Chapter 2
Autophagy-Based Treatment Approaches in Neuropsychological Diseases

Şebnem Yıldırımcan Kadıçeşme
https://orcid.org/0000-0002-8908-9464
Kafkas University, Turkey

ABSTRACT

Autophagy is an extremely important molecular pathway for the maintenance of cellular and organismal balance. According to recent research, cognitive diseases like dementia, Alzheimer's disease, Parkinson's disease, Huntington's disease, attention-deficit hyperactivity disorder, schizophrenia, and bipolar disorder are all influenced by defective autophagy. Neuropsychiatric disorders are extremely important because they affect the brain function, emotions, and mood of patients. Treatment of neuropsychiatric disorders is a very difficult process, and some problems are encountered in response to treatment. Therefore, new treatment approaches are needed. Given its significance in the pathophysiology of neuropsychological diseases, the autophagy pathway appears to be a promising target for the development of novel therapeutic approaches for these conditions. New research should be focused on explaining the relationship between this pathway and neuropsychological disorders. The data obtained from these studies will pave the way for the development of new therapeutic agents.

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INTRODUCTION

Autophagy is a physiological process that eliminates infections, damaged macromolecules, long-lived proteins, misfolded or aggregated proteins, and malfunctioning organelles (Klionsky et al., 2021). Autophagy maintains intracellular homeostasis by breaking down and recycling proteins and organelles (Liu et al., 2023). Autophagy occurs through three different mechanisms: microautophagy, macroautophagy, and chaperone-mediated autophagy; however, the most prominent mechanism is macroautophagy (Liu et al., 2023).

Numerous neuropsychiatric and neurodegenerative disorders have been linked to abnormalities in the autophagy system. The onset and progression of neurodegenerative disorders are significantly influenced by precipitate-forming protein aggregates in nerve cells. The ubiquitin-proteasome system and autophagy do not remove these disease-associated aggregates from the cell. Therefore, disruptions in these pathways trigger synapse loss, nerve cell abnormalities, and cell death. For this reason, creating autophagy-based treatment plans for various illnesses requires an understanding of the molecular mechanisms underlying autophagy (Li et al., 2024). An overview of the connection between neuropsychological diseases and the autophagy pathway, as well as autophagy-based therapy options, is intended to be given to readers in this section.

BACKGROUND

Autophagy

Long-lived proteins, malfunctioning organelles, cytosolic fragments, damaged macromolecules, and pathogens are all degraded by autophagy, which uses proteolysis to maintain cellular and organismal homeostasis (Yamamoto, 2023). Based on membrane dynamics and cargo delivery mechanisms, three categories can be used to classify autophagy: chaperone-mediated autophagy, microautophagy, and macroautophagy (Figure 1). In macroautophagy, a structure with two membranes known as the autophagosome is formed as a result of membrane elongation (Yamamoto, 2023). The precursor of the autophagosome is the cup-shaped, double-membrane phagophore. The phagophore isolates cytoplasmic material and closes to form the autophagosome (Menzies et al., 2017). The autophagosome then fuses with lysosomes, and the cytoplasmic contents are degraded. Macroautophagy is