

Effects of corticosterone and amyloid beta on the corticosteroid receptors in organotypic brain slice cultures

Assistant Professor Merve Alaylioglu², **Professor, PhD Selma Yilmazer¹**, Professor PhD Erdinc Dursun², Professor PhD Duygu Gezen-Ak²

¹Dept. of Medical Biology, Halic University, Faculty of Medicine, Istanbul, Turkey, ²Brain and Neurodegenerative Disorders Research Laboratories, Department of Neuroscience, Institute of Neurological Sciences, Istanbul University- Cerrahpasa, Istanbul,, Turkey

Background

Stress is accepted as an important risk factor for Alzheimer's disease (AD) (1,2). High levels of cortisol, which is the stress hormone, in the cerebrospinal fluid (CSF), plasma and serum of Alzheimer's patients and the decrease in hippocampus volume and declarative memory disorders in patients with major depression and chronic corticosteroid treatment give rise to thought for a possible relationship between AD and stress (2,3,4). This suggests that the increase in glucocorticoid levels, which occurs as a result of stress, may participate in the formation of pathological mechanisms seen in AD, and raises the question of whether stress triggers the pathways that cause neurodegeneration or not.

Methods

In the study; in organotypic brain slice cultures, which allows to obtain results closest to in vivo models by protecting tissue architecture and microenvironment, circadian rhythm and stress models with corticosterone application and Alzheimer-like model with amyloid beta 1-42 (A β 1-42) peptide application were generated. The effects of these treatments on glucocorticoid receptor (GR) and mineralocorticoid receptor (MR) expressions, which are corticosteroid receptors, were investigated at both mRNA and protein levels. Regional localizations of these proteins in the brain were also examined by immunofluorescence method.

Results

As a result of our study, we found that GR and MR expression levels and their localizations in the hippocampus region changed both in circadian rhythm and stress models created by corticosterone applications and in AD-like models created by amyloid beta 1-42 application, and we determined that these changes differ depending on the dose. When we evaluate the findings of corticosterone and A β 1-42 applications we obtained in our study together, we observed that GR protein level, and GR localization in the hippocampus, especially in the stratum pyramidalis region, were similarly affected.

Conclusion:

Our findings point out that the increase in corticosterone caused by stress may be involved in the formation of pathological mechanisms seen in AD.

Keywords:

Alzheimer's disease, corticosterone, organotypic brain slice cultures

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