied in 20 patients with PD, 10 patients assigned to anodal 2-mA tDCS for 25 minutes during physical therapy and 10 patients to sham tDCS for 25 minutes during physical therapy. Both groups are done for 2 weeks. The Parkinson’s Disease Cognitive Rating Scale and verbal fluency test performances increased only in the anodal tDCS with a stable effect at 3-month follow up. This study revealed that anodal tDCS is a novel therapy for PD patients with mild cognitive impairment.29

In 2016, Stephens et al.30 randomized 90 healthy older adults to receive sham, 1 mA, or 2 mA of tDCS stimulation for 15 min during five sessions of working memory training. The anode electrode was placed over the right DLPFC (F4), and the cathode was placed over the contralateral cheek. All participants showed improvements in the trained verbal and visual working memory tasks. This study revealed that anodal tDCS can increase far transfer benefits (processing speed, cognitive flexibility, arithmetic) at 1 month after anodal tDCS at the right DLPFC (F4).30

In 2016, Yun et al.31 studied the effects of repeated tDCS on glucose metabolism and cognitive performance in 16 MCI. The 2mA anodal tDCS over left DLPFC (F3) and cathodal tDCS over the right DLPFC (F4) with bilateral frontal stimulation were applied for 30 min, 3 times per week for 3 weeks. Using Positron emission tomography (PET), revealed a significant increase in cerebral metabolic activity in the medial prefrontal cortex, precuneus, midtemporal regions, and the anterior cingulate cortices in the anodal tDCS group. Multifactorial Memory Questionnaire (MMQ) was performed to assess the participant’s subjective memory functioning. MMQ scores and glucose metabolism were significantly improved only in the anodal tDCS group. This study revealed that active tDCS can change the
Novel cognitive ageing rehabilitation with transcranial direct current stimulation

Safety of tDCS

There is no report evidences of brain damage, seizure or syncope when treatment with tDCS. The only side effects are local skin and scalp effects as irritation, itching, redness.

Conclusion

tDCS is cost-effective and safety for cognitive ageing rehabilitation. The evidences of tDCS appeared less than 20 years, it is emerging novel non-invasive brain stimulation in both research and clinical settings. As a safe, painless, inexpensive treatment for modulating the excitability of brain tissue, tDCS has strong potential for application in cognitive ageing rehabilitation. The succeed of tDCS treatment depend on the knowledge and experiences of the physicians to select the patients, put the correct area of 10-20 EEG montage and select the protocols.

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

References


