Aging Research Institute Newsletter

Tabriz University of Medical Sciences (TUOMS)

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Special Issue: Healthy aging congress (5th International Alavi meeting)

National Elderly Week 1401;
The Resilience and Contributions of Older Women

Jules Zermati (1875_1925)

Messages about the congress

Dr. Yunes Panahi
Deputy of Research and Technology, Ministry of Health and Medical Education

I extend my greetings and best regards to the respected guests of the healthy aging congress being held in the honor of Professor Abass Alavi at Tabriz University of Medical Sciences. I am really delighted that this congress coincides with the meeting of the research deputies of the country's medical sciences universities in Tabriz.
It is noticed that the world's population is aging and in our country about 10% of the population is elderly at this time, which will increase up to 30% due to improving the quality of life and life expectancy. The point needing attention is that the elderly population faces various problems. There is a wrong believe people at the age of 60 or older have no place in social activities. In fact, this misbelief along with their health problems like cardiovascular disorders, neurological disorders, dementia, cancer, musculoskeletal diseases, and etc. increase the risk of social isolation in elderly.
The point is that we should improve the health status and quality of life of this population by developing research in the field of aging. The development of research centers and networks related to aging is necessary in parallel with the increase in the number and proportion of the elderly population. It is very important that the research centers and universities with proper infrastructures and specialized human resources should have the promotion of education and research in the field of aging in their road map, so that they can meet the needs of the ever-increasing elderly population and manage the related concerns.
The development of geriatric knowledge can reduce the years of life spent with disability and disease and improve the quality of life of the elderly by possible reduction of exposure to common problems of aging.
Once again I am grateful for participation of Prof. Alavi and other professors and researchers in this meeting and I proudly announce our readiness to support research in the field of geriatric.

Dr. Bahman Naghipour
Dean of Tabriz University of Medical Sciences

The world's population is rapidly aging, and this population shift will affect all aspects of society. Aging is associated with changes in biological, psychological, behavioral, and social processes. Having the opportunity to live a long and healthy life and enjoying a healthy life is an inalienable right of all human beings. Due to the importance of paying attention to healthy aging and improving the lives of the elderly, the United Nations has named the current decade the Decade of Healthy Aging (2021-2030).
Healthy aging does not necessarily mean the absence of any disease or disability because most elderly have one or more diseases that, when properly controlled, have little effect on their health. According to the World Health Organization, healthy aging is defined as "the process of developing and maintaining the functional ability that enables wellbeing in older age". Healthy aging emphasizes the need for action in various sectors and enables older adults to remain a resource for their families, community, and economy.
Scientific communication plays a significant role in knowledge transfer. Congresses are necessary for the scientific growth and development of societies by creating an atmosphere for the exchange of information on various scientific and research topics. Scientific conferences are an opportunity to exchange new and valuable information and achievements, and provide easy access to up-to-date scientific resources. Moreover, they provide a platform for companionship and communication as well as knowledge transfer between seniors and younger researchers. Holding the Healthy Aging Congress as a scientific event is a great opportunity to get acquainted with the latest scientific findings and a step towards improving the scientific, research and health level of society.

Prof. Abass Alavi
Honorary Professor of Tabriz University of Medical Sciences

It's a great pleasure for me to meet you. Being honest with you, I was going to give my speech in Turkish, because Tabriz is very dear to my heart and some of the best years of my life were spent in Tabriz. I was grown up in this beautiful city, so my heart is still in Tabriz. I love to come to Tabriz very soon and hopefully this is going to happen. So, this is a really great opportunity and it is truly a big pleasure for me to take part in this great occasion. As you know, aging is a big part of my academic life. I have done a lot of research in many aspects of aging and in 2015, when I was at the university, we had a conversation about aging and I thought that, it was fantastic and was exactly what I wanted to do and I couldn't make it happen in a better place than my beloved Tabriz. So, when we discussed it with Dr. shakouri and colleagues, it was very clear that we wanted to emphasize on the three of major elderly problems. Following the progress that have been made in medicine, the world is aging very rapidly. People are living much longer, so if you live longer you are going to develop some medical problems, on top of which there are brain disorders as was discussed in dementia, and other abnormalities occurring in the brain. The second common problem that elderly people would face, is cardiovascular diseases, following the number one killer in the world, also in Iran, atherosclerosis, in which a hardening of arteries developes clots in the heart. And the third common problem is the musculoskeletal problems, in which old people develop significant problems with joints and muscles. So, I really thought that it should be emphasized and some investments must be considered by the university at national level on these problems, and this will be a great help for the university of Tabriz as well as the rest of country. I really was satisfied during that visit which we established aging research institute and I want the greatest and the best tuition for young members to get involved at these projects and in fact when I come to Tabriz, that I am hoping it is going to happen soon, we really have to establish

some major awards. So I will be able to support that and I really want to do this. I want to just encourage young people in medicine to get interested about research and start it particularly about aged reached disorders, so really this is going to be a very important contribution not only for the people of Tabriz and Azerbaijan but also for the entire country. Actually, I want my homeland to be visible in the world's scene and I really would like to help as many people as I can, to write papers that can be published in international journals. Persians are just smart as anybody in the world and we have to shine as we did 2000 years ago. We were the leaders in any level, science and other things. Hopefully, this fall I will come to Tabriz. I'm going to visit my homeland and country and my "HAMSHAHRIES", and start another beginning in age related researches. This is going to make me very happy because fortunately I am a healthy old person and I am able to work as hard as anybody; I work 7 days a week and 10 hours a day and I have to help young people, of course in medicine, because I lost my father when I was four years old and my mother was 24 years of age and since that time, she wanted me to help mankind. So I want to do it not only for the world, but also for my country's people and Tabrizi patients. So, this is my greatest desire, I really hope to be there again to see you face to face, rather than by internet. I also hope to seriously examine the projects related to this important issue not only in my motherland but in the whole of Iran.

Dr. Hassan Soleimanpour

Deputy of Research and Education, Imam Reza Medical Research and Training Hospital

Dr. Hassan Soleimanpour, Vice-Chancellor for Education and Research, Imam Reza (AS) Hospital, Tabriz, and one of the founders of Professor Alavi Aging Research Institute , Tabriz University of Medical Sciences, at the opening of the 5th International Alavi Meeting on the global crisis of covid-19 and its impact on older adults mortality, noted:

According to the World Health Organization in April 2020, more than 95 percent of covid-19 deaths were in people over the age of 60 , and more than half of covid-19 deaths were in people over 80 years old. In fact, older people have the highest risk of developing covid-19. Perhaps one of the main reasons for this significant incidence in this age group is poor immune responses and efficacy.

It was also noted that, based on studies, the main difference between covid-19 and influenza pandemic is in the age distribution of patients with severe disease.

Mortality rates in people affected with covid-19 increase dramatically with age, with most mortality occurring in the population over 50, with most people with H1N1 influenza being younger than 60 years. In comparison, most of the covid-19 hospitalized individuals were over 60 years old.

Dr.Soleimanpour, professor of intensive care at Tabriz University of Medical Sciences, stated that the mortality rate of the elderly in Covid-19 was higher than that of the influenza pandemic as the mortality rates in Spanish influenza and H1N1 were in the age groups of 15-44 and 59-59 years old, respectively. Therefore, special attention to this vulnerable age group should be given priority

in the policy-making of public health authorities.
In continuation of his speech, while honoring the scientific and moral status of Professor Abbas Alavi, he emphasized that:
Honoring scientists and introducing them to the present and future generations, as well as justifying the scientific efforts of the greates literati, is highly effective in educating the youth and turning these actions into a public culture.
The city of Tabriz, like many other cities in Azerbaijan, has been distinguished by cultural and scientific honors throughout the history of civilization and culture of our dear homeland. And ,undoubtedly, Professor Abbas Alavi, who is one of the pioneers of modern nuclear medicine , is the shing star of this vast land.
Dr. Soleimanpour continued ,
Professor Alavi is undoubtedly one of the wonders in the field of medicine . With his extraordinary intellgence and knowledge in various fields, he is a prominent and special scholar and scientist, and if we consider only his published works, the comprehensiveness of Professor Abbas Alavi will be revealed.
In 2016, the esteemed President of the University, Dr. Mohammad Hossein Soomi, with regard to my proposal and also due to the privileged scientific and moral position of Professor Abbas Alavi, issued the order to establish the Aging Research Institute of Tabriz University of Medical Sciences in honor of this world-renowned scientist and a leader in modern nuclear medicine.
Following this commendable action, in May 2022, we witnessed the formation of the fifth Alavi International Meeting in Tabriz University of Medical Sciences.
In his closing remarks, he made another request to the current President of Tabriz University of Medical Sciences, Dr. Bahman Naghipour, as follows:
Appreciating the support of the current board of the university and especially the esteemed president of the university, Dr. Bahman Naghipour in holding this glorious meeting, I, as a small member of the large famiy of teachers, request to make this ethical action of the university in establishing an aging research institute, an even more praised deed by building the head statue of Professor Abbas Alavi in front of the faculty of Medicine of Tabriz University of Medical Sciences in honor of this valued and eminent scientist of Tabriz, to introduce a successful model of science and ethics to students and academics.

Before the congress ....

Honestly, We have been working for several months to organize better the fifth International Alavi meeting, the healthy ageing congress. Since January, we have collected retraining questions to upload, arranged programs, and managed lecture files. Going through this process which I reported in a few words, required much effort. We got disappointed and tired many times through this journey. Still, with our colleagues' help and having meetings, we aimed to do our best and hold the congress on the announced date. We were struggling even in our night dreams. We have been through ups and downs, we were told to change the date of the congress, but we were so keen to do it and tried until the last moment. Our Dear colleagues in different departments who were aware of our difficulties did their best and helped us achieve our goal. We greatly appreciate their efforts.

It was Wednesday morning, May 12. After finalizing the programs, checking connections with online hosts, preparing the refereeing files, and planning for the airport reception, we were finally ready.

The opening ceremony began just on time with reciting verses from the Holy Quran and playing the national anthem in the VIP hall of the medical school. As the meeting of the research assistants of the Iran's medical universities was being held in Tabriz, We were delighted to have a video connection with them. Our other online guests were Dr Panahi, Professor Alavi, and other foreign judges. The first lecture presenters were Dr Naghipour, President of Tabriz University of Medical Sciences, and Dr Farhang, President of the Aging Research Institute. After that, we heard encouraging statements from Professor Alavi supporting the Aging Research Institute and the city of Tabriz, his hometown, which brought tears to our eyes. Then, Dr Soleimanpour asked Dr Naghipour for a statue of Professor Alavi to be made in his Gratitude and installed at the medical school entrance.

In addition to holding webinars with retraining points, the research section included judging the projects and awarding grants to selected ones. The student projects were so productive and creative. The judges and professors encouraged them, and we wished we could support more student projects. Finally, research workshops were held.

We hope to experience these wonderful memories in the future again and reiterate our cooperation with our dear colleagues and students in holding coming congresses and meetings. We wish this meeting to begin a noteworthy change in the science and culture of this country. Eventually, we are grateful to each of the professors, colleagues, and students and their support.

Healthy aging congress (5th International Alavi meeting)

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Opening ceremony

The opening ceremony began with the recitation of verses from the Holy Quran and the playing of the national anthem of the Islamic Republic of Iran in the VIP hall of the Medical School. Due to the coincidence of holding the Healthy Elderly Congress with the national meeting of research vice chancellors of medical universities in Tabriz, the opening ceremony was held with the presence of the esteemed president of the university, university professors, judging teams from different universities, video conference and live communication with research venues of Universities of Medical Sciences and the online presence of Dr. Panahi, Deputy Minister of Research and Information Technology of the Ministry of Health, Professor Abbas Alavi, Professor of the University of Pennsylvania and the foreign judges of the Congress.

In the opening ceremony, Dr. Naghipour, President of Tabriz University of Medical Sciences, Dr. Panahi, Deputy Minister of Research and Technology of the Ministry of Health, Professor Alavi, Professor of the University of Pennsylvania, Dr. Farhang, Director of the Aging Research Institute, Dr. Akhondzadeh, Professor of Tehran University of Medical Sciences, and Dr. Hassan Soleimanpour, Vice Chancellor of Research in Imam Reza Hospital, gave a speech.

Part I

Scientific webinars with retraining scores: This section consisted of five scientific webinars with retraining points which were held in collaboration with Covid Studio of Imam Reza (AS) Hospital. In the scientific webinars section of the congress, speakers from Tabriz University of Medical Sciences, Tehran University of Medical Sciences, Shiraz University of Medical Sciences, Shahid Sadoughi University of Yazd, Rehabilitation Sciences and Social Health, Babol University of Medical Sciences, Kermanshah University of Medical Sciences, Turkey and Thomas Jefferson University were present. The specifications of the executed panels are as follows:

Part II

The research section began after the official opening ceremony of the Congress on Wednesday, May 11, 1401 and continued until the third day of the Congress. The research section consisted of two parts: 1- judging academic projects and 2- judging student projects. On the first day of the congress research section, 11 academic research projects were reviewed, and on the second day, 13 student research projects were reviewed. The refereeing team consisted of internal and external referees. The foreign referee team consisted of 5 judges from three universities: University of Copenhagen, University of Southern Denmark, and Tampere University.The team of internal judges included 22 judges from the Ministry of Health and Medical Education, Tehran University of Medical Sciences, Tabriz University of Medical Sciences and Kermanshah University of Medical Sciences.

In the research section, in addition to judging research projects, Professor Albert Gjedde, professor at the University of Copenhagen, Denmark, spoke for 20 minutes on the subject of the Aging Congress .

Part III

Workshop section: In this section, a workshop on writing review-systematic and meta-analysisarticles was held with the target group of students and professors.

Lecture

The Healthy Brain: From the Beginning to the End

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We are here to resolve the issues of healthy aging. This is also the topic of my presentation here. Of course, we are only at the beginning of the scientific examination of the process of healthy aging that I think is so important for us to understand. So, with my thanks for being able to present a talk at this conference, I will begin my presentation by asking how brains actually benefit humans and other animals.

My answer is that brains are important to mammals in general and particularly are important to humans because I have come to the understanding that the purpose that brains fulfill is to predict the future. The reason this is important is because brains enable movement and when you move, you move from the time now to a time in the future. It is vitally important that it appears that brains evolved to predict the kinds of movement, and the importance of the movements, and the directions of the movements, and the method of movement that would to some sufficient extent raise the likelihood of survival in the future to a level of certainty as people move or animals move.

This prediction of how to move and where to move and how fast to move is to me one of the most important functions of the brain, and it is almost certainly the reason that animals have brains. An example of a life form is plants that have no brains. They do not have brains, probably because they do not move and hence do not need to predict the future because they are just sitting there, unable to do anything about their fate.

There are even hybrid forms of life that are animals that move when they are young and have brains. When they age, they become plants that fix themselves to the bottom of the ocean and lose their brains, apparently, because you do not need brains when you cannot move. That is the kind of hypothesis that lurks behind the examples I will now discuss with you. In the course of five short items of presentation, I hope to be able to keep the time sufficiently but we will see, depending on my powers of prediction and control over the motions of the muscles of speech:

We predict because we move, and we use the past to predict the future for obvious reasons. We use emotions to choose among different futures that we predict from the course of actions that we are about to take: There are predictions that we are happy with and there are other predictions that we are not happy with, and the latter kind are the ones that will determine the movements that we undertake. The use of the past evolves during early development, but it takes some time for the necessary memories to develop sufficiently. Finally we now that the use of the past unfortunately declines with age because of the increasing difficulties with the keeping of items in memory that we must use to predict the movements that we need to do. The first item to consider is the claim that we predict because we move.

We have obtained some insight into the evolution of animals on land since the time when they left the primordial oceans some 375 Million years ago, aided by three drives that would determine whether anyone of these animals or species would survive, that is the challenges of being able to live, to eat, and to reproduce. Eat to survive oneself, survive to win the competitions with other animals, and reproduce to be able to put offspring into the world. The species that did this successfully evolved to the stage we are at now.

Then humans arose. There is some discussion as to when this happened, but most scientists now say it hap-

pened 200,000 years ago. The evolution of humans went forward by means of a new fourth drive that supported the urge of humans to understand how things work and what purpose life serves. The new urge drives humans to try to discover what we need to know of the prospects of humanity with the help of science and cultural and artistic interactions. The efforts help us predict the future and they help us to predict in a more appropriate way the specific movements into the future we need to undertake if and when we understand the purpose of these movements.

Here is an image of a real brain but not as a single human brain but as an average human brain constructed from brain images from 85 young people where you clearly see the gyri also known as folds and sulci also known as grooves. It is remarkable that scientists only realized what the surface of brains really looks like no earlier than 250 years ago. Observers before that claimed that brains look like clouds and serve mostly as radiators than cool blood during the circulation.

The different regions and networks of the brain serve different functions. For these functions as well as for the work of the brain as a whole, a major functional distinction between brain regions is the so-called executive brain in the front and the receptive brain in the back. The executive brain is associated with the frontal lobe that we may call the output side of the brain, while the receptive brain consists of the three hind lobes with the functions associated with hearing and vision and sensation. The receptive functions provide the basis for the ability of the frontal to make the predictions that are important to the planning of purposeful movements.

Nowadays we use tomography to determine the activity of brains cells. The problem is that the number of brain cells as you know is so enormous that we need to examine brains by imaging larger groups or regions of cells. The images represent positron emission tomographic records of activity such as glucose consumption in the brain shown in this particular recording of the uptake of a tracer that we give to show the amount of glucose that the regional cells actually consume. Figure 1 shows you how the tracer amount increases in two selected regions, the cortex and the caudate nucleus.

You can study the brain's work with these impressive images of the metabolism of the brain showing that the cerebral cortex is particularly active in terms of the glucose consumption as are some regions of the basal ganglia and other subcortical places in the brain.

When we use the past to predict the future by means of the brain, the past must of course be stored in memory. This is one of the main functions of memory and one of the reasons why there are parts of the brain that store the past activities of brain in such a way that we can use the records again to predict the future. We can perhaps say with a nod to Shakespeare that "predictions are the dreams that stuff is made on", and I shall call this mechanism the generator of "memories of the future". When we think about the future challenges that we need to meet and observe, we resort to the stores of long-term memory. Those are stores where so-called declarative facts in particular remind us of how to do things.

The declarative facts that are stored in the brain are the facts of episodes we remember but also the meaning of words. This is why I can speak English to you and you understand what I say but if you spoke to me in a language other than the few that I know, such as in Azeri or Persian for example, you probably would not be able to make me understand what you said. Therefore, it is the items we learn that form the contents of memories that are important to the ability to predict the future and that is why we call this ability by the amusing term "memory of the future".

There is a network in the brain that is active when you think of the future or the past. It is known as the default mode network that connects neurons in the frontal lobes of the brain with neurons the posterior lobes of the brain such as the medial temporal lobes. Here we find the neurons engaged in activities of the brain associated with the past, while the frontal lobes are engaged in the activities that you plan for the future.

We can explore the default mode network when we place a volunteer in a brain imaging device and ask the person to think about the past such as when you "remember taking a daytrip last summer and walking on the beach" or about the future when you "imagine picking out a puppy at the pet shop next year". Surprisingly we actually find that there are no differences between the two maps of activity. We activate the same two places in the brain whether we are thinking of the past or the future.

The regions connected by the network include a part of the cortex in the back of the brain called the precuneus. It is a name that only means that it is a region just in front of another region called the cuneus or "fold". In the cortex in the front of the brain there is the medial frontal lobe or ventromedial prefrontal cortex that we think works to control the precuneus when we direct our brain to think of or

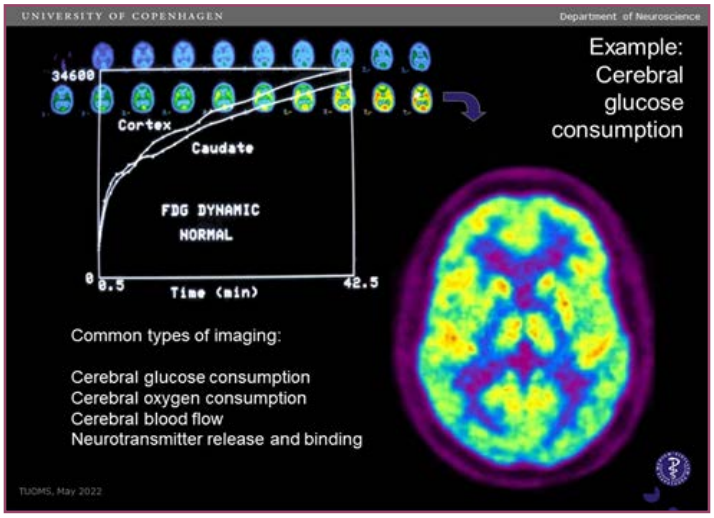

Fig. 1

be conscious of the past or the future that both of which we generate from memory.

There are other important networks besides the default mode network that is active when you are thinking about the past or the future. Another network is the attention network and particularly the so-called dorsal attention network that is the one that active when you choose to pay close attention to the world associated with the here and now. It is active when you think of the present rather than the past or the future that is the activity of the default mode to which you "default" when you are more or less forced to focus on the present.

It is important to know that humans, by and large, use emotions to choose among the different futures presented by memory. It means that we have feelings when we weigh the reasons for the future acts that we are about to carry out, positive or negative feelings.

We know that positive emotions are associated with brain activity recorded in the anterior of the intermediate prefrontal cortex. Figure 2 gives 25 examples of sites of activation in human brains exposed to positive emotions about the past or the future, visible in the anterior or the intermediate prefrontal cortex shown for a number of different contexts. The sites of positive feelings about the future appear to be associated with sites in front of the sites that are associated with negative emotions. There are 15 examples of sites that appear more active when you think negatively about things that happened in the past or about things that are going to happen in the future.

We find the sites linked to negative emotions in more posterior parts of the intermediate prefrontal cortex. When we put the evidence together, we find that the brain region known as Brodmann Areas 25 and 32pl are associated with the negative emotions, while Brodmann Areas 10m, 10r, and 32ac are associated with positive emotions. We can actually understand how some neurologists have tried to treat depression by putting electrodes in Area 25 that successfully inhibited the sites of negative emotions

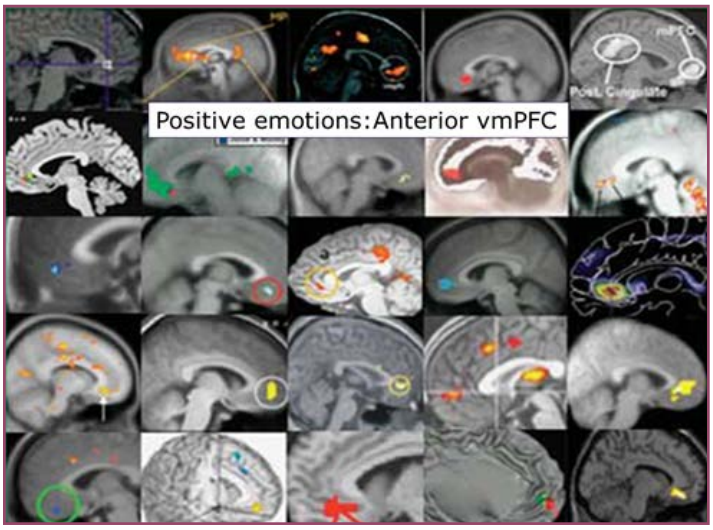

Fig. 2

in a number of cases. I don't think anybody actually tried to activate positive emotions from Area 25 by drugs other than by accident, and I have not heard of electrodes being placed in Areas 10 or 32ac to increase the intensity of positive emotions.

The use of the past evolves in early development: This happens as children grow extensions of the dendrites of neurons that we call dendritic spines, and you see here two such nerve cells with dendrites and dendritic spines in Figure 3. The spines are the little pointed extensions sitting on the dendrites that are now held to be the places of truly physical storage of the memories. The spines connect neurons and when they are active, we are conscious and remember things, depending on which spine connections we activate.

The process of development of spines is a form of plasticity occurring during development that depends on the generation of new spines as more experiences are stored as memories. It works almost as an old-fashioned gramophone record with the physical storage of the memories. Brains turn out to be record players and the spines are the records that hold the memory items that are important for us to think about in terms of the past or the future. When the spines connect and depolarize and the more we use, store, and reuse particular memory items, the more the spines grow and the more they multiply until the number reaches a maximum at puberty.

When we look at the neuronal connectivity established by dendritic spine activity, we can see that the spines are not fully developed in children. In 7-year-old children, we see that the spines supporting the connections between the ventromedial prefrontal cortex and the precuneus are not yet fully developed. When we then compare with the adults, we see the massive growth of memory stores in the precuneus. The development is associated with the process of growing up of course. We can then see what the difference is when we compare adults with children. When we compare the connectivity of 25-30 year old adults with 7-year-old children, we see that the development of memory stores in the precuneus is characteristic of growing up.

The spines evolve as people go through the early postnatal, adolescent, early adult, and adult phases of life, and the spine numbers keep rising until puberty as you gain more and more experiences and grow memory stores to hold the experiences. It is a common experience that some of the new spines may not be useful because they may no longer serve any purpose in adulthood and that they may then undergo decline and removal when they are no longer useful. When some spines are removed, it is of course important to make sure that the right ones are removed and the useful ones are maintained into adulthood which is where these physical structures store the memories that must serve us until the end of life.

Sadly the use of the past declines with aging and we tend to forget because the connections between the an-

terior part and the posterior parts of the brain decline with aging when dendritic spines are lost with age. We know much about the dendritic morphology, the dendritic spines, the number of dendritic spines per micrometer, and we now know that the diameter and the density decline with aging from ages of 40 to 85. You actually lose the spines during aging and with them the memory stores where you placed your consciousness and your predictions of the future.

We know that the annual rate of change is somewhat different in different parts of the brain, and we know that the one with the highest loss of brain volume associated with loss of spines is the hippocampus that plays a role in the administration of spines. Other regions have varying degrees of decline that average about 0.5 percent per year that you lose in terms of regional volume and also in terms of dendritic numbers as you age. This includes the precuneus and the medial orbitofrontal and middle frontal cortices as important sites of communication between the memory stores and consciousness.

The declines show that the glucose consumption that is important to the maintenance of the activity of neurons actually declines and reflects an evolution of dementia, particularly as Alzheimer's disease. A normal value of the common Mini-Mental State Examination is a score of 30, but your ability to obtain normal scores in this examination declines as glucose consumption declines. Some regions are more sensitive than others are, and at an MMSE score of 11 there are very significant declines of glucose consumption in parietal and frontal lobes and they are of course precisely the lobes that must communicate. When these two parts of the brain no longer communicate with each other because they have lost the connections that are maintained by the dendritic spines, the functions of memory and predictive coding no longer work.

In Alzheimer's disease, the occipital, frontal, and parietal lobes have particularly low activity compared to healthy controls. When this is compared to the accumulation of a particular substance such as PiB measured as binding potentials of this Pittsburgh Compound B, we see that the substance appears to be a marker that is consistent with the degree of dementia. It is particularly high in the frontal lobe in Alzheimer's disease (AD) and it seems to be confined mostly to the white matter in healthy control subjects.

Fig. 3

The problem is that many people differ greatly in terms of the amount of PiB present in their brains as a marker of the substance known as amyloid β in the brain. We know that healthy control subjects with perfectly high values of the MMSE exam also can have very high degrees of accumulation of the PiB substance as a marker of amyloid β.

The significance of PiB accumulation therefore is not clear. Let's note first that patients with Alzheimer's disease have high values of amyloid β accumulation while completely healthy control subjects vary greatly, including some with very high levels. Is there a possible answer to this puzzle? I collaborated with a group that just had a paper accepted with the title "In Alzheimer's disease, β amyloid accumulation is a protective mechanism". The claim is that amyloid β accumulation may be a protective mechanism that ultimately fails because it is overwhelmed by the pathology. We claim that amyloid β accumulates to protect brain regions, and the claim led us to predict that more amyloid β accumulates in regions of the brain that are able to maintain higher rates of glucose metabolism, reaching a maximum that is followed by increasing dementia. The maximum accumulation of amyloid β is of course characteristic of AD but apparently it does not correlate with the cognitive decline, unlike the rates of glucose metabolism.

We compared regionally averaged and individual estimates of regional binding of patients of PiB with regionally averaged and individual values of the rates of metabolism of tracer FDG that is a marker of glucose metabolism, and we did this in brain regions of volunteers with AD. We found that healthy control subjects as expected have little PiB accumulation but in mild cognitive impairment the PiB marker increases in proportion to the amount of glucose that are used in different parts of the brain such as hippocampus, parahippocampus, and other regions.

We noted interesting things when we compared different regions of the brain in AD. The PiB signal appeared to signify the highest accumulation of amyloid β on average in regions with the highest FDG-measured glucose consumption. This was true originally of two separate reference studies that we cited to generate the hypothesis. We also noted that control subjects had comparatively little PiB binding. The authors did observe that accumulation of PiB in AD is highest in the regions with highest glucose consumption, and it is also true in the intermediate stages of mild cognitive impairment.

When we then looked at the published evidence from the same brain regions individually in different parts of the brain of individual subjects, we noted the strange observation that the correlation was the reverse for every re-

gion separately. The PiB signal was highest in the individuals with the lowest consumption of glucose. It was true in the majority of the regions of the cortex including the precuneus in AD and in control subjects of both studies that we used to generate the hypothesis that the correlation between PiB accumulation and the FDG signal was reverse inside individual regions.

To test this hypothesis we did our own study. We tested the hypothesis by correlating individual glucose consumption values and PiB binding potentials in different regions of the brains of volunteer patients in Aarhus. We observed the inverse correlation in terms both of logarithmic scaling and with linear scaling. When we compared mean PiB binding potentials with mean glucose consumption rates of different regions of the brain, in marked contrast, we found a direct linear correlation as predicted by the hypothesis. This finding means that PiB accumulation is highest in the regions of the brain with the highest averages of glucose consumption rates, as shown in Figure 4.

We concluded that the claim tentatively explains the cognitive decline in some patients at significantly lower levels of amyloid β deposition than in other patients, as well as the presence of cognitively healthy individuals with elevated amyloid β accumulation. With further support of the hypothesis it may be necessary to revise the understanding of the origin and effects of amyloid β accumulation in brains of patients with AD. Additional findings may then support the understanding of amyloid β as a protective substance. That understanding may explain why removal of amyloid does not really help any of the patients. At the same time it is indeed likely that the protective mechanism eventually is overwhelmed in the cases of fully developed AD and dementia.

I am very happy to have had the opportunity to discuss this possible novel understanding of amyloid β accumulation a protective mechanism that may support healthy aging in some cases. Thank you very much for the opportunity to speak to the attendants at the 5th Alavi meeting and for your kind attention.

Thank you very much. I am so happy with the collaborations that exist between us and I see co-authors of mine in the audience so I think of this as a very nice occasion that I hope will be a meeting in person at the next Alavi gathering. I did expect critical questions but perhaps I have used too much of your time. The finding has been accepted for publication but I still think that the possibility that amyloid β may be a protective substance may for obvious reasons be a controversial claim for some observers.

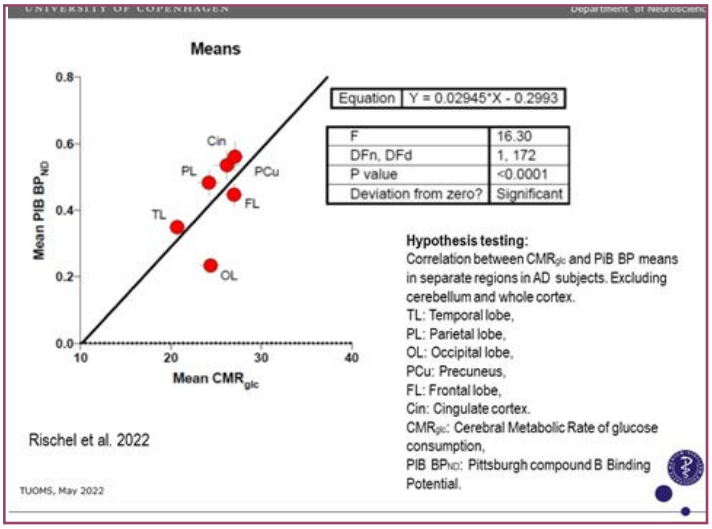

Fig. 4

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Research Status of Gerontology and Geriatrics in Iran

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Greetings and best regards to my dear friends and colleagues

I am very happy of accompanying my dear friends here at the 5th international congress on aging.

The data used in today's presentation are up-to-date and extracted from new sources. I reviewed and analyzed the articles on geriatric medicine and gerontology subset of Scopus database. In this slide, you can see countries around the world based on their indexed scientific output in Scopus. You can also see the world's prestigious universities that work in this field, which are mainly American and European universities, with Britain and France having the largest number of papers in this field up to 2022 so far.

It is worth to note that most of the institutions that support geriatric research are also countries for which this issue is a priority, and it is interesting to note that Japan is one of the countries where aging is very important and has a large number of elderly people. As you can see, Japan is one of the countries that support aging research.

If you look at the list of countries that are ranked in the field of geriatrics and gerontology, the thirty-third country is Iran. This shows that research and production of science in this subject in Iran is somewhat under-developed. Now, if you take a look at all of Iran's citations in this regard, you will find that we are also ranked 40th in citations related to geriatrics, which is even worse than the status of published articles. While in the general investigation of Iranian citations in all fields, it can be seen that our country's citations in all fields are on average in a better position than the number of articles in each field.

Note that if you look at the rank of Iranian articles on aging in the middle-east, you will notice that the occupying regime of Jerusalem, which is usually not among the first 4 or 5 countries, is on the first place in this subject area, while Turkey is in second place and Iran is in the third place. After Iran, Saudi Arabia is in the fourth place. This is while our country is generally ranked first or second in other fields.

Also, looking at the rankings based on citations, Iran have the third rank in the region with a clearly large gap from the second country, and it shows that we have to work hard to be able to compensate the vast lag in this area. The reason is also clear: The research in this field in Iran has a history of about a decade and is not a field with an extensive history. Therefore, the research that has been conducted in this field is relatively new and has not been yet having good citations. Also, in terms of the number of students and graduates in this field, we have not yet been able to improve ourselves because each student in this field will have two or three articles.

Also note that Iran ranks 16th in the world in terms of average science in all fields and 15th in terms of citations

in all fields, but in geriatric medicine it ranks 31st in terms of number of articles and 40th in number of citations. This shows that the production of science in this field in Iran is far from the average total production of science in Iran.

The number of Iranian articles in this field has grown reasonably, but because our base in this field was zero, it has caused us to not yet gain our place in the region and in the world.

The best approach to solving a problem is to move towards solving it. That is why, the Ministry of Health, Tabriz University of Medical Sciences, Tehran University of Medical Sciences, Welfare and other institutions that work in this field, should provide financial support for research in this field so that this field can grow.

Having an overview of the research in this filed in the past years, you will see that the main research done in this field is in the field of neuroscience, nursing (which is currently increasing and accounts for most of the research in this area), and psychiatry (which unfortunately has not yet grown significantly compared to the field of neuroscience).

In this slide, you can see a simple comparison of the average science in Iran in comparison to gerontology, which shows that in sections such as the publication of articles in prestigious journals and the number of citations, Iran is behind its own average and this must be compensated. Of course, it is obvious that fortunately, in the field of international relations, we are ahead of the Iranian average in this field. This means that scientific exchanges in this field are done well, and this shows that there are probably a few people who are the so-called pacemakers in this field in Iran, and they do their job well.

Finally, the most active university in the country regarding publication of articles in this field is the University of Social Welfare Sciences, which has launched the field of geriatrics and has taken students and has been active. However, despite the fact that the number of articles in this university is good, it has not performed well in terms of number of citations, and this shows that it has not published very high quality articles. In the next ranks Tehran University, Iran University of Medical Sciences and other universities of medical sciences are placed.

Investigating the active authors of the country in the fields of geriatrics and gerontology, the top researchers of the country are listed in the table above, among who are professors from the University of Social Welfare and Dr. Fadaei Vatan who has launched the field of geriatrics in Iran, as well as researchers from other universities of the country.

Thank you very much for your attention. I hope I have been able to give my dear friends a good view of geriatric and gerontologic research with this presentation.

Grants

Academic Prejects

1. Mitochondrial transplantation in combination with mitochondrial boosters, MitoQ and melatonin, as a surviving strategy to counteract myocardial reperfusion injury of aged rats

PI: Dr. Reza Badalzadeh
Professor of Physiology, Tabriz University of Medical Sciences

2. Prevalence of multimorbidity, polypharmacy and related risk factors in people over 50 years of age in a combined population of "Azar Cohort study" and "Tabriz longitudinal study on Aging"

PI: Dr. Elnaz Faramarzi
Associate Professor of Nutritional Sciences, Tabriz University of Medical Sciences

3. The implementation of Cognitive Rehabilitation Therapy (CRT) on cognitive frailty of community dowelling of older adults

PI: Dr. Maryam Chehrehgosha
Ph.D. in Gerontology, Golestan University of Medical Sciences

4. Evaluation of the protective and anti-aging effect of curcumin-loaded niosomes against oxidative stress and mitochondrial dysfunction in breast cancer stem cells

PI: Dr. Nosratollah zarghami
Professor of Clinical Biochemistry, Tabriz University of Medical Sciences

5. The effect of astrocyte -derived exosomes and reelin glycoprotein on neurogenesis and neural tissue regeneration in the animal model of hippocampal photothrombotic stroke

PI: Dr. Mohammad Karimipour
Associate Professor of Anatomical Sciences, Tabriz University of Medical Sciences

Student Prejects

1. Cortical and Subcortical Structural changes in MCI converted to AD using T1-MRI data

PI: Jafar Zamani
Ph.D. candidate in mechanical engineering, Amirkabir University

2. Designing Conceptual Framework and the Age- friendly Health System Assessment tool for Iran: Case Study of Tehran City

PI: Badrye Karami
Ph.D. candidate of health service management, Tehran University of Medical Sciences

3.The Aging Urban Brain: Mapping the cities through the senses of its consisting older adults

PI: Sama Rahnemayan
Medical student, Tabriz University of Medical Sciences

4. Evaluation of Berberine loaded grape nano-vesicles effects on young and elderly individuals mesenchymal stem cell aging profile status

PI: Mohammad Sadegh Soltani-Zangbar
Ph.D. of immunology, Tabriz University of Medical Sciences

5. Evaluating protective effects of Melatonin plus Quercetin on senescing of mesenchymal stem cells by down/up-regulating of age-related genes

PI: Amir Valizadeh
Ph.D. candidate of biochemistry, Tabriz University of Medical Sciences

6. The prevalence of potentially inappropriate prescribing among older adults in community settings: An overview of systematic review

PI: Nafiseh Ghassab-Abdollahi
Ph.D. candidate of gerontology, Tabriz University of Medical Sciences

7. The association of dairy products consumption and Longitudinal Changes in Cardiovascular Risk Factors in the elderly

PI: Mohammad Nosrati-Oskouie
Ph.D. candidate of Nutrition, Tabriz University of Medical Sciences

Editorial Board

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