



Aging with MS

Presenter:
Dr. Augusto Miravalle

Yahaira Rivera:

Hello. Good evening. On behalf of the Multiple Sclerosis Association of America, we extend a warm welcome to all of you. Thank you for participating in our seminar “Aging with Multiple Sclerosis,” which will be presented by a neurologist specializing in multiple sclerosis, Dr. Augusto Miravalle. My name is Yahaira Rivera and I am the Director of Mission and Program Development for the Multiple Sclerosis Association of America and I will be the moderator of this program. This seminar is part of our series “Together Finding Resilience, Living with Multiple Sclerosis,” a series dedicated to our Hispanic and Latino community living with multiple sclerosis. And this series is made possible thanks to the generosity of our sponsors, Biogen, Genentech, and Sanofi Genzyme.

Before starting our talk, I would like to tell you about the services we offer. The Multiple Sclerosis Association of America is a national nonprofit organization dedicated to improving the quality of life of the multiple sclerosis community through life-saving and supportive services. These services include a toll-free telephone line that provides services nationwide in English and Spanish, Monday through Friday from 8:30 a.m. to 8:00 p.m. Eastern Time. We also have an equipment distribution program with products designed to improve your safety, mobility, exercises and also to help with heat sensitivity. We also have an MRI access program. We offer educational programs, publications and digital resources to keep you informed and to help you make decisions and monitor the progress of the disease.

All of our programs and services are available to people living with multiple sclerosis in the United States and its territories. Many of these resources are already available in Spanish, so I invite you to visit our website that you see on the screen, so that you can continue to learn about our programs, services and also the events we have for the community. You can also follow us on social media, contact us via email or give us a call.

Now I'd like to share some reminders for tonight's program. You will have the opportunity to share comments and ask questions using the question and answer icon. If time permits, we will do our best to have a question and answer section at the end of the presentation. We also ask that you please help us by completing a brief survey that will appear on your screen at the end of the program. We will also share the survey link in the chat. And lastly, I want to let you know that this show is being recorded and will be available in our digital library over the next few

weeks, so if you know someone who couldn't be here with us, you can share the video with your family and friends.

We want to remind you that this program is for informational and educational purposes only and does not constitute or replace medical recommendations previously provided. If you have any questions that are specific to your diagnosis or treatment, we recommend that you contact your doctor or healthcare provider.

And now, without further ado, I want to introduce you to our guest speaker. Tonight, our guest is Dr. Augusto Miravalle. He is the chancellor of the Multiple Sclerosis Center and Associate Professor of Neurology at Rush University Medical Center in Chicago. He is a board-certified neurologist specializing in multiple sclerosis and has participated in much scientific research in the field of multiple sclerosis and neuroimmunology. Dr. Miravalle is also a member of several organizations, including the Healthcare Advisory Council and the Hispanic and Latino Advisory Board of the Multiple Sclerosis Association of America. Welcome Dr. Miravalle. Thanks for being with us. I'll pass it over to you.

Dr. Augusto Miravalle:

Thank you Yahaira. It is a pleasure to be here with you and thank you for the invitation. This is a very important topic that will surely bring up many conversations and many questions, so I invite the audience to please post questions in the chat, and if we have time at the end we will answer them. So if I would like to start, this talk is titled *Aging with Multiple Sclerosis* and this is very important to discuss since there has been recent data that is giving us a slightly more accurate guideline on how to approach the treatment of multiple sclerosis in those people who are at an advanced age.

So, today's content is going to be organized according to these guidelines. First I'm going to give a very brief overview of what multiple sclerosis is. I am also going to define what is called the age of aging and how different ages, whether chronological or biological age, influence the treatment and management of multiple sclerosis. We are also going to talk about a relatively recent concept, which is what is called neurological reserve and how to understand this concept of neurological reserve that helps us appreciate a little more how the disease perhaps affects certain people and understand that sometimes the disease, although it appears stable from a radiological point of view, the symptoms of the disease may progress. Finally, we are going to start talking a little about what brain health is and at the end we are going to discuss what are the strategies to increase brain health and have a much healthier life.

So, without further ado, let's start giving a very brief overview of multiple sclerosis. Multiple sclerosis is a disease whose cause is not known, but it is known to be autoimmune, which means that the immune system plays a leading role in initiating and maintaining the disease. So, there are immune cells that have somehow been confused and that are attacking myelin, which is that substance that surrounds and protects the fiber, the optic nerves, many parts of the central nervous system that myelin plays a predominant function not only in the protection of the nerves, but also in the conduction of nerve impulses. All activity of the brain, whether the activity that leaves the brain such as for motor function, the function of rolling balance, as well as the functions that reach the brain, such as sensory, auditory and other functions that require myelin for that information be transmitted. So, if there is a lack of myelin, if there is demyelination, those functions may be affected and of course, if the disease is not treated, there is a high incidence of disability, whether motor disability or sensory disability, of walking, as well as cognitive impairment.

So it is very important that these initial symptoms of the disease are recognized so that there is a timely diagnosis and adequate treatment, because one knows that today, with these treatment tools that we have, the disease can be controlled to the point of almost a complete review. It is very important that either the patients are already diagnosed, as well as those family members who have been educated about what the initial symptoms are. Also symptoms that must be taken into account if you are receiving treatment and have these symptoms of relapse, talk to your doctors, or it may be an indication that you should change the treatment you are receiving. More frequent are fatigue. It is an unusual fatigue. It is a fatigue that goes far beyond simply being tired, having a long day, a fatigue that is really motor, a fatigue of muscular movement, but also a cognitive fatigue. Being tired, not being able to concentrate, not having attention.

But visual symptoms are also very common, problems when walking, spasticity, stiffness, weakness, dizziness, instability, whatever, also sensory problems, as we said before. It must also be remembered that multiple sclerosis can cause emotional disorders and this is very important to emphasize, since it is very common that these emotional disorders, whether anxiety or depression, are not perceived early and that patients become... they tend to be depressed or irritable, to lack concentration at times, which manifests itself in a very subtle way, as well as anxiety. So there are times when family members are the ones who recognize these problems. So, it is very important to discuss it and for you to discuss it with your doctors because it is treatable and quality of life generally improves when you have timely treatment. As I said before, multiple sclerosis can also cause memory problems, attention to other cognitive functions that are different from dementia. And we are going to talk about this today. I'll make it simple - it does not cause dementia, however it can cause cognitive disorders.

As I said before, one does not know what the cause of the disease is, but it is a disease that is called multifactorial. That means there are many factors that independently contribute to an increased risk of contracting the disease. Among them there are genetic factors in which one knows that 10% to 15% of patients with multiple sclerosis have a family member who suffers from the disease, but 80%, 90% of the patient does not have these genetic factors, they do not really determine what the chances are. However, one can inherit if one terminates genes that increase the risk of disease.

Children of people with multiple sclerosis, if they have only one parent with multiple sclerosis, have a higher risk of the disease, but it is a risk that is estimated between 2% to 3%, which is a very, very small risk. That risk increases if both parents have multiple sclerosis, which can be as high as 10%, but it is still a generally very small risk.

There is an association between multiple sclerosis and certain viral infections, especially the virus that causes infectious mononucleosis. The virus called Epstein-Barr, which in very recent studies and research has found that the presence of this virus, especially when it is symptomatic and the patient has certain genes, can increase the risk of disease up to 32%, it is very high. But as you know, not all patients who have had infectious mononucleosis develop multiple sclerosis. We know that the presence of the virus alone does not mean that someone will develop the disease, many times this virus does not cause symptoms. So it is very likely that patients who have had multiple sclerosis, who have multiple sclerosis, do not know that they have been infected by the Epstein virus. So there's no kind of role or diagnostic utility to really see if it's present, because that's not going to change in any way the kind of therapeutic approach.

And finally, it is not known that environmental factors that increase the risk of multiple sclerosis, as well as the presence of certain environmental factors in patients who already have multiple

sclerosis, may be associated with a worse prognosis. Things such as smoking, vitamin D deficiency, and an excessive consumption of salt in the diet are factors that are now recognized as having a worse influence on the course of the disease.

As I said before, we are going to talk a little about age, and this usually confuses everyone. But one, of course, knows the chronological age, right? Those are the years from birth. It is an age that changes every year and we cannot do much to alter the course of chronological age. However, there is another type of age called biological age, and this one is a little more difficult to understand. But biological age is something that one has control over. Biological age is a measure of the individual's physiological functioning and health, which can be equal to or greater than chronological age. And of course, one has to treat it as much as possible so that each biological age is younger than the chronological age. Which would mean that if one is of a certain age, but their health, in terms of organic, physiological functioning is much healthier, if one is much younger than one's chronological age, that is what one aspires to through health, through education, through certain activities that are lifestyle type, to stay healthy or stay young as a result of what one does despite the fact that chronological age continues.

So chronological age, biological age, and aging is a continuous process in which one has control over certain factors, of course, not in aging or in chronological age, but in biological age. And why is this important? Because the notion of health estimates that aging and health between 2015 and 2050, the percentage of the planet's inhabitants over 60 years of age will double, going from 12%, which is what was estimated in 2015 to the highest 20% in 2050. We are getting older, which is a good sign. The population is aging, it is reaching much older ages, so it is very important that one begins to understand how to influence the biological age so that even though one ages, the biological age is reduced, so that one can reach advanced ages in a very healthy way.

And this genetic study is very interesting in that there are regions of the chromosome that are called two telomeres, and that chromosomal region is found at the ends of each chromosome. And it has a fundamental function in protecting our genes, in protecting our nucleotides in our DNA. They also play a very important role in preserving the information in our genome. In prevention, for example, it makes certain mutations that may be associated with cancer, premature aging and so on. And then what has been seen is that there are certain conditions in which chronic smoking can lead to a shortening of the telomeres through damage to the entire inflammation, for example, in lifestyle issues. And they can shorten those telomeres, which has a direct consequence to DNA damage, damage to our genomes that can influence quality of life, life expectancy.

So there's a lot of interest in really understanding what the association is between telomeres and multiple sclerosis, between telomeres and lifestyle factors that may have a direct relationship to health. So, in patients with, for example, primary and progressive multiple sclerosis, greater telomere shortening has been seen, especially in those patients who have not been controlled with medications and this shortening has been associated with greater clinical disability and greater conversion to advanced stages of the disease. It has also been seen that this telomere shortening has been associated with greater brain atrophy and, of course, greater oxidative stress, which further contributes to greater inflammation and this generates an almost vicious cycle in which this greater inflammation is subsequently, to have a shortening of their second telomeres. It is very important that this is understood to say well, when one says we must control the inflammation of multiple sclerosis, one is saying from the point of view not only therapeutic to reduce the disability or reduce the injuries, but also to reduce all these secondary consequences that perhaps one does not think about, but that are very important.

So, let's now talk a little about what those environmental, CDM or epigenetic factors are. Epigenetics means beyond genes that have a direct influence on biological life. You imagine the physical state of physical and fundamental health to have a better biological age, average or younger in healthy eating, lifestyle, diseases associated with diabetes, hypertension, obesity, smoking has an influence directly on biological age. As well as mental health, note that in patients who have depression, anxiety, bipolar illnesses, they have a worse illness, biological age, a worse quality of life and a lower mental health, perhaps not only directly due to these illnesses, but also indirectly, so these diseases lead to quality of life, greater social isolation and less physical activity. As a whole, social life is also very important from a communication point of view, but also to improve certain emotional factors, of course stress and hours of sleep. Then I think it would be the epigenetic categories, which I have seen have a direct effect on biological age.

So, now we are going to review a study that has been done between certain years in patients between 20 and 40 years old, patients who have multiple sclerosis and what has been seen was the percentage of patients plus the incidence and prevalence of patients at certain ages at certain times. So what this is and is being done is a longitudinal study that was carried out for a long time to see what is not only the incidence of multiple sclerosis, but also at what age patients develop the first symptoms. And from what you see in this graph, what you are seeing are two things. One is that the incidence of multiple sclerosis continues and increases. There are many more cases each year, and that is perhaps not only because of better recognition of the disease, but because the disease is also more common today than the disease was many years ago.

But notice that when one compares, for example, in 1984, which is on the line below, on the light blue line, with light blue points such as the incidence in 2004, not only does one see that there is an incidence and a prevalence increased, but the median age of multiple sclerosis also increased. That is telling us that there are not only more cases of multiple sclerosis, but a greater accumulation of cases at a later age. So not only is the disease prevalent at a later age, but it is accumulating more. Patients have longer survival. There is also an aging of the population in general, which means that today there are more patients with multiple sclerosis, but also more elderly patients with multiple sclerosis. Therefore, it is essential that one understand not only what the implications of age and multiple sclerosis are, but also what is the timely and appropriate care of elderly patients who have multiple sclerosis.

This study has made a comparison between pediatric patients with multiple sclerosis and patients with an advanced age and what are the risk factors that different ages have with multiple sclerosis according to when the disease began. And I know that for patients who have a pediatric or adolescent onset, the biggest risk factors are low levels of vitamin D, exposure to the Epstein–Barr virus that causes multiple sclerosis, such as obesity. These three factors are the major risk factors, while patients who have had an onset of the disease at later ages are closer to 50, 60 years. The risk factor changes and conditions such as, for example, environmental pollution, oxidative damage, chronic inflammation, certain hormonal changes have a much higher risk and a much greater influence on not only the risk of contracting the disease, but also on the prognosis of the disease.

So, now let's review a little what the natural history of multiple sclerosis is. It is very likely that if you have participated in previous talks you have already seen this very popular graph, in which what you measure is age or time in the X graph and disability in the Y graph. So, in these black bars one can see what would be the representation of relapses or those exacerbations or

clinical syndromes of multiple sclerosis that sometimes improve completely and it is seen that the line goes down to the baseline level, but many times there is a progressive accumulation of disability due to incomplete recovery from the symptoms of relapse. And that leads to the fact that at a certain point in the disease, patients go from a period of relapses and recurrences to a period of secondary progressive disease. And these are generally seen in patients who have not received any type of treatment. And this change from limiting recurrence to a secondary progressive one occurs between 15 and 25 years of age. After the first symptoms.

But what I want to bring to your attention is the blue square is to your right that's titled Immunosenescence. And what does that mean? It is a word that is relatively recent. Immunosenescence means that as we age and our body ages, our immune system also ages. That, in many ways, means that the immune system is aging. And that's just a natural thing that happens to all of us. Whether you have multiple sclerosis or not, this immunosenescence happens to all of us. And that explains why when one is at certain ages over 60, 65, 70, one begins to have more infections, one begins to get sicker, the incidence of certain cancers, or neoplasms increases, and one of the factors that determines this increased risk of infection and neoplasia is immunosenescence, which means that the immune system weakens as a result of aging. That happens to all of us.

Now, if one puts immunosenescence in the context of multiple sclerosis, there are two fundamental consequences. One is that any consequence of the immune system or attack will improve, the incidence will decrease, let's say, the lesions, the relapses, will decrease over time as a direct consequence of immunosenescence. That's why it's good news, because what it means is that the probability of having new lesions, the probability of having new relapses, or in older people, 60, 65 years old, is lower than in people who are 30 years old. But like everything, it's not all good news, because one also sees that the risk of infections, the risk of complications, the risk of cancer and other associated diseases increases in a late stage of the disease.

Surely that patient is asking, well, what does one have to do with the medications? I don't know, the medications are immunosuppressing and if I remember, if I am of an advanced age and I know that my body itself is going through a process of immunosenescence, I have to stop my medications, I have to reduce it. So, there are questions, very important questions. There is no one answer that can be applied to everyone and there have been recent studies that have tried to find that answer, but unfortunately they have not given us an answer that can be generalized to everyone. So, what is recommended today is that you individually discuss it with your neurologist, whether the decision to continue with immunosuppressed drugs or suppressants, to continue with medications in elderly patients has to be made on an individualized basis. But it's probably kind of a good idea to start having those conversations, which is a very important question to ask your neurologist if you're older, whether or not you should really continue your multiple sclerosis treatment.

So a question you asked me is good. If the immune system ages, could my multiple sclerosis go into remission with advancing age? Well, as I said before, it may be. So this immune senescence has many consequences or those consequences are directly in the cells of the immune system, there is an adaptation of the behavioral cells of the immune system, such as the production of antibodies or the production of certain cells that have a predominant role in inflammation, multiple sclerosis. So it is very likely that everything that is the direct inflammation of multiple sclerosis will decrease as a consequence of age.

As I said before, another question that you might have, that perhaps you are asking yourself at this moment, is, well, if the frequency of relapses and lesions decreases as a consequence of immunosenescence and advanced age, why do my symptoms worsen? And that is a very common question. A question that many patients have. And this can really be applied from many points of view, but perhaps the most generalized way to explain it is the concept that we simply call neurological reserve. The neurological reserve, then, is the ability of the brain to compensate for certain brain functions through a reserve.

The number one function is aging. As you age, your brain shrinks. The volume of tissue shrinking is something called atrophy. That happens to all of us with or without multiple sclerosis. It is brain atrophy, it is a direct consequence of aging. Number two is when the brain slows down what one does to compensate for that brain loss, one begins to use its neurological reserve to be able to continue doing the usual things. Why does it happen in multiple sclerosis? Sometimes, especially if brain atrophy has not been treated, it is much more accelerated in patients with multiple sclerosis, especially those patients who are not receiving medicine at these ages. What has a direct consequence is that if brain atrophy is more accelerated, the neurological reserve will be more diminished. Then the brain's ability to compensate for the effects of aging will be diminished. Well, that directly explains why, even though immunosenescence results in fewer lesions, a lower frequency of relapses, there is a greater progression of disability because there is less compensation for this lack of neuronal reserve.

So it is a process that is very complicated to understand, but it is essential to understand it, because this can explain why there are times when you feel worse, your symptoms are getting worse and you do an MRI and the injuries are the same, there is no change, there is no new injury. And you say, well, how do I explain why I feel worse? Well, that is explained in several ways, as I said before, perhaps due to this lack of neuronal reserve it can also be explained by that brain atrophy that what they have is a direct consequence of the lack of brain compensation for aging and progression, of the illness.

So, this is a graph that tries to explain what the consequence is on brain mass or volume over time, with or without multiple sclerosis. If you look at the graph, at the orange color, it shows loss of neuronal or brain mass that occurs simply due to aging in healthy patients. And the one in gray shows that in untreated multiple sclerosis, this loss of brain volume can be accelerated. The good news is that there are many treatments today and there are some treatments that are considered highly effective, that are so highly effective that they reduce the probability of brain atrophy almost to the levels of healthy patients. So, that is one of the findings of science in multiple sclerosis, perhaps the most fundamental, that through this medicine that we use to care for patients, it can not only alter the natural course of the disease, but also reduce the probability of an accelerated atrophy of the brain.

So, as I said before, what is neurological reserve? It is the ability of the brain to tolerate changes related to age and pathology related to brain disease. We must remember that the brain is a very flexible organ. There is a concept called neuronal plasticity, and what that means is that the brain changes, it is very changeable. You cannot influence the brain to change function, to improve function, to change behavior through what you do. And without going any further, you have been doing it since you were born. When you learned to ride a bicycle, the brain did not know how to move the legs in a coordinated manner and how to maintain balance. Through practice, what you did is train your brain so that these functions now become automatic.

And with that example one can apply it throughout life. When you exercise, when you need the muscle, when you are trying to learn a new language, what you are doing is exercising that

neuron that did not have a certain function so that they learn to function in a certain way, whether through language, music education or whatever you want to do. But, it is essential that training is continuous and progressive. If you try to learn a language overnight, you will not learn it. What you have to do is do it progressively, gradually and continuously. Our audience is likely to be bilingual or perhaps speak more than two languages. And it has happened to all of us that if you do not practice it, even though you have learned it, the ability to speak fluently is lost. So, with that function of the brain, that applies to all types of functions, whether motor, cognitive, intellectual or even emotional. So, this adaptation is always changing and it is essential that one understands that one has control over the functioning of their brain.

And maybe this can be all together, not what we were talking about until now. That is the concept of the loss of neuronal reserve, that concept of brain atrophy that is seen in the upper part of the figure, clinical relapses, lesions in the brain. Well, everything is related, let's say this whole process is related. It is not that one process is independent of the other. So, if one wants to achieve optimal brain function with multiple sclerosis, an intervention alone is not enough. The optimal treatment of multiple sclerosis should include controlling the disease, controlling inflammation, relapses, reducing brain lesions or the probability of new lesions, reducing the probability of brain atrophy, slightly this is done with the medications that one has that are highly effective, as well as training, physical, mental, cognitive training, so that this neuronal reserve capacity increases.

And this is an example, let's say graphic, but it tries to represent what I said before, that the volume of the brain and the number of neurons is not as important as how efficient they are in coordinating them. And generally I explain this by making an analogy, if you compare a brain with an office and you have an example, one is a very large brain, the same as an office with 3000 employees. The second example is a smaller brain, like an office with 300 employees. But the office with 3000 employees, no one talks to anyone, no one enjoys working with anyone, they don't have good communication, they never meet. What's more, there is a little toxicity. The second example is an office of 300 people, everyone enjoys working with each other and they are constantly communicating, they have meetings. So, I'm going to ask you, which office is going to have better results, the first or the second? Well, surely you would say the second one, right? Because despite being a smaller office, it has better communication, is more efficient and has less toxicity. And well, the same thing happens in the brain, the size of the brain is not as important as the optimal functioning of the brain, how optimal the brain functions are. So, even though one is going through a process of brain atrophy, it is very important to remember that size does not justify function. What has a fundamental influence on function is efficiency, how efficient those brain connections are. So, you might ask now, how can we influence greater efficiency in neurological reserve? That is a fundamental question.

So, a question that leads us to perhaps the last part of this talk, which is what is brain health and why is it important? So, brain health refers to the optimal functioning of the brain in the ability to remember, learn, play an instrument, concentrate, maintain an active and clear mind. Brain health is simply trying to get the most out of your brain and helping reduce some of the risks that come with aging. And this is my vision of brain health. This is something that I always talk about with my patients, that there are certain pillars of brain health and this is something that I have seen through research, from the results of studies that have given an idea of what they are, the factors that have a direct influence on brain health. As we said initially, lifestyle is essential. Associated diseases are also essential; patients who have obesity, smoking, diabetes, and hypertension have a worse influence on brain health. So if you have any of these diseases, it is very important that you talk to your doctors to try to control that disease, those actions. Genes, as we said before, have a fundamental influence on brain health that very few

people can do otherwise, but what they can do is reduce inflammation in the brain, which has a direct influence on the activation of certain genes. Then, as we said, in multiple sclerosis it is essential to reduce inflammation.

Access to health care is also fundamental, and that is something that is perhaps too complicated to talk about much today, but it is fundamental that patients have access to health care, have access to doctors, hospitals, medical care, to education. What they are doing today is essential to try to educate themselves, understand this, communicate with other patients, with foundations such as the Multiple Sclerosis Association of America, because access to them is essential, whether through education or patient care. I know it has a direct relationship to brain health. As we said previously, environmental factors, whether infectious, air pollution, for example, or second-hand smoking, are factors that have a direct effect on brain health. And also education. It has been seen that in regions of the world in which education is not as accessible, in which children do not have access to secondary education, for example, they have a higher incidence of diseases and dementia. So education, cognitive training, has a direct relationship on brain health.

Regarding nutrition, I know that the Multiple Sclerosis Association of America has many resources regarding nutrition, so I will be very brief, but it is known that one of the diets that has a direct relationship with brain health is the DASH diet, which is the diet that has more vegetables, fruits, grains, like the Mediterranean diet, which also adds fish, along with a moderate consumption of dairy products. For example, the MINE diet is like the Mediterranean diet, but it also has more emphasis on green vegetables such as blueberries. There is also the Ketogenic diet, which is a bit more controversial. The Ketogenic diet, since it has more emphasis on fats, and especially saturated fats, has a negative effect on brain health. And finally, there is vegetarianism. It is good that some research studies say that it is healthy, however we must keep in mind that the consumption of vegetables without the consumption of animal protein can have a negative influence on vitamin B12 levels. Vitamin B12 is essential for brain health. So, consuming only vegetables, it is important to talk to your doctor to check your vitamin B12 levels and whether they are low.

Where there is a lot of agreement in terms of what one understands about diet is what dietary processes are negative and have a negative influence on brain health, and processed foods, and sugar, especially in high concentrations, and salt in high concentrations, and excessive alcohol, and saturated fats. And all of those are, whether in any type of diet that one looks at, it has been seen to have a negative influence on brain health.

As I said before, the Mediterranean diet is perhaps the most popular. It is a diet that has been studied in multiple sclerosis, it has been studied in cardiovascular disease. It is a diet that has also been seen to have a benefit in terms of weight and obesity. So perhaps of all the diets that have been studied with multiple sclerosis, it's the one that has the most information and data to be recommended. As I said before, salt has a negative effect on brain health. It is recommended that you consume less than two grams per day of salt and if you start counting all the products one eats they generally include salt. Then it is very easy to reach two grams per day, which is why it is recommended that you try to cook your own meals as much as possible and not add salt, and perhaps supplement them with other types of seasonings. Smoking has a direct negative effect on the brain. So it is very important not to smoke. And finally, the associated diseases, as I said before, depression, anxiety, hypertension and the incidence of these associated diseases changes over time. Let's say when you age, the incidence of hypertension increases, the incidence of depression also increases, of... cholesterol,

hyperlipidemia and diabetes. So it is very essential that one keep in mind that with aging there is also a higher incidence of certain diseases.

And finally, let's talk a little about exercise. That's something that lately there is a lot of information on the benefits of exercise in multiple sclerosis, as well as brain health. Exercise increases aerobic capacity, increases muscle strength, motor activity, balance, reduces fatigue, reduces depression, as well as this has been seen less frequently, but it has been seen in association that exercise, given adequately and progressively can have a direct effect on some disease patterns seen on nuclear magnetic resonance, such as a decrease in lesion volume and an increase in brain volume. So, brain and health exercise is lately being viewed as a therapeutic intervention as it has many benefits in many areas of brain health.

This study has been done in a rigorous manner, in which patients with multiple sclerosis were divided into four groups. The first group had a very intensive training series of exercise between 10 to 30 minutes plus a cognitive training of 45 minutes. Patients in group one had a very rigorous, very strict exercise and cognitive training intervention. The second group only had cognitive training, but they did not have exercise training, they had what is called a placebo. That placebo was doing passive stretching exercises for 45 minutes. The third group had an active exercise intervention lasting between 10 and 30 minutes with placebo cognitive training, that was using the internet for 45 minutes a day. And finally, the fourth group had both placebos, the cognitive placebo and the exercise placebo. Well, the hypothesis of this study was that patients in group one were going to have better eating, cognitive and physical fitness than patients in group two and three and that patients in group four were going to have worse cognitive fitness.

Now let me tell you the results. Patients in group one, as stipulated at the conclusion of this study, had an increase in cognitive function and an increase in physical function. What happened to group two? Well, those who received the cognitive increase, they increased cognitive function. What happened to the patients who received the exercise placebo? Also, they increased physical fitness and that increase in physical fitness was very similar to the increase in physical fitness of the first group. Now, we see what happened in group three. Group three were patients who had very intense exercise with a placebo cognitive intervention. Well, they increased both, they increased cognitive function and they increased physical function comparable to the first group. Well, now let's see what happens in the last group. The group that received both placebos, cognition placebo and physical activity placebo. They also increased.

So what happened here? The authors concluded that the study was negative because they could not corroborate that the hypothesis that group one was going to be better than group four was valid. But when you analyze the results it was not a negative study, it was a positive study. What happened here? Everyone improved, and it's not that they improved because they learned the answers or because they were more familiar. They improved because cognitive and physical function really improved. And the conclusion is that what had been specified as a placebo or something that was expected to have no type of advantage, really was not a placebo, what one learned again from this study is that even if it is a minimal activity, whether cognitive or physical, even a 45-minute passive stretch has a fundamental benefit on brain health. What one learned from this study, which has been published very recently, is that it is not necessary to do intensive exercise, an intensive cognitive program, you have to keep the brain active continuously in a progressive way, even if it is with interventions that seem minor or minimal, because this intervention has a very positive result in physical and cognitive fitness.

So with that I would like to finish, because we are reaching the end of the talk. To say what the consequences are, as I said before, physical exercise and brain health are essential, even though there is no recommendation that can be applied to all. In general, one says that adults need at least 150 minutes of moderate activity or 75 minutes of vigorous activity per week. And for those who have dogs, walking the dog helps, even if it's a moderate walk for 25 or 30 minutes, that helps. As I said before, you have to eat healthy. There are two types of diets that have a greater or lesser influence on brain health, but what is known is that in addition to the components of the diet, which are fundamental, you have to put colors on your plate, have a varied and balanced diet, and also put fiber, because fiber is essential to improve your healthy gut bacteria and reduce salt and sugar consumption. And finally, we must socialize, we must increase cognitive function, through puzzles, reading, painting, music, meditation and social activities.

So, in summary, biological age can be improved through lifestyle. The immune system ages over time, something called immunosenescence. However, some symptoms of multiple sclerosis may worsen or progress due to a lack of compensatory neurological reserve. Neurological reserve can be improved with a healthy lifestyle and it is never too late. You can start promoting greater and better brain health today. And with this I would like to finish by thanking the Multiple Sclerosis Association of America for the invitation and of course for their attention.

Yahaira Rivera:

Many thanks to Dr. Miravalle for this very informative presentation and for giving us such important information for our Hispanic community, especially people who are aging and are living with multiple sclerosis. We have a few minutes for some questions from the audience. One of the questions, Dr. Miravalle, is about life expectancy and prognosis of multiple sclerosis. Is there an approximate lifespan for patients living with multiple sclerosis?

Dr. Augusto Miravalle:

Not today. It is the same as patients without multiple sclerosis. In the past one said that yes, there was a lower life expectancy, between five and ten years shorter. But today with the treatments available, life expectancy is similar to that of a patient without multiple sclerosis.

Yahaira Rivera:

Thank you so much. Another question I received is... the person says, why do some of my symptoms continue to worsen if the brain lesions are stable?

Dr. Augusto Miravalle:

A good question and we talked about it a little during today's talk, is because of this lack of neurological reserve compensation. So, as one ages, one needs more neurological reserve to compensate for aging. So it is very possible that this decrease in compensation will cause some injuries that previously did not cause symptoms to begin, to cause symptoms that begin to cause problems. Finally, these symptoms do not mean that there are new lesions, but rather that there is less brain compensation.

Yahaira Rivera:

Okay. Thank you very much for your answer. Another question goes like this: How do you know if an ailment is due to the normal aging process or is due to a relapse of multiple sclerosis?

Dr. Augusto Miravalle:

Very good question, and to be honest, it is best if you have doubts, talk to your doctor, because it is very difficult. You alone at home really know the difference and that is why you have trained doctors to help you. If you have any questions, you should consult your doctor. Generally one says that if the symptoms last more than 24, 48 hours, that is generally symptoms that mean that there is a new attack, a new injury.

Yahaira Rivera:

Thank you so much. We have several female participants who have asked questions about how menopause affects the aging woman with multiple sclerosis.

Dr. Augusto Miravalle:

Surely. A very good question. You know that estrogens have a protective role in multiple sclerosis, since high levels of estrogen have a direct influence on certain cells, the immune system causing less inflammation. That is why one sees that during pregnancy estrogen levels are so high, generally multiple sclerosis remains very stable. In menopause what happens is that estrogen levels decrease. So it has been seen that postmenopausal women have a greater probability of disease progression. Estrogen supplementation is not recommended today, as estrogen supplementation, although it may be beneficial, has also been found to be associated with greater risks. Cancers such as uterine cancer and breast cancer are feared. So the benefit is not greater than the risks that estrogen supplementation can bring to your health.

Yahaira Rivera:

Thank you so much. That answer is very interesting and we hope that we have been able to offer the answer that our audience is looking for. Dr. Miravalle, another question is: what advice would you give to people who need to improve their mobility and muscle pain?

Dr. Augusto Miravalle:

It is essential to work with a physical therapist, since physical therapists are essential in helping them understand what type of exercise to do in a healthy way, but also safely. Because if you have ambulation problems, balance problems. The worst thing you can do is exercise that is not appropriate as it can cause more damage. Then work with someone who is a physical therapy professional to understand what type of exercise that is so frequent and gradual that you need to have this restraint, especially early, so that you can make the decision fully.

Yahaira Rivera:

Thank you so much. We have another question and you touched on this topic that we think is very important, especially for people who are entering an older age and that is about continuing or discontinuing disease-modifying therapies.

Dr. Augusto Miravalle:

Yes, a good question, since as we said before, immunosenescence means that the immune system's immunity decreases. So there are times when, let's say, adding an immunosuppressant can increase the risk of infections, can increase the risk of neoplasia, so it's something that's very important to consider. There are some, as I said before there is no rule that can be applied to everyone. So the recommendation is that you discuss it individually, talk to your doctors. Generally, what you do is if the patient is in a stable state for at least ten years and that means no relapses, no progression of the disease, is without lesions in the brain, which are new, and is over 65 years old, that's where you start to say well maybe it's safe to reduce or

stop the treatment. However, there are many treatments that are not healthy abruptly, such as Tysabri, Gilenya, and other treatments. So before you discontinue, please talk to your doctors.

Yahaira Rivera:

Very good advice, thank you very much. And one question we received tonight is about hearing loss, whether this is a symptom due to multiple sclerosis, old age, or both.

Dr. Augusto Miravalle:

Most likely it is old age. However, yes, it has been seen that injuries, especially in the spinal cord, can cause hearing loss, but generally this hearing loss is acute, from hearing well to hearing loss. Hearing loss due to aging is more gradual and progressive.

Yahaira Rivera:

Thank you very much, Dr. Miravalle. We only have one minute left before saying goodbye. Any last tips or advice you want to offer our audience about aging with multiple sclerosis?

Dr. Augusto Miravalle:

Of course. Well, it's never too late to be healthy. So you can start today to talk about your health. Exercise, educate yourself, socialize. These are all critical functions and ones that you have control over.

Yahaira Rivera:

Definitely. Thank you very much. On behalf of the Multiple Sclerosis Association of America we once again thank Dr. Miravalle for his time, for this very informative talk, and sharing with the Hispanic community such important information and vital advice for aging with multiple sclerosis, but in a healthy way. We thank our wonderful audience for being here with us. Thank you for participating. We hope you have enjoyed the learning and that it has been of great help and that you can apply it to your life. Please don't forget to complete the survey that will appear on your screen soon. I invite you to visit our website to continue learning about our services, programs and events. I remind you that this program was recorded and will be available on our website in the coming weeks. Thank you very much to all! Good night and happy Hispanic Heritage Month! Until next time.