ANODAL HIGH DEFINITION TRANSCRANIAL DIRECT CURRENT STIMULATION FOR NEUROREHABILITATION OF CHRONIC STRESS AND DEPRESSION

A THESIS

submitted by

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(Enrollment No. D15050)

Under the supervision of

Dr. SHUBHAJIT ROY CHOWDHURY

for the partial fulfilment for the award of the degree

of

DOCTOR OF PHILOSOPHY

SCHOOL OF COMPUTING AND ELECTRICAL ENGINEERING

INDIAN INSTITUTE OF TECHNOLOGY MANDI

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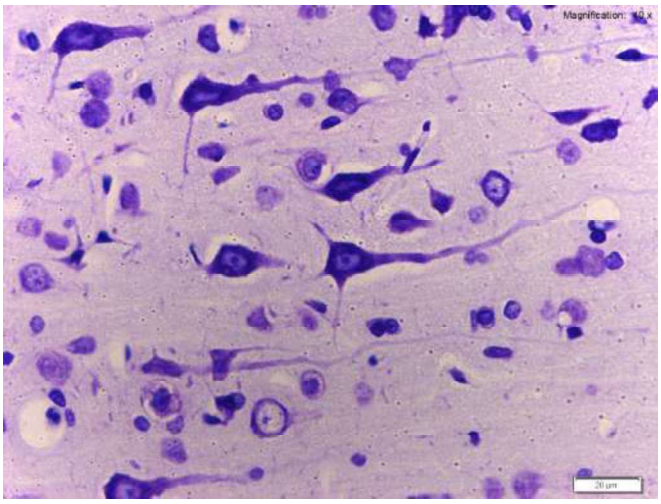
There is nothing as sublime and pure as knowledge!

Shrimadbhagavadgita

Dedication

The work is a gratitude to surviving patients from neurological and psychiatric disorders worldwide. I would really hope that this work could contribute to the field of “Neuroscience and Biomedical Engineering”



The thesis is dedicated to my respected parents Mr. M. R. Sharma (Father), Mrs. Kamla Sharma (Mother), as their blessing made the journey a lot easier. I would also dedicate this to my sister Mrs. Priyanka Sharma and Mr. Anuroop Sharma (Brother-in–law) and my two little nieces Smita Sharma and Aanya Sharma and my uncle Mr. C. L. Sharma, for their unconditional love and moral strength. I would also dedicate this to my respected guru Shri Rudra Nand Maharaj Swami Sugrivanandji for his continuous blessing that helped me to move forward to achieve my goal of life.

Declaration by the Research Scholar

I hereby declare that the entire work embodied in this thesis is the result of investigations carried out by me in the ***School of Computing and Electrical Engineering***, Indian Institute of Technology Mandi, under the supervision of ***Dr. Shubhajit Roy Chowdhury***, and that it has not been submitted elsewhere for any degree or diploma. In keeping with the general practice, due acknowledgments have been made wherever the work described is based on finding of other investigators.

Place : IIT Mandi, Himachal Pradesh.
Date: 21-08-2021

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Declaration by the Research Advisor

I hereby certify that the entire work in this Thesis has been carried out by ***Gaurav Sharma***, under my supervision in the ***School of Computing and Electrical Engineering (SCEE)***, Indian Institute of Technology Mandi, and that no part of it has been submitted elsewhere for any Degree or Diploma.

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THESIS CERTIFICATE

This is to certify that the Thesis titled *"ANODAL HIGH DEFINITION TRANSCRANIAL DIRECT CURRENT STIMULATION FOR NEUROREHABILITATION OF CHRONIC STRESS AND DEPRESSION"*, submitted by ***Gaurav Sharma***, to the ***School of Computing and Electrical Engineering (SCEE)***, Indian Institute of Technology, Mandi, for the award of the degree of ***Doctor of Philosophy***, under Visvesvaraya scheme for Ministry of Electronics and Information Technology (MeitY) is a bonafide record of the research work done by him with my supervision. The contents of this Thesis, in full or in parts, have not been submitted to any other institute or university for the award of any degree or diploma.

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CERTIFICATE

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दिनांक: 11/12/2020

Certificate

This to certify that study proposal entitled, **'Validate the fabricated electrodes by investigate physiological effects before and after high definition transcranial direct current stimulation (HD-tDCS) dose'** has approved by the Institutional Animal Ethics Committee (IAEC) in the meeting held on 13 December, 2019 Vide Approval No. IAEC/IHBTP-10/Dec 2019.

(Yogendra Padwad)
Member Secretary, IAEC
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Gaurav Sharma (IIT Mandi)

Abstract

Neurological and psychiatric disorders are recognized as the leading cause of disability-adjusted life-years (DALYs) and the second leading cause of deaths. Neurodegeneration conditions or cognitive impairments are one of the serious problems related to the disturbances in the lifestyle of surviving patients and surrounding caregivers. Generally, stress and depression are associated with the neurodegeneration condition, which also leads to cognitive impairment by a decline in the cognitive function skills, including loss of memory, trouble in thinking, learning new things, state of confusion and many more. In recent years, non-invasive brain stimulation (NIBS) techniques through transcranial direct current stimulation (tDCS) are a promising and effective tool for neurorehabilitation, as confirmed by the evidence related to the recovery of the surviving patients from neurological disorders. Such stimulation techniques are found to enhance the cognitive functionality skills by modulating the neuronal activity.

In this thesis work, simulation based study has been used, to find out the best multi-electrode anodal high definition transcranial direct current stimulation (HD-tDCS) configuration, and the appropriate amount of weak direct current intensity in terms of enhancement in focality of the targeted surface area. Further, a small sized high definition dual-purpose spiking electrode has been fabricated for sensing EEG signal and stimulating using HD-tDCS. The main benefit of these sensing and stimulating fabricated electrodes is to record EEG signals before and after injecting the weak amount of direct current on targeted locations of the brain with the same fabricated electrodes. Two different types of dual-purpose electrodes have been fabricated namely Au/AgCl and Pt/AgCl. The I-V characteristics of both sensing electrodes were providing a good response. Moreover, I-V characteristics in the case of Au/AgCl show a better response than Pt/AgCl. Further, an experimental trial has been carried out to validate the fabricated sensing electrodes for recording EEG signal after required impedance matching, which is less than 50 kΩ*. The analysis involving current density studies confirms that the electric field provided by the fabricated electrodes can penetrate deep into the cerebral cortex region. These fabricated electrodes can also play a significant role in maintaining high focality of HD-tDCS of the brain.*

A preclinical validation study of the research work has been carried out after develop-

ing chronic stress and depression-like behaviour rat model over a period of 14-days; and the effects of a single anodal HD-tDCS antidepressant dose (2.00 mA *× 5 minutes) have been validated, which has been done by placing the fabricated Au/AgCl electrode on the region of interest of the rat brain. This study has provided strong positive evidence in terms of improvement in behavioural tests and EEG signal in the treatment group rats after a single anodal HD-tDCS antidepressant dose as compared to the rats with naive and chronic stress or depression-like behaviour. Also, the present study has provided evidence in terms of improvement in the glutamate/GABA (E/I) ratio, both in the cortex and hippocampus regions of the treatment group rats after single anodal HD-tDCS dose, as compared to the rat group with chronic stress or depression-like behaviour, which is also associated with an enhancement in the memory and learning ability of the rats. It is worthy of note that the single anodal HD-tDCS dose has provided strong evidence related to the significant increase in the microglia labelled ionized calcium binding adaptor molecule 1 (Iba1) expression in both cortex and hippocampus region of treatment group rats as compared to the rat group with chronic stress or depression-like behaviour. The study also provides evidence related to the reduction in the count of partially degenerative neurons after a single anodal HD-tDCS dose in the treatment group rats as compared to the rat group with chronic stress or depression-like behaviour. Hence, the fabricated electrodes have an ability to provide stimulation through HD-tDCS dose that can penetrate up to the cortex and hippocampus region from the surface of the brain within tolerable and safety limits. Moreover, the single anodal HD-tDCS antidepressant dose (2.00* mA *× 5 minutes) has the capability to treat patients suffering from chronic stress and depression. The final outcome of this work is the development of a prototype of an HD-tDCS device, which is also compatible with fabricated dual-purpose electrodes. The prototype of the HD-tDCS device has the capability of providing a weak amount of direct current ranging from 1.00* mA *to 4.00* mA *with a maximum error of less than 2%. Such type of emerging advancement in the HD-tDCS device can help patients suffering from cognitive disorders without a permanent support from the caregivers.*

Contents