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## Cathodal Transcranial Direct Current Stimulation (c-tDCS) Primed Intermittent Theta Burst Stimulation (iTBS) over Left Dorsolateral Prefrontal Cortex for Depression: A Case Report

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# Cathodal Transcranial Direct Current Stimulation (c-tDCS) Primed Intermittent Theta Burst Stimulation (iTBS) over Left Dorsolateral Prefrontal Cortex for Depression: A Case Report

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## Case Report

# Cathodal Transcranial Direct Current Stimulation (c-tDCS) Primed Intermittent Theta Burst Stimulation (iTBS) over Left Dorsolateral Prefrontal Cortex for Depression: A Case Report

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## Abstract

**Background:** Newer treatment modalities such as non-invasive brain stimulation techniques including transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) are being studied for the treatment of depression. In this paper a patient is reported with treatment-resistant depression who responded to treatment with a novel cathodal tDCS primed intermittent theta burst stimulation (iTBS) protocol targeted at the left dorsolateral prefrontal cortex administered over five consecutive days. Possibly, the inhibitory effect of cathodal-tDCS facilitates the excitatory effects of iTBS by homeostatic metaplasticity and improves efficacy by reducing the inter-hemispheric imbalance in prefrontal cortex activity.

**Keywords:** non-invasive brain stimulation (NIBS), transcranial direct current stimulation (tDCS), repetitive transcranial magnetic stimulation (rTMS), intermittent theta burst stimulation (iTBS), dorsolateral prefrontal cortex, major depressive disorder.

## Introduction

Major depressive disorder is a common and debilitating mental illness with a lifetime prevalence of 5.3% as per the recent National Mental Health Survey of India [1]. Nearly half of the patients do not respond to a sequential trial of two antidepressants and are considered to have treatment-resistant depression (TRD) [2]. Newer device-based, non-invasive brain stimulation techniques (NIBS) such as transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) that can induce neuroplastic changes in the cortex

have been investigated as add-on therapy in TRD [3, 4]. In this paper a patient is reported with TRD who was successfully treated with a novel cathodal tDCS primed intermittent theta burst stimulation (iTBS) protocol at our neuromodulation centre.

## Case report

A 48-year-old right-handed married lady presented with a history of recurrent depressive disorder, with onset at the age of 32 years. She had nine previous episodes with a mean duration of 4.3 months, treated with multiple antidepressants and electroconvulsive therapy, with good interepisodic functioning. There was no family history of mental illness and no psychosocial stressors preceding the current episode. She has been on regular treatment for hypothyroidism for the past three years with 50 µg of thyroxine tablet daily.

The current episode began six months ago while she was on a combination of 900 mg of lithium carbonate and 20 mg of escitalopram oxalate tablets.

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It was characterized by a persistent and pervasive sad mood, anhedonia, death wishes, disturbed sleep, feelings of guilt, a pessimistic view of the future, reduced libido, and panic attacks. After two months into the episode, she received an adequate trial of vilazodone with no response. At the presentation, she was on a combination of 20 mg of vilazodone hydrochloride and 1.5 mg of cariprazine. On mental status examination, she had ideas of worthlessness and hopelessness, pervasive and persistent sad mood, depressed affect, and grade 4 insight. Vilazodone and cariprazine were discontinued, and she was started on 37.5 mg of venlafaxine hydrochloride, which was gradually increased to 75 mg twice a day along with 1.5 mg of clonazepam. The thyroid-stimulating hormone level was normal (serum TSH 2.07  $\mu$ IU/mL); hence, thyroxine was continued at 50  $\mu$ g per day. She was also diagnosed with anaemia (haemoglobin 9.8 g/dL) and Vitamin-D deficiency (serum Vitamin D 12.7 ng/ml) and was thus started on iron and vitamin supplementation. Considering treatment-resistant depression (failed trials of escitalopram and vilazodone), she was offered NIBS treatment, to which she agreed.

## Discussion

We found a good response to cathodal tDCS primed iTBS protocol in a middle-aged patient with TRD. Theta burst stimulation (TBS) is a novel form of patterned rTMS that requires less stimulation time and exerts longer-lasting effects when compared to conventional rTMS. While iTBS is known to be excitatory, continuous TBS (cTBS) is inhibitory [7]. Despite preliminary evidence for its efficacy in major depression, there is considerable heterogeneity in response and long-term effects [8, 9].

The rTMS-induced cortical plasticity changes depend on the functional state of the cortex, which can be altered by preconditioning or priming with tDCS. Inhibitory cathodal tDCS increases the excitatory effect of iTBS through the principle of homeostatic metaplasticity [10, 11]. According to the imbalance hypothesis of depressive disorder, there is relative hypoactivity of the left DLPFC compared to the right DLPFC [12]. While cathodal-tDCS is inhibitory, iTBS is excitatory, and

when both are given sequentially over left DLPFC, the inhibitory effect of cathodal-tDCS facilitates the excitatory effects of iTBS further by homeostatic metaplasticity and results in improved efficacy by reducing the inter-hemispheric imbalance.

We have recently established the Centre for Neuromodulation in Psychiatry, in Kasturba Medical College, Manipal, as a part of a multicentric research project funded by DBT India Alliance, along with NIMHANS, Bengaluru and CIP, Ranchi, which offers NIBS treatment for psychiatric disorders [13]. Although, NIBS therapies are effective and have fewer side effects than pharmacotherapy, the treatment protocols need optimization, specifically during maintenance phases. The cathodal tDCS primed iTBS protocol is a promising option for the management of TRD.

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