Chapter 5
Brain Aging and Glial Cells: What Is the Link?

Kamal Smimih
Faculty of Sciences and Techniques, Sultan Moulay Slimane University, Morocco

Chaima Azzouhri
Faculty of Sciences and Techniques, Sultan Moulay Slimane University, Morocco

Fatima Ez-Zahraa Saad
Independent Researcher, Morocco

Youssef Ait Hamdan
https://orcid.org/0009-0005-8616-8852
Higher Normal School, Cadi Ayyad University, Morocco

Jawad Laadraoui
https://orcid.org/0000-0002-9784-1265
Faculty of Sciences, Hassan II University of Casablanca, Casablanca, Morocco

Nadia Zouhairi
Faculty of Sciences and Techniques, Sultan Moulay Slimane University, Morocco

Mohamed Merzouki
https://orcid.org/0000-0002-9837-4312
Faculty of Sciences and Techniques, Sultan Moulay Slimane University, Morocco

ABSTRACT

Brain aging is a complicated and diversified process that includes an ongoing decline in cognitive performance as well as various cellular and molecular changes in the brain. During an individual's life, glial cells such as oligodendrocytes, microglia, and astrocytes are crucial for maintaining healthy brain function. Astrocytes support neurons but may become less efficient with age, contributing to cognitive decline. Microglia, the brain's immune cells, can turn overactive with age, causing inflammation which can lead to neuronal damage. Oligodendrocytes, responsible for myelin sheath maintenance, also undergo changes, affecting neural communication. With advancing age, changes in glial cell function may lead to neuroinflammation, oxidative damage, and abnormalities in neural circuitry, all of which contribute to age related cognitive decline and neurodegenerative disorders. This chapter delves into the intricate dynamics of brain aging, focusing on the profound influence of age-related changes in glial cells.

DOI: 10.4018/978-1-6684-9675-6.ch005

1. INTRODUCTION

Brain aging is characterized by a multitude of dynamic changes in glial cells, particularly astrocytes (Palmer and Ousman, 2018) and microglia (von Bernhardi, Eugenín-von Bernhardi, and Eugenín, 2015), which have far-reaching implications for neural function and age-related neurodegenerative diseases (Suksuphew and Noisa, 2015). Astrocytes, until thought to be inert supporters, reveal an unseen dynamism as they age (Matias, Morgado, and Gomes, 2019). Their cellular hypertrophy, the swelling of cell bodies and processes, and the reconfiguration of their structural components paint a vivid portrait of their evolution (Verkhratsky et al., 2019; Clarke et al., 2018; Stogsdill et al., 2017). In turn, microglia, the brain's vigilant sentinels, metamorphose in response to neuroinflammatory cues or cellular distress (Muzio, Viotti, and Martino, 2021). They transition from a state of constant surveillance, characterized by long, branched processes, to an activated, amoeboid form replete with pro-inflammatory attributes (Hickman et *al*., 2013).

This change brings about long-lasting inflammation in the brain, which is a common sign of brain aging. It may significantly affect cognitive performance and potentially cause neurodegenerative diseases (Jin et *al*., 2022). These changes in the shape of glial cells with the age course suggests that the aging brain is always changing, and this can affect the complex functioning of the brain.

This chapter explores the changing role of glial cells in the aging brain, exploring their morphological and functional changes. As well, it examines how these changes impact brain function, including synaptic activity, neurotransmitter regulation, and susceptibility to oxidative stress. Additionally, it highlights the glial cell contributions to age-related neurodegenerative diseases like Alzheimer's, Parkinson's, and multiple sclerosis, underscoring the significance of aging in these conditions.

Additionally, it investigates the delicate interplay of oxidative stress, inflammation, genetics and epigenetics, to understand the mechanisms causing these changes in order to figure out the mysteries of brain aging, enabling the development of new strategies for preserving the healthy aging and combatting age-related neurological disorders.

2. AGE-RELATED CHANGES IN GLIAL CELLS

2.1 Structural Alterations

2.1.1 Changes in glial cell morphology

The alteration in glial cell morphology, notably that seen in astrocytes and microglia, is one indicator of brain aging. Astrocytes show significant morphological changes with age. These changes include cellular hypertrophy, an increase in the size of the cell bodies and processes, and a reorganization of their structural components (Stogsdill et *al*., 2017; Clarke et *al*., 2018;Verkhratsky et *al*., 2019). As a result, the intricate network of fine astrocytic processes that intimately associates with synapses and neurons becomes altered, impacting synaptic function and neurotransmitter regulation (Kim, Park, and Choi, 2019).

Microglia, the brain's resident immune cells, also undergo striking changes in morphology during aging. When they are young, microglia have a ramified shape, characterized by long, branched processes, facilitating their constant surveillance of the brain microenvironment (Vidal-Itriago et *al,*. 2022). However, in response to neuroinflammatory cues or cellular stress, microglia in aged brains transition