Major depressive disorder: Brain signals as biomarkers for depression

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Tiago Costa from Delft University of Technology explores the potential of neuroimaging techniques, specifically non-invasive electroencephalography (EEG), in detecting biomarkers for depression

Major Depressive Disorder (MDD) is a prevalent and complex mental disorder posing significant challenges to both individuals and societies worldwide. An early and accurate diagnosis of depression is essential for effective treatment and management. In recent years, advancements in neuroimaging techniques have opened new avenues for identifying biomarkers that could aid in the diagnosis and understanding of depression.

Among these techniques, non-invasive electroencephalography (EEG) has gained attention in the last decade for its potential to detect depression biomarkers. While there is significant heterogeneity in terms of methodologies, sample sizes, and research objectives, several consistent patterns and findings emerge.

EEG is a non-invasive neuroimaging technique that measures the electrical activity of the brain. By placing electrodes on the scalp, EEG records the collective firing of neurons, producing a series of wave patterns that reflect brain function and cognitive processes. It is widely used in clinical settings to diagnose conditions like epilepsy, monitor brain activity during surgeries, and assess brain health.

Additionally, EEG aids in understanding sleep patterns, cognitive states, and neurological disorders. Its real-time monitoring capability makes it valuable in researching brain dynamics, neural connectivity, and mental states, offering insights into the intricate workings of the human brain.

EEG signals as biomarkers for depression

Among the most prominent EEG biomarkers associated with depression are abnormalities in alpha wave activity. (1) Alpha waves (8-13 Hz) are linked to a state of relaxed wakefulness and sensory processing inhibition. Individuals with depression often exhibit reduced alpha power in resting-state EEG recordings, particularly over frontal brain regions. This reduction in alpha power has been correlated with cognitive deficits and challenges in emotion regulation. The power ratio of different frequency bands has also garnered attention as a potential biomarker for depression.

For example, the Alpha/Beta ratio was recently shown to decrease in individuals with depression when compared with healthy individuals. (2) EEG studies have also uncovered frontal asymmetry patterns that could serve as biomarkers for depression. (3)

Greater relative right frontal activation and diminished left frontal activation have been associated with negative affect and depressive symptoms. Frontal asymmetry has been proposed as an indicator of emotional processing biases in depression, shedding light on the neural underpinnings of mood disorders.

Event-related potentials (ERP), which are distinct EEG responses triggered by specific events or stimuli, have also been explored as a biomarker for depression. (4) The P300 component, an ERP associated with cognitive processing and attention allocation, has consistently shown reduced amplitude in depression. This reduction in P300 amplitude points toward deficits in cognitive resource allocation and attention, which are often observed in individuals with depression.

Finally, the study of functional connectivity networks using EEG has revealed alterations in depression. (4) The default mode network (DMN), responsible for self-referential thinking, frequently displays hyperconnectivity in depression. Conversely, connectivity between the DMN and executive control networks is diminished, highlighting disrupted communication between brain regions associated with self-regulation and goal-directed behavior. (4)

A critical look at recent findings

Despite the progress made in identifying depression biomarkers using non-invasive EEG, several methodological considerations emerge from the systematic mapping. The diversity in participant characteristics, such as age, gender, and comorbidities across studies, can impact the generalizability of findings.

Future research should strive for more homogeneous samples to enhance the reliability of results. Similarly, the variation in EEG recording protocols and data preprocessing techniques can introduce inconsistencies. Standardizing these procedures across studies would enhance the comparability and reliability of results. Furthermore, most studies reviewed here employed cross-sectional designs, limiting insights into the dynamic changes of EEG biomarkers over time. Longitudinal studies are crucial for understanding the progression of depression and its neural correlates.

Biomarkers for depression: Implications and future directions

The systematic mapping of studies using non-invasive EEG to detect depression biomarkers underscores the potential of this technique in advancing our understanding of depression’s neurobiological underpinnings. The consistent alterations observed in frequency domain analysis, ERPs, and connectivity patterns provide valuable insights into the neural dysregulation associated with depression. Additionally, the emergence of machine learning approaches holds promise for creating objective and accurate diagnostic tools.

However, this mapping also highlights the need for rigorous methodological standards in the field. Establishing standardized protocols for EEG recording, preprocessing, and analysis will enhance the comparability of findings across studies. Furthermore, the

integration of longitudinal designs and multi-modal imaging techniques could offer a more comprehensive view of the temporal dynamics and complexity of depression-related neural changes.

The use of EEG signals as a biomarker detection may also provide in the future the means to develop a closed-loop therapy for the treatment of depression. Brain stimulation has been explored as a potential treatment for several symptoms of depression.

However, brain stimulation is usually performed without relying on the information that specific brain signals of patients show at any given moment in time.

Hence, by coupling EEG recordings with a brain stimulation modality, such as focused ultrasound, a minimally- invasive personalized therapy for depression may provide better outcomes for depression patients. The UPSIDE project is an EU-funded initiative striving to achieve this goal, for which updates can be found on the project website.

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