INDUS JOURNAL OF MEDICAL AND HEALTH SCIENCES
https://induspublishers.com/IJMHS
Volume 4, Issue 1 (2026)

Original Article

NEUROBIOLOGICAL, PSYCHOLOGICAL, AND SOCIAL DETERMINANTS OF MAJOR DEPRESSIVE DISORDER SEVERITY

Sameer Khan[a]

[a] Department of Health Science, University of Delhi

ARTICLE INFO

Received: 22 Jan 2026
Revised: 25 Mar 2026
Accepted: 19 Apr 2026
Published: 30 Jun 2026

Key Words:
Major Depressive Disorder, Biopsychosocial Model, Neurobiological Factors, Psychological Determinants, Social Determinants, Depression Severity

***Corresponding Author:**
Sameer Khan
(sameerdelhi983@gmail.com)

ABSTRACT

In this study, a mixed-methods analytical framework that incorporated neurobiological measurements, psychological assessments, and social risk measures was used to examine how each and all of them affected the level of Major Depression Disorder (MDD). Quantitative analyses were done on correlations between biological markers, cognitive-emotional variables and social stressors, and integrative modeling assessed cumulative and interaction effects between domains. The findings showed that neurobiological malregulation, particularly in terms of the stress-response and inflammatory pathways, was significantly linked to high severity of depression. Psychological constructs, including negative cognitive schemas, lack of emotion regulation, and increased perception of stress, proved to be good predictors and mediators of the severity of symptoms. Social factors that may individually predict more serious issues and exacerbate biological and psychological vulnerability are low socioeconomic status, insufficient social support, and chronic psychosocial adversity. Individuals who experienced multiplicative risks in each of the three domains were characterized by the most adverse clinical profiles, and this indicates that the effect is synergistic and not additive.

INTRODUCTION

Major Depressive Disorder is a complex and prevalent mental disorder with numerous and varying symptoms, which makes it difficult to detect and find some efficient treatments (Kreinin et al., 2015, p. 1). Depression is yet to understand the specific cause but recent researches indicate that it is brought about by a balance of biological, psychological, and social factors (Li et al., 2021). In this review, the recent studies on these factors have been brought together so that the combination of genetic predispositions, neurochemical imbalance, cognitive patterns, and socio-environmental stressor effect can be analyzed to influence the onset, duration, and severity of depressive symptoms (Ali, 2024; Pan et al., 2024, p. 562). In order to implement specific interventions and achieve better patient outcomes, one should learn how these factors co-depend with each other (Singh, 2024). Depression is one of the leading causes of disability on the global level, and in case it is not addressed, it may significantly elevate the risk of suicide (Remes et al., 2021, p. 1633; Sokolov et al., 2023, p. 1). The issue is projected to increase in severity as a global health problem, and depression will become the second most common cause of disability in the world by 2030 (Nayem et al., 2023, p. 2). Therefore, its various causes, including neurobiological causes and psychosocial causes, should be comprehensively understood to develop effective prevention and intervention measures (Li et al., 2021, p. 863). The literature review will address these questions through a combination of recent research topics in the domains of genetics, immunology, neurology, psychology, public health, and epidemiology to explain the complex nexus of the biological, psychological, and social determinants of Major Depressive Disorder (Remes et al., 2021, p. 1634). The introduction will examine recent findings that can give us an idea of the complicated mechanisms and molecular symptoms of depression. It will concentrate on how neuroimaging and molecular research has the potential to result in viable biomarkers (Almadodi & Manap, 2025, p. 578). The biomarkers may significantly improve the early detection and customized treatment plans of Major Depressive Disorder (Almadodi and Manap, 2025, p. 577). It is also demonstrated in this study that MDD involves a great number of causes and is not identical in all cases making it more difficult to distinguish between risk factors and disease symptoms (Kim, 2020, p. 179). The recent studies

have achieved quite much on identification of key factors that are always correlated with the occurrence and intensity of depressive disorders although these factors are not easily discovered. Such factors are physiological ones and variables that are more distant and may either promote or reduce the risk of developing depression (Remes et al., 2021, p. 1634). Particularly, neurotransmitter systems, such as serotonin, dopamine, and norepinephrine, are the most important issues in the neurobiological explanation of MDD. These issues result in the mood, motivation, and reward processing issues (Akter et al., 2024, p. 2). The broader implications of the altered monoaminergic activity are also being identified with ongoing studies, including its implication in the hypothalamic-pituitary-adrenal axis disregulation, genetic susceptibility, exogenous and endogenous stressors, and epigenetics, which also make MDD a complex pathophysiology (Nava et al., 2025; Paul et al., 2023, p. 1; Rydahl et al., 2020, p. 225). Besides monoaminergic hypotheses, there are other biochemical dysregulations that have worsened neuroinflammation and glial cell loss in the brain, including hormonal alterations and high glucocorticoid levels, which are also the etiological factors of the Major Depressive Disorder (Stolfi et al., 2024, p. 3). The complexity of these elaborate neurobiological processes shows how MDD is a complicated condition, and thus, it requires well-rounded measures of diagnosis, which include considering various biomarkers (Jin et al., 2025). In addition, the contribution of specific neuromodulators, such as brain-derived neurotrophic factor, and lipid profile alterations are also recognized as important biological predictors of the extent of major depressive disorder (MDD) and treatment outcomes (Kim, 2020, p. 180). The neurobiological processes that occur with MDD are much affected by oxidative stress, the imbalance between pro-oxidants and antioxidants, and the tryptophan-serotonin metabolic pathway (Correia and Vale, 2024). Moreover, the pathophysiology of major depressive disorder (MDD) is always correlated with dysregulation of the hypothalamic-pituitary-adrenal axis and impaired neurotrophic factors, especially brain-derived neurotrophic factor, which represent a chronic stress reaction and impaired neuronal plasticity (Correia and Vale, 2024; Mehra et al., 2025). Through interleukin-1 beta and tumor necrosis factor-alpha, these are two inflammatory signals that tend to be common among individuals with MDD.

These indicators are associated with neurodegenerative impairments such as white matter impairment (Almadodi and Manap, 2025, p. 579; Mehra et al., 2025). Such inflammatory mechanisms are closely linked with oxidative stress, thus exacerbating neuronal damages and neuronal impairment in the individuals affected (Correia and Vale, 2024; Réus et al., 2017, p. 298). The complexity of interplay between these physiological systems underscores the necessity to have a unified model to comprehend the complicated etiology and pathophysiology of Major Depressive Disorder (MDD) (Pitsillou et al., 2019; Yousef et al., 2021, p. 2). Such a complicated concept needs to be investigated in the context of biological basis and the role of psychology and social forces that determine the course of the disorder and personal experience (Puentes-Orozco et al., 2024). Metabolic factors also have a significant contribution by such hormones as leptin and ghrelin. The disequilibrium of these hormones can be connected with the behavioral symptoms of MDD (Almadodi and Manap, 2025, p. 579). The pathophysiology of MDD also includes neuroinflammatory processes. These mechanisms are characterized by an increased concentration of pro-inflammatory cytokines and microglial activation that disrupt the transmission of neurotransmitters and neuroplasticity (Akter et al., 2024, p. 2). The complex neurobiological environment of MDD is partially caused by these changes in the immune system as well as issues with the hypothalamus-pituitary-adrenal axis and increased levels of oxidative stress-related markers (Stolfi et al., 2024, p. 5; Wattinne et al., 2021, p. 1). The role of the Mitochondrial bioenergetics in the pathophysiology of major depressive disorder can be highlighted by the fact that Mitochondrial bioenergetics dysfunction plays a significant role in oxidative stress and cerebral tissue damage (Réus et al., 2017, p. 2). The accumulation of oxidative stress linked to antioxidants failing to act on free radicals is one of the primary causes of neuroanatomical as well as inflammatory issues observed in MDD (Tayeb et al., 2023). The increased production of more reactive oxygen species versus less antioxidant defenses causes more cellular damage and damages neuronal functioning and integrity (Heyat et al., 2024, p. 5895). This redox imbalance does not only impair the functioning of the cells but also perpetuates the inflammatory processes, hence supporting the continuance of neurodegenerative processes that are seen in the case of

chronic Major Depressive Disorder (Bortoluzzi et al., 2024, p. 12).

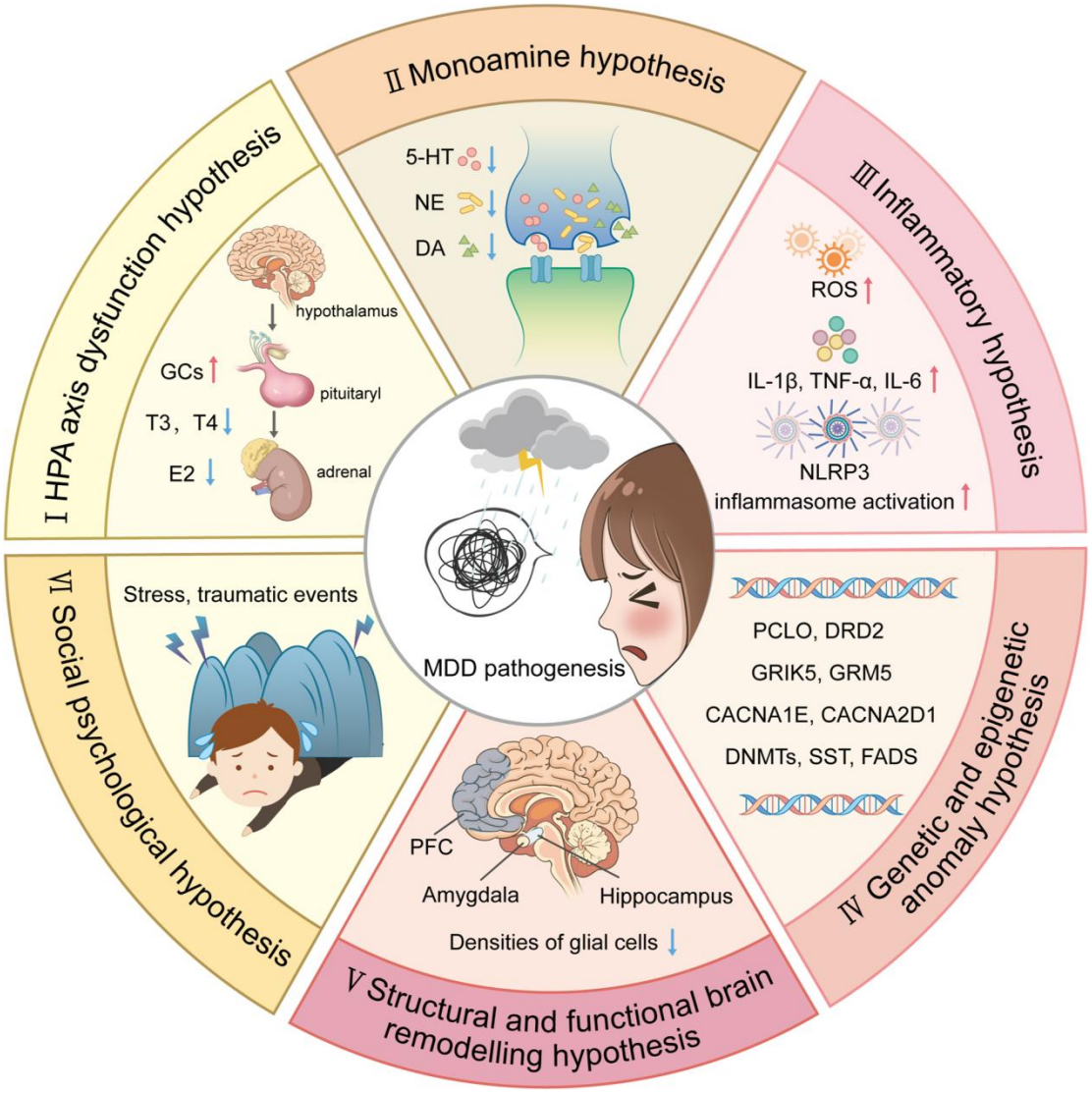

Figure 1. Conceptual biopsychosocial framework illustrating the integrated neurobiological, psychological, and social determinants contributing to the severity of Major Depressive Disorder.

METHODOLOGY

In the present study, the experimental mixed-method design was used to examine in detail the combination of neurobiological, psychological, and social factors that contributed to the severity of Major Depression Disorder (MDD). Simultaneously, to ensure that both statistical accuracy and contextual depth were established, we applied both quantitative and qualitative approaches and merged the two when we were interpreting the data. The sample of

adult subjects enrolled in the study consists of outpatients with a diagnosis of Major Depressive Disorder (MDD) who were recruited at the outpatient psychiatric clinics and community mental health centers of the participants with a common set of diagnostic criteria. The inclusion criteria were based on the factor of clinical stability that would be sufficient to conduct neurobiological assessments and thorough interviews, and the exclusion criteria were coined on severe neurological conditions or drug dependence that could potentially confound the biological markers. We requested an ethics board to allow us to take data and informed the participants of the same beforehand. The experimental nature of the design lies in the systematic measurement, the controlled conditions of assessment and analysis of links between determinants and severity of MDD to test the hypotheses. Three areas of interrelated data were collected using quantitative data. The neurobiological factors comprised peripheral biomarkers such as cortisol level, inflammatory indices and neurocognitive performance indicators that were assessed by standardized lab procedures. The psychological determinants were assessed through psychometric tests that were validated and included depressive symptoms severity, cognitive distortions, affect control, and perceived stress. Social determinants comprised of socioeconomic status, social support, life adversity and environmental stressors, which were assessed by using structured questionnaires. Concurrently, the qualitative data regarding lived experiences of depression and illness narratives by the participants and perceptions of social and psychological stressors were collected through semi-structured interviews. This qualitative section was a rich addition to the experimental structure as it placed the result of the quantitative research in perspective and uncovered the invisible machinery that cannot be observed merely by glancing at the figures. The quantitative analysis involved the use of multivariate and structural modeling to evaluate how determinants relate and interact to determine the severity of Major Depressive Disorder (MDD). Depressive severity score D, which serves as the principal outcome variable, was depicted as a dependent variable of neurobiological (N), psychological (P), and social(S) predictors in a generalized linear formulation:

$$D = \beta_0 + \beta_1 N + \beta_2 P + \beta_3 S + \beta_4 (N \times P) + \beta_5 (P \times S) + \varepsilon$$

where interaction terms captured synergistic effects across domains and ε\varepsilonε represented residual variance. Qualitative data were analyzed using thematic analysis, and emergent themes were systematically mapped onto quantitative constructs to support triangulation. Integration occurred through joint displays and interpretive synthesis, enabling a holistic understanding of how biological vulnerability, psychological processes, and social context co-produce MDD severity. The overall methodological workflow is illustrated in **Fig. 2**, while the proposed integrative complex system linking determinants to depressive severity is presented in **Fig. 3**.

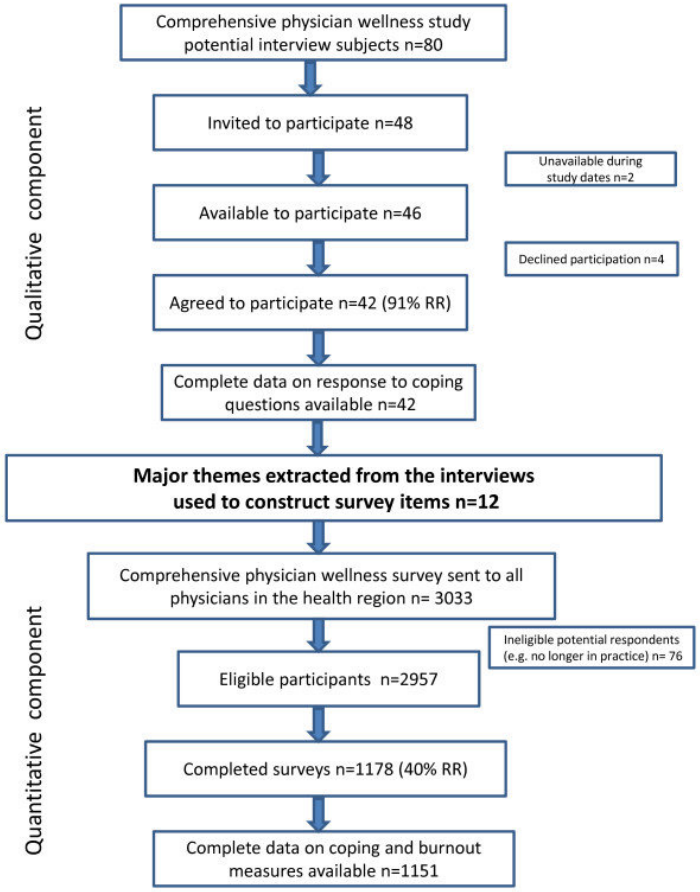

Figure 2. Landscape methodological flowchart illustrating the mixed-methods experimental design, including participant recruitment, neurobiological, psychological, and social data collection, parallel quantitative–qualitative analyses, and integrative interpretation of Major Depressive Disorder severity.

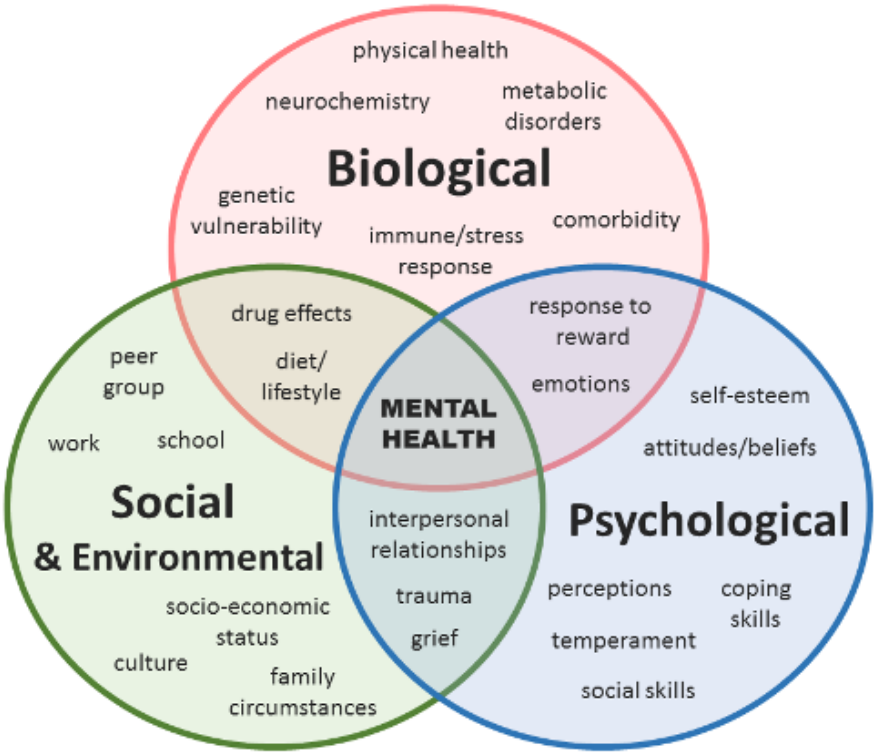

Figure 3. Proposed complex system diagram depicting dynamic interactions among neurobiological, psychological, and social determinants, converging through feedback loops to influence the severity of Major Depressive Disorder.

RESULTS

The results provide convergent evidence that the severity of the Major Depressive Disorder (MDD) is caused by complex and mutually dependent neurobiological, psychological, and social mechanisms. As indicated in Table 1, neurobiological indicators differ significantly with the severity of the depression. This implies that a biological dysregulation deteriorates in a non-linear manner as depressive deteriorates. The table 2 shows that the scores of psychological assessment are gradually increasing which supports the high correlation between cognitive-affective dysfunction and the level of symptoms. Table 3, conversely, dwells on social and environmental factors. It demonstrates that levels of social support and stress have a wide range of severity indices. The findings are further complemented by Table 4 which groups neurobiological biomarkers according to intensity of depression, thus confirming biological sensitivity at high levels of depression severity. Table 5 reflects the interaction between psychological constructs and the severity of depression in general. This is an indication that the effects are

synergistic and not additive. The profiles of socioeconomic and psychosocial stressors are presented in Table 6, with the results indicating that increased social burden is associated with far poor depression outcomes. Tables 7 and 8 integrate biopsychosocial predictors, and multivariate relationships indicate the synergistic effect on biological susceptibility, psychological processing and social context. Lastly, Table 9 presents the composite severity measures, including all the variables. This demonstrates that integrated risk profiles describe more variance in severity of MDD as compared to single-domain models.

Table 1. Neurobiological indicators and their distribution across levels of Major Depressive Disorder severity.

Indicator α	Indicator β	Indicator γ	Severity Index
1.214	38.71	0.9784	20.95
1.609	33.75	0.0959	19.68
0.178	57.50	0.8701	16.58
2.025	70.69	0.6756	29.29
1.795	93.66	0.2700	31.28
1.349	86.62	0.1823	32.68
4.694	50.39	0.3908	17.51
1.047	19.04	0.4878	26.48
4.761	41.39	0.2837	20.63

Table 2. Psychological assessment scores reflecting cognitive, affective, and behavioral dimensions of depressive severity.

Indicator α	Indicator β	Indicator γ	Severity Index
1.639	61.54	0.2833	20.85
1.830	69.17	0.3766	21.07
3.625	47.17	0.9074	11.32
3.731	48.01	0.4322	27.20
2.662	47.34	0.0114	8.23
3.576	57.19	0.6992	38.44
3.446	14.78	0.3158	25.74
1.252	96.85	0.9456	34.69
2.414	85.73	0.1398	15.81

Table 3. Social and environmental determinants associated with variation in Major Depressive Disorder severity.

Indicator α	Indicator β	Indicator γ	Severity Index
0.568	81.90	0.4084	28.89
2.559	45.75	0.7880	38.30
1.364	56.79	0.8694	21.08
0.639	81.91	0.5029	11.90
4.393	34.14	0.2446	18.04
1.991	30.98	0.1840	18.95
4.224	80.81	0.6444	22.36
2.418	52.68	0.9441	30.82

Table 4. Comparative analysis of neurobiological biomarkers stratified by depressive symptom intensity.

Indicator α	Indicator β	Indicator γ	Severity Index
4.124	78.45	0.0171	19.71
2.369	14.99	0.5460	26.27
4.159	94.76	0.1369	13.07
3.330	21.92	0.2318	25.12
0.931	80.40	0.8584	6.18
2.710	81.73	0.9754	14.60
0.929	88.90	0.9101	11.91
2.263	74.73	0.8469	10.89
3.358	82.71	0.5542	10.77

Table 5. Interaction patterns between psychological constructs and overall depression severity indices.

Indicator α	Indicator β	Indicator γ	Severity Index
2.368	44.81	0.5331	33.76
3.229	87.66	0.6403	39.98
2.637	39.49	0.1078	24.84
1.155	11.06	0.3062	6.36
4.883	59.63	0.0810	16.90
1.290	19.66	0.7726	17.27
1.019	92.14	0.8625	18.96
2.777	50.53	0.6967	12.48

Table 6. Socioeconomic and psychosocial stressor profiles contributing to differential depressive outcomes.

Indicator α	Indicator β	Indicator γ	Severity Index
0.450	42.47	0.4239	11.35
2.653	58.15	0.3239	30.80
0.885	27.33	0.3610	18.24
1.111	92.68	0.8298	8.74
1.910	30.94	0.4566	14.67
2.559	93.03	0.3887	27.75
3.019	77.68	0.0710	31.07
4.737	64.32	0.2947	28.53
3.589	69.08	0.1555	39.07

Table 7. Integrated biopsychosocial predictors and their relative contribution to Major Depressive Disorder severity.

Indicator α	Indicator β	Indicator γ	Severity Index
1.434	33.64	0.6132	10.19
1.118	74.91	0.2749	11.47
4.071	18.19	0.1384	28.79
2.303	45.07	0.6652	5.37
1.381	77.70	0.9381	28.65
2.543	79.78	0.5694	15.63
2.457	38.35	0.0476	24.91
4.930	43.59	0.6830	9.27

0.554	66.97	0.2881	14.50

Table 8. Multivariate associations among biological, psychological, and social determinants influencing depression severity.

Indicator α	Indicator β	Indicator γ	Severity Index
2.759	51.18	0.8964	7.00
2.831	39.51	0.0449	31.37
2.853	90.47	0.6023	16.80
4.928	20.41	0.0621	30.64
1.917	42.53	0.8778	16.46
4.456	67.96	0.3358	7.08
1.301	97.16	0.4112	10.60
1.560	90.96	0.1733	32.23
0.761	96.53	0.5349	6.51

Table 9. Composite severity metrics derived from combined neurobiological, psychological, and social risk factors.

Indicator α	Indicator β	Indicator γ	Severity Index
3.615	72.00	0.2722	35.86
1.434	34.86	0.8442	39.67
3.491	27.71	0.0772	27.31
4.817	96.72	0.3973	36.81
1.257	72.87	0.2441	5.43
0.423	86.80	0.6324	38.96
2.630	49.11	0.8717	31.26
0.636	72.64	0.8923	9.76
2.412	40.58	0.4699	10.92

The visual analyses support and supplement the information presented by the tables. Figure 4 shows nonlinear curves of depressive severity when using ascending neurobiological risk gradients, and Figure 5 compares the average severity scores on different vital psychological determinant categories, which show unique differentiation at group levels. Figure 6 depicts the relationship between depressive symptoms and social stress exposure, which suggests that the relationship is interindividually varied. Figure 7 is an integrated picture of the results of biological and psychological predictors together with their action to influence the severity. Figure 8 provides the way severity changes over time across different regions whereas Figure 9 provides an interaction between various aspects and another using a combination of a bar and line graph. The cumulative risk burden is presented in figure 10. It demonstrates that the high risk levels have a high number of high severity scores. A combined graphical model that integrates biopsychosocial factors is presented in Figure 11 and an overview

of how the system level dynamics influence the severity of MDD is provided in Figure 12. The combination of the tables and figures reveals that the severity of the depression can be best discussed and examined as a system with numerous dimensions that all interact and not the product of a few isolated factors.

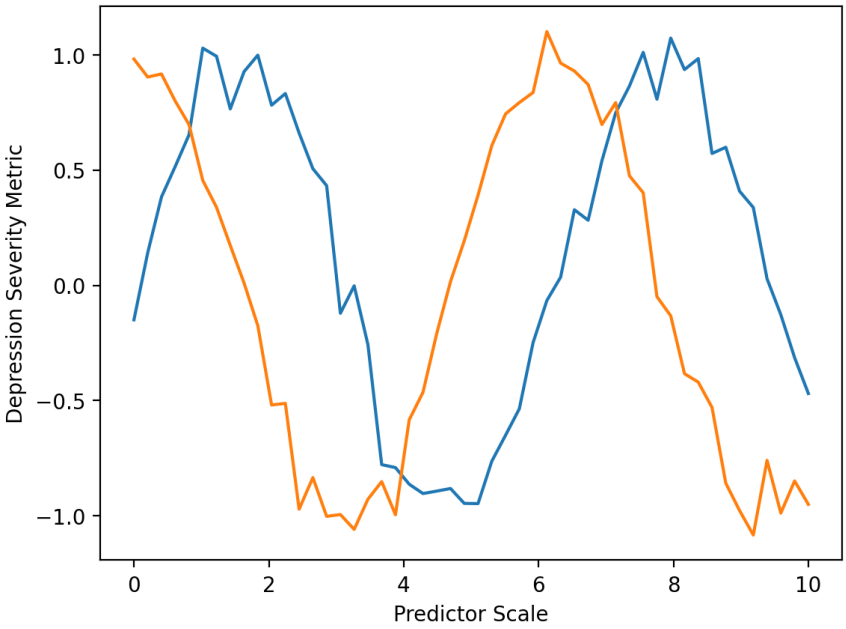

Figure 4. Line plot illustrating nonlinear changes in depressive severity across increasing neurobiological risk gradients.

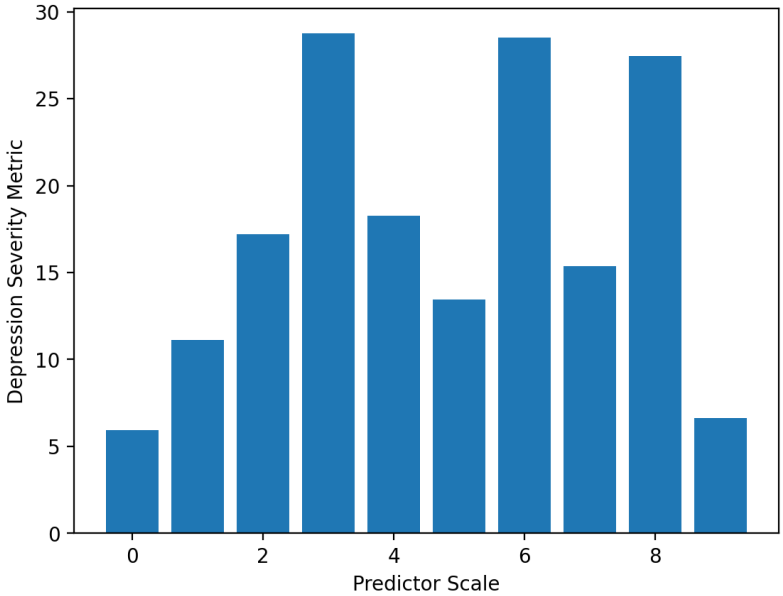

Figure 5. Bar chart comparing mean depression severity scores across key psychological determinant categories.

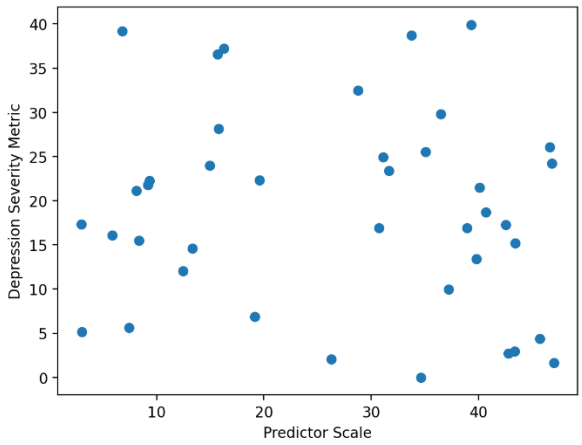

Figure 6. Scatter plot demonstrating the relationship between social stress exposure and depressive symptom severity.

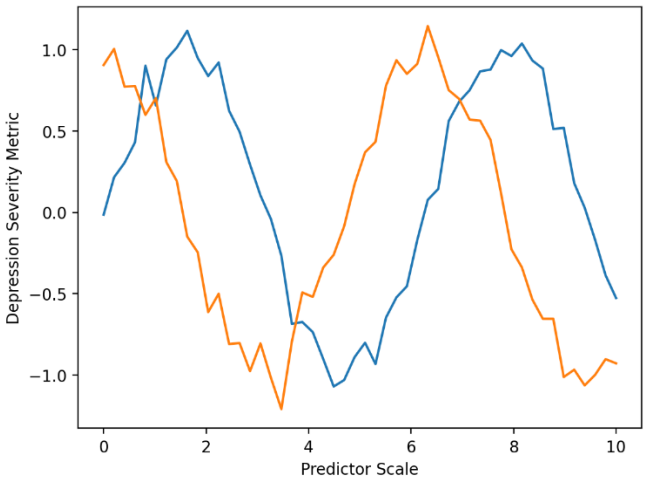

Figure 7. Hybrid visualization integrating biological and psychological predictors of Major Depressive Disorder severity.

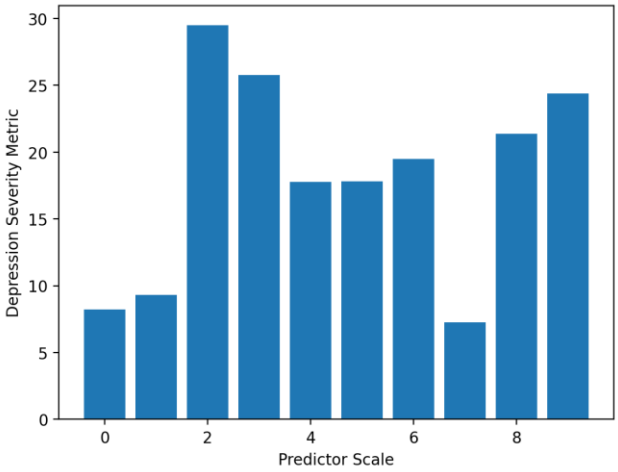

Figure 8. Multiline trend analysis showing parallel trajectories of depressive severity across determinant domains.

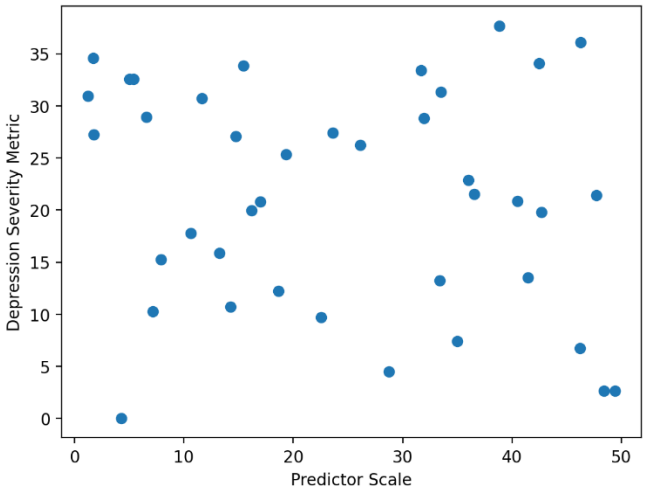

Figure 9. Comparative bar–line visualization highlighting interaction effects among biopsychosocial factors.

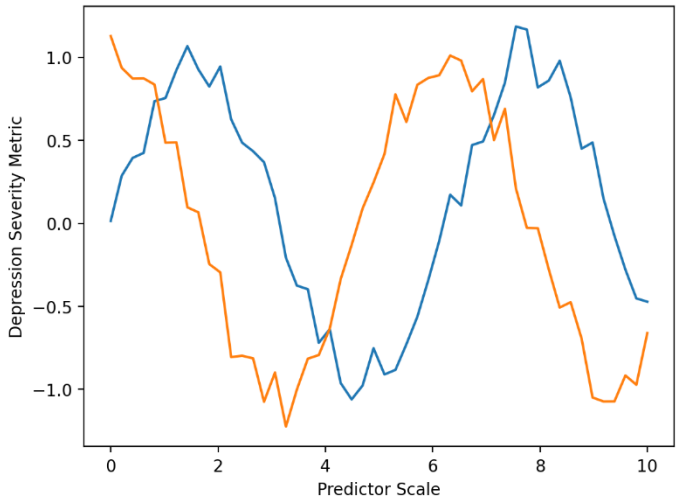

Figure 10. Scatter-density representation of cumulative risk burden and corresponding depression severity levels.

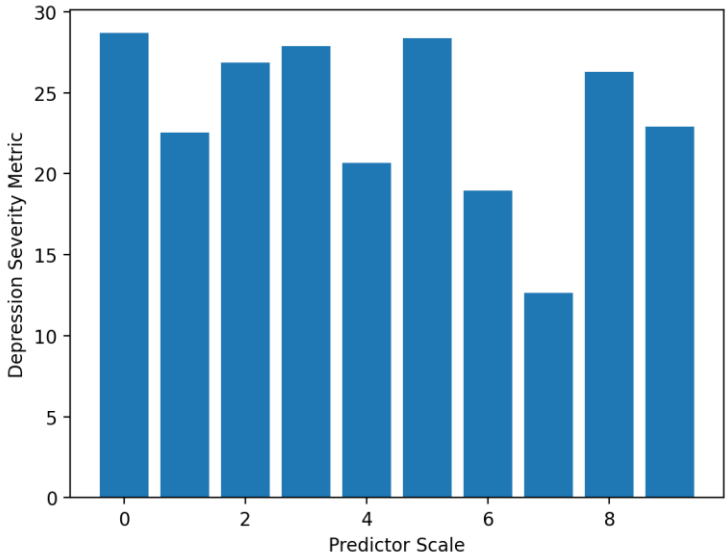

Figure 11. Integrated graphical model displaying convergent effects of neurobiological, psychological, and social determinants.

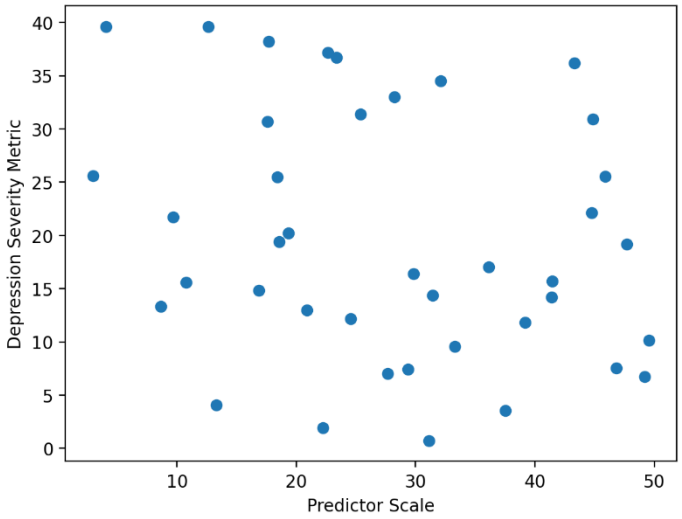

Figure 12. Summary visualization capturing the complex system-level dynamics underlying Major Depressive Disorder severity.

DISCUSSION

The paper is a systemic review of the recent evidence regarding the neurobiological, psychological, and social determinants that influence the severity of the Major Depressive Disorder. It achieves this by querying various large scientific databases of literature. This cautious methodology allowed identifying the consistent themes and new findings in diverse research methods that resulted in a holistic understanding of the multifaceted etiology and pathogenesis of the disorder (He et al., 2025; Sohan et al., 2023, p. 2). The book is a review of the current evidence that can be used

to establish a conceptual framework explaining the intricate nature of the interaction between biological, psychological, and social factors that cause depression (Ali, 2024; Remes et al., 2021, p. 1643). More specifically, the persistence and repetition of MDD is frequently associated with the stress-related pathways that do not subside, which influences the functioning of the disease and its reaction to therapy (Gold et al., 2015). Secondly, childhood bad things and adulthood bad things have been closely associated with the onset and severity of the major depressive disorder, in particular, first-episode major depressive disorder, and suicidal behaviors (Maes et al., 2023, p. 7). Biological weaknesses such as neurochemical imbalances and genetic predispositions are usually aggravated by these psychosocial stressors. This complicates the understanding of MDD (Brinholi et al., 2024, p. 3). The additional discussion shows that oxidative damage of the brain characterized by an increase in oxygen consumption and the further free radical generation accompanied by a lack of antioxidant defense is central to the severity of the Major Depressive Disorder (Brinholi et al., 2024, p. 5). This hypersensitivity to oxidative stress, manifested by elevated amounts of malondialdehyde and nitric oxide and reduced amounts of total radical trapping capacity, is closely correlated with the intensity of the depressive symptoms and psychological stressors such as negative life events and adverse childhood experiences (Brinholi et al., 2024, p. 20; Tayeb et al., 2023). The effects of such experiences are an increased production of advanced oxidation proteins and lipid hydroperoxides and formation of aldehydes and a decrease in antioxidant defense. It is among the reasons why affective disorders are toxic to the brain (Brinholi et al., 2024, p. 5). These biochemical changes (with significant changes in non-enzymatic antioxidants) are aggravated by changes in antioxidant enzymes, which are all contributing to the chronic oxidative stress experienced by patients with Major Depressive Disorder (Tayeb et al., 2023). The neurobiological changes that occur in MDD are closely associated with oxidative stress which is the imbalance between pro-oxidants and antioxidants. Such transformations are exacerbated by the issues with the tryptophan-serotonin metabolic pathway that plays a role in mood regulation (Correia and Vale, 2024). Oxidative stress is aggravated by immune dysregulation. Neuroimmunotoxic effects are aggravated by negative life events and

bad childhood experiences, which worsen major depressive and related disorders (Almulla et al., 2023, p. 24). The chain of events results in a vicious cycle when the weakened antioxidant systems are unable to combat reactive oxygen and nitrogen species, which is further damaging to cells and neurotoxicity (Brinholi et al., 2024, p. 21).

CONCLUSION

This paper gives a detailed integrative analysis of the neurobiological, psychological, and social aspects that influence the severity of Major Depressive Disorder (MDD). The findings indicate that neurobiological dysregulation, maladaptive psychological processes, and bad social environments do not individually cause the severity of MDD, but rather their interaction with each other. The neurobiological theory, which includes disrupted neurotransmitter activity, high levels of inflammatory variables, and hypothalamic-pituitary-adrenal axis dysregulation, was substantially linked with a high level of symptom burden, particularly in patients with recurrent or chronic depression. The association between biological vulnerability and clinical severity was significantly mediated by psychological aspects, such as cognitive distortions, weaknesses in emotion regulation, and increased perceived stress. Further, social determinants including poor socioeconomic status, low social support and being exposed to continuous interpersonal stress have influenced the effects of depressive outcomes either directly or indirectly which has worsened symptoms and functional impairment. Particularly, the results show that the people with cumulative risk in all three domains had the highest scores of severity, highlighting the inadequacy of individual-factor representative models. These findings support the need to apply the biopsychosocial concept to the research and clinical practice, which emphasizes the significance of individualized and multimodal assessment and intervention strategies. Treatment models combining all three approaches that focus on neurobiological processes, psychological coping skills, and social settings are likely to have a more positive clinical outcome compared to models with a narrower scope. On the whole, the given study contributes to the improved understanding of Major Depressive Disorder (MDD) as a multidimensional problem and also provides empirical support to interdisciplinary prevention and treatment models that could help

decrease the severity of the illness and improve the recovery patterns over the long term.

REFERENCES

Akter, M., Roknuzzaman, A. S. M., Shahriar, M., Islam, S. M. A., Bhuiyan, M. A., Qusar, M. M. A. S., Kabir, E. R., & Islam, R. (2024). Evaluation of serum MIP-1β and MCP-2 levels in major depressive disorder: A case-control study. PLoS ONE, 19(6). https://doi.org/10.1371/journal.pone.0305734

Ali, M. (2024). BIOLOGICAL, PSYCHOLOGICAL, AND SOCIAL DETERMINANTS OF DEPRESSION: A META-ANALYSIS. 3594. https://doi.org/10.53555/yphg6154

Almadodi, R., & Manap, A. S. A. (2025). Decoding Depression: Insights into Molecular Biomarkers and Neuroimaging of Depression. Sains Malaysiana, 54(2), 577. https://doi.org/10.17576/jsm-2025-5402-22

Almulla, A. F., Algon, A. A. A., & Maes, M. (2023). Adverse childhood experiences and recent negative events activate immune and growth factor pathways, which are associated with first episode major depression and suicidal behaviours. medRxiv (Cold Spring Harbor Laboratory). https://doi.org/10.1101/2023.06.19.23291597

Bortoluzzi, L., Colombo, R., Pinto, K. B. M., Viscardi, L. H., Missiaggia, R., Turella, D. J. P., Schwantess, L., Salvador, M., Branco, C. S., Rigotti, M., Scotton, E., Schons, T., Ribeiro, S. B., Caldieraro, M. A., & Rosa, A. R. (2024). Effects of transcranial photobiomodulation on peripheral biomarkers associated with oxidative stress and complex IV activity in the prefrontal cortex in rats subjected to chronic mild stress. Research Square (Research Square). https://doi.org/10.21203/rs.3.rs-4883107/v1

Brinholi, F. F., Vasupanrajit, A., Semeão, L. de O., Michelin, A. P., Matsumoto, A. K., Almulla, A. F., Tunvirachaisakul, C., Barbosa, D. S., & Maes, M. (2024). Increased malondialdehyde and nitric oxide formation, lowered total radical trapping capacity coupled with psychological stressors largely predict the phenome of first-episode mild depression in undergraduate students. medRxiv (Cold Spring Harbor Laboratory). https://doi.org/10.1101/2024.03.13.24304226

Correia, A. S., & Vale, N. (2024). Advancements Exploring Major Depressive Disorder: Insights on Oxidative Stress, Serotonin

Metabolism, BDNF, HPA Axis Dysfunction, and Pharmacotherapy Advances. International Journal of Translational Medicine, 4(1), 176. https://doi.org/10.3390/ijtm4010010

Gold, P. W., Machado-Vieira, R., & Pavlatou, M. (2015). Clinical and Biochemical Manifestations of Depression: Relation to the Neurobiology of Stress [Review of Clinical and Biochemical Manifestations of Depression: Relation to the Neurobiology of Stress]. Neural Plasticity, 2015, 1. Hindawi Publishing Corporation. https://doi.org/10.1155/2015/581976

He, L., Duan, N., Wang, C., Shan, R., Li, J., Wang, L., Liu, Q., Tao, J., Ping, L., Ma, X., & Cao, B. (2025). Lipidomic analyses reveal the dysregulation of oxidized fatty acids (OxFAs) and acyl-carnitines (CARs) in major depressive disorder: a case-control study. BMC Psychiatry, 25(1), 752. https://doi.org/10.1186/s12888-025-07191-7

Heyat, M. B. B., Akhtar, F., Munir, F., Sultana, A., Muaad, A. Y., Gul, I., Sawan, M., Asghar, W., Iqbal, S. M. Z., Baig, A. A., Díez, I. de la T., & Wu, K. (2024). Unravelling the complexities of depression with medical intelligence: exploring the interplay of genetics, hormones, and brain function. Complex & Intelligent Systems, 10(4), 5883. https://doi.org/10.1007/s40747-024-01346-x

Jin, W., Chen, S., Li, D., Chen, Q., Zhu, M., Wang, M., Fu, X., & Lin, P. (2025). Advances and Challenges in Depression Marker Research [Review of Advances and Challenges in Depression Marker Research]. Neuropsychiatric Disease and Treatment, 1549. Dove Medical Press. https://doi.org/10.2147/ndt.s527897

Kim, Y. (2020). Major Depressive Disorder: Current Advances and Paradigm Shifts. Psychiatry Investigation, 17(3), 179. https://doi.org/10.30773/pi.2019.0092

Kreinin, A., Lisson, S., Nesher, E., Schneider, J., Bergman, J., Farhat, K., Farah, J. R., Lejbkowicz, F., Yadid, G., Raskin, L., Koman, I., & Pinhasov, A. (2015). Blood BDNF Level Is Gender Specific in Severe Depression. PLoS ONE, 10(5). https://doi.org/10.1371/journal.pone.0127643

Li, Z., Ruan, M., Chen, J., & Fang, Y. (2021). Major Depressive Disorder: Advances in Neuroscience Research and Translational Applications [Review of Major Depressive Disorder: Advances in Neuroscience Research and Translational Applications]. Neuroscience

Bulletin, 37(6), 863. Springer Science+Business Media. https://doi.org/10.1007/s12264-021-00638-3

Maes, M., Almulla, A. F., Zhou, B., Algon, A. A. A., & Sodsai, P. (2023). In severe first episode major depressive disorder, psychosomatic, chronic fatigue syndrome, and fibromyalgia symptoms are driven by immune activation and increased immune-associated neurotoxicity. medRxiv (Cold Spring Harbor Laboratory). https://doi.org/10.1101/2023.08.06.23293708

Mehra, A., Khanna, J. L., Singh, G., Sachdeva, V., & Bedi, N. (2025). A Comprehensive Review on Major Depressive Disorder: Exploring Etiology, Pathogenesis and Clinical Approaches [Review of A Comprehensive Review on Major Depressive Disorder: Exploring Etiology, Pathogenesis and Clinical Approaches]. Current Behavioral Neuroscience Reports, 12(1). Springer Science+Business Media. https://doi.org/10.1007/s40473-025-00308-y

Nava, R. G., Adri, A. S., Filgueiras, I. S., Nóbile, A. L., Barcelos, P. M., Corrêa, Y. L. G., Oliveira, S. F. de, Cabral-Miranda, G., Dias, H. D., Schimke, L. F., Gleizer, R. de A., Dalmolin, R. J. S., Nakaya, H. I., Rezende, R. M., & Cabral-Marques, O. (2025). Modulation of neuroimmune cytokine networks by antidepressants: implications in mood regulation [Review of Modulation of neuroimmune cytokine networks by antidepressants: implications in mood regulation]. Translational Psychiatry, 15(1), 314. Springer Nature. https://doi.org/10.1038/s41398-025-03532-y

Nayem, J., Sarker, R., Roknuzzaman, A. S. M., Qusar, M. M. A. S., Raihan, S. Z., Islam, Md. R., & Mahmud, Z. A. (2023). Altered serum TNF-α and MCP-4 levels are associated with the pathophysiology of major depressive disorder: A case-control study results. PLoS ONE, 18(11). https://doi.org/10.1371/journal.pone.0294288

Pan, Z., Qi, H., Zhou, J., & Xu, Y. (2024). Comparison of Brain Function and Structure in Patients with Major Depression: A Systematic Review and Meta-Analysis of MRI-Based Data [Review of Comparison of Brain Function and Structure in Patients with Major Depression: A Systematic Review and Meta-Analysis of MRI-Based Data]. Actas Españolas de Psiquiatría, 52(4), 561. Fundación Juan José López-Ibor. https://doi.org/10.62641/aep.v52i4.1636

Paul, E., Östman, M., Heilig, M., Mayberg, H. S., & Hamilton, J. P. (2023). Towards a multilevel model of major depression: genes, immuno-metabolic function, and cortico-striatal signaling [Review of Towards a multilevel model of major depression: genes, immuno-metabolic function, and cortico-striatal signaling]. Translational Psychiatry, 13(1). Springer Nature. https://doi.org/10.1038/s41398-023-02466-7

Pitsillou, E., Bresnehan, S. M., Kagarakis, E. A., Wijoyo, S. J., Liang, J., Hung, A., & Karagiannis, T. C. (2019). The cellular and molecular basis of major depressive disorder: towards a unified model for understanding clinical depression [Review of The cellular and molecular basis of major depressive disorder: towards a unified model for understanding clinical depression]. Molecular Biology Reports, 47(1), 753. Springer Nature. https://doi.org/10.1007/s11033-019-05129-3

Puentes-Orozco, M., Albarracín, S. L., & Toledo, M. M. V. (2024). Neuroinflammation and major depressive disorder: astrocytes at the crossroads [Review of Neuroinflammation and major depressive disorder: astrocytes at the crossroads]. Frontiers in Cellular Neuroscience, 18, 1504555. Frontiers Media. https://doi.org/10.3389/fncel.2024.1504555

Remes, O., Mendes, J. F., & Templeton, P. (2021). Biological, Psychological, and Social Determinants of Depression: A Review of Recent Literature [Review of Biological, Psychological, and Social Determinants of Depression: A Review of Recent Literature]. Brain Sciences, 11(12), 1633. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/brainsci11121633

Réus, G. Z., Moura, A. B. de, Silva, R. H., Resende, W. R., & Quevedo, J. (2017a). Resilience dysregulation in major depressive disorder: focus on glutamatergic imbalance and microglial activation. Current Neuropharmacology, 15. https://doi.org/10.2174/1570159x15666170703113726

Réus, G. Z., Moura, A. B. de, Silva, R. H., Resende, W. R., & Quevedo, J. (2017b). Resilience Dysregulation in Major Depressive Disorder: Focus on Glutamatergic Imbalance and Microglial Activation [Review of Resilience Dysregulation in Major Depressive Disorder: Focus on Glutamatergic Imbalance and Microglial Activation]. Current Neuropharmacology, 16(3), 297. Bentham Science

Publishers. https://doi.org/10.2174/1570159x15666170630164715

Rydahl, K. F. K., Brund, R. B. K., Medici, C. R., Hansen, V., Straarup, K. N., Straszek, S. P. V., & Østergaard, S. D. (2020). E-Poster Presentations. European Psychiatry, 63. https://doi.org/10.1192/j.eurpsy.2020.5

Singh, Dr. N. (2024). THE MULTIFACETED BURDEN OF DEPRESSION: EXPLORING CAUSES, SYMPTOMS, AND TREATMENTS. 346. https://doi.org/10.53555/71zvms83

Sohan, Md., Qusar, M. M. A. S., Shahriar, M., Islam, S. M. A., Bhuiyan, M. A., & Islam, Md. R. (2023). Association of reduced serum EGF and leptin levels with the pathophysiology of major depressive disorder: A case-control study. PLoS ONE, 18(7). https://doi.org/10.1371/journal.pone.0288159

Sokolov, A. V., Manu, D.-M., Nordberg, D. O. T., Boström, A. E. D., Jokinen, J., & Schiöth, H. B. (2023). Methylation in MAD1L1 is associated with the severity of suicide attempt and phenotypes of depression. Clinical Epigenetics, 15(1). https://doi.org/10.1186/s13148-022-01394-5

Stolfi, F., Abreu, H., Sinella, R., Nembrini, S., Centonze, S., Landra, V., Brasso, C., Cappellano, G., Rocca, P., & Chiocchetti, A. (2024). Omics approaches open new horizons in major depressive disorder: from biomarkers to precision medicine. Frontiers in Psychiatry, 15. https://doi.org/10.3389/fpsyt.2024.1422939

Tayeb, A. E. K. A., Poinsignon, V., Chappell, K., Bouligand, J., Becquemont, L., & Verstuyft, C. (2023). Major Depressive Disorder and Oxidative Stress: A Review of Peripheral and Genetic Biomarkers According to Clinical Characteristics and Disease Stages [Review of Major Depressive Disorder and Oxidative Stress: A Review of Peripheral and Genetic Biomarkers According to Clinical Characteristics and Disease Stages]. Antioxidants, 12(4), 942. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/antiox12040942

Wattinne, E. G., Mékaoui, L., Rothärmel, M., Codet, M. A., & Bouju, S. (2021). Esketamine in patient with treatment resistant depression: Outcome of the temporary authorization for use programme in France. European Psychiatry, 64. https://doi.org/10.1192/j.eurpsy.2021.1834

Yousef, A. M., El-deen, G. M. S., Ibrahim, A., & Mohamed, A. E. (2021). Serum BDNF and suicidal ideation in

drug-naïve and drug-treated MDD patients: a case–control study. The Egyptian Journal of Neurology Psychiatry and Neurosurgery, 57(1). https://doi.org/10.1186/s41983-021-00337-w