Chapter 3
Cognitive Function Involving Glial Cells:
The Surprising Role of Astrocytes

Samira Boulbaroud
Polydisciplinary Faculty of Beni Mellal, Morocco

Hanane Khalki
Polydisciplinary Faculty of Beni Mellal, Morocco

Fatima Zahra Azzaoui
Laboratory of Biology and Health, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

ABSTRACT

Astrocytes, once considered passive support cells in the central nervous system, are now recognized as dynamic contributors to neuronal processes. They play pivotal roles in regulating synaptic transmission, modulating excitability, and influencing synapse formation. These non-neuronal cells release gliotransmitters like glutamate, affecting synaptic activity. Dysfunctions in astrocytes are linked to neurodegenerative and psychiatric disorders. In neurodegenerative disorders like Alzheimer's and Parkinson's, astrocytic dysfunction plays distinct roles. While astrocytes may not significantly contribute to Alzheimer's progression, they are involved in neuroinflammation, Aβ metabolism, and calcium regulation. Conversely, in Parkinson's, astrocytes contribute to mitochondrial dysfunction, impacting dopaminergic neurons. This comprehensive exploration sheds light on the intricate and multifaceted roles of astrocytes in cognition and their potential implications for therapeutic interventions in neurological and psychiatric conditions.

INTRODUCTION

Glial cells, a heterogeneous group of non-neuronal cells, are crucial for modulating and supporting neuronal function in the central nervous system (CNS). Glial cells, including astrocytes, microglia, and oligodendrocytes, constitute the majority of cells in the CNS (Jakel & Dimou., 2017). While neurons

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have received more attention traditionally, glial cells are increasingly acknowledged for their essential roles in maintaining brain homeostasis, synaptic function, neuronal survival, and information processing. Glial cells provide metabolic support, regulate extracellular ion concentrations, recycle neurotransmitters, contribute to the blood-brain barrier, and actively participate in immune responses and synaptic plasticity (Barker et al., 2008).

Astrocytes, the most abundant glial cell type in the brain, have been traditionally associated with functions such as metabolic support, regulation of extracellular ion concentrations, and maintenance of the blood-brain barrier (Herculano-houzel., 2014; Vasile et al., 2017). However, recent studies have unveiled their unexpected involvement in cognitive functions, challenging the conventional view of astrocytes as passive support cells., Research has shown that astrocytes actively participate in various cognitive processes, including learning, memory, and synaptic plasticity (Dossi et al., 2018). They regulate synaptic transmission, modulate neuronal excitability, and influence the formation and elimination of synapses. Additionally, astrocytes release gliotransmitters, such as glutamate, ATP, and Adenosine, which can directly modulate synaptic activity and contribute to information processing in the brain (Park et al., 2015; Chen et al., 2013; Lee et al., 2013; Fujii et al., 2014; Sibille et al., 2014, 2015). Astrocyte dysfunctions have been implicated in several neurodegenerative and psychiatric disorders, further highlighting their importance in cognitive functions. Dysregulated astrocyte calcium signaling, impaired glutamate uptake, and disrupted astrocyte-neuron interactions have been observed in conditions such as Alzheimer's disease, Parkinson's disease, and schizophrenia. Overall, the coexistence and intertwining of protoplasmic astrocytes and varicose projection astrocytes in the human cortex suggest that they are distinct subtypes of cells with specialized functions in regulating synaptic activity and supporting the communication between different brain regions. Astrocytes, previously known as supportive cells, are now recognized as active contributors to cognitive processes. The multifaceted nature of their roles, encompassing metabolic assistance, modulatory control over synaptic activity, and involvement in neural plasticity, underscores the complex interplay between neurons and astrocytes within the CNS (khakh & Sofroniew., 2015). Gaining insight into the functions of astrocytes in cognition may offer novel avenues for therapeutic interventions aimed at addressing neurodegenerative and psychiatric conditions (Liddelow & Barre., 2017; Dallerac & Rouach., 2016).

THE MULTIFACETED ROLES OF ASTROCYTES IN COGNITIVE FUNCTION: INSIGHTS AND IMPLICATIONS

Heterogeneity of Astrocytes and the Multiplicity of Their Origin

Astrocytes, a type of glial cells in the CNS, perform various functions, including metabolic and structural support for neurons, regulation of the extracellular environment, and contribution to neural development and signaling (Chen and Swanson, 2003). The existence of two basic subtypes of astrocytes in rodents, the protoplasmic and fibrous astrocytes, has been established (Miller & Raff, 1984).

Protoplasmic astrocytes exhibit bushy and highly branched morphology, with numerous fine processes emanating from the cell body. They are primarily located in the gray matter of the CNS, particularly in the cerebral cortex, where they are closely associated with neurons and synaptic structures. Protoplasmic astrocytes play a vital role in maintaining microenvironment surrounding neurons, providing metabolic support, regulating neurotransmitter levels, and modulating synaptic activity (Tabata, 2015).