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Original Article

The Interaction of EBV-Derived MicroRNAs with Bipolar Disorder-Associated Genes: Insights from Bioinformatics

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Abstract

Background and Aims: Bipolar disorder (BD) is a complex psychiatric condition characterized by episodes of mania and depression. While genetic factors contribute significantly to BD, they do not fully account for the disorder's variability, suggesting that additional elements, such as infections and immune dysregulation, may play a role. Recent studies have implicated Epstein-Barr virus (EBV) in various psychiatric conditions due to its ability to produce microRNAs (miRNAs) that influence host gene expression. However, the specific interactions between EBV miRNAs and BD-related genes remain underexplored. This study aims to investigate the potential interactions between EBV-derived miRNAs and genes associated with BD, using both text-mining and experimental data to identify relevant gene targets.

Material and methods: We utilized data from the VirMirna database to identify EBV miRNAs and their target genes in human cells. Additionally, genes associated with BD were sourced from the DISEASES database, with data filtered to ensure medium to high confidence associations. Using network analysis in Cytoscape, we explored the interactions between EBV miRNAs and BD-related genes. Genes were further categorized based on their regulation status (upregulation, downregulation, dysregulation) in BD.

Results: The analysis identified 21 unique EBV miRNAs targeting 30 BD-associated genes. Of these, 27 genes were linked through text-mining data, while 3 genes had evidence from both text-mined and experimental sources. Key findings include that miRNAs such as ebv-miR-bart22 and ebv-miR-bart19-3p target multiple genes, suggesting broader regulatory influence. Genes impacted by these miRNAs include those involved in neurotransmitter pathways, neuroplasticity, and immune responses, potentially contributing to the pathophysiology of BD.

Conclusions: This study highlights the potential role of EBV miRNAs in modulating gene expression related to BD, suggesting that viral factors could influence the disorder's onset and severity. The findings open new avenues for therapeutic strategies aimed at mitigating the impact of EBV miRNAs on psychiatric health. Further research is necessary to confirm these interactions and explore their clinical implications.

Keywords: Bipolar disorder, Epstein-Barr virus, microRNAs, Gene regulation, Psychiatric disorders, Neuroplasticity, Immune response.

Introduction

Bipolar disorder (BD) is a chronic psychiatric condition characterized by alternating episodes of mania and depression, significantly affecting patients' quality of life. It is a complex disorder with a multifactorial etiology, encompassing genetic, environmental, and neurobiological factors. While extensive research has identified numerous genetic risk factors associated with BD, these findings alone cannot fully explain the variability in disease onset and progression. This gap in understanding has led researchers to explore additional contributing factors, including the

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role of infections and immune dysregulation in psychiatric disorders (1).

Emerging evidence suggests that viruses with potential CNS-relevant effects, which can infect the nervous system, may influence the pathophysiology of psychiatric conditions (2, 3). Among these, Epstein-Barr virus (EBV) has garnered significant attention due to its ability to establish lifelong latency in the host and modulate immune responses. EBV is a ubiquitous herpesvirus known to infect over 90% of the global population, often remaining dormant within B-cells. However, during its latent phase, EBV produces viral microRNAs (miRNAs) that can regulate both viral and host gene expression(4, 5). This regulatory capability allows the virus to evade immune detection and persist in the host, potentially altering host cellular pathways in ways that could influence psychiatric health.

Although EBV primarily establishes latency in B cells, increasing evidence supports plausible CNS-relevant effects of EBV infection. EBV-related neuroinflammatory responses and CNS manifestations have been reported, and glial responses to EBV infection have been proposed as a potential contributor to inflammatory reactions in the brain. In addition, EBV gene-expression programs differ across latent and lytic states, and viral non-coding products (including EBV-encoded miRNAs) may contribute to sustained modulation of host pathways relevant to neuroimmune signaling and psychiatric phenotypes (5).

MicroRNAs (miRNAs) are small non-coding RNA molecules that play critical roles in post-transcriptional regulation of gene expression. By binding to target mRNAs, miRNAs can suppress protein translation or promote mRNA degradation, thereby modulating various cellular processes, including neurogenesis, synaptic plasticity, and immune responses (6-8). Dysregulation of miRNA expression has been linked to several psychiatric disorders, suggesting that miRNAs could be key players in the molecular mechanisms underlying mood instability and cognitive dysfunction(9, 10).

Given the potential for viral miRNAs to influence host gene expression, there is growing interest in understanding how EBV miRNAs might impact genes associated with psychiatric disorders like BD. Recent studies have highlighted the role of miRNAs in modulating genes involved in mood regulation, stress responses, and neuroplasticity. However, the specific interactions between EBV miRNAs and BD-related genes remain largely unexplored (10). Addressing this gap could provide new insights into how latent viral infections may contribute to the development or exacerbation of psychiatric conditions.

In this study, we sought to investigate the potential connections between EBV miRNAs and genes associated with BD. By leveraging data from both text mining and experimental sources, we aimed to identify viral miRNAs that may influence the expression of genes implicated in BD.

Methods and Materials

Data Collection and Preprocessing

To investigate the potential role of EBV microRNAs in BD, we collected relevant data from multiple bioinformatics databases. First, EBV microRNA target data were sourced from the VirMirna database, which specializes in viral microRNA interactions with host target genes (11). After downloading the full target dataset, we filtered it to retain only the interactions involving EBV microRNAs and their associated targets in human cells. This dataset served as the foundation for identifying EBV microRNAs that might impact genes associated with BD.

Next, we gathered data on genes associated with BD from the DISEASES database (https://diseases.jensenlab.org/), which compiles gene-disease associations based on both literature mining and experimental evidence. The database is divided into two sections ,Text-mining (Gene-disease associations derived through computational text mining of scientific literature) and Experimental (Gene-disease associations based on empirical data from various studies)

We combined data from both sections to maximize coverage of BD-associated genes. Genes with a medium to high confidence level in their

association with BD were selected to ensure the reliability of the dataset. This preprocessing step yielded a refined list of genes implicated in BD that we could cross-reference with the EBV microRNA targets.

Identification of Relevant microRNA-Target Interactions

Following data collection, we organized and displayed the combined dataset in Microsoft Excel for further analysis. The goal was to identify EBV microRNAs with target genes that overlap with our BD gene list. By filtering the dataset for shared targets between EBV microRNAs and BD-associated genes, we identified a subset of interactions that potentially link EBV microRNAs to the regulation of BD-relevant genes. This subset of interactions was used for subsequent network and regulatory analyses.

Gene Regulation Categorization and Functional Annotation

To enhance our understanding of the role of identified target genes in BD, we performed an additional analysis of gene regulation status using the STRING(12), DisGeNET(13), and Gene Cards (14) databases. These databases provide curated information on gene expression regulation, interaction networks, and disease associations. Each gene was classified based on its regulatory role in BD into three main categories, Downregulation(Genes that showed decreased expression levels in BD, potentially reducing their functional activity), Upregulation(Genes with increased expression levels in BD, which could contribute to disease pathology through enhanced activity) and Dysregulation or Unknown(Genes for which data were inconclusive or indicated both upregulation and downregulation under different conditions, suggesting an imbalance in gene expression).

This classification provided a framework for interpreting the functional impact of EBV microRNAs on BD genes. By combining network visualization with regulation categorization, we aimed to identify patterns that may reveal how EBV microRNAs influence molecular pathways related to BD, thereby contributing to its pathogenesis.

Network Construction and Visualization in Cytoscape

The selected data were imported into Cytoscape (15) to construct a network of microRNA-gene interactions. This network visually represented the interactions between EBV microRNAs and BD-associated genes identified across various databases, facilitating the identification of key patterns and interactions within the network.

In Cytoscape, each interaction was represented as an edge connecting a source (EBV microRNA) to a target (BD-associated gene). The network was styled to reflect the type of regulation exerted by each interaction. This visualization allowed us to observe patterns in the regulatory network, facilitating the identification of key EBV microRNAs that may have substantial influence over BD-related pathways.

Results

Through text mining of the DISEASE database, we identified a total of 265 unique genes associated with BD. These associations were evaluated using Z-scores, where scores between 4 and 6 indicate *moderate confidence* and scores greater than 6 indicate *high confidence*. In our dataset, 253 genes showed a moderate confidence level (Z-scores between 4 and 6) and 12 genes demonstrated high confidence associations (Z-scores above 6).

The 12 high-confidence genes associated with BD in this analysis provide valuable insights into potential biological underpinnings of the disorder. Key genes like SLC6A4, HTR1A, and HTR2A are integral to serotonin signaling, which is critical in mood regulation and implicated in various psychiatric conditions. Dopamine-related genes, such as SLC6A3 and DRD2, contribute to reward and mood pathways, while COMT and MAOA are involved in the breakdown of dopamine and other neurotransmitters.

Table 1. SCZ-Associated gene in experimental dataset.

Reference ID	Gene name	ID	Disease	Source	Confidence score	Functional relevance to BD
ENSP00000242257	MRM2	DOID:14042	Bipolar I disorder	TIGA	1.404	Mitochondrial rRNA modification; energy metabolism/neuroprotection.
ENSP00000247001	SUGP1	DOID:14042	Bipolar I disorder	TIGA	1.086	RNA splicing regulator; implicated in neuronal gene expression.
ENSP00000252575	NCAN	DOID:14042	Bipolar I disorder	TIGA	1.086	Extracellular matrix proteoglycan; neuroplasticity/synaptic stability.
ENSP00000262815	MAU2	DOID:14042	Bipolar I disorder	TIGA	1.086	Cohesin loading factor; cell cycle/chromatin regulation.
ENSP00000266376	CACNA1C	DOID:14042	Bipolar I disorder	TIGA	1.012	Voltage-gated Ca2+ channel; neuronal excitability/mood regu-lation.
ENSP00000291481	HAPLN4	DOID:14042	Bipolar I disorder	TIGA	1.086	Neural ECM linker; synaptic organization/neurodevelopment.
ENSP00000305071	RFXANK	DOID:14042	Bipolar I disorder	TIGA	1.086	MHC class II transcription factor; immune egulation/inflammation.
ENSP00000374014	TM6SF2	DOID:14042	Bipolar I disorder	TIGA	1.086	Lipid metabolism transporter; neuronal membrane homeostasis.
ENSP00000385334	MAD1L1	DOID:14042	Bipolar I disorder	TIGA	1.404	Mitotic spindle assembly checkpoint; cell cycle/neurogenesis.
ENSP00000402154	MEF2B	DOID:14042	Bipolar I disorder	TIGA	1.086	Transcription factor; neuronal differentiation/survival.
ENSP00000402756	NR2C2AP	DOID:14042	Bipolar I disorder	TIGA	1.086	Nuclear receptor coactivator; gene regulation in neurons.
ENSP00000425864	BORCS8	DOID:14042	Bipolar I disorder	TIGA	1.086	Lysosomal trafficking regulator; neuronal protein clearance.

Genes like CACNA1C and ANK3 play roles in calcium signaling and neuronal excitability, while ZNF804A, DISC1, and BDNF contribute to neurodevelopment, synaptic plasticity, and neuronal survival. Together, these genes highlight pathways relevant to mood stabilization, neuroplasticity, and neurotransmitter regulation, making them strong candidates for further research aimed at unraveling the complex genetic landscape of BD.

Also, Our analysis, based on experimental data from the DISEASE database, identified 12 genes with a confidence score of 1 or higher, underscoring a robust association with BD. This dataset was curated to include only genes with medium to high confidence, as we excluded entries with confidence scores below 1 to ensure data reliability.

Among the top genes, MRM2 and MAD1L1 had the highest confidence scores (1.404).

MRM2 plays a role in mitochondrial function, essential for cellular energy, while MAD1L1 is involved in cell cycle regulation, potentially influencing neuronal growth. Additional genes, such as SUGP1 and NCAN (both at 1.086), contribute to pathways relevant to cellular structure and neuroplasticity, with NCAN linked to extracellular matrix components important in neural connectivity. Other genes like MAU2 and RFXANK (1.086 each) also emerged, with RFXANK being crucial for immune response, hinting at potential links between immune regulation and neuropsychiatric disorders. The remaining genes, including HAPLN4, TM6SF2, and MEF2B, are associated with brain structure and function, pointing to roles in neuronal integrity and resilience (Table 1). These genes highlight critical

Table 2. Associations of EBV-Derived miRNAs with BD-Related Genes Identified from Text Mining and Experimental Data

EBV miRNA	Data Source	Target Gene	Status in BD
ebv-miR-bart9*	BD-Textmining	NR3C1	Downregulation
ebv-miR-bart22	BD-Textmining	NEK4	Dysregulation
ebv-miR-bart10	BD-Textmining	PER2	Upregulation
ebv-miR-bart20-3p	BD-Textmining	PPIG	Downregulation
ebv-miR-bart9	BD-Textmining	RORA	Upregulation
ebv-miR-bart1-3p	BD-Textmining	CALM3	Unknown
ebv-miR-bart19-5p	BD-Textmining	GRIA2	Downregulation
ebv-miR-bart15	BD-Textmining	ZNF804A	Upregulation
ebv-miR-bart19-3p	BD-Textmining	GSK3B	Dysregulation
ebv-miR-bart14	BD-Textmining	NDEL1	Downregulation
ebv-miR-bart18-5p	BD-Textmining	HOMER1	Dysregulation
ebv-miR-bart1-3p	BD-Textmining	DGKH	Upregulation
ebv-miR-bart21-5p	BD-Textmining	FXR1	Upregulation
ebv-miR-bart17-3p	BD-Textmining	FMR1	Dysregulation
ebv-miR-bart6-5p	BD-Textmining	PRKACB	Dysregulation
ebv-miR-bhrf1-3	BD-Textmining	HDAC1	Unknown
ebv-miR-bart19-3p	BD-Textmining	MTHFR	Dysregulation
ebv-miR-bart14	BD-Textmining	BCL2	Dysregulation
ebv-miR-bart7	BD-Textmining	FOXP2	Unknown
ebv-miR-bart22	BD-Textmining	CREB1	Downregulation
ebv-miR-bart19-3p	BD-Textmining	NLGN1	Dysregulation
ebv-miR-bart2-5p	BD-Textmining	MECP2	Dysregulation
ebv-miR-bart5	BD-Textmining	DISC1	Downregulation
ebv-miR-bart21-3p	BD-Textmining	IMPA1	Unknown
ebv-miR-bart13	BD-Textmining	IL10	Unknown
ebv-miR-bart6-3p	BD-Textmining	CLOCK	Dysregulation
ebv-miR-bart13	BD-Textmining	C9orf72	Dysregulation
ebv-miR-bart22	BD-experimental	NEK4	Dysregulation
ebv-miR-bart22	BD-experimental	SF3B2	Unknown
ebv-miR-bart15	BD-experimental	FADS1	Dysregulation
ebv-miR-bart6-5p	BD-experimental	EIF1AD	Unknown

pathways in mood stabilization, neurotransmitter function, and neuroplasticity, underscoring their importance as candidates for further research to better understand the genetic underpinnings of BD.

In this study, we retrieved data from the VirMirna database to identify miRNAs related to EBV and their associated target genes. After filtering, we identified 48 unique EBV miRNAs, which collectively target 3013 unique genes in *Homo sapiens*. These interactions were derived from experimental evidence, providing insights into the potential regulatory roles of EBV miRNAs in host cellular pathways (Supplementary Materials).

In this analysis, we identified 30 unique genes linked to both BD and 21 viral miRNAs, sourced from both experimental and text-mined data. Of these genes, 27 were associated through text mining, while 3 genes were connected through both experimental and text-mined data. The associations with BD are

categorized as 6 genes were connected through downregulation, 5 genes are associated via up-regulation,12 genes are linked through dys-regulation and 7 genes have an unknown asso-ciation type. Among the miRNAs, ebv-miR-bart22 and ebv-miR-bart19-3p stood out with connections to three genes each, indicating a higher level of interaction. Additionally, five other miRNAs were each linked to two genes, while the remaining miRNAs each associated with a single gene.

Furthermore, three specific miRNAs—ebv-miR-bart22, ebv-miR-bart15, and ebv-miR-bart6-5p—were found to interact with genes associated with BD from both experimental and text-mined data sources, highlighting their significance across multiple data types. Key genes with high miRNA associations include NEK4, BCL2, C9orf72, CALM3, and CLOCK (Table 2) (Figure 1).

Discussion

BD is a complex psychiatric condition charac-terized by extreme mood swings, ranging from manic highs to depressive lows. Its etiology is multifactorial, involving a combination of genetic and environmental factors. Genetic studies have identified various susceptibility genes associated with BD, yet genetics alone does not fully explain the disorder's onset or progression (1, 16, 17).

Recently, research has begun to explore the influence of external factors, such as infections and immune responses, on psychiatric disor-ders. This growing body of work suggests that viral infections with potential CNS involve-ment and immune dysregulation may play roles in triggering or exacerbating psychiatric symptoms, particularly in genetically suscepti-ble individuals (18-20).

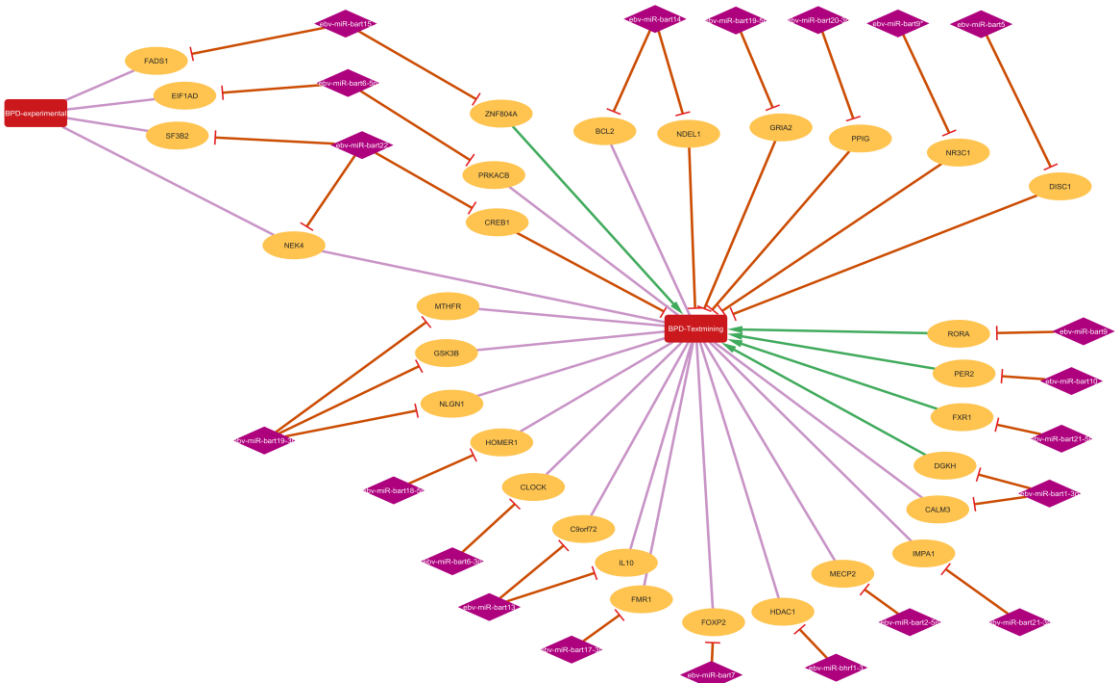

Fig 1. Network visualization of interactions between EBV-associated miRNAs and genes linked to BD, incorporating regulatory direction. The diagram includes connections sourced from both experimental (left, in red) and text-mined data (right, in red). Each miRNA (purple diamond shapes) targets specific genes (yellow ovals) with regulatory relationships indicated by color-coded lines: **green arrows** represent upregulation, **purple lines** indicate dysregulation or unknown association, and **red lines** signify downregulation.

EBV is a widespread pathogen known for its affinity for infecting B-cells and establishing lifelong latency in the host. EBV's persistence in the body can lead to chronic, low-grade inflammation, which may contribute to neuro-inflammatory pathways associated with psy-chiatric disorders. This low-level inflammatory

state, driven by a persistent viral infection, could impact neural circuits involved in mood regulation (21-23).

EBV's potential role in psychiatric disorders is thought to involve its impact on immune regulation and gene expression within the brain. The virus produces its own miRNAs, small non-coding RNAs that allow it to control both viral and host gene expression. Through these miRNAs, EBV can modulate host cell pathways to maintain latency and evade immune detection (5, 24, 25). However, this manipulation of host cellular processes may inadvertently affect neural circuits related to mood and cognition, potentially contributing to psychiatric symptoms.

In our study, we identified 21 unique viral miRNAs associated with genes linked to BD. This number suggests a significant level of interaction between EBV miRNAs and genes involved in psychiatric pathways, indicating that EBV infection may play a role in modulating gene expression related to BD. The presence of multiple viral miRNAs targeting BD-associated genes suggests that EBV may influence the expression of genes critical for mood regulation and cognitive function. This finding implies a potential role for EBV in affecting the genetic and molecular landscape of BD, possibly contributing to its onset or exacerbating symptoms in susceptible indivi-duals. The results add weight to the hypothesis that viral infections and immune responses might be involved in psychiatric disorders, particularly when the virus persists and establishes latency.

While the field of psychiatric genetics is still exploring the influence of viral miRNAs, studies have increasingly shown links between viruses with demonstrated CNS-relevant effects, such as EBV, and psychiatric disorders (22, 26). For instance, research has found associations between herpesviruses and psychiatric conditions such as schizophrenia and depression, with viral miRNAs identified as potential modulators of neural pathways (27). However, studies specifically examining EBV miRNAs and their role in BD are limited. This makes our study pioneering in identifying specific EBV miRNAs potentially targeting BD-related genes.

Related evidence supporting biological plausibility comes from studies discussing EBV-associated inflammatory responses in the brain and CNS manifestations of EBV infection, as well as work highlighting how EBV persistence and immune modulation may intersect with neuroinflammatory pathways. Moreover, prior literature has emphasized that EBV produces regulatory miRNAs during infection/ latency that can modulate host gene-expression programs, which provides a rationale for investigating EBV miRNA–host gene intersections in psychiatric disorders. Nevertheless, BD-specific experimental studies directly testing EBV miRNA effects on BD-relevant molecular phenotypes remain limited; therefore, our network results should be interpreted as hypothesis-generating and as a prioritization map for follow-up experiments.

These findings suggest that while most miRNAs target a single protein, a few, such as ebv-miR-bart22 and ebv-miR-bart19-3p, exhibit broader regulatory potential, potentially impacting multiple proteins associated with BD. This variation in targeting capacity highlights certain miRNAs as more influential in modulating pathways related to the disorder, warranting further investigation into their specific roles and mechanisms.

In this study, we observed three distinct types of interactions between EBV miRNAs and BD-associated genes, each suggesting a different potential mechanism of influence. Some miRNAs in our data are associated with genes that are downregulated in BD. Since miRNAs inherently act as downregulators of gene expression, these interactions suggest that certain EBV miRNAs could directly contribute to the downregulation observed in the disorder. By reinforcing the suppression of these genes, these miRNAs might exacerbate pathways associated with depressive symptoms or mood regulation deficits in BD. This direct downregulatory effect indicates that EBV miRNAs could have a significant and straightforward role in modulating gene expression patterns linked to the disorder (28, 29).

Another category involves miRNAs that downregulate genes which are upregulated in BD. This might seem counterintuitive initially, but

one possible explanation is that while these miRNAs induce downregulation, the effect may not be strong enough to fully counteract the cell's tendency to upregulate these genes in response to internal cues. Instead, the miRNA-mediated downregulation could serve as a stimulus, prompting the cell to attempt to re-establish balance by further upregulating the gene, thereby disrupting homeostasis. This mechanism could create a feedback loop where the miRNA's influence indirectly contributes to gene upregulation in BD, potentially influencing the disorder's manic or depressive states by disturbing the cellular response mechanisms (30, 31, 32).

The third category includes miRNAs that target genes known to be dysregulated in BD, meaning they may be upregulated in one phase (e.g., mania) and downregulated in another (e.g., depression). Given that BD alternates between these two phases, miRNA effects on dysregulated genes could contribute to the cyclical nature of the disorder. By targeting such genes, miRNAs might tip the balance in favor of one phase over the other, potentially influencing the shifts between manic and depressive states. This model suggests that miRNAs might not just impact overall gene expression levels but could also play a role in the dynamic regulation of genes that vary depending on the disorder's phase (33, 34).

A key mechanistic question is whether and how EBV-derived miRNAs might influence CNS-relevant gene regulation despite the blood–brain barrier (BBB). A plausible, but not directly tested, route is that EBV-infected or activated immune cells may traffic across the BBB under inflammatory conditions and thereby deliver viral products to the CNS microenvironment. In addition, it has been proposed that extracellular vesicles (including exosomes) released from infected immune cells could transport viral miRNAs systemically and potentially facilitate intercellular transfer to recipient neural or glial cells. These mechanisms remain hypotheses in the context of BD and require direct experimental validation in disease-relevant models.

Immune cells, particularly activated B-cells, have the ability to traverse the blood-brain barrier under conditions of inflammation or immune activation. This means that once EBV has infected these cells, it can use them as Trojan horses to gain access to the brain. As these infected immune cells cross the BBB, they can release viral particles or, more importantly, EBV miRNAs in the brain's microenvironment. Once inside the brain, the virus can persist in a latent state, which is particularly relevant since many of the identified miRNAs in our study are known to be produced during the latent phase of EBV infection (21).

Exosomes are small extracellular vesicles that can carry proteins, lipids, and nucleic acids, including miRNAs, from one cell to another. Infected B-cells can release exosome-derived miRNAs, which can travel through the bloodstream and potentially cross the BBB. This has been previously demonstrated, where B-cell-derived exosomes carry functional products, including viral miRNAs. Once EBV miRNA-laden exosomes cross the BBB, they can be taken up by neural cells. Exosomes have a natural affinity for cell membranes and can fuse with target cells, releasing their cargo directly into the cytoplasm. In the context of the brain, these exosomes could interact with neurons, astrocytes, or microglial cells. Once inside these cells, the EBV miRNAs can exert their regulatory effects, potentially influencing genes involved in mood regulation, neuronal plasticity, and stress responses. This mechanism suggests that EBV could indirectly modulate brain function and contribute to psychiatric symptoms associated with disorders like BD (35, 36).

These potential pathways underline the plausibility that EBV miRNAs produced during the virus's latent phase could reach the brain and modulate gene expression in neural cells. The ability of immune cells to cross the blood–brain barrier, together with the role of exosomes in miRNA transport, may provide routes through which EBV infection contributes to the development or exacerbation of psychiatric disorders. Understanding these pathways could also reveal therapeutic opportunities, such as targeting the transfer of viral miRNAs via extracellular vesicles, to mitigate their impact on brain function. However, as this study is

computational and relies on curated and text-mined resources, the identified relationships should be considered hypothesis-generating rather than causal and will require targeted experimental validation in disease-relevant models.

Future Directions

Further studies are needed to elucidate the exact mechanisms by which EBV miRNAs modulate gene expression in the brain. Understanding how these miRNAs influence pathways related to mood regulation and neuroplasticity could provide new insights into the molecular underpinnings of BD. The identification of specific EBV miRNAs that interact with BD-related genes opens up potential therapeutic strategies. Developing approaches to inhibit the transfer of EBV miRNAs via exosomes or blocking their interactions with target genes could mitigate their effects on psychiatric symptoms.

Investigating the presence and activity of EBV miRNAs in patients with BD over time could provide valuable information on how viral factors influence the progression of the disorder. Such studies could help establish EBV miRNAs as biomarkers for disease onset or severity. While this study focused on EBV, other viruses with potential CNS involvement may also contribute to psychiatric disorders.

Future research should explore whether similar mechanisms involving viral miRNAs are at play in other infections and how they may interact with genetic susceptibility factors.

Conclusion

Our findings highlight the potential role of EBV miRNAs in influencing gene expression related to BD, suggesting that these viral factors could be contributors to the disorder's onset or severity. The interplay between viral infections, genetic susceptibility, and environmental factors adds a new dimension to understanding the etiology of psychiatric conditions. By uncovering how EBV miRNAs interact with BD-associated genes, this study opens up new possibilities for diagnostic and therapeutic interventions aimed at mitigating the impact of viral factors on psychiatric health.

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Disclosure

None

Conflict of Interest

No conflict of interest is declared.

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Ethics Approval and Consent to Participate

Not applicable

Data Availability Statement

All data generated or analyzed during this study are included in this article.

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