Involvement of Astrocytic Tetraploidy in Pharmacoresistant Epilepsy: Role of The P2x7 Receptor

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Abstract

Introduction: Pharmacoresistant epilepsy is a significant public health problem, affecting 25–33% of patients who do not respond to current antiseizure treatments. This situation highlights the urgent need to identify new therapeutic targets. This study analyzes the role of astrocytic tetraploidy (a state with 4C DNA content) in pharmacoresistance, as well as its impact on neuronal excitability.

Method: Two experimental models were used: (i) a human astrocyte cell line (CRL-8621), and (ii) primary astrocyte cultures obtained from resected cortical tissue of patients with pharmacoresistant epilepsy. The cell line was differentiated in serum-free conditions. Methodologies included immunocytochemistry to detect membrane receptors, and intracellular calcium homeostasis was assessed to evaluate receptor functionality.

Results: Our results show that purinergic P2X7 receptors are present in the cell line and their expression significantly increased after serum deprivation and differentiation. The presence of tetraploid astrocytes was confirmed, and functionally, they responded to various stimuli such as KCl, bradykinin, ATP, and Bz-ATP. Similarly, primary astrocytes expressed P2X7 receptors and functionally responded to the agonists Bz-ATP and ATP.

Discussion: Altogether, the results suggest that tetraploid astrocytes are functional and may be involved in pharmacoresistant epilepsy. These findings may contribute to identifying new therapeutic targets of interest in the future.

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