Zinc deficiency induces apoptosis via mitochondrial p53- and caspase-dependent pathways in human neuronal precursor cells

ABSTRACT: As reviewed in the previous chapter above, tryptophan utilization for serotonin synthesis increases the necessary precursor for the melatoninergic pathways. The changes and susceptibility factors associated with Alzheimer’s disease (AD) regulate, and can be regulated by, the melatoninergic pathways. In this chapter we look at the role of the melatoninergic pathways in more detail in relation to changes and interventions relevant to AD. Many pharmaceutical and dietary factors, with efficacy in AD and/or AD models, regulate the melatoninergic pathways, either directly or indirectly. As such, much of the experimental data pertaining to regulators of the etiology, course and treatment of AD, such as zinc, selenium, acetylcholinesterase inhibitors and valproate, may be intimately intertwined with the melatoninergic pathways. In this chapter, we review the role of the melatoninergic pathways in AD, highlighting its previously little recognised involvement in a host of susceptibility factors and treatment approaches. More insight as to the relevant changes occurring in AD should allow treatments to better target relevant biochemical targets, thereby improving the management of this poorly conceptualized, and therefore poorly treated, disease.

ABSTRACT: parkin loss associated early-onset of Parkinson's disease, involves mitochondrial dysfunction and oxidative stress as the plausible decisive molecular mechanisms in disease pathogenesis. Mitochondrial dysfunction involves several up/down regulation of gene products, one of which being p53 is found to be elevated. Elevated p53 is involved in mitochondrial mediated apoptosis of neuronal cells in Parkinson's patients who are folate deficient as well. The present study therefore attempts to examine the effect of Folic acid (FA) supplementation in alleviation of anomalies associated with parkin knockdown using RNAi approach, specific to Dopaminergic (DA) neurons in Drosophila model system. Here we show that FA supplementation provide protection against parkin RNAi associated discrepancies, thereby
improves locomotor ability, reduces mortality and oxidative stress, and partially improves Zn levels. Further, metabolic active cell status and ATP levels were also found to be improved thereby indicating improved mitochondrial function. To corroborate FA supplementation in mitochondrial functioning further, status of p53 and spargel was checked by qRT-PCR. Here we show that folic acid supplementation enrich mitochondrial functioning as depicted from improved spargel level and lowered p53 level, which was originally vice versa in parkin knockdown flies cultured in standard media. Our data thus support the potential of folic acid in alleviating the behavioural defects, oxidative stress, augmentation of zinc and ATP levels in parkin knock down flies. Further, folic acid role in repressing mitochondrial dysfunction is encouraging to further explore its possible mechanistic role to be utilized as potential therapeutics for Parkinson's disease. Copyright © 2015. Published by Elsevier Inc.

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