Summary. Oxidative stress, inflammation and the aggregation of oxidized, misfolded or aberrant proteins in the brain induces deregulations in programmed cell death: apoptosis and autophagy. Apoptosis is one of the processes implicated in aging and neurodegenerative pathologies, and for the last decade, has been one of the most studied processes due to its essential role, not only in aging, but also in many neurodegenerative diseases, including Parkinson’s, Alzheimer’s and Huntington’s. However, autophagy being the major intracellular pathway for the degradation and recycling of long-live proteins and organelles is widely involved in the pathogenesis or prevention of many age-related diseases, including neurodegenerative conditions. Recently, autophagy activation has been considered as part of the cellular responses to elevated oxidative stress, eliminating unwanted, damaged and oxidative structures; thus favouring, in this way, the key anti-aging mechanism associated with the caloric restriction. Longevity factors, such as sirtuins, and redox-sensitive transcriptional factors, such as NF-κB and p53, can also regulate basal autophagy in cells, with a direct impact on longevity and the development of inflammation and neurodegeneration. Here, we reviewed the critical changes of autophagy in the aging and neurodegenerative brain and the role of key regulators of autophagy, which are directly related to oxidative stress, inflammation and longevity pathways.

Key-words: Neurodegeneration, Autophagy, Sirtuins, NF-κB, p53

Introduction to oxidative stress and inflammation in the aging brain

Aging is defined as a complex, irreversible and multifactorial process that leads to changes over time, affecting multiple biological functions, with a gradual deterioration in the adaptability of the organisms to environmental changes and stressful conditions. These changes are detected at all levels, molecular, cellular, tissular levels and organismal (Yu and Chung, 2006), leading to functional systemic disorders related to the aging process and a higher risk of succumbing to age-related pathologies, such as neurodegenerative disease, diabetes, autoimmune and inflammatory diseases and cancer. Initially, aging was proposed as the major risk factor in most neurodegenerative disorders (Floyd and Hensley, 2002). The incidence of neurodegenerative diseases, such as Alzheimer’s disease (AD) and Parkinson’s disease (PD) increases significantly with age (Wilson et al., 2007). Given that the ratio of elderly people is increasing, it is crucial that research uncovers the mechanisms associated with senescence and implicated in the transition from benign aging to degenerative disease to prevent the development of the age-related pathologies and in particular, the cognitive decline associated with aging. In the central nervous system, the neuroendocrine changes observed during aging appear to be more related to disorders of the relationship between neural and hormonal signals, rather than alterations of specific structures (Ferrari and Magri, 2008; Ferrari et al., 2008).

However, in a review of aging, it is essential discuss the previously well-known processes underlying the aging phenomenon, such as oxidative stress and its subsequent inflammation. Oxidative stress is the main causal factor of aging and the development of various diseases, including age-related sporadic degenerative