Brain Fog: A Neurocognitive and Pathophysiological Review of Mechanisms and Clinical Correlates

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Abstract

"Brain fog" is a non-specific clinical term describing subjective cognitive impairment characterized by reduced clarity of thought, memory disturbances, and impaired concentration. While commonly reported across multiple conditions, it lacks formal diagnostic classification. This narrative review examines the neurocognitive and pathophysiological mechanisms underlying brain fog, including neuroinflammation, neurotransmitter imbalance, metabolic dysfunction, and network-level brain connectivity disruption. Understanding these mechanisms provides a framework for interpreting brain fog as a manifestation of underlying systemic or neurological processes rather than a standalone disorder.

This article is a narrative review based on existing literature and does not present original experimental data.

Keywords

brain fog, neuroinflammation, cognitive dysfunction, brain networks, neurotransmitters, fatigue, neurobiology

Introduction

Brain fog is increasingly recognized as a clinically relevant symptom complex observed in conditions such as chronic fatigue syndrome, post-viral syndromes, metabolic disorders, and neuropsychiatric illnesses. Despite its prevalence, it remains poorly defined within formal diagnostic frameworks. Advances in neuroscience suggest that brain fog reflects dysfunction across multiple interconnected systems rather than isolated pathology [1].

1. Neuroinflammatory Mechanisms

Neuroinflammation is a key contributor to cognitive dysfunction. Elevated cytokines such as IL-6 and TNF-α can disrupt synaptic signaling and impair neuronal communication. Microglial activation further contributes to altered neural processing and cognitive fatigue [2].

2. Neurotransmitter Imbalance

Cognitive clarity depends on balanced neurotransmitter activity. Brain fog has been associated with:

- Reduced dopamine (affecting motivation and focus)
- Altered serotonin (mood and cognition)
- Acetylcholine dysfunction (memory and attention)

These imbalances impair efficient neural signaling [3].

3. Metabolic and Mitochondrial Dysfunction

Energy metabolism plays a critical role in brain function. Mitochondrial dysfunction reduces ATP availability, leading to:

- Mental fatigue
- Slowed cognitive processing
- Reduced neuronal efficiency

This is particularly relevant in systemic illnesses and chronic fatigue states [4].

4. Brain Network Dysregulation

Functional connectivity studies demonstrate disruption in:

- Default Mode Network (DMN)
- Executive Control Network
- Salience Network

These alterations impair attention, working memory, and cognitive flexibility [5].

5. Systemic and Clinical Associations

Brain fog is associated with:

- Post-viral syndromes (e.g., post-COVID states)
- Autoimmune disorders
- Sleep disturbances
- Psychological stress

These factors often interact, contributing to persistent cognitive symptoms [6].

Discussion

Brain fog represents a multidimensional phenomenon involving neuroinflammatory, neurochemical, metabolic, and network-level disruptions. Rather than being a discrete disorder, it should be viewed as a clinical manifestation of underlying systemic and neurological dysfunction. Integrating these mechanisms allows for a more comprehensive understanding and targeted therapeutic approaches.

Conclusion

Brain fog is a complex neurocognitive symptom rooted in identifiable biological mechanisms. Recognizing its pathophysiological basis enhances diagnostic clarity and supports the development of targeted interventions. Future research should focus on objective biomarkers and standardized clinical definitions.

Table 1. Mechanisms Contributing to Brain Fog

Mechanism	Pathophysiology	Clinical Effect
Neuroinflammation	Cytokine-mediated disruption	Cognitive fatigue
Neurotransmitter imbalance	Dopamine/serotonin changes	Poor focus
Mitochondrial dysfunction	Reduced ATP production	Mental exhaustion
Network dysregulation	Connectivity disruption	Impaired cognition

Figure 1. Pathophysiological Model of Brain Fog

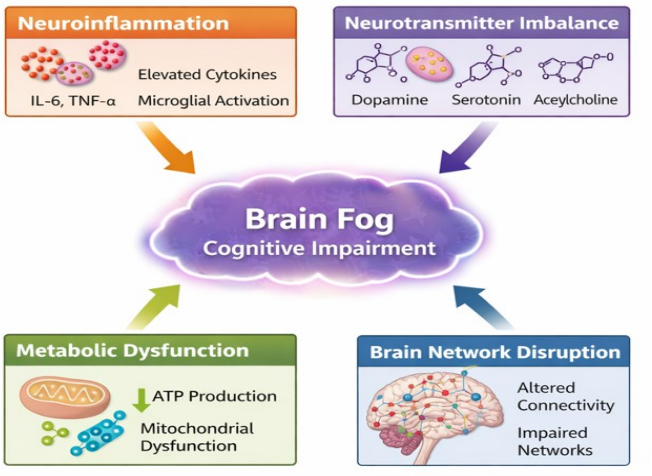

Fig. 1. *Diagram illustrating the interaction of neuroinflammation, neurotransmitter imbalance, metabolic dysfunction, and brain network disruption leading to cognitive impairment and subjective brain fog.*

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