Chapter 5

Alternation of Mitochondrial and Golgi Apparatus in Neurodegenerative Disorders

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ABSTRACT

Neurodegenerative disorders (NDs) are characterized by dysfunction and loss of neurons associated with altered proteins that accumulate in the human brain and peripheral organs. Mitochondrial and Golgi apparatus (GA) dysfunctions are supposed to be responsible for various NDs. Damaged mitochondria do not produce sufficient adenosine triphosphate (ATP) and produce reactive oxygen species (ROS) and pro-apoptotic factors. Mitochondrial dysfunctions may be caused by various factors such as environmental causes, mutations in both nuclear or mitochondrial deoxyribonucleic acid (DNA), that code many mitochondrial components. Three factors that are mainly responsible for the morphological changes in GA are certain pathological conditions, drugs, and over expression of Golgi associated proteins. In this chapter, common aspects of mitochondrial and GA dysfunction concerned about NDs are summarized and described for Alzheimer’s disease (AD), Parkinson’s disease (PD), amyotrophic lateral sclerosis (ALS), and Huntington’s disease (HD).

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INTRODUCTION

NDs are characterized by bioenergetics defect, oxidative stress (OS) and progressive loss of physiologically or anatomically related neuronal system in the human brain (Schapira, 2008; Malkus et al, 2009; Oliveira, 2010). Neurons are the fundamental structure and functional unit of the nervous system of living beings which includes the spinal cord and brain. The neuronal diseases are incurable conditions result in progressive degeneration of nerve cells and cause ataxias or dementias (Beal, 2005; Manczak et al, 2005). The examples of NDs are AD, PD, ALS, prion disease, motor neuron diseases (MND), HD, spinocerebellar ataxia (SCA) and spinal muscular atrophy (SMA). The exact molecular, cellular and pathological mechanism responsible for the progression of these diseases and neuronal cell death are not fully understood. Every cell is a complex communications of various organelles such as endoplasmic reticulum (ER), GA, mitochondria, nucleus, etc. carrying out several functions. These organelles exchange materials and signals to make the cell functional properly without producing and defects. Nowadays, advanced techniques are allowing researchers to understand the connecting link between these organelles. Among the cell organelles, defective connections between mitochondria and GA have been concerned in several NDs. Generation of ROS in mitochondria and GA has been identified as an important factor for the cell death (Swerdlow & Khan, 2004; Lin & Beal, 2006; Reddy & Beal, 2008; Reddy, 2008). Mitochondria are exceptional amongst other organelles, as they dispose their own, mitochondrial DNA (mtDNA), which is mainly inherited from the mother. Their number is very high in neurons, mainly in synaptic terminals, as they are the major energy producers through tricarboxylic acid cycle (TCA) and oxidative phosphorylation. They undergo continual fusion and fission leading to their elongation or fragmentation respectively. GA is associated with protein trafficking in a cell and plays an important role in the pathogenesis of NDs. The objective of the chapter is to focus on the impact of dysfunctional mitochondria and GA on various NDs.

BACKGROUND

Various NDs have been recognized for centuries and research into their causes and effects has been taking place for decades. NDs are characterized by progressive loss of anatomically related neuronal systems. As life expectancy continues in developed countries, the occurrence of these disorders also increases. In the literature, much knowledge is being available concerning the mechanisms of disease, but the causing factors of these problems are still not well known. To date, many mechanisms have been recommended for explanation of protein aggregation metabolism, and misfolding, protein neuronal function, and cell signaling, but still it is difficult to understand the mechanism clearly at the cellular and molecular level (Tan et al, 2014). To understand these diseases, we need to understand how these cells function, their response to local environment and effect of dysfunctional organelles on these diseases. In this book chapter, authors focused on the role of mitochondria and GA on the dysfunction of neurons that result in various NDs. Mitochondrial play an important role in $\text{Ca}^{2+}$ homeostasis, ATP generation, ROS formation, and even apoptosis etc. and any dysfunction in these processes results in the dysfunction of neurons in a large number of NDs (Baloyannis, 2006). Functional or structural alterations of the Golgi pathology also recognized as a constant pathological characteristic of various NDs including PD, AD, HD, ALS, and prion diseases (Canet-Avilés et al, 2004). The neuropathological changes observed in these diseases can vary with the type of mutation in mtDNA, and level of Golgi dysfunction. GA marked as...