Chapter 1
The Aging Brain:
From Physiology to Neurodegeneration

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ABSTRACT

Neurodegeneration is the progressive and gradual dysfunction and loss of axons in the central nervous system. It is the main pathological characteristic of chronic and acute neurodegenerative conditions like Alzheimer's disease (AD), Parkinson's disease (PD), and multiple sclerosis (MS). The usual aspects of pathogenesis of disease can be abridged with regards to the downstream implications of uncontrollable protein oligomerization and aggregation from postmitotic cells. The brain structure constantly changes in normal aging without any dysfunction accompanying the structural changes in brain. The decline in cognitive capabilities, for example, processing speed, memory, and functions related to decision making are the sign of healthy aging. The reduction in brain volume in healthy aging is possibly related to neuronal loss at some marginal extent. The following chapter discusses the structural and functional alterations in the brain in ageing and neurodegeneration.

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INTRODUCTION

Aging of the brain is described through various anatomical, molecular and functional changes directing to enhance susceptibility to numerous diseases (Glorioso, Oh, Douillard, & Sibille, 2011). During aging, structural brain changes include volumetric shrinkage of brain and change in specific brain morphology in some region (Peters, 2006). Apart from the damage in structural integrity and neural plasticity, progressive declining in reserves of cellular homeostatic and variation in the mechanism of calcium dependent signaling has been recommended as the significant events associated in brain aging (Cai & Tammineni, 2017). Brain aging is also associated with some chemical and molecular alteration such as changes in hormones and neurotransmitter levels, accelerated formation of reactive oxygen species (ROS), dysfunctioning of mitochondria, accretion of nuclear and mitochondrial DNA damage convoyed by age related failure in DNA repairing and aggregation of intracellular and extracellular proteins (Wallace, 2010). Such severe changes in cellular and molecular levels cause difficulties in regular activities like attention, sleep, language, speech, decision making and cognitive abilities like work memory and long term memory (Alhola & Polo-Kantola, 2007). Higher-order brain system breakdown in aging is associated partially to myelinated fibres disruption which connects neurons to various cortical regions. Though the minimal neuronal loss in most of the cortical region is a part of normal brain aging, variation in synaptic physiology of neurons aging may participate in alteration of connectivity and higher order integration (Bishop, Lu, & Yankner, 2010). Significantly, these changes reduced down the coordination of brain activity which leads to weak performance in numerous cognitive domains.

Neurodegeneration is continuous loss of structural and functional properties of neurons corresponds to some pathological conditions which including neurons death (Gorman, 2008). In manner, neurodegenerative disorders (NDs) signify a huge assembly of neurological disorders with varied pathological and clinical expressions disturbing particular neuronal sets in detailed functional anatomic systems that progress in a persistent manner (Lin & Beal, 2006). Different NDs like PD, AD, Huntington disease (HD) and amyotrophic lateral sclerosis (ALS) are common in therapeutic research studies. NDs are mostly characterized through the factors like genetic risk factors, certain age ranges, courses of progression, clinical symptoms, dysfunctioning and neuronal death particular biochemical abnormalities, and presence of extracellular and intracellular protein (Kovacs, 2016). In the advance study, the beginning of NDs are instigated by the protein aggregation which are called proteinopathies (Shelkovnikova, Kulikova, Tsvetkov, Peters, Bachurin, Bukhman, et al., 2012). In this case, the aggregation of soluble monomers or oligomers cause toxic conditions subjected to consideration like some slight variations in the synthesis of α-synuclein and tau protein cause the occurrence of certain stressful condition which lead to PD and frontotemporal dementia respectively (Wang & Roberts, 2010). For these proteins, it is common that the holoprotein comparatively or entirely benign and with a series of cleavage of these protein lead to the production of toxic species or fragments. Likely, the rate of full length protein production is not a significant issue with respect to the rate of cleavage level of that protein. The example of ongoing studies on this fact is the cleavage of full-length amyloid precursor protein (APP) resulted to the production of toxic product called amyloid β (Aβ) peptide which get aggregated onto the neurons and cause AD (O'Brien & Wong, 2011). Similarly, this toxic-fragment model appears to be appropriate to some polyglutamine diseases like spinocerebellar ataxia type 3 and HD (Shao & Diamond, 2007). This notion also proves to be helpful in therapeutically tracing of NDs. The chapter highlights the physiological functioning of brain, structural and functional brain changes in ageing and neurodegeneration. The chapter also focusses on the factors which are responsible for aging and neurodegeneration.