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Short Communication

Title: Reactive Oxygen Species (ROS), Mitochondrial Dynamics & Functionality in Parkinson's Disease - A Brief Communication

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ABSTRACT

Parkinson's disease (PD), is the second common and deadliest neuronal & a multisystem disorder in the world with significant morbidity and healthcare burden. Still now, the proven therapeutics is lacking mainly due to the poor understanding of this disease. The previous and some new neurological and pathological studies of Parkinson's disease brains reported that the irreversible relapse of dopaminergic neurons in substantia nigra and other brain regions, and loss of dopamine (DA) in the striatum may be one of the main reasons for this disease. Along with that now a days while increasing research with mitochondria, we got to know that it has also a key role in many neurological disorders along with Parkinson's disease. The result of mitochondrial dis-regulation and generation of reactive oxygen species (ROS), that's activated some specific pathways and ultimately leads to cell damage and neurological disorder like PD. So, in future it is warranted to know more about the disease and targeting the all pathways related to this field. Here in this short article we described in brief about the Parkinson's disease and how the mitochondrial dynamics and Reactive oxygen species are impacting the disease progression with some therapeutic approaches.

Introduction:

Parkinson's disease (PD), is the second common and deadliest neuronal & a multisystem disorder that contributes to significant morbidity and healthcare burden in the world [1]. Characteristics of the disease include tremor at rest, rigidity, bradykinesia and postural instability [2]. The symptoms of Parkinson's disease [3] both non motor and premotor include constipation, hyposmia, REM-sleep behaviour disorder, as well as cognitive, neuropsychiatric, autonomic and sensory disturbances (https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/symptoms-causes/syc-20376055).

About the Parkinson's disease (PD):

Recent Neuro-pathological studies of Parkinson's disease brains show that the irreversible relapse of dopaminergic neurons in substantia nigra (SN) and other brain regions, and a simultaneous loss of dopamine (DA) in the striatum may be one of the main reasons for th is disease [4]. The A9 type of dopaminergic neurons death in the substantia nigra and the protein-aceous aggregates in neurons, are pathological characteristics of Parkinson's disease (PD) [5, 6]. At present, the pathogenic implication of these is a birthplace of much debate among researchers but the alpha-synuclein (SNCA) which codes for alpha-Syn- a, was the first gene in which mutations causing PD (PARK1; or PARK4) were recognized [2]. Lewy bodies are formed from these SNCA and caused degeneration of dopaminergic neurons, and leads to Parkinson's disease (PD). Most of the symptoms like mainly related with brain injury (https://medlineplus.gov/druginfo/meds/a601068.html) are presently treated with L-3,4-Dioxyphenylalanine (Levodopa) with carbidopa, which increase the stability and efficacy. Apart from this, Tolcapone and Bromocriptine is also important drugs are currently used for the treatment[https://www.amboss.com/us/knowledge/Medication_for_Parkinson_disease]. The Synuclein (SNCA) is highly connected to the genetic factors of PD and thus plays a key role in both autosomal dominant and recessive type of PD. Synuclein (SNCA) and leucine-rich repeat kinase 2 genes were shown to induce autosomal dominant PD with Lewy pathology, respectively [7, 8]. Independent of Lewy pathology, recessive autosomal mutations in PINK1, PARKIN and DJ-1 (PARK7), have been found to induce an early development of Parkinsonism with slower progression [2,4,9]. Mutations in all of these proteins cause for all intents and purposes the same clinical characters and pathology, proposing that they all participate in a communal pathogenetic path [10]. As Lewy bodies holding are present in most PD patients, so the possibility to impact in this common pathway of alpha-Syn is high [11,12]. These destructive pathways can be neutralized by the using of cytoprotective pathways like transcriptional factors, nuclear factor erythroid, 2p45 related factor 2 (Nrf2), it neutralizes the oxidative stressors and plays a key-roles in mitochondrial factors [13-18].

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Brief Relation with Reactive oxygen species and mitochondrial dysfunction:

Although there are several aspects to which scientist are working to cure the disease but the flow of research gets a new way when we got to know the key functional role of mitochondria in many neurological disorders along with Parkinson's disease. It is well known that mitochondria, is a metabolic center of a cell with own genome that is mainly engaged with a variety of metabolic processes [19]. Its main functions are manufacturing the cellular ATP, nucleotides, fatty acids, and iron-sulfur collections [20]. It also helps to maintain the cellular integrity and homeostasis. Interestingly, the SNCA is also found on the mitochondria in the animal models [21]. Mitochondria are necessary to be rising up in sites where high amount of energy or calcium buffering are desired for neural activities [22]. In quite a few neurodegenerative diseases & disorders interrelated to mitochondrial failings. The neurons show modifications in the oxidative phosphorylation, the homeostasis of intracellular ROS and the levels of calcium are gets disturbed, as well as in the mitochondrial kinesis, mitophagy and fusion/fission dynamics also found to altered [23,24]. Defects in neuronal development and neuronal plasticity for the deregulation of the mitochondrial fusion or fission has also been associated with both in ex vivo and in vivo models [25]. It was discovered that -synuclein is active in electron chain transport complex I dysfunction, which impairs mitochondrial function and causes dopaminergic cell death [26].

So it is the concluding point that the loss of mitochondrial functionality related with so many neurological disorder, including Parkinson's disease. According to current evidence, Mitochondrial damage, production of ROS, loss of calcium supply, Imbalance between fission and fusion of mitochondria, & mitochondrial fragmentation leading eventually to neuronal death & loss of neuron to neuron communication [24]. Thus, strategies to adjust abnormal mitochondrial dynamics & ROS warranted, therapeutic target for the treatment of neurodegenerative disease including Parkinson's disease. [27-28]

In a very recent paper [29] it has been discussed that the same dysfunction of mitochondria if found in astrocytes that is well known for regulating calcium signaling, fatty acid and glutamate antioxidant production can lead to disease progression.

Parkinson's is more a genetic disorder thus personalized treatment; molecular analysis and drug sensitivity test will help in future to increase the overall survival in this disease.

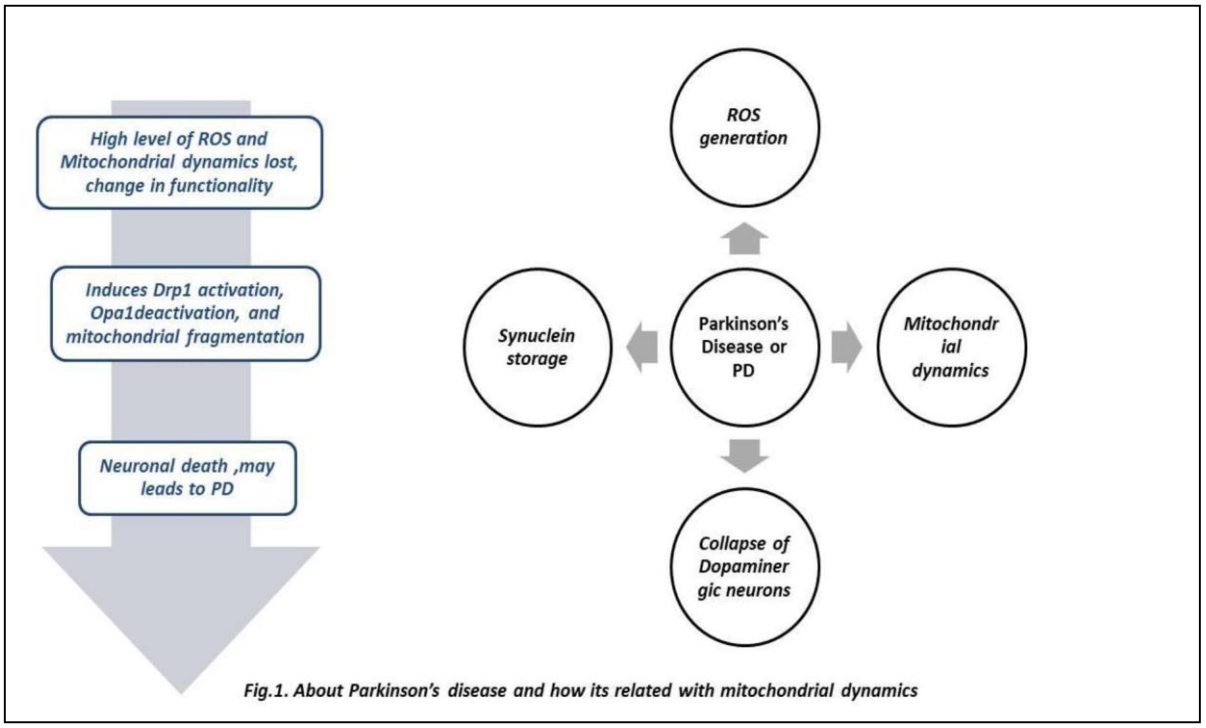

Fig.1. About Parkinson's disease and how its related with mitochondrial dynamics

Conclusions and therapeutics:

Finally, we can say that the alteration of mitochondrial dynamics is important mediators of several neurodegenerative diseases like Parkinson's disease. The cellular ROS levels influence the expression and activity of Drp1, Opa1, and mito-fusions, which in turn modulate the neuronal fate. The role of ROS in the regulation of mitochondrial dynamics is critical for several neurodegenerative disorders thus more detailed clinical works are needed. In this field some of the approaches are very important are listed below.

- Anything that can be acts as antioxidant in nature mainly plants bio active molecules can be used to reduce the level of ROS. Thus more research in medicinal plants is warranted.
- As the neuronal death occurs in this case so anything (Growth factor) that can promote the growth of the damaged neurons can be used along with the drugs to increases the treatment effect. Combinational approaches may be more meaning full. To establish this scientist should practice some approaches.

- Stem-cell technologies represent a promising approach for treating neuronal diseases. IPS technology is also now very popular that helps to know better about the disease and it can be help in new therapies.
- Any immunological (e.g.: astrocytes) or others cells with defective mitochondrial activity are very prominent target for the PD.

Thus, strategies to modify and targeting both the ROS production and abnormal mitochondrial dynamics and its function is very important therapeutic approach for the treatment of in Parkinson's disease.

Declarations:

The author declares that; this work is original. Use or Modification of other's articles (open access) data, idea related in this field done after giving appropriate credit to the original author(s) and the sources. The author's, furthermore, makes no representations that the data available in the referenced papers is free from error. PC prepared the manuscript and referencing. Final editing done by DM. The web-links that's used in this short communication are not mentioned in the reference section they are used as in text citation only.

Conflict of Interest: None

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