Astrocytes and Their Role in Psychiatric Disorders

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Abstract

Astrocytes are the most abundant glial cells in the central nervous system. They are recognized as active participants in neurodevelopment, neurotransmission and synaptic plasticity. Astrocytes are increasingly associated with the modulation of neuronal circuits and regulation of neurotransmitter balance. The dysregulation of these functions may contribute to the progression of psychiatric illnesses. The understanding of astrocytes and their relation to psychiatric disorders such as schizophrenia, bipolar disorder, and major depressive disorder is constantly evolving. Targeting astrocytes in the development of therapeutic interventions for psychiatric disorders is an emerging avenue of exploration. This paper discusses the exact function of astrocytes, their part in synaptic plasticity and how they play a crucial role in the development and presence of psychiatric illnesses, specifically schizophrenia and mood disorders.

What Are Astrocytes?

One of the most integral components of one's central nervous system are astrocytes. In the past, astrocytes were thought to act only as supporting cells for neurons; however, modern research suggests that they may play additional, multifaceted roles crucial to the proper functioning of the nervous system. Structurally, astrocytes possess numerous fine processes extending from their cell bodies, which form intricate networks that wrap around neurons and their synapses. It is oftentimes said that astrocytes are in "close structural association with synapses" (Notter, 2021). This feature in astrocytes greatly helps in regulating synaptic transmission. Functionally, they contribute to the maintenance of neuronal health and homeostasis by regulating nutrient and ion levels, as well as participating in the formation and maintenance of the blood-brain barrier.

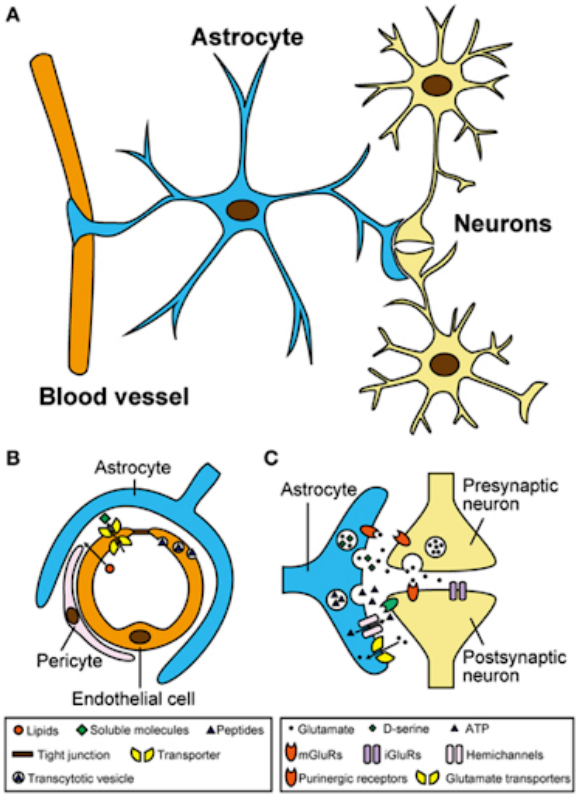

Figure 1. Visualization of Astrocyte Structure and Some of its Roles (Research Gate, 2016)

The Role of Astrocytes in Neurotransmission and Synaptic Plasticity

Neurotransmission and synaptic plasticity are critical functions of astrocytes that are necessary for the nervous system's essential processes and function. By actively contributing to the control of neurotransmitter levels in the synaptic cleft (the narrow space between two neurons in which chemicals are exchanged), astrocytes have a significant impact on neurotransmission. The process by which neurotransmitters—chemical messengers in the brain—are reabsorbed into presynaptic neurons following their release into the synaptic cleft is known as neurotransmitter reuptake. Ensuring appropriate neurotransmitter levels and controlling neuronal transmission depend on this mechanism. Neurotransmitters like gamma-aminobutyric acid (GABA), a major inhibitory neurotransmitter, and glutamate (the most abundant neurotransmitter in the body), a major excitatory neurotransmitter, are taken up by astrocytes after their release into the postsynaptic cell. Astrocytes assist in stopping the signaling between neurons by removing these neurotransmitters from the synaptic cleft, avoiding overstimulation and preserving the equilibrium of neuronal activity. In addition to neurotransmission, they also play a crucial role in synaptic plasticity. They release signaling molecules, such as gliotransmitters, which can modulate the strength of synaptic connections. Synaptic connection is what controls the consistency of transmissions between two specific cells. The significance of these connections between two neurons can be influenced by various factors such as the frequency of activation, the relevance of information and neurotransmitter type, just to name a few. Moreover, astrocytes control a process known as synaptic pruning, which strengthens and improves significant synaptic connections while removing less significant ones. (NIMH. 2023, March). Astrocytes influence long-term potentiation (LTP) and long-term depression (LTD), two forms of synaptic plasticity associated with learning and memory. LTP is the process by which synaptic connections strengthen and LTD involves weakening them. Glutamate, ATP and cytokines are all compounds that astrocytes regulate in the process of plasticity (Ota, Y., Zanetti, A. T., & Hallock, R. M. 2013).

These factors modulate LTP and LTD, influencing the persistence and strength of synaptic changes associated with memory formation.

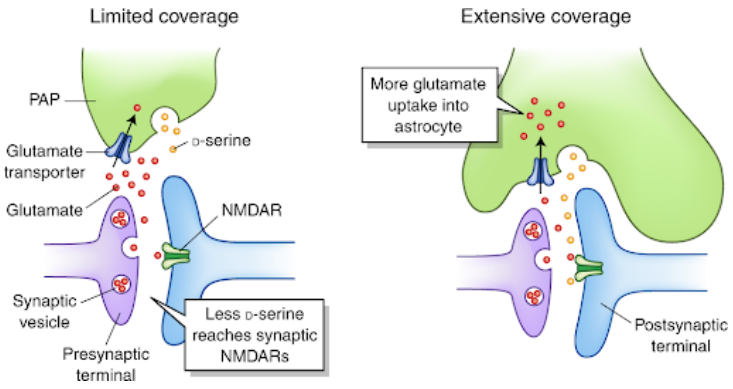

Figure 2. Diagram of Plasticity of Structural Interactions, Synaptic Elements and Astrocytes (Santello et al., 2019).

Psychiatric Disorders and Their Prevalence

Psychiatric disorders, also referred to as mental health disorders, are a broad category of problems that impact a person's thoughts, feelings, actions, and general state of health. These complicated illnesses are frequently caused by a mixture of biological, psychological, environmental, and hereditary variables. They impact a wide range of individuals and, as shown in a study from The World Health Organization in 2019, approximately 1 in 8 people suffered from some variation of mental illness. Additionally, these numbers drastically increased after the COVID-19 pandemic (World Health Organization, 2022). There are a broad range of categories for psychiatric disorders such as, depressive, anxiety, bipolar, neurodevelopmental, etc. are a few amongst the many different types of illnesses. The prevalence of psychiatric disorders varies upon many different factors such as which disorder it is, geographic location as well as cultural factors. Mental illness encompasses many different conditions ranging from mild to moderate to severe. There are two distinct categories when it comes to mental illnesses: Any Mental Illness (AMI) and Serious Mental Illness (SMI). AMI includes all recognized mental illnesses. SMI is a smaller and more severe subgroup of AMI. (National Institute of Mental Health, 2023).

Schizophrenia & Mood Disorders

Schizophrenia is a serious and chronic mental disorder that greatly impacts a person's thinking, emotions and behavior. Symptoms of schizophrenia can be characterized as either positive and negative. Positive symptoms involve things that are physically/outwardly visible and add factors into one's behavior, whereas negative symptoms are much more subtle, difficult to observe and tend to subtract a factor from one's behavior. (National Library of Medicine, 2019). Mood disorders are another type of psychiatric illness. They significantly impact one's mood regulation and can impact their daily tasks and overall mental well being. Some common mood disorders include major depressive disorder and bipolar disorder. They also impact one's emotions and behavior through a series of hallucinations, disorganized thinking, etc. However, mood disorders emphasize a persistent feeling of sadness and can eventually lead to a lack of interest in everyday activities that an individual once enjoyed (National Library of Medicine, 2019).

How Do Astrocytes Relate to these Disorders?

Dysfunctional synaptic pruning has been observed in schizophrenia (Sekar et al., 2016), which can lead to inflammation in the brain, disruption of balance of neural circuits as well as irregular brain connectivity (Birnbaum & Weinberger, 2017). These genetic variations in affecting astrocyte function can cause individuals to be more susceptible to this disorder. Moreover, astrocytes play a critical role in neuroplasticity, which is commonly known as the brain's ability to adapt and reorganize. Neuroplasticity is oftentimes impaired in such psychiatric conditions (Santello, M., 2019). In mood disorders, dysfunctional astrocytes can influence weak synaptic connectivity and prevent regulation in reuptake and release of neurotransmitters, leading to such disorders. In addition to this, it has been noted that astrocytes also help in regulating neurotransmitter levels which are typically dysregulated in the disordered brain. They play an intricate role in maintaining the balance of these neurotransmitters and dysfunction of this role may contribute to symptoms of such disorders (NIMH, 2023). Dopamine imbalance is highly common in schizophrenia (Correll, C. 2020). If astrocytes are unable to undergo the process of neurotransmitter uptake and regulate their levels, it may lead to something similar to dopamine imbalance which eventually contributes to the symptoms of schizophrenia.

Conclusion

The evolving understanding of astrocytes and their roles in the central nervous system emphasizes their importance to psychiatric disorders. Through their regulation of neurotransmitter balance, synaptic transmission, and plasticity, they have exerted great influence over the neuronal circuits necessary for mood regulation. By investigating the complex relationship between astrocytes and psychiatric disorders, further research may lead to new approaches for managing complex conditions and improving treatment for individuals that suffer from such illnesses. Thus, continued research and studies on astrocytes holds immense potential to advance and better our understanding and treatment of psychiatric disorders.

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