Tentative Outline

Special Thematic Issue for Current Neuropharmacology

Title of thematic issue: MITOCHONDRION AS A SELECTIVE TARGET FOR THE TREATMENT OF ALZHEIMER DISEASE AND OTHER DEMENTIA

Guest Editor: Professor, Doctor Gjumrakch Aliev, MD&PhD

Aims & Scope: Mitochondrion as a hallmark for the disease development, maturation, progression, and effectiveness of the treatment represents a completely new and more effective strategy to treat almost all of human diseases including stroke, Alzheimer disease (AD), and/or other neurodegenerative conditions that are characterized by mental retardation and memory loss. The main goal of this proposed special issue is to summarize recent evidence the mechanisms behind mitochondrial induced oxidative imbalances in pre-clinical experimental models that mimic human AD and/or AD itself. Future expanding research regarding the implication of this strategies in the clinical trials will provide crucial information in the development of new, more effective diagnoses as well as therapies for the treatment of atherosclerosis, including cerebrovascular athero- and arteriosclerotic pathology that are found in mild cognitive impairment (MCI) and AD with the consequence of the mental deterioration and progressive neurodegeneration.

Keywords: Alzheimer disease, Mitochondria, Mitochondrial DNA Overproliferation and/or Deletion, Cellular Hypometabolism, Vascular Dementia, Clinical Sign, Drug Development, Multitarget Treatment Strategies, Myocognitive Impairment, Integrative Treatment.

Subtopics:
The subtopics to be covered within this issue are listed below:

Stroke and arteriosclerosis with neurological consequences such as Alzheimer disease (AD) are two leading causes of age-associated disability, dementia, and death. The Center for Disease Control and Prevention and the National Center for Health Statistics recently reported that AD has surpassed diabetes as a leading cause of death. AD is now the sixth-leading cause of death in the United States. With our nation facing an unprecedented population shift of aging baby boomers—and AD poised to strike 10 million of them—it is clear this escalating epidemic must be addressed now with our help. Estimates for the US tell us that AD affects 4 million people (rising steeply from <1% of the population aged 65 to 40% of those aged 90) and costs $600 billion per year, which is equivalent to the total cost of stroke, heart disease, and cancer combined. In addition, neurological disease and psychiatric disorders are some of the most heavily funded research areas today. Although tremendous strides have been made, the study of the brain cellular compartment many questions unanswered.

Scientific research programs across the globe are working on the cause, prevention, and treatment of neurodegenerative disorders. From academic institutions to nationally lead initiatives, each are aggressively trying to find ways to help reduce the staggering numbers of people affected on an annual basis. Overall, there are no effective strategies in use for determining, controlling, and treating this devastating disease.

Conventional wisdom for the almost over last 30 years has decreed that AD is a ‘neurodegenerative’
disorders caused primarily by abnormal deposition in brain tissue protein called ‘amyloid-beta’ (Aβ), and is characterized by loss of cognitive function and inappropriate death of nerve cells in areas of the brain that control such functions as memory and language. The trigger for nerve cell death is unknown in the case of AD. The finding of Aβ deposition in AD brains after death led to the so-called “amyloid hypothesis”.

For over a decade, the amyloid hypothesis has so influenced and guided research in the field of Alzheimer dementia that many workers consider it as the gold standard of scientific investigation. Personally I have extensively reviewed the literature which claims that AD is caused by the deposition of Aβ within structures called senile plaques that invade AD brains and that such plaque formation then leads to further abnormalities within the nerve cells, eventually killing them. I was not able to found evidence to support this claim and ample to question it. Moreover, the amyloid hypothesis has been criticized because its research findings up to now have not generated any benefits in the clinical management and treatment of AD patients nor to an understanding of how the elderly are preferentially affected. By contrast, there is now significant and still growing strong evidence from the fields of epidemiology, pharmacology, neuroimaging, clinical medicine, microscopic anatomy, and molecular biology which indicate that AD is a oxidative stress induced mitochondrial failure that initiates cerebrovascular disorder whose underlying cause is impaired blood flow to the brain during advanced aging.

This evidence can be summarized as follows: (1) numerous epidemiologic studies link AD risk factors such as stroke, heart disease, hypertension and atherosclerosis to reduced cerebral blood flow and therefore cellular and subcellular hypoperfusion and energy failure; (2) evidence that AD and vascular dementia (VaD), an acknowledged vascular disorder, share practically all the same risk factors and may benefit from the same treatments; (3) drug therapy reported to improve AD symptoms (including prescriptive drugs now available for AD) all increase blood flow to the brain; (4) people who are likely to develop AD but do not yet show dementia symptoms can be identified by using brain blood flow measurements and brain PET scans; (5) the clinical symptoms are very similar in most AD and VaD patients; (6) parallel abnormalities occur in brain vessels and brain tissue including Aβ laden plaques in AD and VaD patients; (7) low levels of brain blood flow in aged humans and human models can lead to abnormal cell metabolism, tissue damage and memory problems independent of Aβ; (8) mild cognitive impairment (a term used to describe a preliminary stage leading to AD) can convert equally to AD or VaD; (9) and small vessels, especially of the vascular mitochondrion damage, are present in the AD brains after death.

During the last decade our basic and clinical studies clearly demonstrated that during the neuronal energy crisis, cerebral hypometabolism and vascular (e.g. all of brain cellular compartment) hypoperfusion are major and potentially treatable contributors to the loss of function in patients with stroke as well as AD. Re-classification of AD from a poor neurodegenerative to a mitochondrion failure induced cerebrovascular disorder would speed the development of truly beneficial treatments or a cure, improve patient management, provide earlier
diagnosis, and reduce the number of AD cases in the future by aggressively treating the risk factors that can turn on this dementia. In addition, recent research that trying to make connection between the amyloid and mitochondrion failure appeared to be another misunderstanding not only regarding the etiopathophysiology of AD but also blocking developing selective treatment strategies against this devastating diseases.

Schedule:

- Manuscript submission deadline: July 31, 2019
- Peer Review Due: September 10, 2019.
- Revision Due: September 20, 2019
- Announcement of acceptance by the Guest Editors: October 10, 2019.
- Final manuscripts due: October 31, 2019.

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