

# Biomarkers of Response to tDCS in Clinical Depression: A Neuroimaging and EEG Study

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## Introduction

Clinical depression is a highly prevalent and debilitating mental health disorder, characterized by a range of affective, cognitive, and physical symptoms that significantly impact an individual's quality of life. Despite the availability of multiple treatment options, including pharmacotherapy, psychotherapy, and newer interventions such as transcranial direct current stimulation (tDCS), many patients experience suboptimal response or fail to respond altogether to these treatments. As a result, identifying biomarkers that can predict treatment outcomes is becoming increasingly important in both clinical practice and research. Biomarkers can serve as objective indicators of treatment efficacy, allowing for personalized, precision medicine approaches that tailor interventions based on individual neurobiological profiles. In the case of tDCS, a non-invasive neuromodulation technique, identifying biomarkers of response is particularly crucial because the effects of stimulation can vary widely across individuals. While tDCS has shown promise in improving symptoms of depression, particularly in patients who are treatment-resistant, understanding the underlying mechanisms and identifying reliable biomarkers of treatment response remains an ongoing challenge [1].

## Description

tDCS involves the application of a low-intensity electrical current to specific regions of the brain via electrodes placed on the scalp. The current is believed to modulate cortical excitability, either enhancing or inhibiting neuronal activity depending on the polarity of stimulation. The most commonly targeted brain region for depression is the dorsolateral prefrontal cortex (DLPFC), an area implicated in emotion regulation, executive functioning, and cognitive control. DLPFC hypoactivity has been consistently observed in individuals with depression, and modulating this region via tDCS has been shown to improve mood and cognitive function. However, despite its efficacy in many cases, the response to tDCS is not universal, and some patients fail to experience meaningful improvements. This variability has prompted interest in identifying biomarkers that can predict which individuals are most likely to benefit from tDCS, and why certain individuals do not respond as well to the treatment [2].

Neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), have been used to explore brain activity patterns before, during, and after tDCS treatment. These studies have revealed that tDCS can alter the activity of brain networks associated with depression, such as the default mode network (DMN), the salience network,

and the cognitive control network. Specifically, tDCS over the left DLPFC has been shown to increase cortical excitability in this region and improve connectivity between the DLPFC and other brain areas involved in mood regulation, such as the ventral striatum. However, it remains unclear which specific brain activity patterns or connectivity changes serve as reliable biomarkers of tDCS response. Some studies suggest that baseline DLPFC activity, as measured by resting-state fMRI or electroencephalography (EEG), may be predictive of treatment outcomes. Higher pre-treatment activity in the DLPFC may indicate a greater potential for responsiveness to tDCS, as individuals with lower baseline activity may require more substantial stimulation to induce therapeutic changes [3].

EEG is another promising technique for identifying biomarkers of response to tDCS in depression. EEG provides real-time measures of cortical electrical activity and offers high temporal resolution, allowing researchers to track changes in brain oscillations associated with treatment. One specific EEG marker that has been identified as a potential predictor of tDCS response is the alpha rhythm, which is typically associated with relaxed, calm states. Alterations in the alpha rhythm, particularly in the frontal regions, have been linked to depression, and modulation of alpha activity via tDCS may indicate treatment efficacy. Other EEG markers, such as theta and beta rhythms, have also been implicated in depression and may serve as potential biomarkers of response [4]. Theta waves, often associated with emotional processing and memory, have been found to be altered in individuals with depression, and changes in theta activity following tDCS may reflect improvements in emotional regulation and cognitive control. Beta waves, which are involved in motor control and cognitive engagement, may also be modulated by tDCS, with changes indicating improvements in executive function and motivation [5].

## Conclusion

In conclusion, identifying biomarkers of response to tDCS in clinical depression represents an exciting avenue for advancing personalized medicine in psychiatry. By using neuroimaging techniques such as fMRI and EEG, as well as genetic and neurochemical analyses, researchers are beginning to uncover the brain activity patterns, genetic profiles, and neural biomarkers that predict who will benefit from tDCS. These biomarkers have the potential to inform treatment decisions, ensuring that patients receive the most appropriate and effective interventions for their unique neurobiological profiles. While much progress has been made, further research is needed to refine these biomarkers and develop standardized protocols for tDCS application. By improving our understanding of the mechanisms underlying tDCS treatment response, we can optimize its therapeutic potential and provide more effective, targeted treatments for individuals suffering from clinical depression.

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## Conflict of Interest

None.

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