

Yoga—Impact on Mitochondrial Health: Clinical Consequences

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Mitochondria are cytoplasmic organelles responsible for life and are the power house of the cell. They play an important regulatory role in energy metabolism, apoptosis, reduction–oxidation potential, free radicals scavenging, and intracellular calcium regulation. Mitochondrial dysfunction can result in a broad range of degenerative disorders such as encephalopathies, cardiomyopathy, aging, cancer, diabetes, Alzheimer’s disease, Parkinson’s disease, and Huntington’s disease.¹ Unhealthy social habits, genetic mutations, epigenetic factors, stress, exposure to infections, allergens, and toxins may contribute to selective disease susceptibility associated with increased mitochondrial fragmentation and dysfunctional mitochondria. Such mitochondria produce supraphysiological levels of free radicals and low levels of adenosine triphosphate. Mitochondrial diseases are highly recessive in nature and exhibit a threshold effect. When the number of mutant mitochondria crosses a certain threshold, it adversely impacts the tissue function. Thus, tissues with high energy demand first manifest the disease as they have a lower threshold and thus low levels of mutant mitochondria can disrupt the function of such tissues. A group of diseases are caused by the damage to mitochondria such as the Kearns–Sayre syndrome, chronic progressive external ophthalmoplegia, mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes, myoclonic epilepsy with ragged-red fibers, neurogenic weakness with ataxia and retinitis pigmentosa, or Leigh syndrome, and Leber hereditary optic neuropathy (LHON).² Yoga is an ancient mind and body practice that enhances wellness, promotes health, prevents the onset of diseases, and can be used as an adjunct therapy in complex diseases. Yoga improves the mitochondrial and nuclear deoxyribonucleic acid (DNA) integrity and positively impacts the sperm epigenome.^{3,4} Yoga is a profound science that works through a well-defined psycho-neuro-immune axis, which affects a variety of processes from basic metabolism, epigenetics, DNA repair, oxidative bioprocesses to aging, blood pressure, organ system maintenance, subjective well-being, and reproductive health.^{3,5–8} A pilot study from our lab showed that there was a reduction in blurring and clouding of vision after eight weeks of

yoga-based lifestyle intervention (YBLI) in LHON patients. There was no further deterioration in vision, and they were able to complete visual tasks such as recognizing faces and objects after the regular daily practice of yoga. This could be explained by the improvement in mitochondrial integrity post-yoga practice as there was an increase in the mitochondrial membrane potential, levels of nicotinamide adenine dinucleotide (NAD⁺), cytochrome c oxidase (COX-II), mitochondrial copy number, and expression of genes that maintain mitochondrial integrity and promote mitochondrial biogenesis (*AMPK*, *IGF1R*, *PRC-1*, *TFAM*, *SIRT-1*, *TIMP-1*, and *KLOTHO*).⁴ It also increases the levels of melatonin, a master regulatory molecule that regulates the sleep–wake cycle and is a potent antioxidant whose highest subcellular concentration is in mitochondria and since mitochondria are both the source and target of free radical-induced damage, an increase in melatonin levels plays a key role in minimizing the oxidative damage to mitochondrial (mt) DNA and thereby reducing mt mutations. LHON is a rare mitochondrial retinopathy caused by the respiratory chain dysfunction that leads to oxidative stress (OS) and insufficient energy supply, which results in enhanced apoptosis of retinal ganglion cells (RGCs). This is an underlying pathology of LHON, and in primary open-angle glaucoma (POAG) too, there is enhanced apoptosis of RGCs. Although it was believed that intraocular pressure (IOP) is the only modifiable risk factor in glaucoma, recent studies have shown that an increase in IOP, ischemia, hypoxia, OS, glutamate excitotoxicity, low levels of brain-derived neurotrophic

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factor (BDNF), inflammation of glial cells, and increased levels of tumor necrosis factor alpha (TNF- α), interleukin (IL)-6, and nuclear factor kappa B (NFkB) are the factors which cause enhanced apoptosis of RGCs in POAG.^{9–11} In LHON, treatment strategies included giving anti-inflammatory, antioxidants, neuroprotectants, and antiapoptotic agents. Recent studies from our lab showed that yoga and meditation cause a decline in expression levels of pro-inflammatory genes such as TNF- α , NFkB, and IL-6, and upregulation of anti-inflammatory, antiapoptotic, antioxidant genes and genes maintaining neuroplasticity [BDNF, dehydroepiandrosterone (DHEA), nerve growth factor receptor (NGFR), and neuregulin] and regulating the blood flow in POAG.^{8,9,12–14} This has also been documented in other complex diseases such as unexplained male factor infertility and rheumatoid arthritis (RA). Thus, yoga by improvement in mt integrity and mt copy number may be beneficial in diseases where there is a reduced energy production secondary to mitochondrial dysfunction, and hence yoga warrants larger studies in different mitochondrial diseases and some of such studies are ongoing in our laboratory.

Yoga optimizes self-regulatory mechanisms by stress modulation on physical, emotional, and psychological levels via high-level and low-level brain networks.¹⁵ Yoga enhances focused attention during different *asanas* (physical postures), *pranayama* (breathing techniques), *dhyana* (meditation), and *savasana* (relaxation techniques), and is termed as “meditation in motion.” It works through many mechanisms and has been associated with many positive and objectively measurable changes in an individual, which include reducing stress and anxiety, warding off depression, improving sleep, reducing sympathetic distress, reducing hypertension symptoms, decreasing inflammation, and improving the quality of life.^{8,13,14,16–18} The relaxation response elicited due to yoga leads to an elevation of β -endorphins, improvement in cardio-vagal tone, reducing sympathetic overactivity, lowering of IOP, and reduces further damage to RGCs.^{12,19,20} Yoga is also known to enhance cognitive abilities, boosting memory, increasing thickness of cerebral cortex, neural connectivity, positive changes in electroencephalogram (EEG), and improving neuroplasticity.¹³ Yoga aids in the maintenance of genomic stability and chromosomal integrity, reducing the rate of cellular aging by maintaining telomere length and upregulation of telomerase activity and the increase in expression levels of sirtuins.^{13,14} Yoga normalizes the levels of transcripts involved in DNA repair, cell cycle checkpoint control, and causes the downregulation of pro-inflammatory genes.²⁰ A study from our laboratory documented positive effects of YBLI in RA, which is a severe autoimmune inflammatory disorder characterized by chronic pain and swelling, primarily affecting the peripheral joints.^{21,22,23} Our recent randomized controlled trial (RCT) on the impact of yoga on RA patients published in *Frontiers in Psychology*, 2020 supports yoga as an adjunctive therapy to treat this chronic progressive debilitating disease as it aids in decreasing systemic inflammation by its beneficial effects on the

psycho-neuro-immune axis and normalization of dysregulated transcripts (IL-6, TNF- α , NFkB1, TGF- β , and CTLA4).⁸ Yoga improves the mitochondrial integrity by altering the expression levels of transcripts that maintain mitochondrial integrity, which aids in the maintenance of optimal free radical levels, holds the key to increase the mitochondrial copy number, improves COX-II activity, increases NAD⁺ levels, optimizes OS markers, and increases the expression levels of transcripts that maintain mitochondrial integrity, reduces disease activity and its associated consequences on physical and mental health, and hence can be beneficial as an adjunct therapy.^{4,22,23}

The regulation of cellular OS within physiological limits after YBLI suggests the potential of this intervention in protecting cells from OS-induced nuclear and mt DNA damage and telomere attrition and in reversing epigenetic changes, which accumulate due to unhealthy lifestyle and adverse environmental conditions. The multifaceted dimensions of yoga enhance psychological and physical health by its underlying cumulative effects on maintaining the mitochondrial and nuclear genome. Yoga is a cost-effective emerging health discipline which unlike drugs has no side-effects and aids in reducing disease severity, optimizes OS levels, increases transcript levels associated with immune homeostasis, immune system metabolism, mitochondrial architecture, and mitochondrial biogenesis, and hence has the immense potential to be used as an adjunct therapy in the management of mitochondrial diseases.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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