Tabriz University of Medical Sciences

AGING RESEARCH INSTITUTE NEWSLETTER

Tabriz University of Medical Sciences (TUOMS)

Editorial

Gut microbiota: a route for a healthy aging

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Over the past decade, the proportion of ages over 65 in the population of developed countries has increased by more than 10%. Moreover, the percentage is expected to reach over 20% by 2030 [1]. To maintain the health of the elderly, a proper function of the homeostatic systems (nervous, endocrine and immune) and appropriate interactions between these systems and gut microbiota is required. However, these systems are affected by aging which reduces the functional capacity of all the organs in the body. In turn, a chronic low-grade inflammatory state may appear, evolving into "inflammaging". "Immunosenescence" is a physiological decline in immune system in both adaptive and cellular immunity, resulting in age-related oxidative stress, a low-grade inflammatory state, and intestinal dysbiosis. There might be a correlation between immunosenescence and a perturbed gut microbiota and frailty in the elderly [2].

Due to the effects of the gut microbiota on the process of immunosenescence and inflammaging, it can be considered that gut microbiota homeostasis along with the prohibition of the pathogen colonization and their proliferation and toxin production, can ultimately affect the host's lifespan [3]. In this respect, it can be possible to promote lifespan with strategies targeting microbiota, such as pro/prebiotics consumption. However, the studies covering the whole lifespan of humans are obviously not possible at the moment, and the results are not expected to be available soon [4].

Alternations in the gut microbiota composition can be thought as one of several different age-related physiological processes. These alterations determine the process of aging in human beings. It is certain that the aging gut microbiota shows several features affecting the health status of the aged. An approach to prevention and treatment of diseases, as well as for the promotion of healthy aging and longevity, can consider the aging human being as a meta-organism. One of the strategies in this approach might be the manipulation of the gut microbiota composition through the use of pro/prebiotics. Indeed, the use of pro/prebiotics seems to be a promising approach despite limited available studies [5].

Genetic background and lifestyle of the people can influence the links between healthy aging, microbiota and longevity. In this respect, there are many studies suggesting that by making some [cont.]

Autobiography: Albert Gjedde

I came to Odense as Professor of Translational Neurobiology in 2018, after time Copenhagen where I became head of a new Department of Neuroscience and Pharmacology in 2008. Before Copenhagen, I headed the Positron Emission Tomography (PET) Center at Aarhus University Hospital since 1994, including the new Center of Functionally Integrative Neuroscience (CFIN) established there in 2001 to study live and intact human and animal brains.

I left Canada in 1994, persuaded by Danish Research and Education Minister Bertel Haarder to establish PET in Aarhus. In Montreal, I headed the McConnell Brain Imaging Center at McGill University where I originally had a one-year fellowship to study PET but I ended up staying for eight years, during which time I also supervised the PhD of a neurobiologist from Tabriz, Manouchehr Vafaee.

My interest in PET goes back to medical school in Copenhagen where physiology professor Christian Crone advised me to study blood-brain [cont.]

Founder's Message

Prof. Seyed Kazem Shakouri, M.D.

Since honouring the bygone scientists is a sign of every nation's legacy and pride, we can hardly find people who ignore this significance. Avicenna (c. 980 – June 1037) as the father of early modern medicine and Muhammad ibn Zakariya al-Razi (854 CE – 925 CE), famous Iranian chemist, are among the best scientists of Iran and the whole world whose two precious treasures, "The Canon of Medicine" and "al-Hawi" have been inherited for us. Therefore, 23rd and 27th of August are named as the doctor's and pharmacist's day in Iran showing our sincere appreciation. Congratulations to all the experts in medicine and pharmacy in the light of these great days. Furthermore, we are pleased to invite all researchers to the 4th Alavi Meeting from October 9-11, 2019 in the Aging Research Institute of TUOMS.

Director of RCPBS's Message

Prof. Ali Fakhari, M.D.

Modern psychiatry is a novel look to psychiatry 100-year widespread history from psychoanalysis and psychology to neuroscience. With a precise look to the history of psychiatry, the pioneer psychiatrists would be considered as magicians who have tried to treat or intervene of the mind disorders in their arbitrary own way. Modern psychiatry, however, is not based on speculation or supposal but is based on accurate, calculated, and non-prejudice studies and tries to find the causes and context of human behavior and disorders that are called psychiatric disorders.Clinical trials that benefit from blind or even triple blind methods can be considered as examples of serious intention of psychiatric studies and researches to eliminate bias and speculation in human studies.In this regard, modern psychiatry contains a wide range of scientific studies including sociology and human behavior in societies, crises, different situations as well as molecular changes, and the role of genes, neurotransmitter and receptors in psychiatric disorders. Therefore, basic, molecular, genetics and cognitive studies, psychology, imaging techniques, and other modern sciences are used in this field.

Researchers of this research center, in accordance with their mission, are considering this wide range of scientific studies and, of course, their main aim in research in psychiatry and aging with design, innovation and structured studies in these fields aspire to play an important role in national, regional and international modern psychiatry studies. The main goal of this research center is to understand the current concerns of society such as the elderly, psychiatric disorders, addiction and psychotic in order to take steps in resolving the mentioned problems.

Editorial [cont.]

principal changes in lifestyle and related factors, including caloric restriction diets, intake of probiotics [6], reduction of the proinflammatory status [7], enhancement of antioxidant activity, prevention of insulin resistance [8] and lipid dyshomeostasis [9], microbiota transplantation, physical activity and maintenance of immune homeostasis, it is possible to enhance the quality of life during the process of aging.

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References:

1. United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population. Ageing 2017 - Highlights (ST/ESA/SER.A/397).
2. Bischoff SC. Microbiota and aging. Curr Opin Clin Nutr Metab Care. 2016;19(1):26-30.
3. Martin R, Nauta AJ, Ben Amor K, Knippels LMJ, Knol J, Garssen J. Early life: gut microbiota and immune development in infancy. Beneficial Microbes 2010;1:367–82.
4. Biagi E, Candela M, Franceschi C, Brigidi P. The aging gut microbiota: new perspectives. Ageing Research Reviews 2011;10:428–9.
5. Biagi E, Candela M, Turroni S, Garagnani P, Franceschi C, Brigidi P. Ageing and gut microbes: perspectives for health maintenance and longevity. Pharmacological research. 2013 Mar 1;69(1):11-20.
6. Perez Martınez G, B€auerl C, Collado M. Understanding gut microbiota in elderly's health will enable intervention through probiotics. Benef Microbes 2014;5:235e246.
7. Lowry C, Smith D, Siebler P, et al. The microbiota, immunoregulation, and mental health: implications for public health. Curr Environ Health Rep 2016;3:270e286.
8. Zhang X, Zheng X, Yuan Y. Treatment of insulin resistance: straight from the gut. Drug Discov Today 2016;21:1284e1290.
9. Nehra V, Allen J, Mailing L, et al. Gut microbiota: modulation of host physiology in obesity. Physiology 2016;31:327e335.

Research Center of Psychiatry and Behavioral Sciences

Research Center of Psychiatry and Behavioral Sciences has been established from the second half of 2007 as the research team of psychiatry and behavioral sciences of Tabriz University of medical sciences with faculty members including psychiatrists, psychologists, psycho-pharmacologists, physiologists, radiologists, neurologists, social medicine specialists and epidemiologists at Razi hospital of Tabriz. The research team was gradually promoted to the Clinical Psychiatry Research Center by establishing the Board of Directors and with the efforts of Professor Ali Fakhari in March 2011 receiving the permission of Ministry of Health. And in 2017, it was finally approved as Research Center of Psychiatry and Behavioral Sciences; the center is currently a subsidiary of the Aging Research Institute. Our Studies in previous years have been largely human-induced, and research in this area continues. Some researches in the human domain briefly includes:
Psychiatric disorders (case-control, interventional, ...)
Brain Mapping Studies (QEEG) and MRI
Genetic studies in the field of psychiatric disorders
Cognitive studies

The center is currently conducting several research projects in cooperation with various domestic and foreign universities such as Iran University of Medical Sciences, Orumieh, Semnan, Ardebil, Tabriz Universities, Islamic Azad University of Tabriz, and Groningen University of the Netherlands. About 250 research projects have been running and publishing valid papers at this center. Since 2017 with the recruitment of the first full-time research faculty member (a physiologist with a research orientation on the role of the nervous system in psychiatric and behavioral disorders) The Center's research has entered a new phase in the development of animal model studies beside human studies. During the years 2017 to 2018, with the cooperation of Tabriz University of medical sciences and the Aging Research Institute our animal models laboratory was set up and the office has also been expanded. By increasing the facilities, the activities necessary for obtaining a license to admit PhD by research students have begun, which is expected to be completed in 2019. It should be noted that in the animal laboratory various models have been set up and studies in the following areas (human and animal) have been added to the activities of the center:
1) Cognitive science animal models: These models are used to examine the complications of psychiatric disorders on cognitive abilities.
2) Psychiatric animal models:
- Anxiety tests
- Depression induction models
- Recording and analyzing depression behaviors
- Animal Model of Post-Traumatic Stress Disorder (PTSD)
- Animal Model of Social Behavior
- Addiction models:
  - Inducing addiction
  - Withdrawal
- Autism model

3) Electrophysiological studies (under construction)
- Recording EEG signals from animal brain
- Recording single-brain signals from animal animals
- Recording short term potentiation (Paired Pals)
- Recording Long Term Potentiation (LTP)

4) Stereotactic surgery
- Cannulation of the rodent brain to inject different drugs in any area of the brain

5) Exercise studies
- Using special treadmills for laboratory animals to study the effects of forced exercise on psychiatric disorders and other diseases.

6) Sleep studies: To study sleep physiology and the effects of sleep deprivation on psychiatric and behavioral disorders
- Full sleep deprivation
- REM sleep deprivation

7) Pain studies
8) Molecular studies

Autobiography [cont.]

glucose transport in rats and to go to New York after my medical degree in 1973, to learn about the energy metabolism of brains under the tutelage of neurologist Fred Plum at the New York Hospital.
The years 1973-76 in New York were the years when psychiatrist Louis Sokoloff in Bethesda developed autoradiography of brain metabolism with labeled 2-deoxyglucose (2DG) that was quickly extended to fluoro-deoxyglucose (FDG) for use in people. The first experiments with FDG were done by another Tabrizi scientist, the nuclear medicine physician Abass Alavi whom I met in Philadelphia.
The ambition to work with PET actually arose earlier when I went to Berkeley in California in 1964 where I witnessed the onset of the Free Speech Movement (FSM) of students who wanted to modernize university education and to extend voting rights to black Americans. In Berkeley I met the physicist, physiologist, and physician Thomas Budinger who completed a PhD project on medical physics, and he also played an important role in the development of PET at the Lawrence Berkeley Laboratory where he still works. It was here that Ernest Lawrence invented the cyclotron and discovered positrons.
I returned to Copenhagen in 1976 to become a neurosurgeon but the interest in PET caused me to choose neuroscience with PET as the tool. PET didn't come to Denmark till after my transfer to Montreal when I sold an older PET device to Copenhagen in 1989. The urge to develop PET facilities caused me to help move another older PET device from Montreal to Dresden in East Germany, at the time when students and others breached the Berlin Wall, an event that I witnessed 25 years almost to the day after the FSM in Berkeley.
Physicist Clifford Patlak from the NIH paid a visit to Copenhagen in 1977 on the occasion of conferences on neurochemistry and brain circulation. He shared an idea with me of how to measure blood-brain barrier permeability that I combined with a method of bolus injection and automated blood sample integration into what became known as the Patlak or Gjedde-Patlak Plot.
With no PET in Denmark, and no prospects for one, I had to do PET during shorter visits to other places, including the PET Laboratory of Wolf-Dieter Heiss in Cologne-Merhaim and the nuclear medicine department of Henry N. Wagner, Jr., in Baltimore, MD, where I met my long-term friend and colleague Dean F. Wong who helped me apply the "Plot" to neuroreceptor binding studies with PET. An obvious approach now presented itself to combine neuroreceptor and metabolism studies with PET into investigations of how the processes interact in the service of brain function.
This is what I want to do here in Odense, with the help of friends from McGill in Montreal, Johns Hopkins in Baltimore, and TUOMS in Tabriz. My focus is on dendritic spines and their role in network integration that may shed light (positrons and photons) on the origins of consciousness.

Top Article

Congratulations to Dr. Reza Badalzadeh, Associate Professor of Physiology, TUOMS, on having his articles entitled: Signaling mediators modulated by cardioprotective interventions in healthy and diabetic myocardium with ischaemia-reperfusion injury published in journal of European Journal of Preventive Cardiology (IF=4.542) which have been selected as the top articles of this issue. To show greetings, Aging Research Institute has given him a special grant.

Correspondence

MRI: a promising tool for early-stage wake up stroke detection

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Abstract
Wake up stroke (WUS), as a neurovascular emergencies, has high prevalence particularly in elderly people. In other hand, the patients with WUS are not eligible to receive any fibrinolysis treatment due to unknown time of symptoms onset. Fortunately, today MRI is a specialized diagnostic tool to identify patients within preceding 3-4.5 hours onset of symptoms and subsequently could improve the WUS management to receive proper treatment.

Keywords: Wake up stroke, elderly people; fibrinolysis treatment; MRI

Aging is considered to be as golden, valuable and respectful period throughout human life. Due to physiological imbalances, elderly people are more susceptible to various diseases such as cardiovascular disorders, neurodegenerative conditions, and cancers. Given that the stroke (CVA[1]) is the second leading cause of death following cardiovascular events in Iran and worldwide, it has been an interesting field of research for many researchers or clinicians. Recent epidemiologic studies noted the stroke occurs almost a decade earlier in Iran compared to developed countries have arisen concerning to make necessary and strategic decisions for the management and proper treatment because of socio-economic irreparable and heavy cost [1]. In fact, age is one of the non-modifiable items for stroke while there is a correlation between the increasing incidence of stroke and older people growing within the population, which poses predictable challenges for health care systems. Regarding stroke is considered as one of the acute and neurological emergency, precise and prompt therapeutic approaches play an important role in stroke management. Awareness of symptoms onset time also has importance in the therapeutic strategy of stroke. Receiving of fibrinolysis treatment is also restricted to a time window of 3- 4.5 hours' onset. Wake-up stroke (WUS) is a frequent condition, affecting patients with stroke. Approximately one-third of patients with ischemic stroke represent the symptoms of stroke when they wake up. Consistent with recent studies, our unpublished results showed that the prevalence of wake-up stroke is almost similar in women and men with age range between 68-72 years old. Chronic hypertension is thought to be as the main risk factor for stroke occurrence. Some cardiovascular [cont.]

Correspondence [cont.]

risk factors involve in WUS also listed below:

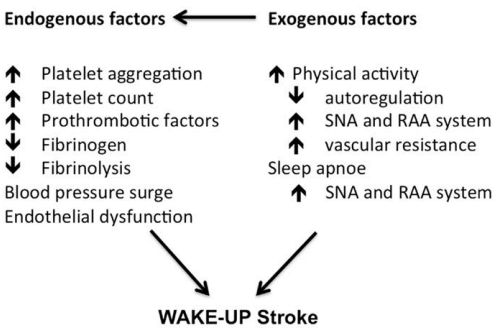

Figure 1. Changes of cardiovascular factors resulting in contributing to a higher risk of stroke in the morning hours. [5].

CT (computerized tomography) or MR (magnetic resonance) angiography, as known diagnostic tools, have adequate sensitivity and specificity in identifying an occlusion of large proximal vessels. In WAKE UP trial as one the major European clinical study which was conducted by Glasgow University (UK), the physicians were able to manage all patients with suspected stroke who eligible benefit from fibrinolytic treatment by using a combination of two types of MRI scans [3]. Diffusion-weighted imaging (DWI) is able to show early changes in the brain after CVA, while pathologic changes in the second type of MRI sequences, FLAIR (fluid-attenuated inversion recovery) is not observable till after passing several hours. If changes are shown on DWI but not FLAIR, then a patient's stroke is most likely to have happened within 4.5 hours. Today, DWI/FLAIR mismatch called 'tissue clock' applicate to identify the patients whose stroke occurred within 3 to 4.5 hours from symptoms beginning. With a positive DWI lesion and a negative FLAIR sequence, it has been declared a 78%–93% specificity and 65% sensitivity to predict whether the stroke happened in the preceding 4.5 hours or not. These findings supported the hypothesis that MRI would be used as a tissue clock to determine the infarct region occurred less than 4.5 hours previously (Figure 2 and Figure 3) [4]. Like CT/ MR perfusion, NIHSS[2] also is a worthy surrogate for detection of tissue at risk. To interpret, the larger area of perfusion lesion gains a higher score of NIHSS [4].

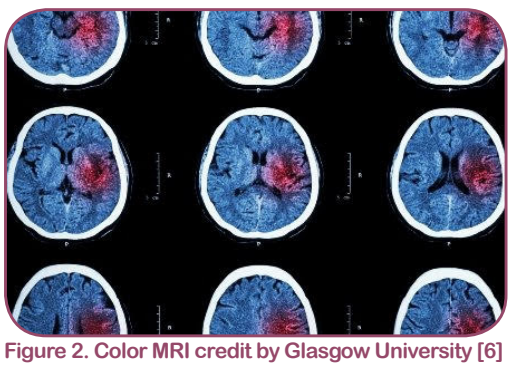

Figure 2. Color MRI credit by Glasgow University [6]

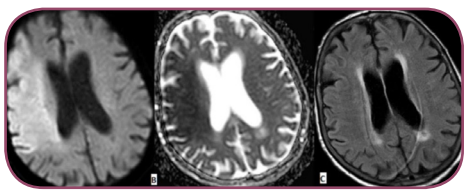

Figure 3. Wake-up stroke typical MRI scan: A. DWI showed an area of hyperintensity in the right middle cerebral artery (MCA) zone; B. Restricted diffusion on apparent diffusion coefficient (ADC) map; C. FLAIR is negative [4].

Although there is not approved treatment paradigm for WUS, nevertheless according to the more recent guideline, stroke patients who present with an unclear onset of stroke symptoms up to 24 hours could be potential candidates for intravenous thrombolysis treatment (such as t-PA, Alteplase) and/ or mechanical thrombectomy (endovascular stroke treatment) [5]. It has been shown that alteplase as a choice treatment for hyperacute stroke is better in elderly patients with 80 ≤ years old. Over the last decade, to improve management of stroke patients especially in elderly subjects, the care units transferred from general wards into multidisciplinary and specialized units. For the first time, the organized stroke care defined in the 1980s but implemented following meta-analysis which conducted in 2013. Remarkable reduction in mortality (20%) and disability were the major outcomes of this study. The improvement of stroke unites particularly has importance for older patients, who often fright having to move into a nursing home [6].

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References:

1. Azarpazhooh MR, Etemadi MM, Donnan GA, Mokhber N, Majdi MR, Ghayour-Mobarhan M, Ghandehary K, Farzadfard MT, Kiani R, Panahandeh M, Thrift AG. Excessive incidence of stroke in Iran. Stroke. 2010;41: e3-e10.
2. Parr E, Ferdinand Ph and Christine Roffe Ch. Management of Acute Stroke in the Older Person. Geriatrics 2017, 2, 27; doi:10.3390/geriatrics2030027.
3. Dekker L, Hund H, Lemmens R, Boiten J and Wijngaard I. Unknown onset ischemic strokes in patients last-seen-well >4.5 h: differences between wake-up and daytime-unwitnessed strokes. Acta Neurol Belg. 2017; 117(3): 637–642.
4. Huang X, Alakbarzade V, Khandanpour N, Pereira AC. Management of a wake-up stroke. Pract Neurol 2019; 0:1–6. doi:10.1136/practneurol-2018-002179.
5. Atkinson G, Jones H, Ainslie PN. Circadian variation in the circulatory responses to exercise: relevance to the morning peaks in strokes and cardiac events. Eur J Appl Physiol (2010) 108(1):15–29. doi:10.1007/s00421-009-1243-y.
6.https://www.gla.ac.uk/news/archiveofnews/2018/may/headline_585728_en.html

1. Cerebrovascular Accident
2. National Institute Health Stroke Scale

International Project (No.3)

Interaction of aging with cardioprotective interventions in myocardial ischemia-reperfusion injury: focusing on autophagy and mitochondrial biogenesis mechanisms

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Aging is a complex process characterized by the progressive failure of cellular repair pathways such as autophagy and mitophagy (mitochondrial autophagy), resulting in a gradual accumulation of dysfunctional macromolecules and organelles. The incidence of ischemic heart disease increases dramatically with age. Myocardial ischemia/reperfusion (I/R) injury is always inevitable during and following cardiac procedures such as angioplasty (PCI), CABG surgery, and heart transplantation. It is believed that aging can interact with I/R pathophysiology and may inhibit the cardioprotective effects of therapeutic modalities (like postconditioning). In this interaction, autophagy and mitochondrial function can be the two main determinants because they have critical roles in I/R injury, aging process as well as cardioprotection. Thus, it seems logical that activating mitochondrial biogenesis through autophagy/mitophagy stimulators would modulate the burden of cardiac diseases in aging.

In spite of extensive preclinical investigations on cardioprotection, there is still no translation of knowledge from basic to clinical settings. One reason is likely attributable to the research settings and methodological designs. Human [cont.]

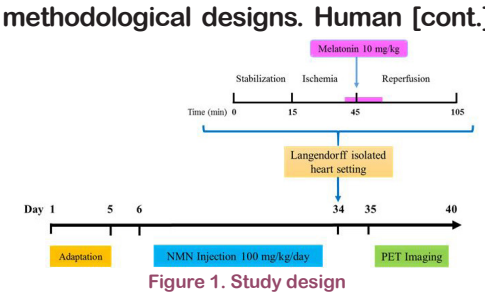

Figure 1. Study design

Student Letter

Stem-Cell Therapy: Toward An Evolution in Treatment of Parkinson's Disease

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Parkinson's disease (PD) is the second most prevalent neurodegenerative disease in the world, that affects more than 1% of population over 65 years; and it is predicted that with the aging of population, especially in developed countries, this number will increase gradually in the near future [1,2]. PD has some principle motor symptoms, including bradykinesia, resting tremor, rigidity, and postural instability, as well as non-motor symptoms that include depression, cognitive decline, intestinal dysfunction, and gradually decreased life quality [3].

The exact pathogenesis of PD is not clear, yet one of the hallmarks of PD occurrence is the loss of dopamine neurons in the midbrain (mDA). For this reason, dopamine (DA) replacement therapy is now considered as the gold standard medical treatment for PD. Other successful interventions to relieve PD symptoms include surgical applications (e.g. deep brain stimulation) or gene therapy; however none of these treatments actually prevents or reverses the loss of mDA neurons [4]. In this situation, the only possible option to reverse the disease progression is to replace the lost neurons; and since the neurodegeneration in PD remains relatively local, it is considered to be a good candidate for cell-based treatments [5].

The first steps for cell-based therapy of PD were taken by worldwide efforts to replace the lost DA neurons, using fetal midbrain tissue; some of which showed great success and long lasting survival because of the physiological release of DA in host bodies. The fetal transplant work was groundbreaking, but the problem was that the material itself was scarce [6]. Technically, multiple fetal donors are required for a single fetal transplant to be possible; besides, it is not ethical to request or demand tissue from electively aborted fetuses [7].

Embryonic stem-cells (ESCs) are another potential source for DA neurons, which are extracted from the human blastocyst and are therefore representative of early embryo [8]. The study of human ESCs is still in the pre-clinical stage, since some of the conducted animal studies suggested that ESCs may cause behavioral and neurochemical complications in animal models of neurodegenerative diseases. Moreover they are only available on embryonic stage which is a very short stage of life and not always attainable [9].

To overcome these obstacles, it is possible to derive mDA neurons for transplantation from non-fetal or non-embryonic sources; and a reasonable way to do so, is to induce stem cell sources by reprogramming skin fibroblasts through a pluripotent stage, and make induced pluripotent stem-cells (iPSCs). These cells offer a variety of advantages, including accessibility, immunoacceptability, and avoiding ethical issues, in comparison to fetal and embryonic stem cells [10].

iPSC is the very technology which makes it possible to generate patient and disease specific cells, without any need to embryos or fetuses. and therefore, is able to revolutionize personalized medicine [11,12], but on its way to become a feasible choice for PD treatment, still much work is needed to be done. For instance PD is a heterogeneous disease that may have multiple etiologies or variable unsets, with different responses to cell-therapy [13]. Hence Therefore, factors such as patient selection criteria for initial clinical trial design, need to be taken into consideration carefully.

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References:

1. Samii A, Nutt JG, Ransom BR. Parkinson's disease. Lancet (London, England). 2004;363(9423):1783-93.
2. Dorsey ER, Bloem BR. The Parkinson Pandemic-A Call to Action. JAMA neurology. 2018;75(1):9-10.
3. Lees AJ, Hardy J, Revesz T. Parkinson's disease. Lancet (London, England). 2009;373(9680):2055-66.
4. Sonntag KC, Song B, Lee N, Jung JH, Cha Y, Leblanc P, et al. Pluripotent stem cell-based therapy for Parkinson's disease: Current status and future prospects. Progress in neurobiology. 2018;168:1-20.
5. Barker RA, Drouin-Ouellet J, Parmar M. Cell-based therapies for Parkinson disease-past insights and future potential. Nature reviews Neurology. 2015;11(9):492-503.
6. Master Z, McLeod M, Mendez I. Benefits, risks and ethical considerations in translation of stem cell research to clinical applications in Parkinson's disease. Journal of medical ethics. 2007;33(3):169-73.
7. Barinaga M. Fetal neuron grafts pave the way for stem cell therapies. Science (New York, NY). 2000;287(5457):1421-2.
8. Towns CR, Jones DG. Stem cells, embryos, and the environment: a context for both science and ethics. Journal of medical ethics. 2004;30(4):410-3.
9. Kim JH, Auerbach JM, Rodriguez-Gomez JA, Velasco I, Gavin D, Lumelsky N, et al. Dopamine neurons derived from embryonic stem cells function in an animal model of Parkinson's disease. Nature. 2002;418(6893):50-6.
10. Towns CR. The science and ethics of cell-based therapies for Parkinson's disease. Parkinsonism & related disorders. 2017;34:1-6.
11. Tapia N, Scholer HR. Molecular Obstacles to Clinical Translation of iPSCs. Cell stem cell. 2016;19(3):298-309.
12. Hockemeyer D, Jaenisch R. Induced Pluripotent Stem Cells Meet Genome Editing. Cell stem cell. 2016;18(5):573-86.
13. Schapira AH, Jenner P. Etiology and pathogenesis of Parkinson's disease. Movement disorders : official journal of the Movement Disorder Society. 2011;26(6):1049-55.
2002:295-309.

International Project (No.3) [cont.]

patients with myocardial I/R injuries commonly have underlying cardiovascular risk factors such as aging, which is usually ignored in the settings of preclinical studies. Therefore, it is necessary to design targeted and multi-dimensional studies with two or more therapeutic approaches (combination therapy) instead of monotherapy. Accordingly, the aim of this study was to evaluate the protective effects of nicotinamide mononucleotide (NMN) and postconditioning with melatonin, alone or in combination together, on myocardial I/R injury in aged rats. In this study, we had postulated that administration of anti-oxidative and cell-surviving treatments (e.g. melatonin) beside the activators of mitochondrial biogenesis (e.g. NMN) can restore I/R heart's normal physiology and overcome the failure of cardioprotection in aging setting.

This experimental study (figure 1) was conducted in the cardiovascular laboratory of Department of Physiology in Tabriz University of Medical Sciences. Our study revealed the therapeutic potential of NMN and melatonin against I/R injury in aged rat hearts, specifically when they were used in combination. We found that NMN and melatonin had protective effects against I/R injury by reducing the infarct size and restoring myocardial contractile and electrical function toward normal values. Co-application of NMN and melatonin could provide stronger cardioprotection through reducing mitochondrial membrane depolarization and its ROS generation as well as boosting the expression of genes regulating autophagy and mitochondrial biogenesis (Foxo1-LC3B-P62-mfn1/2 and Sirt3-PGC1α-Nrf1-TFAM-mtDNA).

Two articles derived from this project have recently been published in European Journal of Preventive Cardiology (IF: 4.542) (doi:10.1177/2047487318756420) and in Biogerontology (IF: 3.702) (doi:10.1007/s10522-019-09805-6), and two other articles are under review. For the second part of the study, we want to collaborate with Odense University to use the animal PET scan machine for assaying the extent of myocardial infarction in aged rat hearts, in vivo. To this end, a mini-project for Danish part has been written, in collaboration with Dr. Vafaee and Dr. Flemming in Odense, and after providing the required facilities, we can conduct the PET section of the project in Odense University in Denmark.

Ibn Sina (23 August 980 AD)

Happy National Doctors' & Pharmacists' Days!

Keepers of health, gaurdians of living
Great doctors we all believe in
Although noteworthy, not everyone knows
How much to these men, our science owes
Ibn Sina, Father of medicine. Al-Razi, Founder of Pharmacy
And to this day, remained their legacy

Sketch: Ali Shamekh, Medical Student of TUOMS
Poem: Pooriya Sadeghi, Medical Student of TUOMS

Al-Razi (27 August 840 AD)