Sains Malaysiana 54(2)(2025): 577-587
http://doi.org/10.17576/jsm-2025-5402-22

Decoding Depression: Insights into Molecular Biomarkers and Neuroimaging of Depression

(Penyahkodan Kemurungan: Pandangan tentang Molekul Penanda Biologi dan Pengimejan Neuro Kemurungan)

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Received: 12 January 2024/Accepted: 26 November 2024

ABSTRACT

In this review, we explore the recent insights on major depressive disorder (MDD) and emphasizes the involvement of specific genes, particularly in MDD development. The paper consolidates and examines various biological, epigenetic, and environmental factors contributing to depression, illustrating the intricate interplay among these elements. Interestingly, molecular and neuroimaging findings are summarized and discussed, acknowledging the current absence of reliable biomarkers for MDD. This absence is attributed to the structural and functional complexity of the brain, the limitations of available technology, and the weak correlations between genetic markers and clinical manifestations of depression. Interestingly, in somatic treatment, only electroconvulsive therapy (ECT) has been proven effective in treating resistant depression. In conclusion, this article critically reviews the molecular biomarkers and neuroimaging of depression. Existing mechanisms such as the biogenic amine hypothesis and genetic and environmental factors are recognized for explaining depression's pathophysiology. The potential for neuroimaging and molecular studies to yield promising biomarkers for depression is highlighted.

Keywords: Depression; dopamine; environmental; genetics; MMD; MRI

ABSTRAK

Dalam ulasan ini, kami mengkaji pandangan terkini tentang gangguan kemurungan utama (MDD) dan menekankan penglibatan gen tertentu, terutamanya dalam pembangunan MDD. Kertas ini menyatu dan meneliti pelbagai faktor biologi, epigenetik dan persekitaran yang menyumbang kepada kemurungan, menggambarkan interaksi rumit antara unsur ini. Menariknya, penemuan molekul dan pengimejan neuro diringkaskan dan dibincangkan, mengakui ketiadaan semasa penanda biologi yang boleh dipercayai untuk MDD. Ketiadaan ini dikaitkan dengan kerumitan struktur dan fungsi otak, batasan teknologi sedia ada serta korelasi yang lemah antara penanda genetik dan manifestasi klinikal kemurungan. Menariknya, dalam rawatan somatik, hanya terapi elektrokonvulsif (ECT) telah terbukti berkesan dalam merawat rintangan kemurungan. Kesimpulannya, kertas ini mengkaji secara kritis penanda biologi molekul kemurungan dan pencitraan saraf. Mekanisme sedia ada, seperti hipotesis amina biogen serta faktor genetik dan persekitaran diiktiraf untuk menjelaskan patofisiologi kemurungan. Potensi untuk kajian pengimejan neuro dan molekul untuk menghasilkan penanda biologi yang berpotensi untuk kemurungan dibincangkan.

Kata kunci: Alam sekitar; dopamin; genetik; kemurungan; MMD; MRI

INTRODUCTION

Depression is not a monoetiological disease; it is a psychiatric condition characterized by a persistent low mood, significant loss of enjoyment in activities, difficulties with focused attention, disruptions in appetite and sleep, cognitive problems, feelings of worthless, excessive guilt, and thoughts of self-harm and suicide (Zakaria et al. 2022). Depression is recognized as a heritable condition. Multiple studies have demonstrated the hereditary transmission of affective disorders across generations (Ivanets et al. 2021). According to the World Health Organization (WHO), depression is projected to be recognized as a worldwide problem by 2030, impacting approximately 300 million individuals across all age groups (Zhu et al. 2018). The development of depression may be influenced by exposure to environmental stressors. Abundant evidence indicates that environmental stress, particularly childhood trauma, significantly contributes to the development of depression.

Several review papers present evidence indicating that environmental factors can induce epigenetic alterations in humans (Padurariu et al. 2010; Penner-Goeke & Binder 2019). Epigenetics encompasses mechanisms that influence the activation and interpretation of genes, without altering the DNA sequence. These mechanisms include DNA methylation (DNAm), microRNAs (miRNAs), and modifications to histones (Penner-Goeke & Binder 2019). Consequently, specific stressors have the ability to modify the way genes are activated, potentially leading to heritable changes in subsequent generations (Provençal et al. 2020). People who have been abused or neglected as children or as adults are at risk of developing depression as a result of stressful life events, and depressive symptoms can develop as a consequence of adverse childhood experiences (Hu, Yiu & Clark 2021).

Research has shown that individuals suffering from depression exhibit decreased levels of serotonin, whereas antidepressant medications have demonstrated the ability to elevate serotonin levels in the brain. Moreover, the reduction of tryptophan, a specific amino acid involved in the production of melatonin and serotonin, can trigger depressive symptoms in patients undergoing treatment for depression, but it does not affect untreated patients. The results indicate that elevating serotonin levels is crucial for achieving antidepressant effects, although a decrease in the level of this neurotransmitter alone may not be sufficient to generate the desired outcome (Hu, Yiu & Clark 2021; Provençal et al. 2020). Figure 1 depicted the monoaminergic neurotransmitters and the regulation of mood, emotion, and cognitive function. The identification of depression relies on symptoms since there is an absence of biological markers that sufficiently meet the criteria for diagnosis (Gururajan et al. 2016). Clinicians utilize various psychometric scales to evaluate different aspects of depressive functioning, with the Hamilton Depression Rating Scale (HDRS) being the most frequently employed (Kiecolt-Glaser et al. 2011). However, laboratory-based diagnostic tests in molecular biology have the potential to enhance the precision of diagnosing major depressive disorders. These tests can pinpoint factors that define patients and support the customization of therapeutic approaches (Redei et al. 2014). The influence of genetic factors on the risk of MDD is widely recognized. A comprehensive study conducted on a large group of twins in Sweden estimated that approximately 37% of the risk for MDD can be attributed to genetic factors (Sullivan, Neale & Kendler 2000). Conversely, it is widely recognized that environmental factors, particularly stress, and exposure to unfavorable life events, play a role in increasing the likelihood of the risk. For instance, a comprehensive analysis of 26 studies showed a robust correlation between childhood trauma, particularly neglect and emotional abuse, and the development of depression in adulthood

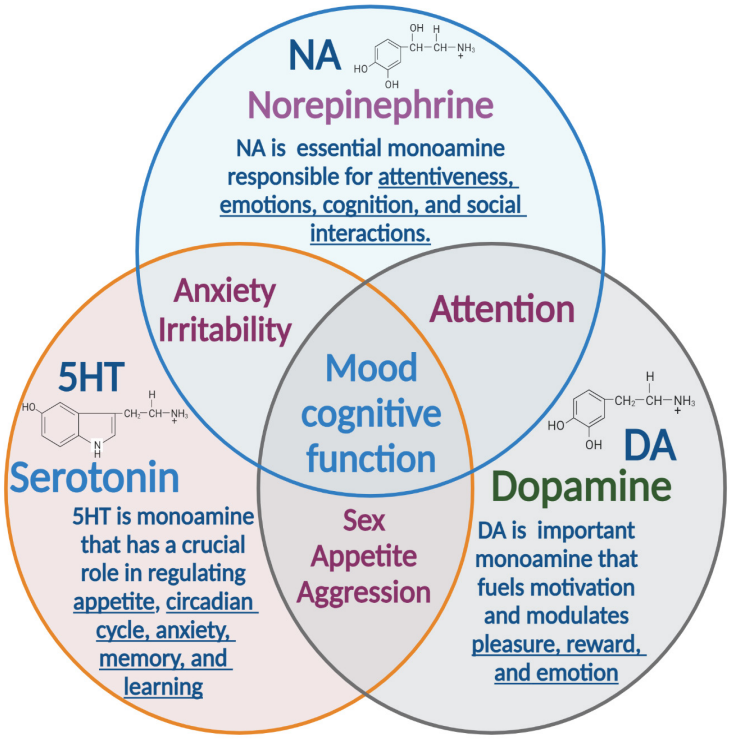


FIGURE 1. Monoaminergic neurotransmitters and the regulation of mood, emotion, and cognitive function

(Kendler, Karkowski & Prescott 1999; Mandelli, Petrelli & Serretti 2015; Penner-Goeke & Binder 2019). This article aimed to provide a thorough analysis of the underlying mechanisms, factors that contribute to, and molecular indicators of depression. The potential of neuroimaging and molecular investigations to produce promising biomarkers for depression is emphasized.

RECENT INSIGHTS

Emerging research on MDD sheds light on its intricate biological landscape, showing that MDD is tied to complex interactions across neurotrophic, metabolic, inflammatory, and endocrine systems (Rimti et al. 2023). Key biomarkers such as Brain-Derived Neurotrophic Factor (BDNF), are closely linked to stress resilience and neuroplasticity. Their levels are often reduced in individuals with chronic stress or depression, highlighting their relevance in MDD pathogenesis (Emamzadeh 2016). Inflammatory signals, especially cytokines like interleukin-1 beta (IL-1b) and tumor necrosis factor-alpha (TNF-α), are elevated in many MDD patients. They are frequently associated with neurodegenerative changes (Dos Santos et al. 2018) including white matter disruption, which may contribute to cognitive impairment and the persistence of depressive symptoms (Lim et al. 2021). A study found that individuals with MDD who showed elevated levels of TNF-α also had reduced BDNF levels, which increased the chances of developing the Val66Met polymorphism (Caldieraro et al. 2018). Furthermore, neuroendocrine disruptions in the hypothalamic-pituitary-adrenal (HPA) axis, marked by altered cortisol and other stress hormones, underscore the role of prolonged stress response in the disorder (Chávez-Castillo et al. 2019). Moreover, metabolic factors, including hormones like leptin and ghrelin, are also implicated, suggesting that metabolic imbalances may intertwine with MDD's behavioral manifestations. For instance, patients with MDD also show varied insulin resistance, with indicators like elevated HDL cholesterol and hyperglycemia (Pan et al. 2012) seen more in cases with poor physical health metabolomic technologies that enable precise identification of these biomarkers. This could be achieved by using molecular panels that show distinct biochemical signatures linked to MDD (Zheng et al. 2017). Notably, AI-assisted models utilizing glucose and lipid metabolic profiles have been shown to effectively predict MDD diagnosis, supporting the hypothesis that oxidative stress and impaired antioxidant defenses may influence depression pathology (Liu et al. 2015). Patients with recurrent MDD episodes exhibit high levels of oxidative DNA damage markers (8-Oxo-2′-deoxyguanosine), which correlate with the severity of depressive symptoms (Maes et al. 2012). Gastrointestinal biomarkers and the microbiome also play roles, as gut-brain interactions appear to influence mood and inflammatory status, providing new angles for therapeutic exploration.

MOLECULAR BIOMARKERS AND NEUROIMAGING IN DEPRESSION

MOLECULAR BIOMARKERS

The identification of reliable molecular biomarkers for depression is an ongoing area of research, and multiple factors contribute to the complexity of this condition. Firstly, depression biomarkers possess distinct characteristics. Sampling biomarkers post-mortem cannot yield dependable outcomes due to the absence of a singular brain structure accountable for the disease (Jakubczyk et al. 2014). A panel of biomarkers derived from blood samples can be used to identify major depressive disorder (MDD). This panel measures the levels of nine specific markers in the blood transcript, namely ADCY3, DGKA, FAM46A, IGSF4A/CADM1, KIAA1539, MARCKS, PSME1, RAPH1, and TLR7 (Redei et al. 2014).

Chronic stress leads to the condition of hypercortisolemia, and depression has consistently been associated with increased cortisol levels (Stetler & Miller 2011). An increase in cortisol (glucocorticoids) in the biological fluids correlates with symptoms of MDD, suggesting it could be a potential biomarker (Jakubczyk et al. 2014). Kenis et al. (2020) conducted a meta-analysis study to investigate various biomarkers as potential predictors for the diagnosis and treatment of depression. Out of the various gastrointestinal factors, such as neuroimaging, neurotrophic factors, neurotransmitters, hormones, immunology, and oxidative stress, only cortisol is relevant for diagnosing MDD. There was a relationship between cortisol levels and the onset, relapse, and recurrence of the disease, but this relationship depended on the baseline level of depression. Moreover, the level of cortisol can be measured in a variety of specimens, including blood, urine, saliva, and even hair (Nobis, Zalewski & Waszkiewicz 2020). In contrast, reduced levels of cortisol are indicative of atypical depression (Krishnan & Nestler 2008) and can be valuable in distinguishing between the melancholic and atypical subtypes of the condition (Lamers et al. 2013).

Recent research has substantiated the involvement of non-coding RNAs, specifically microRNAs (miRNAs), in the development and manifestation of depression (Guo et al. 2022). MiRNAs are single-stranded RNA molecules that control mRNA expression by either degrading RNA or suppressing protein translation. They can modulate the expression of numerous genes, allowing them to control multiple cellular signaling pathways (Bartel 2018). Belzeaux et al. (2012) discovered that 14 microRNAs exhibited differences in peripheral blood samples between individuals with depression and those who were healthy. Examinations of RNA-Seq conducted on blood samples obtained from individuals with MDD have uncovered noteworthy alterations in the miR-let-7 and miR-34 families (Lopez, Kos & Turecki 2018). These changes are observed in depressive patients and exhibit promise as diagnostic

biomarkers for depression. MiRNAs also have a significant impact on the effectiveness of antidepressant treatment. Specifically, miR-146a5p, miR-146b-5p, miR-24-3p, and miR-425-3p show promise as potential indicators for predicting the outcome of depression treatment (Guo et al. 2022).

It has been conclusively proven that inflammation is linked to depression, and a wide range of reviews have been conducted (Bartel 2018; Belzeaux et al. 2012; Jakubczyk et al. 2014). For instance, conditions such as systemic lupus erythematosus, traumatic brain injury, and multiple sclerosis are linked to elevated rates of major depression in the brain (Perez-Caballero et al. 2019). Individuals suffering from inflammatory disorders exhibit elevated rates of depression (Osimo et al. 2020). Neuroinflammation can be induced by peripheral inflammatory cytokines crossing the blood-brain barrier to cause depression symptoms (Jesulola, Micalos & Baguley 2018). As cytokines rise, the HPA axis is stimulated, and cortisol releasing hormone (CRH) is produced, resulting in higher cortisol levels (Raison, Capuron & Miller 2006). Furthermore, heightened levels of cytokines lead to an upsurge in serotonin transporter expression and trigger the activity of indoleamine 2,3-dioxygenase (IDO), thereby amplifying the kynurenine pathway in the brain. These elements collectively play a role in the onset of depression (Nobis, Zalewski & Waszkiewicz 2020). A meta-analysis conducted by Köhler et al. (2017) described a potential cytokine profile linked to MDD. Among indicators of inflammation, IL-6, C-reactive protein (CRP), Tumor Necrosis Factor-α (TNF-α), and soluble interleukin-2 receptor (sIL-2R) show the most promise as potential markers for identifying depression.

Depression is frequently associated with an increase in IL-6 concentrations among all inflammatory cytokines. Meta-analyses have confirmed this relationship (Carvalho et al. 2020; Haapakoski et al. 2015; Köhler et al. 2017; Nobis, Zalewski & Waszkiewicz 2020). Kunugi, Hori and Ogawa (2015) proposed cerebrospinal fluid (CSF) IL-6 as a biomarker for the neuro-inflammatory subtype of MDD. Elevated IL-6 may serve as an early indicator for cognitive decline in depression, aligning with both the severity of depressive symptoms and heightened activity in the HPA axis (Nobis, Zalewski & Waszkiewicz 2020; Schiepers, Wichers & Maes 2005). In addition to being a potential diagnostic (state) biomarker, IL-6 may also be used as a treatment-response biomarker (Köhler et al. 2018).

Furthermore, IL-6 stimulates the release of CRP from the liver, which is the most commonly used indicator of inflammation. CRP is produced in the liver and is secreted by the cells that produce it (Del Giudice & Gangestad 2018). Hospitalization due to depression is associated with higher CRP concentrations (Wium-Andersen et al. 2013). Multiple studies have demonstrated an association between depression and elevated levels of CRP. This implies a plausible correlation between inflammation and depression (Carvalho et al. 2020; Nobis, Zalewski & Waszkiewicz 2020; Osimo et al. 2020; Strawbridge et al. 2015). Elevated levels of CRP have been proposed to be more precise in identifying female patients with MDD compared to male patients. However, it is important to acknowledge that elevated CRP levels are not exclusive to depression but observed during manic episodes (Köhler et al. 2017). Additionally, it has been reported that the initial CRP levels in individuals with depression may be linked to their response to treatment. Research demonstrated that elevated levels of CRP were indicative of a favorable reaction to pharmacological intervention (Perez-Caballero et al. 2019; Strawbridge et al. 2015; Wium-Andersen et al. 2013). In addition, elevated levels of TNF-α are linked to a higher frequency of depressive episodes (Maes et al. 2012). An inflammatory cytokine TNF-α has also consistently been found to be elevated in depression compared to healthy individuals (Nobis, Zalewski & Waszkiewicz 2020). However, some meta-analyses have found this evidence to be inconclusive (Haapakoski et al. 2015; Tamang, Watanabe & Holzapfel 2016). Importantly Jannelidze et al. (2011) proved that IL-6 and TNF-α levels are higher among patients who are more likely to attempt suicide, suggesting that these substances could be considered as indicators of a person's current condition. Furthermore, scientific evidence has demonstrated that the two cytokines directly impede the process of adult hippocampal neurogenesis (Iosif et al. 2006; Nobis, Zalewski & Waszkiewicz 2020). Depression's pathophysiology involves the participation of BDNF, vascular endothelial growth factor (VEGF), fibroblast growth factors (FGF), and VGF nerve growth factor. These growth factors show great potential as indicators for depression. They are influenced by antidepressant medications. Furthermore, they can be found both in the brain and in the periphery, rendering them appropriate as biomarkers for psychiatric disorders (Castrén & Rantamäki 2010; Clark-Raymond & Halaris 2013; Turner et al. 2006). For the selection of biomarkers, multiple panels may be needed based on the potential pathways that research may implicate (Strawbridge et al. 2015). The abundance of potentially valuable biomarkers poses a challenge for psychobiology in discerning their specific implications and relevance for different individuals. Nevertheless, several endeavors have been undertaken to suggest highly potential biomarker panels (Brand, Moller & Harvey 2015). Table 1 summarizes the recent insights into molecular biomarker based on samples origin and indicator in diagnosis of depression.

NEUROIMAGING IN DEPRESSION

Neuroimaging in depression refers to the use of various imaging techniques to study the structure, function, and connectivity of the brain in individuals with depressive disorders. These techniques provide valuable insights into the neurobiological underpinnings of depression and contribute to a better understanding of the disorder.

Different neuroimaging modalities are employed to examine various aspects of brain function and structure in individuals with depression as shown in Figure 2.

Here are seven forms of neuroimaging that are related to mood disorders: electroencephalography (EEG), structural magnetic resonance imaging (sMRI), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), cerebral blood flow (CBF), magnetoencephalography (MEG), and diffusion tensor imaging (DTI). According to research carried out by Fu and Costafreda (2013), utilizing imaging techniques such as sMRI and fMRI seeks to identify brain abnormalities associated with MDD. Furthermore, the understanding gained from studying the neurobiological factors involved in the development of MDD can elucidate the presence of biomarkers that can be used for diagnosing the condition, predicting its prognosis, and forecasting the response to treatment. Several attempts have been undertaken to utilize the findings of MRI examinations as indicators of depression. MDD patients' MRI showed alterations in the whole brain and in certain parts of it, such as the frontal lobe, ventricles, occipital lobes, and cerebellum. The brain's alterations are dependent on clinical and socioeconomic factors including age, gender, sex, and genetics (Ivanets et al. 2021). Cole et al. (2011) identified a reduction in hippocampal volume during the initial episode of depression. They suggested utilizing these modifications as biomarkers for the initial occurrence of depression. Unlike patients with a history of MDD throughout their lives, there was no observable change in the size of the hippocampus. However, modifications were detected in the insula, thalamus, pallidum, and nucleus accumbens. Kandilarova et al. (2019) found that depression is caused by changes in functional and effective connectivity of

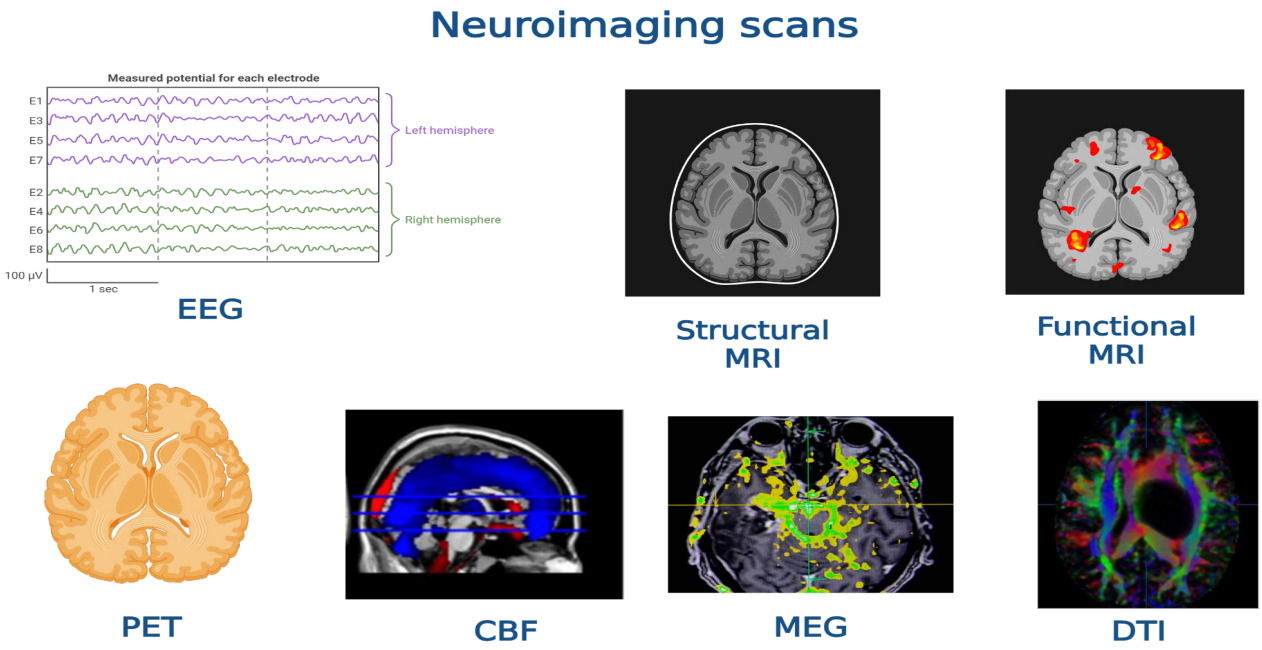
TABLE 1. Summary of molecular biomarkers with sample origin and indicator utilized in diagnosis of depression

Origin/Source	Type of depression	Biomarkers	Indicators	References
Blood	MDD	ADCY3, DGKA, FAM46A, IGSF4A/ CADM1, KIAA1539, MARCKS, PSME1, RAPH1, and TLR7	Elevated levels of biomarkers as indicator for MDD	(Redei et al. 2014)
Biological Fluids	MDD	Cortisol (glucocorticoids)	Chronic stress leads to the condition of hypercortisolemia, and depression has consistently been associated with increased cortisol levels	(Stetler & Miller 2011; Jakubczyk et al. 2014)
Blood	MDD	MicroRNAs (miRNAs)	Alterations in the miR-let-7 and miR-34 families	(Lopez, Kos & Turecki 2018)
Biological Fluids	MDD	Neuroinflammation • Cytokines • Interleukin (IL-6) • Reactive protein (CRP) • Tumor necrosis factor-α (TNF-α)	Elevated level of cytokines, IL-6, CRP and TNF- α	(Raison, Capuron & Miller 2006; Köhler et al. 2017; Carvalho et al. 2020; Haapakoski et al. 2015)
Cerebrospinal fluids (CSF)	MDD	Interleukin-6 (IL-6)	Elevated level of IL-6 as an early indicator for cognitive decline in depression	(Nobis, Zalewski & Waszkiewicz 2020; Schiepers, Wichers & Maes 2005; Köhler et al. 2018)

large-scale brain networks, such as the default mode, executive, and salience networks, using spectral dynamic causal modeling (spDCM) for resting-state fMRI. The study found that depression severity depends on the connectivity of the hippocampal node with other brain regions. A study indicates the right anterior insula plays a crucial role in depression pathophysiology. In a study done by the National Institute of Mental Health on a synopsis of neuroimaging abnormalities associated with mood disorders (Savitz, Rauch & Drevets 2013), they found that depression is increasingly thought to be caused by a mood-congruent processing bias, which increases punishment sensitivity and decreases hedonic capacity. In fMRI studies, this cognitive bias takes two forms. First, some depressed patients have a greater amygdala hemodynamic response to negatively valenced emotional stimuli like sad faces and a lower response to positively valenced stimuli like happy faces (Lamers et al. 2013). Second, some depressed patients have a blunted hemodynamic response in the ventral striatum and orbitofrontal cortex to reward stimuli, which may be linked to anhedonia.

Combining MRI and MEG can be used to investigate the pathophysiological mechanisms of MDD. The involvement of frontal lobes, specifically the anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC), and orbitofrontal cortex (OFC), has been demonstrated in the development of depression. Furthermore, the limbic regions, specifically the hippocampus and amygdala, have shown potential as promising biomarkers for MDD (Ivanets et al. 2021).

Other types of neuroimaging for mood disorders such as the positron emission tomography method (PET), which indicates that MDD is linked to decreased presynaptic dopamine levels. Combining PET with SPECT can identify promising biomarkers based on changes in frontal and limbic regions, including the ACC, DLPFC, and amygdala. However, biomarkers may also be found in the brainstem and midbrain. The authors suggest that the front-limbic regions are ideal for finding promising biomarkers (Dubol et al. 2020). Additional neuroimaging techniques used for mood disorders encompass diffusion tensor imaging tractography (DTI) for evaluating the integrity of white matter tracts, magnetic resonance spectroscopy for assessing variations in chemical composition, and ligand-binding studies for quantifying receptor or monoamine-transporter density (Dunlop & Mayberg 2017).



EEG: Electroencephalogram; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography; CBF: Cerebral Blood Flow; MEG: Magnetoencephalography; DTI: Diffusion Tensor Imaging

FIGURE 2. List of neuroimaging scans to assess various aspects of brain function and structure of individuals with depression

PSYCHOTHERAPY IN HANDLING DEPRESSION

Psychotherapy can be an effective and important component in the treatment of depression. Most psychiatric disorders are treated and prevented through psychotherapeutic interventions. These involves a range of therapeutic approaches aimed at addressing the emotional, cognitive, and behavioral aspects of depression (Bennabi et al. 2019; Karrouri et al. 2021). Psychotherapy enhances the therapeutic bond and empowers patients with depression to track their emotional state, enhance their performance, gain deeper insight into their symptoms, and acquire effective coping strategies for managing stressful situations (Malhi et al. 2015).

Mild to moderate MDD is typically treated with depression-focused psychotherapy. Two specific psychotherapeutic approaches are recommended based on significant clinical evidence: cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT). When severe depression is present, supportive therapy (ST) and psychoeducational intervention (PEI) will typically be used only to augment existing pharmacological treatments (Karrouri et al. 2021).

CBT is a widely used and evidence-based approach for treating depression. It focuses on identifying and challenging negative thought patterns and behaviors that contribute to depressive feelings. The approach is characterized by active participation and pragmatic application, with the therapist and patient engaging cooperatively (Chand, Kuckel & Huecker 2023). Thus, MDD is well treated with cognitive behavioral therapy (National Collaborating Centre for Mental Health 2010) and almost all guidelines recommend it as the first line of treatment (Karrouri et al. 2021). The effectiveness of CBT relies on the patient's ability to observe and change their beliefs and behaviors. To address this challenge, simple techniques, like behavioral activation have been developed. Behavioral activation involves integrating pleasant activities into daily life to boost positive interactions with the environment (Karrouri et al. 2021; Twohig & Levin 2017). Acceptance and commitment therapy, another form of CBT, based on functional contextualism, aids patients in accepting and adapting to ongoing issues. This therapy has shown effectiveness in reducing depressive symptoms and preventing relapses (Kennedy et al. 2016; Lepping et al. 2017). On the other hand, IPT, similar to CBT, is recommended as the initial treatment for adults experiencing mild to moderate MDD episodes. Additionally, IPT is a widely recognized approach for addressing depression in adolescents (Montgomery 1989). IPT is a time-limited therapy that concentrates on improving interpersonal relationships. It helps individuals identify and address specific problems in their relationships that may contribute to their depressive symptoms. The therapist works with the individual to improve communication skills, resolve conflicts, and build social support. Mindfulness-based cognitive therapy (MBCT) is a modern approach that integrates components of CBT. Research has demonstrated that undergoing eight weeks of MBCT during a period of remission significantly decreases the likelihood of relapse. Therefore, it has the potential to serve as an alternative method to decrease or completely discontinue the use of antidepressant medication without raising the likelihood of a relapse into depression (Cladder-Micus et al. 2018; Karrouri et al. 2021).

Somatic treatments can also be effective in treating depression in many situations. Interestingly, electroconvulsive therapy (ECT) is widely recognized as the most prominent treatment for resistant depression, with substantial evidence confirming its efficacy and safety (Karrouri et al. 2021; UK ECT Review Group 2003). ECT is known for its high efficacy, especially in cases of severe depression and when a rapid response is needed. It can be particularly effective in individuals who have not responded well to other forms of treatment. It is generally considered safe, minimizes hospital readmissions, and alleviates the weight of depression, resulting in an enhanced quality of life (McCall et al. 2011; Tørring et al. 2017). Despite the majority of studies indicating that ECT is more advantageous for patients who have had fewer pharmacological treatments, there are still individuals who view ECT as a final resort for treating depression (Anderson & Reti 2009). ECT is commonly prescribed for individuals experiencing severe and psychotic depression, those at an elevated risk of suicide (Fink, Kellner & McCall 2014), individuals with Parkinson's disease, and pregnant patients (Saatcioglu & Tomruk 2011). Additionally, maintenance ECT has demonstrated effectiveness in preventing relapses. Ongoing enhancements in ECT protocols, particularly influenced by advancements in bioinformatics and expanding research in the field, contribute to the continuous improvement of ECT practices (Karrouri et al. 2021).

CONCLUSION

In conclusion, the establishment of a singular marker for MDD is highly improbable. Although depression is currently diagnosed based on clinical signs, biomarkers can serve as a useful tool for categorizing specific patients with the disorder, identifying subtypes, enhancing treatment selection, avoiding certain treatment methods, and predicting treatment response. Currently, ECT is commonly employed for the treatment of depression. The process is generally considered safe and effective. Nevertheless, administering ECT necessitates a collaborative team consisting of a nurse, an anesthesiologist, a psychiatrist, and a neurologist. The positive effects of ECT become apparent after multiple sessions, and the outcomes tend to be long-lasting. The way it operates involves multiple factors; ECT induces alterations in cerebral blood flow and regional metabolism. A majority of individuals undergoing ECT experience positive responses with no unfavorable consequences.

FUTURE PROSPECT

MDD presents with varied symptoms and underlying causes, and its biological and treatment mechanisms remain only partially understood. Current diagnostic tools and treatment options for MDD remain restricted, posing ongoing challenges in effectively managing the disorder (Cui et al. 2024). Future research efforts are likely to contribute to a new generation of antidepressants, as well as further expand our understanding of depression's biological basis (Cui et al. 2024). However, in mental health care, especially in depression, artificial intelligence (AI) has been a transformative force. AI is poised to transform depression care by enabling early diagnosis, tailored treatments, and continuous monitoring (Lee et al. 2021). Emerging technologies will detect early signs of depression through wearable devices and behavioral analysis, supporting timely intervention. Personalized treatment models based on individual health data are also advancing, allowing therapy plans to be adjusted in real time, thus improving effectiveness (Gomes et al. 2023). Additionally, AI-driven virtual therapists and chatbots provide accessible, 24/7 support, which is crucial in regions with limited mental health resources (D'Alfonso 2020). Continuous monitoring using AI may also help prevent severe episodes by tracking changes in mental health and notifying caregivers when needed. Introducing AI into mental health therapy and mental healthcare represents a promising frontier in the field. Although AI holds the potential to revolutionize mental healthcare, it should be implemented responsibly and ethically (Kiseleva, Kotzinos & De Hert 2022). In the nutshell, this article has provided a better understanding on the knowledge of depression and the potential biomarkers. However, a thorough systematic and meta-analysis study encompassing the variables behind depression and associated biomarkers could improve the research in the future.

ACKNOWLEDGEMENTS

Authors would like to express their gratitude to the Deanship of Scientific Research, Vice Presidency for Graduate Studies and Scientific Research, King Faisal University, Saudi Arabia for funding this study. This work was supported by the Deanship of Scientific Research, Vice Presidency for Graduate Studies and Scientific Research, King Faisal University, Saudi Arabia (Grant No: KFU242631).

All authors have no competing or conflicts of interest for this study. Author's contributions is as follows; RA: Conceptualization, Funding acquisition, Investigation, Project administration, Visualization, Resources, Writing–review and editing, Writing–original draft. ASAM: Supervision, Writing–review and editing, Writing–original draft, Data curation, Formal Analysis, Methodology, Resources, Writing–original draft.

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