


Chapter 3

Modulating Neuroinflammation and Autophagy in Psychiatric Disorders Through Mechanisms and Therapies: Therapeutic Strategies and Pathways

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ABSTRACT

The chapter presents the relationship between autophagy and neuroinflammation in major depression, bipolar disorder, and schizophrenia. It emphasizes that oxidative stress coupled with mitochondrial dysfunction can activate mTOR, AMPK, and FOXO1, thereby influencing synaptic function and behavior. The influence of

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microglia, HMGB1, and Toll-like receptors is discussed. The chapter explores how altered gut microbiota and nutrition affect autophagy by regulating short-chain fatty acid levels and inflammatory signals. The effects of lifestyle modifications, such as time-restricted feeding and the use of key phytochemicals (curcumin, resveratrol, hydroxytyrosol, thymoquinone, saffron), on autophagy and inflammation levels are investigated. Summary tables and case studies support the results presented. Neuronal organoids and 3D-printed brain models are introduced as innovative tools to explore disease pathways for future clinical initiatives.

1. INTRODUCTION

1.1. Overview of Inflammation and Autophagy in Neuropsychiatric Disorders

Major neurological, psychiatric, and neurodegenerative disorders are strongly associated with and regulated by neuroinflammation and autophagy (Absalyamova et al., 2025). In this chapter, therefore, three objectives are presented to assist in the main goal of explaining how these processes are related to the corresponding regulatory systems in view of potential treatment. Typically, stressors, including oxidative stress, mitochondrial dysfunction, and toxic protein aggregation, induce neuroinflammation in the CNS. A multitude of these pathogenic stimuli are related to aberrations in autophagy, a cellular process through which damaged proteins and organelles are cleared. Both of these mechanisms are thought to create feedback that worsens neuronal decay and the general pathology of the disease (Gadhawe, et al., 2024).

1.2. Molecular Pathways Regulating Autophagy and Neuroinflammation

Several studies have shown that autophagy is modulated by different signaling networks involving the mechanistic target of rapamycin (mTOR) (Xu et al., 2025), AMP-activated protein kinase (AMPK) (Yang et al., 2025), and Forkhead box O1 (FOXO1) (Wang, et al., 2025). The fine-tuning of these pathways defines the ratio of cell survival to repair and is extensively regulated. For example, under ample energy conditions, mTOR suppresses autophagy, whereas under low energy conditions, AMPK promotes autophagy. These pathways sustain the progression of neurodegenerative disorders such as AD, PD, and ALS and prevent chronic neuroinflammation associated with these diseases (Ragupathi, et al. 2024; Sadeghi, et al. 2023). Autophagy is finely regulated through mTOR, AMPK, and FOXO1

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