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REVIEW

Underexplored Connections Between Diabetes, Hypomanic States and Insecure Attachment

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Abstract: Diabetes, dopamine, attachment style disorders, and hypomania share complex interrelations involving neuroinflammation, dysfunction in brain networks (DMN, CEN, SAL), and emotional regulation. Both Type 1 and Type 2 diabetes induce cognitive and structural changes in the brain through mechanisms such as hyperglycemia, insulin resistance, and chronic inflammation. These processes can affect the dopaminergic system, which plays a pivotal role in motivation, emotional regulation, and the manifestation of hypomania. Dopamine is directly linked to attachment styles, with disturbances in this system increasing vulnerability to emotional disorders, including bipolar disorder and schizophrenia. Hypomania, a hallmark of the bipolar spectrum, is associated with dopaminergic imbalances, often observed in diabetes.

Keywords: diabetes – type 1 and type 2, dopamine, attachment style, hypomania, mania, bipolar disorder

Introduction

According to data from the World Health Organization (WHO), the global prevalence of diabetes has increased significantly, rising from approximately 198 million individuals in 1990 to 537 million in 2021. This figure is projected to reach 783 million by 2045, reflecting a 46% increase from current levels.[1] Insulin resistance, a key feature of type 2 diabetes, impairs reward-related mechanisms, particularly those regulating food intake, which can lead to a loss of dietary control. Research also indicates that diabetes is associated with dopaminergic dysfunction, particularly in the striatum, contributing to cognitive and psychomotor impairments.[2] Given these neurobiological alterations, psychological traits such as insecure attachment and hypomanic tendencies may be especially relevant in individuals with diabetes. These traits can influence key health-related behaviors, including dietary choices, emotion regulation, and treatment adherence. Exploring these associations may shed light on how underlying psychological characteristics contribute to the onset, maintenance, or exacerbation of metabolic disorders. This paper aims to explore the potential links between insecure attachment, dopaminergic dysfunction, and hypomanic states in the context of diabetes.

Dopamine and Diabetes

Arvid Carlsson was the first clinician to identify dopamine as a neurotransmitter.[3] His pioneering research laid the foundation for understanding dopamine's role in the brain. Later, in 1970, Canadian researcher Solomon Snyder, building on the work of John Kebabian and Paul Greengard, investigated dopamine receptors and their relationship with antipsychotic medications.[4] As a result, dopamine was recognized as a neurotransmitter playing a critical role in regulating mood and motivation, as well as being a key component of the brain's reward system. This system is directly

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linked to appetite and insulin regulation.[5] Dopamine contributes to the regulation of food intake and the pleasure derived from eating,[6] processes that are often disrupted in individuals with diabetes.

Diabetes is defined and understood, in accordance with the writings of Aretaeus of Cappadocia, as a chronic metabolic disorder characterized by hyperglycemia (elevated blood glucose levels) resulting from defects in insulin secretion.[7] Diabetes is categorized into two main types – Type 1 and Type 2 – depending on whether insulin production is lacking or the body is resistant to its effects.[8]

On one hand, Type 1 diabetes, marked by impaired insulin production, is predominantly observed in children and accounts for only about 5–10% of all diabetes cases. It progresses rapidly and is often referred to in medical contexts as juvenile diabetes. Rarely, Type 1 diabetes is diagnosed in adults, in which case it is termed latent autoimmune diabetes.

On the other hand, Type 2 diabetes typically progresses at a slower rate and is primarily diagnosed in individuals over the age of 40. It constitutes 90–95% of all diabetes cases. The defining feature of Type 2 diabetes is inadequate insulin production, insufficient for effective blood sugar regulation. Individuals with this type of diabetes may also suffer from obesity and impaired psychomotor function.[8]

In this context, diabetes is regarded as a condition leading to disruptions in the metabolism of carbohydrates, fats, and/or proteins. It may be accompanied by complications affecting various organs or entire systems, including cardiovascular diseases, nephropathy, retinopathy, and neuropathy. In other words, diabetes can be a disabling condition with complex social interactions and severe psychiatric consequences, such as the development of hypomanic or depressive states.

The Dopamine Hypothesis for Hypomanic States

According to the ICD-11, hypomania is a frequently occurring manifestation of bipolar disorder. It is characterized by a persistently elevated mood, increased energy levels, and heightened activity. In contrast to mania, hypomania presents with less severe symptoms and does not typically result in significant social or occupational dysfunction. In clinical and academic literature, the period during which an individual experiences hypomania is referred to as a hypomanic episode or hypomanic state.

A number of studies have demonstrated that manic and hypomanic states can result from dopamine receptor agonists, suggesting a significant role of dopamine in mania.[9] According to Carlsson and Lindqvist and their theory of catecholamine balance, disruptions in the equilibrium between dopamine and norepinephrine may underlie various psychiatric disorders.[10] These authors suggest excessive dopamine activity may lead to mania, while decreased levels may result in depression. Later studies inspired by their ideas show that increased dopamine release in the mesolimbic system leads to symptoms such as hypomania and mania, whereas dopamine hypoactivity in the mesocortical regions contributes to negative and cognitive symptoms, which are typical in schizophrenia and depression.[11]

Chronologically – in 1967, Van Rossum was the first to emphasize that excessive dopamine system activity is directly linked to the symptoms of schizophrenia. He was the first to propose that antipsychotics work by blocking dopamine receptors, thereby explaining their therapeutic effects. This idea was later supported by numerous studies.[12] In 1975, Philip Seeman discovered and described D2 dopamine receptors in the brain and experimentally showed that antipsychotics have a high affinity for these receptors.[13] This supported the notion that hyperactivity of dopamine D2 receptors is central to schizophrenic symptoms.[14] According to Seeman's dopamine hypothesis for schizophrenia, the positive symptoms of the disorder (such as hallucinations, delusions, and hypomanic or manic states) result from excessive dopamine activity in the mesolimbic system. In contrast, reduced dopamine activity in the mesocortical pathway (in and around the prefrontal cortex) contributes to the formation of negative symptoms, such as emotional withdrawal (apathetic-abulic syndrome), psychomotor rigidity, lack of motivation, and cognitive impairments.[15]

Just as in bipolar disorder, Seeman suggests that D2 dopamine receptors are hypersensitive in schizophrenia, which amplifies the response to dopamine fluctuations. This perspective helps explain hypomanic and manic episodes, in which small changes in dopamine lead to excessive arousal and hyperactivity. Several studies support this hypothesis. For example, Seeman's research demonstrates that all effective antipsychotic medications share the common property of blocking D2 receptors, highlighting the central role of dopamine in psychotic disorders.[16] Moreover, imaging studies show increased dopamine synthesis and release in individuals with schizophrenia, further supporting the connection between elevated dopaminergic activity and positive symptoms. Furthermore, pharmacological studies indicate that

dopamine agonists can provoke or exacerbate psychotic symptoms, while dopamine antagonists can mitigate them, emphasizing the importance of dopamine regulation in treating these disorders.

Although Seeman was not a leading researcher in bipolar disorder, his discoveries on dopamine receptors significantly contribute to understanding hypomania as a condition linked to dopaminergic hyperstimulation. The dopamine hypothesis in the context of hypomania, as part of bipolar disorder, has long been known as a leading explanation in understanding the neurobiology of mood disorders. This dopamine hypothesis for affective disorders is primarily associated with the work of Bunney and Davis.[17,18] These authors emphasize that increased activity of the dopaminergic system is linked to manic episodes. Later, Robert Post expanded this idea with his "kindling" concept and the notion of dopamine dysregulation in bipolar disorder, demonstrating how recurrent episodes can intensify dopaminergic abnormalities.[19,20] Similarly, Bruno Giros and Marc Caron explored the role of dopamine transporters (DAT) in hypomanic states within bipolar disorder.[21–23]

In their influential paper, "The Dopamine Hypothesis of Bipolar Affective Disorder: The State of the Art and Treatment Implications", Ashok et al explore how dopamine dysregulation contributes to the development of bipolar disorder. They highlight how abnormal dopamine signaling plays a role in both manic and hypomanic episodes.[9] Consistent with other research,[24,25] they show that increased dopamine activity during hypomania is linked to heightened emotional reactions, impulsivity, and sensitivity to rewards.

Additionally, the work of Herbert Meltzer and Stephen Stahl provides valuable insights, showing that the overactivity of the dopaminergic system in schizophrenia is associated with positive symptoms like hallucinations and delusions, which can be alleviated by antipsychotic drugs that block dopamine receptors. Both psychosis and hypomania are associated with increased dopamine activity in the striatum.[26] Neuroimaging studies suggest that psychotic episodes are marked by excessive dopamine production in the midbrain, leading to heightened sensitivity to stimuli. Similarly, hypomania is linked to higher energy, euphoria, and reduced sleep needs – phenomena that can also be explained by dopamine hyperactivity.[27] While excessive dopamine release in psychosis distorts reality, in hypomania, although the distortion is milder, dopaminergic stimulation is thought to drive increased creativity, impulsivity, and self-confidence.

Some studies hypothesize that both disorders – psychosis and hypomania, involve dysregulation of the dopaminergic system, albeit with different degrees of intensity. Consequently, antipsychotic drugs, which reduce dopaminergic activity, are commonly used in the treatment of psychosis but, at lower doses, are also employed in the management of bipolar disorder, including hypomania. These findings further support the notion that the dopaminergic system plays a central role in both conditions.[28]

Meltzer and Stahl also point out that the dopamine hypothesis cannot fully explain the negative symptoms of schizophrenia, such as emotional withdrawal and cognitive impairments. In this regard, they suggest that other neurotransmitter systems, such as the serotonergic system, may play a role in these aspects of the disorder.[29] Later studies, such as those by Howes and Murray, propose more complex models that include interactions between the dopaminergic system and other neurotransmitter systems, as well as the influence of genetic and external factors on the development of hypomania, mania, and schizophrenia.[30] It has been found that dopamine levels are highly dependent on circadian rhythms (the "internal biological clock"), which explains why some sleep disturbances precede manic episodes. Howes and Kapur further develop the dopamine hypothesis, linking it to neuroimaging and PET scans to demonstrate the hyperactivity of dopamine pathways during mania.[31]

Genetic factors play a crucial role in susceptibility to hypomania and mania, particularly through variations in genes related to dopamine receptors and transporters. The DRD2 gene, located on chromosome 11, encodes the dopamine D2 receptor, which regulates dopaminergic signaling. Variants of DRD2 have been linked to psychiatric conditions such as schizophrenia, addiction, and mood disorders, potentially affecting sensitivity to dopamine and contributing to dysregulation.[32] Similarly, the DRD4 gene, also on chromosome 11, encodes the dopamine D4 receptor, which is involved in cognitive and emotional regulation. Polymorphisms, particularly the 48-base pair VNTR in exon 3, have been associated with traits such as novelty-seeking, ADHD, and schizophrenia. These variations may alter dopamine signaling, increasing vulnerability to dysregulation under stress, which can trigger hypomanic or manic episodes.[33]

Additionally, variations in the DAT1 gene, which are involved in the regulation of dopamine reuptake, have been linked to bipolar disorder, further emphasizing the role of dopamine in mood regulation. These findings highlight the

multifactorial nature of mood disorders, where genetic predisposition interacts with environmental factors to influence disease expression. While these genetic associations are significant, the exact mechanisms remain under investigation, as not all individuals with these variants develop mood disorders.

Psychosocial and environmental factors have a well-documented impact on hypomanic episodes. Stressors such as trauma, interpersonal conflicts, and high-pressure situations can disrupt neurotransmitter balance, particularly dopamine, leading to mood instability. Research suggests that stress-induced increases in dopaminergic activity contribute to hypomanic or manic episodes, and over time, chronic stress and recurrent mood episodes may result in lasting alterations in dopaminergic signaling and brain structure, aligning with Robert Post's "kindling" hypothesis.[34] This connection provides insight into why certain life events precipitate mood episodes in vulnerable individuals.[35] Additional evidence for this relationship comes from studies utilizing quantitative electroencephalography (QEEG) and low-resolution electromagnetic tomography (LORETA). These techniques enable a detailed examination of neural activity (eg, electrical patterns) and the identification of specific regions involved in emotional regulation. For example, a case study of a 54-year-old man experiencing a depressive episode demonstrated that a reduction in prefrontal theta cordance, as measured by QEEG, preceded a transition to hypomania following treatment with clomipramine. This finding suggests that changes in neural activity related to stress and the dopaminergic system can be detected using these methods and may serve as predictors of mood shifts.[36]

The dopamine hypothesis has evolved to recognize the involvement of other neurotransmitter systems, such as serotonin, glutamate, and oxytocin, in modulating dopaminergic activity, particularly in the context of hypomania. Hormonal factors, especially sex hormones like estrogen and testosterone, also influence dopamine activity, adding complexity to the neurobiology of hypomania. Meta-analyses by Michael Berk et al were among the first to correlate dopamine dysregulation with inflammatory processes and oxidative stress, both of which may influence manic states.[37] Neuroimaging studies have shown increased activity in the mesolimbic dopamine pathway during hypomania, linking heightened motivation, hyperactivity, and reduced sleep. Furthermore, dopamine modulates the interaction between key brain networks, including the default mode network,[38] central executive network, and salience network.

In hypomania, hyperactivity in the salience network leads to increased attention to rewards and impulsivity. This is supported by studies showing that elevated dopamine levels promote impulsivity and preference for immediate rewards.[39,40] However, it is clear that hypomanic symptoms cannot be solely attributed to dopaminergic dysfunction, as other neurotransmitters like glutamate, serotonin, and oxytocin also play significant roles.[41,42] Additionally, the mesocortical dopaminergic system interacts with gonadal hormones, such as estrogen and testosterone, influencing mood regulation.[43] Over the past three decades, neurotransmitters such as oxytocin, dopamine, and serotonin have been the subject of extensive research within the context of attachment theories, providing new insights into the emotional and social dimensions of hypomanic states.

Attachment and Dopamine

In this text, when discussing attachment or attachment styles, we adhere to Bowlby's four-factor model. According to this model, an individual's psyche internalizes and is dominated by one of four types of mental working models: a secure attachment style, an insecure attachment style (anxious-avoidant, also known as ambivalent), and a disorganized attachment style. These psychological models are characterized by distinct systems of fantasies, fears, attitudes, reactions, and specific psychological defense mechanisms in interactions with the environment.[44,45] Clinical evidence suggests that early disruptions in attachment styles manifest in adulthood as affective disorders, such as hypomanic states in bipolar depression.[46–49]

On a neurobiological level, the psychological attachment system is linked to the dopaminergic system, which is known to play a role in forming social bonds and fostering a sense of attachment.[50] Dopamine is integral to reward processing and motivation, which underpins the development of both secure and insecure attachment styles. Dysfunctions in the dopaminergic system impair the ability to develop empathy and secure attachments, with significant implications for mental health. Modern neuroimaging and non-invasive techniques have revealed that communication among the brain's three primary neural networks – DMN (default mode network), CEN (central executive network), and SAL (salience network) – is mediated by neurotransmitters such as dopamine, oxytocin, and serotonin. Disruptions in these systems are observed in depression.[51–55]

The first network, the DMN, is engaged in reflective thoughts about the past and future, such as daydreaming about unfulfilled love or other aspirations. This process lacks active psychomotor movement but generates internal representations of "movements" in the mind.[56] The CEN is activated during the resolution of complex tasks requiring focus, deliberate, goal-oriented, and coordinated actions.[56] The SAL (salience network) regulates the transition between passive and active perception of time through emotional and motor responses. It functions as a switch between the internally represented ideas processed by the DMN and the goal-directed actions executed within the CEN.[57] The three neural networks, along with their associated brain regions, are illustrated in Figure 1.

Oxytocin, together with serotonin and dopamine, facilitates communication among these three neural networks. It enhances sensitivity to social stimuli, such as facial expressions or tone of voice, and can activate certain SAL functions. This neurotransmitter also modulates responses to emotional events, playing a crucial role in regulating fear and stress reactions. Like dopamine, oxytocin contributes to social cognition and emotional regulation.[58] Serotonin, on the other hand, is essential for mood modulation, attention, and cognitive flexibility. Both oxytocin and dopamine are associated with reward and pleasure responses, and their release is stimulated by afferent vagal stimulation, touch, massage, food, sex, or sensory nerve activation.[59] Understanding the roles of these neurotransmitters is critical for developing effective treatments for psychiatric conditions such as depression, autism, bipolar disorder, and others.[60]

The role of dopamine in the early interactions between infant and caregiver is crucial for the development of attachment. Studies have demonstrated that the release of dopamine in response to positive social stimuli, such as maternal touch and vocalizations, plays a key role in reinforcing the formation of early bonds between the infant and the caregiver.[61] Dopamine not only facilitates the infant's ability to bond with the caregiver but also contributes to the reinforcement of behaviors that promote social engagement and attachment-related interactions. These early experiences help establish the foundation of the attachment system, which will later influence the child's capacity to form secure or insecure attachment styles.[62]

Neuroimaging studies have shown that the dopaminergic reward system is activated during positive social interactions, such as the exchange of facial expressions, eye contact, and vocal tones between the mother and infant. This activation is thought to be critical for the infant's development of trust and emotional regulation, which are core components of a secure attachment style. Disruptions in dopaminergic signaling, such as those caused by neglect or inconsistent caregiving, can interfere with the child's ability to form secure attachments, potentially leading to the development of insecure or disorganized attachment patterns.[63]

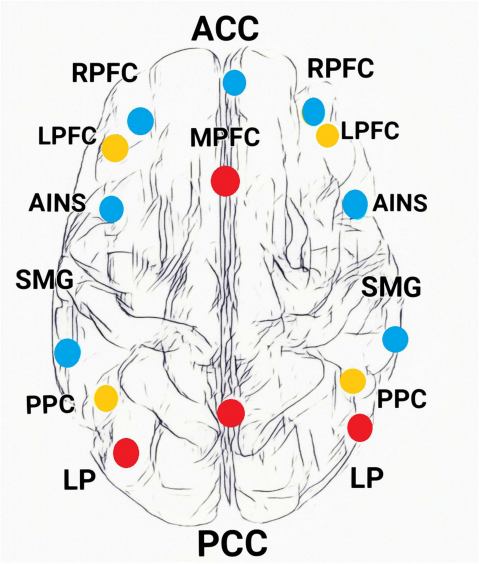

Figure 1 Functional connectivity between SAL, DMN and CEN. Salience Network (SAL) - highlighted in blue, includes the anterior cingulate cortex (ACC), bilateral anterior insula (AINS), bilateral rostral prefrontal cortex (RPFC), and bilateral supramarginal gyrus (SMG). Default Mode Network (DMN) - highlighted in red, includes the medial prefrontal cortex (MPFC), bilateral lateral parietal cortex (LP), and precuneus cortex (PCC). Cognitive Control Network (CEN) - highlighted in yellow, includes the bilateral lateral prefrontal cortex (LPFC) and bilateral.

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The role of dopamine in these early social interactions is further supported by developmental neuroscience research. Money and Stanwood[64] highlight that dopamine is not only essential for reward processing but also plays a critical role in early brain development, influencing synaptic plasticity and neural circuit formation. Their findings suggest that alterations in dopaminergic function during sensitive periods of development may contribute to long-term vulnerabilities in emotional regulation and social behavior, including attachment-related difficulties. These insights align with evidence suggesting that disruptions in maternal care can dysregulate dopaminergic pathways, potentially predisposing individuals to attachment insecurities and affective disorders later in life.[64]

In the context of attachment theory, dopamine-mediated reward circuits reinforce behaviors that align with attachment needs. As the infant interacts with the caregiver, the dopaminergic system strengthens neural pathways associated with feelings of safety and comfort. This mechanism is essential for the development of secure attachment and the subsequent ability to navigate social relationships later in life. Furthermore, early mother-infant interactions and their neurobiological underpinnings highlight the importance of consistent and responsive caregiving for optimal emotional and psychological development.

These claims are supported by research demonstrating that dopamine plays a critical role in the brain's reward system, being involved in motivation and reinforcement learning. Dopaminergic neurons, primarily located in the ventral tegmental area (VTA), release dopamine in response to rewarding stimuli, leading to pleasurable sensations and reinforcing behaviors associated with these stimuli.[65] Moreover, studies on maternal attachment indicate that dopamine is essential for recognizing the infant's affective signals, enabling the caregiver to provide adequate responses that regulate the child's emotional state. Individual differences in maternal caregiving behaviors are linked to dopaminergic system function, with dysfunctions in this system potentially leading to difficulties in emotional regulation and social behavior.[66]

Early mother-infant interactions, particularly through gentle touch, play a unique and crucial role in a child's development. Consistent and responsive touch from the caregiver offers a wide range of benefits for the infant's psychosocial and neuropsychological development, underscoring the importance of such interactions in forming secure attachment bonds.[67] Research indicates that early-life tactile stimulation patterns can alter stress regulation with potential health impacts throughout the lifespan.[68]

Recent research also supports the notion that disruptions in the dopaminergic system, particularly in relation to attachment processes, can contribute to the pathophysiology of affective disorders.[69] Studies have shown that individuals with insecure attachment styles, particularly those with avoidant or ambivalent patterns, exhibit altered dopamine activity in response to social and emotional cues.[70] This altered dopamine function has been linked to difficulties in regulating mood and emotional responses, further corroborating the dopaminergic hypothesis of affective disorders.[71]

For instance, one study found that individuals with insecure attachment styles, particularly those with a history of emotional neglect, exhibit reduced dopamine receptor availability in key brain regions involved in reward processing, such as the ventral striatum and prefrontal cortex.[72] This reduction in dopamine receptor density may impair ability to derive pleasure from social interactions, thereby contributing to the development of mood disorders, including depression and hypomanic states.[73] Similarly, another study found that dysfunctional dopamine signaling in attachment-related brain regions was associated with increased susceptibility to bipolar disorder, suggesting that disruptions in attachment and reward processing systems may underlie the emotional dysregulation characteristic of this condition.[74]

Coordination among the three neural networks – DMN, CEN, and SAL – is fundamental to an individual's cognitive and emotional stability. Their dynamic communication supports the ability to shift focus between internal and external stimuli, recognize salient information, and regulate cognitive processes. Understanding these interactions is essential for accurate diagnosis and therapy for various disorders.[75] Zhong et al provide evidence that changes in the functional connectivity of the DMN, CEN, and SAL networks are associated with cognitive and emotional stability, and disruptions in these networks can lead to various dysfunctions, including mood disorders[76] and hypomania.[77]

Diabetes and Hypomania: A Neuropsychiatric Perspective

An increasing number of studies show a complex relationship between diabetes and the higher frequency of manic or hypomanic episodes, particularly in the context of bipolar disorder. Both Types of diabetes – Type 1 and Type 2 – are associated with an increased risk of psychiatric symptoms, including hypomania. Studies show significant comorbidity between Type 2 diabetes and manic symptoms typical of bipolar disorder type I and schizophrenia.[78,79] Furthermore,

individuals with bipolar disorder have an elevated risk of developing Type 2 diabetes compared to the general population.[78] Conversely, patients with diabetes, both Type 1 and Type 2, show an increased tendency towards depression, bipolar symptoms, and hypomania.[80]

The connection between diabetes and affective disorders is thought to be influenced by disturbances in glucose regulation and the resulting impact on brain function. Insulin resistance, a hallmark of Type 2 diabetes, is associated with cognitive deficits, emotional instability, and an increased propensity for depressive symptoms.[81] Similarly, although Type 1 diabetes involves a deficiency in endogenous insulin production rather than insulin resistance, the continuous management of blood glucose levels through exogenous insulin and fluctuations in glucose levels can also disrupt mood regulation. These disturbances in blood glucose control, especially extreme fluctuations such as hypoglycemia or hyperglycemia, may contribute to mood instability, including the emergence of hypomanic symptoms.[82]

At a neurobiological level, insulin plays a critical role in neuropsychiatric function, synaptic plasticity, and cognitive processes. Disorders in insulin signaling, whether from insulin resistance in Type 2 diabetes or impaired insulin production in Type 1 diabetes, activate microglia and trigger the release of inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α).[83] These inflammatory mediators, in turn, can affect neurotransmitter systems, including those regulating dopamine and serotonin.[84]

The dopamine system, essential for regulating mood and energy, is frequently dysregulated in Type 2 diabetes. Research indicates that both hyperglycemia and insulin resistance contribute to alterations in dopamine signaling.[85,86] Such dysregulation is often associated with heightened dopamine activity, a hallmark of hypomanic episodes. Moreover, this increased dopamine activity may stimulate the release of inflammatory cytokines, thereby establishing a negative feedback loop that exacerbates both metabolic and neuropsychiatric symptoms.[86]

Dopamine Dysregulation Syndrome (DDS) refers to a condition wherein excessive dopamine stimulation leads to compulsive behaviors and mood instability. DDS is most commonly observed in patients with Parkinson's disease, particularly those treated with dopamine replacement therapy.[87] Interestingly, DDS has also been identified in individuals with diabetes, especially those receiving dopamine-affecting medications, such as certain antipsychotics. In these patients, the interaction between insulin dysregulation and medications impacting dopamine pathways may increase the risk of hyperdopaminergic symptoms and exacerbate metabolic instability.[88]

DDS is understood to result from pharmacologically induced dysfunction in the mesolimbic dopamine system,[89] which is crucial in the brain's reward and pleasure mechanisms. This dysfunction leads to personality and behavioral alterations, primarily involving impaired impulse control, and presents similarly to a hypomanic state.[90] A notable similarity between hypomania and DDS is the hyperdopaminergic activity within the mesolimbic system, which includes increased dopamine activity in the nucleus accumbens and striatum. This heightened activity is associated with impulsivity, euphoria, reduced need for sleep, and excessive self-confidence.[88] Furthermore, DDS is sometimes referred to as an artificially induced form of hypomania in patients with Parkinson's disease who are undergoing dopamine replacement therapy.[87]

The intersection of diabetes and hypomania, particularly through the lens of DDS, underscores the critical need for integrated treatment strategies. In patients diagnosed with both diabetes and bipolar disorder, it is essential to manage both the metabolic and psychiatric aspects of the disease. Effective insulin control, reduction of inflammatory markers, and cautious management of dopaminergic medications are key to mitigating the risk of hypomania and other psychiatric symptoms. Acknowledging DDS as a potential factor contributing to mood instability in patients with diabetes emphasizes the importance of a multidisciplinary treatment approach, ensuring that both the neuropsychiatric and metabolic components of the condition are addressed.

Interaction Between Variables: Attachment, Diabetes and Hypomania

While each of the discussed variables – attachment styles, diabetes, and hypomania – has been studied independently, the interaction between them remains underexplored. Recent research into the neurobiological underpinnings of both diabetes and affective disorders suggests a complex relationship between metabolic and psychiatric conditions.[91] A crucial factor linking these elements is the dopaminergic system, which plays a pivotal role in regulating mood,

energy, and behavior. In the context of diabetes, both Type 1 and Type 2, disturbances in dopamine signaling are thought to contribute to alterations in emotional regulation, including the potential emergence of hypomanic episodes.[86]

As we have discussed in previous sections, dopamine dysregulation has been implicated in both diabetes and hypomania. In Type 2 diabetes, insulin resistance and metabolic dysfunction disrupt normal dopamine signaling, leading to increased dopaminergic activity, which is characteristic of hypomanic states. This alteration in dopamine functioning not only affects mood but could also interfere with other cognitive and emotional processes, potentially leading to heightened susceptibility to mood instability. Similarly, in Type 1 diabetes, while insulin resistance is not a primary concern, the need for exogenous insulin and fluctuations in glucose levels can contribute to mood dysregulation and the emergence of hypomanic symptoms.[92]

Interestingly, studies suggest that disturbances in dopamine functioning may also influence the formation and maintenance of attachment bonds, thus adding another layer of complexity to the interplay between these variables.[93] Attachment, as a psychological construct, is crucial in shaping emotional regulation, particularly in the development of interpersonal relationships.[94] The attachment system is modulated by dopamine, which affects reward processing and motivation. When dopamine dysregulation occurs, it may compromise the ability to form secure attachment bonds, potentially contributing to emotional instability and an increased risk for psychiatric conditions, including hypomania.[95]

While the connection between attachment styles and dopaminergic dysregulation remains largely unexplored, there are some emerging insights. Attachment theory suggests that early relational experiences shape the emotional and behavioral responses of individuals in later relationships.[96] Secure attachment is generally associated with a balanced regulation of emotions and effective coping mechanisms, while insecure attachment styles (eg, anxious or avoidant) are linked to heightened emotional reactivity and difficulties in emotional regulation.[96] Given dopamine's significant role in both reward processing and emotional regulation, it is plausible that dopamine dysregulation could impact the formation of attachment bonds. For instance, individuals with dopamine dysfunction may have difficulty experiencing the rewarding aspects of attachment relationships, which could lead to either hyper-attachment (as seen in anxious attachment) or emotional detachment (as seen in avoidant attachment).

However, the direct link between insecure attachment and dopamine dysfunction remains a subject of debate. While some studies suggest that altered dopamine activity may predispose individuals to insecure attachment styles, there is currently insufficient evidence to conclusively establish a causal relationship.[70] Further research is needed to explore whether insecure attachment associated with disrupted dopamine functioning contribute to the development of psychiatric conditions such as bipolar disorder and hypomania.[97]

In addition to the dopaminergic hypothesis, the neuroinflammatory hypothesis offers another perspective on the relationship between diabetes and hypomania. Both Type 1 and Type 2 diabetes are associated with low-grade chronic inflammation, which can influence brain function and exacerbate psychiatric symptoms. Insulin resistance, a hallmark of Type 2 diabetes, triggers the activation of microglia in the brain, leading to the release of inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α).[98] Neuroinflammation activated by diabetes may lead to impaired functioning of neurotransmitters such as dopamine and serotonin, which are crucial for emotional regulation.[99] This could explain the mood instability and the development of hypomanic or manic episodes in individuals with diabetes. Jiang et al explore the mechanisms by which microglia-induced inflammation results in synaptic loss, which, in turn, impacts neurotransmitter systems and cognitive function.[100]

The convergence of these two hypotheses – dopaminergic dysregulation and neuroinflammatory mechanisms – provides a more integrated perspective on the complex relationships between diabetes and psychiatric conditions such as bipolar disorder. These processes are not mutually exclusive but rather work together, influencing both metabolic and psychiatric health. This highlights the need for an interdisciplinary approach to understanding the underlying mechanisms and treatment strategies for individuals who are both diabetic and prone to mood disorders such as hypomania.

Future Research Directions

Given the significance of understanding the interaction between diabetes, attachment styles, and dopamine dysregulation, there is an urgent need for large-scale, longitudinal studies to explore these connections further. A comprehensive

investigation into the neural, metabolic, and psychological factors contributing to mood dysregulation in diabetes would provide valuable insights into the treatment and management of co-occurring psychiatric and metabolic conditions.

To address these gaps, future studies should incorporate advanced neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and quantitative electroencephalography (QEEG), alongside psychometric tools for assessing attachment styles and hypomanic symptoms. By combining these methods with self-report questionnaires, such as the Experiences in Close Relationships – Revised Scale (ECR-RS) for attachment and the Hypomanic Checklist (HCL-32) for evaluating hypomanic symptoms, researchers can identify individuals at higher risk for developing mood instability. These tools may also assist in uncovering any distinct neurophysiological markers that link attachment dynamics, dopamine dysregulation, and mood disorders. Furthermore, the use of biomarkers, including neurochemical markers and inflammatory cytokines, would strengthen our understanding of the underlying physiological mechanisms. The integration of these methodologies will enhance our ability to assess the complex relationship between diabetes, attachment styles, and mood disorders.

In regions like Bulgaria, adapting these research tools and techniques to capture local nuances of attachment, mood disorders, and diabetes would provide invaluable insights relevant not only to local healthcare practices but also to global healthcare challenges. Such studies could potentially guide the development of more personalized and integrated treatment strategies for individuals dealing with both psychiatric and metabolic conditions.

Conclusion

This article examines the complex interactions between diabetes, hypomania, and attachment styles, highlighting the role of dopamine dysregulation and metabolic processes in the development of psychiatric symptoms. Both Type 1 and Type 2 diabetes are associated with an increased risk of hypomanic episodes and other psychiatric symptoms. Impaired glucose regulation, insulin resistance, and inflammatory processes play a crucial role in this interplay, altering dopamine pathways and contributing to psychiatric instability. Although research in this area remains limited, it is essential to explore the mechanisms linking diabetes, hypomania, and attachment, as such studies could offer significant benefits for understanding and treating co-occurring psychiatric and metabolic disorders. This research could provide new approaches for therapeutic interventions and improve the management of patients suffering from these conditions.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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