Westchester County
Staying Sharp
December 1, 2012
THE DANA ALLIANCE FOR BRAIN INITIATIVES

WS: Good morning. I'm just going to make some pre-introductory remarks as people are still filing in. If you did bring food for the Westchester County Food Bank, the totes are in the back. Thank you very much for your generosity. And that line there is to get water and snacks, so if you don't know why you're in that line, that's why you're in that line. My name is Will Stoner. I'm the Associate State Director for Livable Communities at AARP. Some of you probably got a phone call from me, got a piece a mail, an e-mail. We did our due diligence to let as many of our members in Westchester County and the general public know about this event because it's so important to us. I'm going to do some thank-yous in a moment because there's a lot of hard work that goes into putting an event like this together. But I want to do, like I said, some pre-introductory remarks. Whenever we do a member opinion survey at AARP, and some of you may have gotten this survey asking you what you think about different issues,

the number one interest of AARP members is brain health. The number two interest is staying physically fit. The number three interest is eating healthy. The number four interest is staying connected to your community, your family and your friends. Interestingly enough, the program you're about to see incorporate all four of those interests into a fabulous program. So we're thrilled to be able to partner with the Dana Alliance and other partners that I'll be talking about in a moment to actually put on this event for you today. And, of course, the number two concern is brain health. So it's the number one interest, but it's the number two concern behind financial security. I want to thank Collette Phillips. I'm going to point her out on purpose because she did ... let's give her a little applause.

(Applause)

WS: She did a lot of the, I guess the behind-the-scenes organizing for this, so I wanted to get a special applause for her. But AARP is proud to be working with Westchester in so many different ways. Just recently you may have seen an article or some press about how Westchester County just entered into the AARP network of age-friendly communities. AARP is bringing the

age-friendly cities program to the United States, and bringing it down to the community level. So Westchester County put in their designation, said we want to be part of this network. So now they are working purposefully on creating a plan to make sure that all of you can age in place in the community of your choice, and live your best life. And we're proud to be working with the Department of Senior Programs and Services in the Westchester County Executive with their leadership and vision that they have for this program.

Just a quick ... on the way out there will be some flyers. Any veterans or family members of veterans, the Driver Safety Program at AARP is currently free of charge until the end of the year. We've extended it past the month of November because of Super Storm Sandy. So if you're a veteran or a family member of veteran, you can take our driver safety course at zero cost. I encourage you to do it. It's a good way to keep your driving skills sharp.

And to get on with the show. I want to give special thanks to Laura and Simon from the Dana Alliance for working very closely together with us ...

(Applause)

WS: ... putting this together. Westchester County's Deputy County Executive, Kevin Plunckett, thank you very much. And Mae Carpenter from the Westchester County Department of Senior Programs and Services will be making some comments, and of course, I mentioned Collette. Mae is a visionary, and behind that vision is always a lot of hard work, and I know Collette carries a lot of that hard work, and we appreciate that. Special thanks to our AARP volunteers that helped with registration and orientation, and then of course, to all of you for coming on a chilly day to hear about a great program to keep your brain healthy. So without further ado, I want to give the Deputy County Executive, Kevin Plunckett a moment to say some few words, and also Mae Carpenter from the Westchester County Department of Senior Programs and Services.

KP: Thank you. Good morning to everyone. I bring greetings on behalf of our County Executive, Rob Astorino, who is unable to be here this morning. I don't think he sent me because I'm much older than him. (Laughter) But it is a great pleasure to be here certainly with our Commissioner of our Senior

Programs and Services, Mae Carpenter and Collette, Shannon, Dr. Morrison and Dr. Ratan.

As we age, there can be no more important issue than our brain health. We're tall taken up with the health of our body as we grow older, but it's very important as we move forward to focus on how we keep our brain healthy, and that's what today is all about. There are some amazing statistics that I have come to understand. In the Hudson Valley area there are 44,000 people who are suffering from Alzheimer's, 22,000 of those people are here in Westchester County. And it's preventive measures that can help address the issue of Alzheimer's, that can help address the issue of keeping our brains young as we move forward in our years. So I want to thank AARP for putting on today's program. I want to thank NRTA sponsors, the Dana Alliance for Brain Initiatives, the Westchester Public, Private Partnership for Aging Services, and certainly to our Westchester County Department of Senior Programs and Services. And a special thanks to the MetLife Foundation who has provided the grant for this special program. So to everyone here, to all of us, have a great conference. I'm sure the expert information you get will be very

helpful as we all age here in Westchester and everywhere. Thank you.

(Applause)

MC: Good morning. And I, too, would like to thank AARP for working with Westchester County in sustaining a good quality of life and livability for all ages here in Westchester County. Today's program is to empower you to be all you can be. Have you heard that slogan before? Okay, we are an army, too. We want you to be all you can be here in Westchester County, and that means taking care of yourself and empowering yourself with information. Through our Livable Communities Program, and through all of our providers who work with us, we present information through community education programs, through information fairs. We go out and speak in many different venues to carry to you information that's going to help you accomplish that mission of being all you can be. So let's get started with today's program, because we have so much to share. And thank you so much for coming, and have a wonderful holiday.

(Applause)

GD: Good morning, everybody. How's it going?

I'm George DeRan. I'm a personal trainer. I've been a personal trainer for eight years now. My part here is to ... I came here to the brain warm up part of the segment.

(Warm Up Exercise – Not Transcribed)

SW: Thank you. Do you feel invigorated?

ALL: Yes!

SW: It was wonderful watching you. (Laughter) And I must say, my day was made by watching Mae Carpenter and Kevin Plunckett dance to Michael Jackson. Thank you very much. (Laughter) Wonderful to see each and every one of you here. What a great turnout, and what a great event. I had the opportunity to talk with these two men that you're about to hear, and have already learned it feels like a lifelong lesson that I can apply to my own staying fit and having a healthy brain. So just a few words of introduction for myself. My name is Shannon White. For anybody that is a Cablevision prescriber, you may have seen me on News 12. I am a reporter and have been there for the last nine years as a freelance journalist there. I'm also a clergy person. I'm a Presbyterian clergywoman. I'm getting ready in a month from today to start at Wilton Presbyterian Church as the Senior Minister

there, and I'm looking forward to that move. Thank you very much. And I'm also an author, and the lovely young woman over there is selling my latest book, which is "The Invisible Conversations With Your Aging Parents". Because as a Boomer myself, I'm dealing with an aging parent. I've also seen and watched along with people for many years who often don't have the conversations they need to have with the people who are most important to them. So I wrote that book to help people have those conversations and stay connected. So if you're interested in that, I'm happy to sell you a book over there at the end of the program. And actually a portion of the proceeds goes to Alzheimer's research.

And now to our program. I'm very, very delighted, and I'm going to have seat now, to introduce our two guest panelists here. We're going to start over on the far end with Dr. John Morrison, PhD, Dean of Basic Sciences in the Graduate School of Biological Sciences, Professor of Geriatrics and Adult Development and Neuroscience, Mount Sinai School of Medicine. Nice to see you, Dr. Morrison. Let's give him a hand.

(Applause)

SW: And I'd like just for you to give us a couple

minutes about your area of expertise.

JM: Right. Thank you, Shannon, and thank you to the organizers.

(Background Conversation)

JM: I've worked with the Dana Foundation forever, and it's a fabulous organization. So I got my PhD in 1979. We went to the West Coast and immediately started working on brain aging and Alzheimer's disease, so I've been working in that area now almost 30 years. More recently we've become more interested in what I would say is the events in the brain that lead to cognitive aging. So how does synapses change, how do neuron change, and we'll get into that over the next hour. And the distinction between what happens at least to cognitive aging that many of you will experience versus Alzheimer's disease, and there are very important distinctions in that, and we've worked on that for many years. So hopefully we'll be able to translate some of that from the kinds of papers that we write, which would not be very informative to most of this audience, to messages that are very informative to this audience. But that's my scientific background.

SW: Thank you, Dr. Morrison. And Dr. Rajiv

Ratan is the MD and PhD Professor of Neurology and Neuroscience, Associate Dean, Weill Cornell Medical College, and Director of Research at Burke Medical Research Institute. Welcome to you, and please tell us ...

(Applause)

SW: ... tell us about yourself.

RR: So thank you, Shannon. I also would love to thank the Dana Alliance for Brain Initiatives and AARP for having us today. It's great to be here with all of you. I'm a neurologist and a neuroscientist. My interests over the past two decades have been primarily in stroke and how to prevent damage in stroke, and how to encourage recovery, and that's obviously a major focus of our interest at the Burke Medical Research Institute right here in White Plains. My lab has also had a longstanding interest in free radical damage, and antioxidants and how they work in the brain, and we're looking forward to discussing a lot of these different topics with you today.

SW: Wonderful, great. So I would encourage you, if you have pen and paper, you may want to jot down some things. You're going to hear a lot of very interesting things coming out of

these two men. I'd also like to thank the Dana Alliance for Brain Initiatives AARP New York, and the MetLife Foundation for putting this together, as well as Westchester County with the Department of Senior Programs and Services. Okay, so the way that this program is going to be run is we're going to spend an equal ... or maybe not so equal, but we're going to cover three different sections; normal brain function, and then we're going to talk about brain diseases and disorders, and finally successful aging, all right? So then we're going to break that down. And then there will be a time at the end for you to ask some questions of our panelists, all right? So keep your questions in mind, know that we want to have those questions be of interest to everyone so we're not going to be able to answer, you know, specific medical questions for you, but be listening, and if something needs, you know, that you didn't hear or you want to ask more about, those can be asked at the end. So hold your questions for them. You may want to jot them down. Okay, so let's begin. Normal brain function and normal age-related changes. Okay, so Dr. Morrison, I think you agreed to give us a very brief primmer on brain function to kick off the discussion. Go ahead.

JM: Brain function in four minutes. (Laughter) I think the most important thing to remember is that the brain is the organ of behavior. If you grasp that ... and then we'll get finer and finer resolution from there. So what do I mean by that? Well, this exercise that we started with was actually a perfect example. The brain processes all incoming information from the environment, from the outside world. So you were hearing commands to change your behavior, and very, very quickly you were able to adapt your behavior and put your hands up, stomp your feet. I thought it was a great exercise.

W: (Laughs)

JM: So perception of the outside world. Acting on the outside world, both the province of the brain. But very importantly, especially as we move to aging, you almost never perceive something and immediately respond without quote, "thinking". So the human and all primates, for that matter, dedicate an enormous amount of brain to deciding what to do, executive function, planning, planning your day, planning your week, what we call "working memory" in which we'll get back to in a moment. But you spend a tremendous amount of brain energy essentially

deciding what to do, and that is obviously after sensation and before action. And that's the province of the areas that are affected by aging, prefrontal cortex and hippocampus. You probably even read about those brain regions in the newspapers. So how does the brain do that? Well, the brain has certain regions dedicated to certain kinds of information, so you have an area of your brain that perceives vision. In fact, you have 30 different areas of your brain that construct your visual world. Tremendously complicated. How do the visual areas do that? They do that through brain circuits. You have all the information encoded in your brain is encoded by different circuits. The circuits are formed by nerve cells. They're very, very specialized cells, very different from the skin, or the liver, or the muscle, or anything else in your body. Those nerve cells communicate through what we call the synapse. Now, you have billions and billions of nerve cells organized into circuits that carry very specific kinds of information, and you have trillions of synapses. So these are all organized in a way that allows you to do what you do all day every day, which is unbelievably complicated. But they're very, very highly structured, and very highly organized, and when we say trillion of synapses,

they’re not just all over the place, they form these circuits that process information. So the brain is all about information processing. And maybe most importantly for today, the brain can change itself. It is not static, it is not constant. Today, when you walk out of here, you will have learned something, and your synapses will be altered. They will be different than they were when you walked in. And it won't be all your synapses. The synapses in your visual cortex will remain the same. But the synapses in your learning areas, like prefrontal cortex, will be altered. And hopefully they’ll be altered in a very positive way.

SW: All right, so we have men and women here. I’m going to own it right now, I’m postmenopausal woman. I want to know ... and part of my role is to be your voice right now ... is there a difference between the way men and women age when we’re talking about the brain? Who wants to talk about that? Dr. Morrison?

JM: I can start. Actually it’s a big area of research in our lab, and of course, there’s a difference in the way men and women age because of menopause. Menopause is perhaps the single most important event in aging. And it’s become far more

important because the turn of the last century, 1900, the life expectancy for women in America was about the same as the age of onset of menopause, early 50s. Now life expectancy is 80, age of onset of menopause hasn't changed, it's still the early 50s. So women will live for 30 years postmenopausal. So men don't have this abrupt alteration in circulating hormones. It's much more gradual. And as many of you know, I'm sure there's been an enormous of work on this, and enormous amount of attention in the press. There are the WHI studies about ten years ago that frankly confused the issue because they looked at women that were far older than menopausal women. I was just at a meeting in Washington the last two days where we spent two days trying to deal with hormone treatments, and how they impact the brain, and how they impact cognition. Now, hot flashes, most of you may not realize, those are a brain event. It's not a body event, it's a brain event. And so that's a very dramatic effect of aging and menopause on the female brain, which men don't go through. But there are also other things that are mood alterations, there are cognitive alterations with menopause that can be helped by hormone treatments. Now, we have to figure out which are the

right hormone treatments. It's going to take another ten years. But there's no doubt that the brain is a key target of estradiol, and it isn't just the areas that control sexual behavior that are the target of estradiol, the areas that control cognition and memory are a huge target for estradiol. So this is a very, very important and active area of research.

SW: Thank you so much. Do you want to say something, Dr. Ratan?

RR: Well, I think the other point I would just mention, which sort of adds to what John said, is that you might ask well, why not just provide estrogen supplementation as a way of maintaining the brain? And as many of you know, there are potentially adverse side effects of doing that, particularly in the form of developing cancer. So, I think as John points out, part of the challenge for the future is to learn how to stimulate the estrogen receptors in the brain without affecting estrogen receptors in the body, and that's an area of active research.

JM: Yeah, and that's so important, Raj. That was a big topic of conversation at this meeting in Washington. There are receptors that respond to estrogen, and there are actually

several kinds. The idea way to deal with some of these effects in the brain would be to not have to give estradiol because of the risks that Raj referred to, but instead intervene at the receptor level, at the molecular level, and promote the kinds of biochemical actions that would not put you at risk in other organ systems.

SW: Okay. And by the way, I've heard hot flashes are also termed as "power surges". (Laughter) I like to phrase it that way. Okay, so we're all interested in memory. All right? So can you talk to us about the correlation of learning and memory?

JM: You want me to start?

RR: Yeah.

JM: So memory is very intuitive. Memory I think is easy for all of you to understand. It's remembering, at least the way we normally use it, we refer to as declarative memory, which means that you can state what you remember. And it's the memory of life's events. What did I eat this morning, what did I eat yesterday, who did I talk to yesterday? What happened in that car accident 30 years ago? So there are short-term memories, there are long-term memories, and the part of the brain that lays down those new memories is called "the hippocampus", and it's one of

the first parts of the brain affected in Alzheimer's disease, which is why when somebody has early Alzheimer's, the first symptoms are usually memory defects. Cognition is a much more complicated concept, and it is more reliant on the prefrontal cortex, and the prefrontal cortex is not motor, and it's not sensory, it's in between. That's where you make your decisions. So that's executive function, it's planning, it's what we call "working memory", so you're holding information in mind that allows you to make the right decision. It's where you decide how tor each a goal. All of that is cognition. Let me make sure I cover all of these different aspects of cognition. It's thinking intellectual. Work, reasoning, planning, attention. You deciding that you're going to tend to this issue as opposed to that issue is a very, very important cognitive function. These are all affected by age, not in everybody, and not to the same degree, but they are vulnerable to age. Raj?

SW: Do you want to say anything (Inaudible)?

RR: No. I think you covered it very well.

SW: Okay. This may be one of the most important aspects that we cover in this whole event, and so I want you to listen very carefully. We talked about it earlier. John, you

mentioned it in your opening remarks about the good news about the brain that may help us worry less about memory, brain plasticity. What is it, and how does it impact our aging process, and our aging brain?

JM: Right. So this is probably the single most important concept in all of neuroscience right now. When I was taking neuroanatomy in the ’70s, we thought that once circuits developed, that there was a lot of pruning of circuits, and a lot of plasticity in the developing brain, but once you were an adult brain, it was very, very stable. The neurons didn’t change, the synapses didn’t change, the circuits didn’t change. We realize now that that’s an inaccurate view of what the brain is doing, because the brain actually has enormous plasticity, and I’m sure Raj will have something to say about this, too. And what do we mean by plasticity? And it occurs mostly at the synapse, that point of communication between nerve cells, and those synapses can be altered, and they’re altered by experience. They’re altered by stress, they’re altered by learning. If you are depressed, those synapses are taking on a different form than if you’re not depressed. And what it turns out is that you have one set of

synapses that are very, very stable. They're stable for essentially your lifetime. And their coding expertise ... if you learned to play the piano when you were a child, and you can still the piano, that's because you have synapses that don't change at all. Your visual world doesn't change because the visual cortex has relatively little plasticity in the adult. Your prefrontal cortex, where you're learning new things every day, is enormously plastic. The synapses come and go, they're flying all over the place. They're anything but stable. There are stable synapses there, but about half those synapses are not stable, and they will come and go, and they will expand and contract. The molecules that serve those synapses will change all in the context of your daily activities, and what you learn, and what you retain, and what you decide to do.

RR: Yeah, I think ...

SW: Use your example.

RR: I think the way I think of plasticity, I think there are two examples that are helpful. Many of you have children; you remember when they were very young, and how they seem to pick up things so quickly, and in frustrating ways they pick up things quickly. (Laughter) Sometimes the wrong things. But what is

clear is that as you age, it's harder and harder to learn new things, new languages, learning how to play an instrument. But as John pointed out, you still have this ability to learn as you age. And I think the example that I had used earlier is if you look at this table, this hard wood, it's not plastic. You can do anything to it and it won't change. The brain is much more like a piece of stiff foil where if you provide the right inputs, you can shape it into a form that can do things that are positive, learn an instrument, learn how to use a computer, learn how to ride a bike. But also, interestingly, that plasticity can also be maladaptive, can be bad, and that manifests itself as sometimes pain, and some of you have experienced chronic pain, a process called "spasticity". Often after injury to the brain, muscles will be harder to move, the tone is very high, and also a process called "epilepsy" where you can have seizures. So plasticity can be good and bad, and I think one of the important points we want to bring today is that by providing a positive experience, positive training, you can shape that plasticity in ways that ultimately provide resistance to a number of different diseases, including Alzheimer's disease.

SW: Wonderful. So we're going to talk in a few

minutes about brain diseases and disorders, but tell us first of all about the normal changes in memory with age. Because there are ... I mean, I can already tell it, when I go on a live shot on TV, sometimes I'm like what was I supposed to say? (Laughter) So I'm noticing it myself. Go ahead.

JM: So, again, and you're going to learn a little neuroanatomy today, I'm going to go back to this dichotomy between the hippocampus and the prefrontal cortex. Both very, very vulnerable to age. The hippocampus is how you lay down new memories, and a classic example would be where did I park my car?

SW: (Laughs)

JM: Now, I haven't known where I've parked my car since I was 18. (Laughter) I don't have very far to go down. But many people who have very good memories for life's events, remember I said the hippocampus codes life's events, find that that kind of memory is altered with aging. And we know that the synapses in the hippocampus are altered with aging, and the ways in which a synapse is strengthened to allow you to remember something declines with age. Now, if you move to the prefrontal

cortex, remember, that's where I said these is where the more complicated cognitive processes are. Lots of people, not everybody ... that's another very important thing to remember is that chronological age has very little to do with the aging of the brain. In other words some people will see these changes at 60, other people won't see them when they're 80. So lots of people have problems with navigating daily events in life; keeping track of your checkbook, figuring out where you're going, planning the day, planning the week, executive function, in other words complicated processes that get you where you want to go in terms of your goals. Those are coded in the prefrontal cortex. And now we know that the prefrontal cortex actually loses an enormous number of synapses with age. And the number of synapses you lose pretty much predicts your cognitive decline. Now you're getting a very sophisticated view of aging here, believe me. I just published this about a year ago. The synapses that you lose are the ones that are most plastic, and you need those very plastic ones to learn new things, and to formulate new rules of behavior because you formulate new rules of behavior all the time to get what you want. If you did learn to play the piano when you were a child, you can

still play it. That's because the synapses that are very, very stable, you don't lose with age. So you're literally losing your capacity for plasticity. Now, you don't lose it completely, you lose about half of those synapses and so you still have a very high capacity for plasticity. And one bit of good news for the women in the audience ...

SW: (Laughs)

JM: ... is that one of the effects of estradiol is to protect those very plastic synapses. So there are ways we think ... it doesn't have to be estradiol, it could be other ways ... to intervene and protect these very plastic synapses. And I think that that is absolutely key to not only warding off cognitive aging, but maybe in the end also pushing back Alzheimer's disease, which we'll get to in a moment. So promoting synaptic health, and retaining your plasticity, and the synapses that you give that plasticity is really key to warding off the kinds of cognitive declines that we often see with aging.

SW: Raj, do you want to say ... ?

RR: Yes. I think what I'd like to add to that is, you know, the process of aging affects all the organs of our body, and

not just the brain. And there are a number of really intriguing theories of why we age. One theory is that there are these toxins called “free radicals” that come as a result of just breathing oxygen that are generated in our body, and they cause a very low level of damage throughout our whole life, and that damage accumulates and over time damages our tissues in ways that prevent it from being repaired. So for those of you who don’t know what a free radical is, just think about a time when you’ve cut open an apple and you’ve left it on the counter, and if you come back, and you look at that apple, it’s brown. And that process of the apple becoming brown is oxidation due to free radicals. Now, the next time you do this, if you take that apple, and you put some lemon juice over it, you’ll find that you can come back an hour later and the apple will still be white as when you first cut it. And that lemon juice is essentially working as an antioxidant. So all of our organs are affected potentially by free radicals. Another theory has to do with this idea that there are clocks, there is a clock in each one of our cells, and each time our cells divide, there’s a thing called the telomere, which shortens. And so as that telomere shortens, once it’s cleaved off, essentially you’ve exhausted the lifetime of all of

your cells. Now, what's interesting is is that all of these processes, you know, free radical damage, telomere shortening, in some cases too high glucose can be affected by things like exercise, can be affected by cognitive training. And what they do is they build up endogenous defenses in the body that prevent this sort of natural process of aging. And the specific molecular mechanisms by which that is happening are unclear, and that's why it's been so hard to be able to develop a drug that could actually counteract the aging process.

SW: Okay. So we've talked a little bit about what's normal. We're going to go into our second phase now about what's not normal in terms of memory as we age. Certainly for many of us, how many of you are in relationship with someone who has Alzheimer's? Okay. You're not alone; 5.4 million Americans have Alzheimer's disease, 1 in 8 older Americans. That's a lot of people, and 15 million Americans provide unpaid care to those with Alzheimer's. So we're talking about a lot of people, and that's going to grow, perhaps, unless we do a lot of our preventative work. So what I want to do is talk about dementia first, and then about Alzheimer's disease. So how does it relate,

and not relate?

JM: Again, we're back to this same dichotomy. So let's first talk about dementia. Loss of the memory of your life built up over time. That's more the damage to the hippocampus, which usually occurs first. And along with that your inability to form new memories. There's also the loss of the sense of who you are, and your place in the world, and the people that you know. You'll actually get to the point with Alzheimer's disease where you no longer recognize people. There's very importantly a loss of the ability to interpret what is going on around you. That's an important part of dementia. And in the end, you lose your ability to think, reflect, reason, and respond appropriately. So all the things I talked about earlier in terms of your cognitive abilities, those decline dramatically, and that's very, very different than the aging I was talking about ten minutes ago. This is a really dramatic decline. Why is it so dramatic? Because what I was talking about earlier was dependent on your synapses changing with age. Alzheimer's disease, neurons are dying, and the neurons that interconnect important parts of the brain that allow you to think cohesively are precisely the neurons that die. The neurons that

serve your vision don't die, the neurons that allow you to move don't die. It's the neurons in between that allow you think, and reason, and act on the world. And they die. So that's a real problem. We'll talk about this later when we talk about successful aging. But the emphasis now in terms of Alzheimer's disease is prevention rather than treatment, and I think cure is going to be extraordinarily difficult. So you really have to be with treatment and prevention. So much of the effort now is to try to figure out ways to push Alzheimer's back, and Raj has some incredibly scary numbers that he'll probably give you in a moment about how important it is to push it back. Before I turn it over to Raj, let me just read to you what I think is the greatest single description of early dementia, early Alzheimer's disease that I've ever read in the English language. You probably already know who wrote it if it's the greatest thing ever written in the English language, it was written by Shakespeare. And it's King Lear musing about his problems. "I fear I am not in my perfect mind. Methinks I should know you and know this man, yet I am doubtful, but I am mainly ignorant what place this is, and all the skill I have remembers not these garments, nor I know not where I did lodge last night. Do not

laugh at me." Now, the reason that I think ... and there are all kinds of books written on where he is in the progression of Alzheimer's. The reason I think it's early Alzheimer's because of the last sentence, "Do not laugh of me". He still has quite a great deal of self-awareness, yet he's still having all these problems. So to me this is clearly Alzheimer's, but relatively early in the process. So we want to do something over the next 10, 20, 30 years that stops you from even getting here, let alone full-blown dementia.

SW: Okay.

RR: Yeah. So maybe I can go back and reinforce some of the ideas that John has talked about. Alzheimer's starts in an area of the brain called the "limbic system", and it's the area of the brain ... and the structure is called the "hippocampus". This is the seahorse structure that's in the base of the brain, and what is thought to happen ... and this is the area of the brain that's involved in memory, as John said, it's involved in emotions, and it's involved in mood, and that's why some of the initial symptoms of Alzheimer's disease involve memory problems, problems with mood, and emotional ability. What's thought to happen is there's the buildup of a toxic protein in the brain called A beta, and this

forms what are called “senile plaques”, and these senile plaques are able then to give rise to a whole cascade of pathological events in the Alzheimer's brain, which start in the hippocampus, and can move to the parietal lobes. These are the areas that are involved not only in language, but also in helping you to get from one place to another. So a common symptom is someone can’t find their way home, some place they’ve been hundreds of times, they can’t get home. And then finally, the frontal lobes that are involved in, as John said, executive function, being able to plan. Now, over the last decade we’ve learned a huge amount of the causal factors in Alzheimer's disease, not from what we call “sporadic Alzheimer's”, but from familiar forms. And we’ve learned that there are really three major areas. One are areas, genes that are involved in generating this toxic A beta, genes that are involved in cholesterol metabolism like ApoE4, and then genes that are involved in inflammation, and these three areas really form the basis for a lot of the treatments that are going on by different pharmaceutical companies. And many of them have failed, and probably the reason for those failures, as John I think eloquently articulated, is that the treatment comes too late. And we think of the brain ... this

ability to be ... once it's damaged, there can be changes in the brain that prevent you simply from throwing a drug at it and hoping that the symptoms will go away. So I think in understanding, you know, sort of ... I think the point is really to highlight the importance that familiar forms of diseases have played an understanding more common forms of Alzheimer's disease, and that there are a lot of treatments on the horizon. As many of you have heard, there are almost 5 million people with Alzheimer's. The estimates are that if we don't find a treatment, there will be 13 million people in the United States with Alzheimer's by 2050. And the reason we have to focus so heavily on a treatment is a treatment that can delay the onset by simply five years, could result in a 40 percent decrease in the number of people who have Alzheimer's. So we don't have to hit a home run to really make an impact on this disease. A single would be fine.

SW: So I want to ask, and I just want to make sure that everyone knows that there are other types of dementias other than Alzheimer's.

JM: Right.

SW: So let's talk a little bit about that. What is

dementia, and are some dementias reversible?

RR: Right. So a common set of tests that almost everyone who is being considered for dementia undergoes is a B12 level. It's a vitamin that's actually involved in changing methyl groups in our brain. It's something easily taken, but deficiency in B12 can cause dementia. Hypothyroidism can cause dementia. Certain indolent infections can cause dementia, and your doctors can help you to think through that. There are other forms of dementia that are associated with multiple strokes, and Alzheimer's disease tends to have a very smooth course where you have a smooth decline. Having multiple strokes is called "multi-infarct dementia", and that has a more step (Inaudible) course. So sometimes just by piecing together the temporal sequence of events one can get a handle on whether you have one or other of these types of dementias.

JM: I would just add that there are also other neurodegenerative disorders. They're much more rare than Alzheimer's. There's one called Pick's disease, and there's one called frontotemporal dementia. So you may have heard of these. Essentially they're through a different mechanism than

Alzheimer's. They disrupt and kill the same neurons that Alzheimer's kills, and they have a slightly different trajectory. They're usually quicker than Alzheimer's, and they're much more rare.

SW: Can either of you talk to us about how Alzheimer's is diagnosed?

RR: Go ahead. (Laughter) So I'm happy to ...

JM: You've actually had to diagnose it.

RR: Yeah.

JM: I just try and figure out what's going on. (Laughter)

RR: Here, the Alzheimer's expert. So the diagnosis of Alzheimer's is primarily at this point a clinical diagnosis, although as we were talking about before, there's been a huge amount of new information on using imaging, brain imaging. Specifically there is a compound called Pittsburgh B, which binds to these senile plaques and allows you to look at what the plaque burden is in the brain associated with the clinical symptoms. And then also there are some biomarker tests. This is where you can either measure proteins in the blood, or in the

cerebral spinal fluid, the fluid that bathes the brain, and piece together a set of criteria that ultimately allow you to diagnose Alzheimer's disease. But Guy McKhann, who many of you may know, a wonderful leader in the Dana Alliance, developed a series of criteria maybe 20 years ago which based on clinical symptoms and some other tests allows us to categorize people into probable or possible Alzheimer's. And again, those are things that your doctors can go through with you in more detail.

JM: Just to add to that. This is really a very, very important development in the last couple of years that Roger's referred to, this fact that you can diagnose it while the person's still living because the dogma has always been you can only diagnose it pathologically at death. And that still is the most definitive. But these biomarkers combined with imaging are getting pretty accurate. Now, that brings up two issues, one is they're not 100 percent accurate, which is a bit of a problem, so you could say you're very, very likely to have Alzheimer's, and in fact, the person may not. So they have to be combined with whether or not you have signs of dementia. So if you have signs of dementia and you have everything that Raj just referred to, you have a pretty safe

diagnosis of Alzheimer's. But you can have the biomarkers without having dementia. The other thing is do you want to know? (Laughter) Do you want to know because we can't do anything for you. And this is a really, really important issue in terms of insurance companies, in terms of your own stress levels. So I don't know if it will come up in the question and answer period or not, but it's something that the scientific and medical community are going to have to deal with.

SW: And the ethicists, right? (Laughs)

JM: Yes. And the ethicists.

RR: The other thing I wanted to mention, and I don't want to get ahead of us too much, but to highlight what John said about the fact that there was a study done by Bob Katzman in San Diego maybe 15 years ago where they found that between 10 and 40 percent of people who were cognitively normal have pathological evidence of Alzheimer's disease. And so the question is what is it about those individuals that protects them from the deleterious effects of the pathologic changes in the brain that are congruent with Alzheimer's disease? And there is a wonderful neuropsychologist at Columbia, Yaakov Stern, who has developed

this hypothesis called “The cognitive reserve hypothesis”, and the idea is that ... and what he’s shown is that if you ... the higher your education is, or the more cognitively involved your occupation is, the more you’re protected from the pathological effects of Alzheimer's disease. So the example would be that if your gas tank is completely full, then you have to lose many, many more gallons to get to empty, as opposed to your gas tank being a third full. And this sort of gets into the idea of what generates cognitive reserve, and lo and behold, things like exercise, mental activity, doing crosswords puzzles, things like that, and having a social support, all of those things conspire to create cognitive reserve, and I think provide maybe a mechanistic understanding of why these things are important before you actually are symptomatic.

SW: That feels really good knowing I did *The New York Times* crossword puzzle. (Laughs) Up until Wednesday. (Laughs) I can only do Monday, Tuesday and Wednesday. (Laughter) But no further after that. (Laughs)

JM: I was on an airplane one time, and this woman sitting next to me was doing a crossword puzzle, and she said, “Well, I’m kind of a Wednesday girl.” (Laughter) She couldn't

do the Thursday or Friday one. (Laughs)

SW: Yeah, exactly. Not without tremendous help from the Internet. (Laughs) Okay, I need to ask you, before we move off of this, the whole idea of Alzheimer's, any word whether or not there will be a vaccine soon? Any word on that? And I know we're focusing mostly on prevention, but still ...

JM: You may get different answers here. Because I'm ...

SW: Okay, all right. So let's hear both, right?

JM: Yeah, yeah, this is obviously very controversial, and it's a question of whether you buy the amyloid hypothesis completely, or you don't, and I don't. So the vaccine is based on circulating antibodies in your body and brain to amyloid, to the protein that Raj referred to earlier. And the thought is that if you have antibodies circulating, they will remove the amyloid from your brain, and either restore cognitive health or prevent cognitive decline. And they've generally been administered when you already have the plaques that Raj referred to. I think if you already have the plaques, and you already have neuron death, a vaccine is not going to be helpful. I think the time when the vaccine is likely

to be the most helpful is actually ... it's counterintuitive. It's before neuron death, because we now know this same amyloid protein is toxic to synapses. So I think what we're going to have to do with this approach is move anything that is attacking A beta way, way earlier in the process, and try to promote synaptic health with it. And that's going to be difficult to get through FDA and all those sorts of things. But the trials that have failed, that Raj referred to earlier were primarily trials of what we call "plaque busters", and some of those were antibodies to amyloid. And they were just given too late. So will we have a vaccine? Maybe. But if we have one, we're going to have to use it very early in the process.

SW: But when is that? I mean, does that begin at 20, does that ... ?

JM: Oh, I think it's decades. Decades before ...

SW: Decades before. Okay.

RR: So there have been three studies with the vaccine, and two have failed. There was a recent Lilly study that just was completed with an antibody called solomenubab(?), and it failed, but what they did is they did what's called post hoc. After they had done the study, they went back and they re-analyzed the

data looking at people who are more mildly affected and what they found is they found a difference. So I think this really reinforces the idea that the vaccine may work if you get it early enough in the disease. Now, as someone who thinks about brain repair and recovery, I would argue that ultimately no single drug or vaccine is going to treat Alzheimer's disease. It's going to have to be a combination of these types of treatment with the right cognitive retraining because there are enormously complicated number of events that have to go back into getting synapses to form in the right ways in the brain. And so a combination of experience and drugs ultimately is going to be the way forward, and those are the kinds of approaches that we're really looking at at Burke. And I would say that the vaccine idea is not dead yet, and ultimately may be a validation of the A beta hypothesis.

JM: So we actually agree more than I thought we might. (Laughter)

RR: Yeah.

SW: And we'll also get to how to keep the healthy brain going. So we'll get to that whole section.

RR: But there are a number of exciting

treatments, I just want to mention. So I was at a meeting on Thursday at the New York Academy of Sciences, and there also is an interesting hypothesis, which suggests that the accumulation of metals in the brain might be an important way, and what causes these toxic aggregates. Essentially what happens is it's sort of like if you were to put all of your garbage out to have it thrown away, and it all came together in a way that it was so big it couldn't fit in the garbage truck.

JM: (Laughs)

RR: And it's thought that metals kind of clump garbage ... this toxic protein together, and so if you treat with a drug that binds the metals, it dissolves the plaques, and causes amazing recovery, and this is a study that was actually ... it's what's called ... so there are different phases. Phase I is usually safety, phase II is a combination of safety and efficacy, is the drug not only safe, but is it effective, and the phase II studies with this drug called PDB2 show incredible promise for Alzheimer's disease. So I think the message today is not all doom and gloom. There is going to be a lot of optimism, not only about the approaches that you can take every day at home, but also things that are coming

out of the pharmaceutical industry.

JM: Yeah. I totally agree with that.

SW: Very, very interesting. Very, very interesting. And we're getting it ... you know, you've just gone to a research symposium on that. That's fabulous. Can you talk about ... you mentioned, I think, Raj, the impact of stroke on dementia.

RR: Right. So, as many of you know, stroke is the leading cause of disability in the United States. There are 5 ½ million Americans who are disabled from stroke. A stroke for many of those of you who don't know, is caused when you have interruption of blood flow to the brain. And the brain is very highly dependent on oxygen and glucose. So if it is deprived of nutrients even for a short period of time, tissue dies. Another type of stroke is called a "hemorrhagic stroke", and that's where the vessel is interrupted, and the blood leaks out into the brain, and because the skull is a close space, the blood fills the brain, and actually compresses other parts of the brain and kills those areas. The good news about stroke is 80 percent of stroke is preventable, and the key risk factor is high blood pressure. So this is why it's so important if you have high blood pressure to actually have it

treated. Other risk factors; smoking, high lipid levels, especially a high HDL. These are things that you can do to prevent a stroke. But even once a stroke is happening, there are treatments. The key is get to the hospital quickly. I can't tell you how many stories I've heard from my patients, "Oh, I was having a little weakness in my arm, I had dinner, I made, you know, I talked on the phone with my friend, and then I decided to head to the hospital." And the symptoms, to be aware of, so think of this acronym "FAST", F-A-S-T. So face, if you notice any asymmetry in your face. Arm, if you lift your arms up and there's a drooping of one arm. S refers to "speech", so any problems in speech. And T refers to time. Time is of the essence after a stroke. So if you're having any of these symptoms, drop what you're doing. Just like if you were having chest pain and get to the hospital because there is a therapeutic. This is called tissue plasminogen activator. It's widely known as a clot buster, and it's very, very effective. But it would surprise you and astonish you to know that only 1 percent of Americans who qualify for this agent get it because they don't go to the hospital and say, "Do I qualify for TPA?" Or have their family do it. Obviously if you're having a stroke it can be difficult to advocate for

yourself. So you want to get to the hospital within three hours so you can get this clot buster because it will help your recovery. Now, beyond that, we're working on a number of ... there are a number of exciting treatments coming down the pike. At Burke we've very focused on recovery in the brain, and I think we talked a lot about plasticity. Well, I think the best example that plasticity is constrained in the brain, not only in people who are normal, but also after injury is the fact that there are 5 ½ million people who are disabled from stroke. So there are spontaneous mechanisms by which the brain gets repaired, and we're working on strategies, and we can talk more about what those strategies actually are.

SW: Is there any interplay between stroke and depression, and can you address that real quickly?

RR: Right. So stroke is ... about 30 percent of patients who have a stroke will have what's called major depression. And this means that not only will they have feelings of hopelessness, guilt, sadness, but also problems in eating, problems in sleeping, what we call "vegetative signs of depression". And major depression needs to be treated with an antidepressant drug. And about 30 percent of that 30 percent don't

get treatment. And the depression can actually start, it could peak at about three to six months after the initial stroke, even continuing to a couple years out. Now, it's not clear at this point whether the depression is the result of neurochemical changes that actually occur in the brain, or is this simply the appropriate response to an enormously difficult life event. And I think it's probably a combination of both.

SW: Okay, great. I want to talk also real quickly ... I don't know if any of you saw in *The New York Times* this Tuesday about ... and John, you mentioned it for Alzheimer's ... that new research out of MIT shows that people can actually see the progressive damage in brains for Parkinson's currently. Does anyone want to address Parkinson's in terms of how this relates in?

RR: Sure. Yeah. So Parkinson's is a neurodegenerative disease. Stroke, as we talked about is acquired, a more acute event. Parkinson's and Alzheimer's are chronic neurodegenerative diseases. And the commality between those diseases is they both seem to involve this faulty garbage disposal hypothesis, that there is a different toxic protein called

synuclein, which accumulates in an area of the brain called the substantia nigra. And this are of the brain is what generates a neurotransmitter called “dopamine”. And when you lose 80 percent of your dopamine-containing neurons, you start to develop Parkinsonian symptoms, shaking on one side of the body, very slowness of movement, rigidity to your body, what we call bradyphrenia, slow thinking, all of these are signs of Parkinsonism. The good news is is that unlike for Alzheimer's, we do have some symptomatic treatments. The symptomatic treatments for Parkinson’s are very good. The simple idea is if you’ve lost dopamine, replace dopamine. So drugs like Sinemet, or what we call “dopamine agonists”, you know, there are a variety of different trade names for those. They can all be used, and they actually can allow people to live a quite normal life. But part of the challenge, again, with many of these diseases, is since they have such a slow rate of progression, if we had biomarkers, if we had ways to image the progression of the disease, what it allows us to do is to test treatments, and instead of having to wait two years to decide whether a treatment is effective, we can follow the imaging over a much shorter period of time, and this way we can do more trials,

and have a much greater likelihood of having a successful treatment.

SW: Perfect. Yes?

JM: I'd just add a very brief note. As Raj said, Parkinson's disease is the death of one very small nucleus that all uses one neurotransmitter and projects to one particular place. It's a fairly simple circuit, much simpler than the circuits we were talking about that are affected in Alzheimer's disease. So this is a place where stem cell biology actually may end up having an impact on neurologic disorders. I think it's much less likely in Alzheimer's, but Parkinson's, we may be able to replace those neurons and have them get the dopamine to the appropriate place. So that's something to watch out for.

SW: Okay. Fascinating. Okay. Before we get on to successful aging, and I know we want to spend a good amount of time on that, can you talk very briefly about sleep and memory, and how much is needed, and how does it affect memory and healthy brain function. Anybody?

RR: I'm happy to (Inaudible).

JM: Why don't you (Inaudible)? Yeah.

SW: (Laughs)

RR: So as many of you have probably experienced, as you age, you sleep less. And it's well documented that the amount of time that we spend in what's called "slow wave sleep" as we age is significantly diminished. Now, this is the deep sleep that many of us used to enjoy more frequently. (Laughter) And the reason why this deep sleep has become so important ... so what's interesting is there are studies now that show that children who spend more time in slow wave sleep actually do better in school. And interestingly, the connection between sleep and Alzheimer's has recently been made by a series of elegant studies by David Holtzman at Washington University in St. Louis. And what they found is is that during sleep, the toxic protein that actually contributes to the formation of these plaques is produced, but that during these deep sleep moments, actually the production is suppressed. So the thought is, is that the more time you spend sleeping, the more time you can actually spend in slow wave sleep, and the more time that you actually suppress the production of this toxin in your brain that ultimately could cause Alzheimer's disease. And so it's really important from a whole host of standpoints to

really ... if you're not getting a good night's sleep, to try to find out why. And it turns out that, you know, just another quick issue is that many of you may have had to deal with issues of what's called either sleep apnea, or this is a disorder where while you're sleeping, the uvula actually falls back and occludes your ability to get oxygen in your blood. So you become transiently hypoxic during sleep. And what's now shown is that this event can also upregulate enzymes that cause more of this toxin that's found in Alzheimer's. So it's really important to focus on getting a good night's sleep.

JM: And just to add to that, it's very important to realize that sleep is a very active process. It's anything but the brain shutting down. And there are lots of sculpting of synapses and consolidating memories that occur during sleep. So if your sleep is disrupted, your cognitive abilities the next day are going to be disrupted.

RR: I just wanted to add, because I think it's interesting that sleep in our bodies is controlled ... so you know how ... there's no middle ground. You're either awake, or you're not awake, although sometimes I feel like I'm in this middle ground.

(Laughter) So it's sort of like a servo(?). And there is an area of the brain called the VLPO, ventrolateral preoptic nucleus, that regulates, that shuts off the arousal centers when you're falling asleep. Now, as you age, that area degenerates, and that's why you spend less time sleeping as you age. At least it's a hypothesis.

SW: Okay, how are we doing? Everybody still with us? Because we're going to transition now into the hopeful part, right? (Laughs)

RR: Yes.

SW: And talk about successfully aging, and how to do that. In order to get to that point, let's talk about four factors of cognitive fitness, all right? This is something all of us can do, and obviously the fact that you're still engaged, which is fabulous, so we're all successfully aging right now. What can we do to keep our brains healthy and functioning for a lifetime?

JM: There are four major ones, and you've probably heard them before, but the more data we obtain, the more I believe, and the more the scientific community believes that these four are really critical. Increased mental activity, particularly

cognitive exercises, and there actually are now some computer games being developed, mostly at UCSF, UC San Francisco, that seem to be quite useful in maintaining your cognitive abilities. One of the questions has always been, “Well, if I learn to play this game better, do I just know how to play the game better, or will I know how to get to the store and back better?” And that’s really been a very, very important issue. And now they’re showing somewhat we call “transference” from the skills in the game to daily activities. Increased physical activity. This took us all by surprise. We had no idea ... and it’s mice, rats, monkeys, humans ... no idea that physical activity would have such a profound effect on the brain. And we think this is because of various molecules like growth factors that are released during the exercise that then promote neuronal health. My favorite one is increased levels of social engagement because it taps into everything. You’re more physically active if you’re socially active. Social engagement is tremendously demanding in terms of cognitive abilities, and it’s demanding in a very real-world sort of way, and you’re maintaining your friendships, so your sense of wellbeing is maintained, which is very, very important. And the other is what’s good for your heart is

good for your brain. So control vascular risk and maintain heart health. And that makes all the sense in the world. The brain, as Raj pointed out, is tremendously dependent on oxygen and glucose, and the only way for that to get there is through your blood supply. So those four, there are very good data on all four of those now as ways to promote your healthy brain.

RR: Right. So what I would add to that, I think what's really exciting about this is that, you know, at least at this point we can't do much about our genes, we can't do much about the fact that we are aging. We are aging as we are sitting here. These are things that you can have a control on. The one I personally like the best, and I think this is something that we experienced to the start of this is exercise. So 30 minutes of exercise every other day, you know, of moderate intensity, as I think John pointed out, it increases your vascular fitness, so your blood flow to your different organs is great. If you're diabetic, it helps your diabetes. There is now evidence that ... we always thought that the neurons that you were, as John mentioned in the beginning, the compliment of neurons that you had when you were born is the maximum neurons you would ever have, and during life

you were just losing neurons over time. It's now known that there are areas of the brain where new neurons are born, and those neurons can actually be a reservoir of potential replacement neurons for areas that are damaged or sick. And so as you exercise, it's been really elegant studies showing that you get an increase in a growth factor called "brain-derived neurotrophic factor" that increase neurogenesis, and the increased blood flow that happens with that neurogenesis allows those neurons to migrate and incorporate themselves into areas of the brain that are damaged. So exercise is really important, and it really I think ... I will tell you as a clinician, as a scientist, it's biologically plausible ... I mean, all of these mechanisms make sense. Cognitive retraining as, you know, I think John really elegantly articulated in terms of this cognitive reserve hypothesis, the idea is by doing games, any mental activity, talking to your friends, doing things, you create reserves that protects you against Alzheimer's disease. And then finally, I think social networks, exercise and cognitive activity are all ways of dissipating stress. And there's a really exciting *Nature* paper that was published last year from Leewae(?) Si(?) at MIT, and what she shows is that when the glucocorticoids are increased

in your blood, they bind to receptors in the areas of the brain that are involved in memory, and they upregulate brakes on gene expression that's involved in plasticity. So this stress constrains your brain to not be plastic. So anything you can do that sort of dissipates this stress, and all four of these things are included in that, likely will have an affect on the brain.

SW: Okay, so you've said 30 minutes of physical exercise. How much mental activity are we talking about a day?

JM: As much as you can get. (Laughter) One of the exercises that I've always pointed to, because it actually taps into so many components of the brain, is bridge. Bridge, there's a spatial component. You know, that person played one card, that person played another card. There's obviously a memory component. There's communication with your partner through biding, and there's tremendous cognitive tasks. So bridge is one ... how many of you are bridge players? All right, well, that's excellent. My mother was actually a grand master. She was a huge bridge fanatic, and I'm convinced it kept her cognitively healthy for a long time.

RR: So I think this is a question that is much, as

you can see from our answers, it's much less well defined. So most of the studies that have been done that really clearly show that more mental activity is better for you, these are population-based longitudinal studies. And now the question is what is the specific dose, time, and type of mental activity? And obviously computer games are really prominent in this area, and there are some ideas that if you can sort of have computer games that have you shifting what your focus is. Let's say one time your challenge is to, you know, build a series of letters that create a word, but the next week you're doing a whole different set of modifiable tasks. So having different flexible exercises, not necessarily doing the same thing is probably the message that I wanted to get at.

JM: And let me just come back to something else.

SW: Sure.

JM: I'm surprised that stress didn't come up earlier. Don't stress yourself out doing this, because stress (Laughter) ...

SW: Counteractive.

JM: ... stress is really bad for the brain. And we've done studies that show that stress actually causes the

neurons in the prefrontal cortex that you need to function normally, cognitively, to shrink. They actually shrink. And with time away from stress, they come back. Now, one of the problems is as you age, they don't come back as well. So we have to figure out a way to have vacation as you age be just as healthy to your neurons as it is when you're young. But we're working on that.

SW: Is there a difference in ... you know, people often say when your adrenalin is pumping, then you're focused and you can go for it. Is there a difference in the adrenalin and stress, the effects of that? Like if you get ... I mean, I've been told that.

JM: Well, Bruce McEwen has popularized a concept. Bruce, he's a Rockefeller, probably the world's expert on the effects of stress on the brain, and he has actually written a book about this, where there's good stress and bad stress, and the levels of stress that actually make you attend to things, and make you perform at a higher level, and assure your success actually have different effects in the brain than the levels of stress that make you more prone to failure. So stress that is overwhelming. Overwhelming stress, it actually secretes a whole different set of molecules, and has a completely different effect on the neurons.

RR: So I think the connection is that when adrenalin rises, the adrenal glands secrete what's called "cortisol" ...

JM: Right.

RR: ... and it's cortisol that actually has these deleterious effects on brain neurons. So you're absolutely right. As part of the flight or fight response, it definitely ... if it's continuous, I mean, that's usually something like, oh, I almost hit somebody when I came here this morning. You know, you know how that makes your adrenalin go up and your cortisol go up. It's a more, as John says, a more chronic level of anxiety discomfort that I think is probably more problematic.

SW: Would either of you be able to address the importance or the effects on memory of meditation? Do you know anything about that?

JM: It's real. (Laughter) That's about all I can say.

RR: You know, I just was at this meeting on Thursday with a guy named "Rudi Tanzi" who runs the Genetics and Aging Unit at Mass General Hospital, and he just wrote a book with Chopra. That's right.

SW: Oh, Deepak Chopra. Mm-hm.

RR: Deepak Chopra on the super brain, and they talk a lot about this issue, and it sort of gets back to the issue of sleep. The issue is that you can actually slow your brain waves down during meditation, and it's much like getting into that slow wave sleep where you're decreasing the producing of A beta, that toxin in Alzheimer's disease. So there actually is ... you know, it's not sort of a cockamamie, you know, idea that meditation actually might be a therapeutic.

SW: Plus stress.

JM: I was just going to say, it reverses some of the effects of stress, as well.

SW: All right, good. We're going to get to questions in just a minute. Hang on to that, and we'll come to you first. Certainly the financial world has made people not be able to retire, so I'm going back to the social engagement piece. How many of you have had to continue on in work, or go into a second or third career after ... all right, so retirement was delayed, or perhaps being involved with philanthropic. Talk to us more about social engagement. Certainly houses of worship are a way people

can engage, circles of friends. You mentioned bridge clubs. What are some other ways that are important, and what are the effects of the social engagement?

JM: Well, family. Family turns out to be enormously important, and the relationship between, for instance, grandparents and grandchildren is this whole three-generation structure that humans have. And, in fact, other primates do, as well. That is probably one of the most rewarding types of social interaction. Now, of course, it can also be quite stressful. (Laughter)

SW: We've just come off Thanksgiving, right? (Laughter)

JM: So you need to ...

SW: And then the holidays. (Laughs)

JM: Right. You need to promote the rewarding levels of interaction between the family maybe with a little red wine (Laughter) and decrease that, you know, why is Johnny getting Ds in college?

RR: Yeah. I mean, I think that this is really a multifactorial issue. I think an event like today we're all coming

together ...

JM: Yeah, exactly.

RR: ... and we're learning about things that we can do to promote brain health are a form of social engagement. So this is one example. Another example is having emotional supports. Who do you rely on to provide you emotional support? That can come from family, it can come from friends, it can come from, you know, your work, a whole host ... and then, you know, there are person-to-person engagement. And then, you know, more practical things, you know, someone who can help you actually get around to go places that you might want to go. So I think there are a lot of ways in which this ultimately affects the manifestations of dementia or aging, and I would say that there is a little bit of debate about whether social isolation just reflects an early stage in Alzheimer's.

JM: Right.

RR: So if you see somebody who is isolated, and they're a friend, I think the thing is to sort of raise the red flags and say maybe they need to go see their doctor, because it could be depression, it could be Alzheimer's disease, and it's important to

find out.

JM: This is just so important when you pick up on increased social isolation. And Raj brought up a couple examples. Two things that come to mind immediately for me, probably because I've seen it in my own family, are hearing loss, and a broken hip. Both of them, hearing loss leaves a person kind of isolated, they can't follow the conversation at dinner, and a broken hip that leaves you immobile, you can no longer do the social interactions that you were taking for granted earlier. So even things you wouldn't think would cause social isolation in fact, do. So as Raj said, if you see this in one of your friends or one of your family members, I would, you know, try to intervene. Hearing aids are a huge issue.

SW: And just from my own sake, having seen the disconnect in people whether it's, you know, they're isolating themselves, continuing on with the conversations ...

JM: Right.

RR: Right.

SW: ... engaging people in conversations, even if people are pushing you away, to try to come at it from different

angles, that those are key to keeping folks cognitively ...

JM: Yeah.

SW: ... and healthy, you know, in family health.

JM: That's great.

SW: So real quickly, clinical trials, importance of them, engagement in them? Anybody want to talk about that?

RR: Yes, I will. I would encourage ... so I think that if the best example of this is that in this country, if you have cancer, you will go to your doctor and your doctor will say, "If you don't get involved in this clinical trial, you're going to be dead in X number of months." For neurological diseases, I think what we find is we say, "You know, you are going to have a life of disability. You may not be able to play with your grandkids, you may not be able to play golf, you may not be able to engage in the activities." There is sometimes a reticence to get involved in trials that may involve compounds that have theoretical benefits and also theoretical toxicities. I think I would encourage you to really ... this is a personal decision. It's one that involves discussions with your family, but at least be open to considering getting involved in these trials because these are the ways that we actually ... this is kind of

a way that not only you can potentially help yourself, but help those who are affected afterwards to minimize their pain and suffering from a particular illness. So I would encourage involvement in clinical trials when possible.

JM: This might also be a good time to encourage you to be advocates for scientific research. I mean, everything that we've talked about, everything that we do, anything that we do in the future that will help with any of these disorders and any of the aspects of aging that we've talked about today will come from laboratory research that is then translated into clinical innovation. And there is no other way around it. And so it's very, very important if you feel this way that you let your Congress people, and the President's office, and anybody else that's relevant know that you support a biomedical research, and that it needs to be put at a very high priority.

RR: Yeah. Can I amplify that point? So I made this point earlier. Right now in the United States we spend $1.7 trillion a year on healthcare. We spend $30 billion on the NIH budget, less than 2 percent of the cost of health goes to research. The estimates now are that Alzheimer's disease will cost the

United States $1.1 trillion by 2050. This will bankrupt this country. And I think it is collectively our responsibility to do the kinds of things we talked about today, but also to talk to our politicians about how important basic translational and clinical research is in this country, with the caveat of saying I want you to support this research, but I want you to hold the scientists accountable ...

JM: Yes, that's right.

RR: ... for what they are ultimately going to deliver for patients.

JM: That's right.

SW: Okay, and that's one way to be socially engaged, right?

RR: That's right.

JM: Yes.

SW: And in your packets, in your bags that you got, there's this wonderful Brain Connections book. It has wonderful resources in it, including ten ways you can be a brain advocate. I encourage you to look at that. This is all from the Dana Alliance Foundation. Okay. So before we go to questions, we're going to get your questions, we're going to be done by 12:00,

I promise. I want you both to think about the top piece of advice you would offer us for keeping brain healthy. Raj?

RR: Well, I want to say something new, reemphasize what we've talked about. But we haven't talked a lot about nutrition. I would say that there is a lot of unsubstantiated recommendations about taking antioxidants and other supplements. The best thing you can do is eat a balanced diet, eat a diet that, you know, avoids fatty meats, but is balanced. And I think in that way you are more than likely to get all of the types of supplements that you need for keeping the brain healthy.

SW: Okay, so extra supplements, not necessarily?

RR: Well, in certain circumstances they may be appropriate, but those are things that should be done in consultation with your doctor.

SW: Perfect.

RR: So if you have elevated homocysteine levels, you know, if you have high cholesterol, if you have high blood pressure, a lot of these things I think are done in consultation with your doctor because, for instance, there is a bit emphasis on omega-3 fatty acids. If you take too much omega-3 fatty acids,

that's bad. So these are all drugs, and you should treat them as drugs. Just because they're sold over-the-counter in your local grocery store doesn't necessarily mean they're good for you, or they're safe.

SW: Perfect. John?

JM: So I would certainly reinforce what Raj says, especially with the epidemic of diabetes type 2. Diet is incredibly important. But my favorite ... and you've probably already gleaned this from my comments ... my favorite is social engagement. You know, our brain is designed for social engagement. We are incredibly good at communicating, whether it's facial expressions, or verbal communication, or body language, and this is a very complex cognitive task. And it's also fun social engagement, and it's also your friends and family will pick up on cues. We talked earlier, if you see somebody who is becoming more socially isolated, you should try and deal with it. So my advice to all of you, along with what Raj said, and along with a lot of what we said is to be as socially engaged as you can be. I think that will promote brain health.

SW: Perfect. Thank you so much. All right, we're

going to transition now into our questions. Here is how it's going to go. We're just going to travel around with it, or come up here. Okay, so everyone wants to be able to hear your questions. If you are able to get up and come over here to the microphone, please do. If you're not able to get out your seat, please raise your hand and someone will come to you with a microphone. Here are some parameters for us; first of all brevity. All right? We're getting out of here at noon, which means we have 22 minutes. We want to get to as many people as possible. One question only, please, per person, and make them please broad enough so that it relates to everyone. In other words, panelists cannot give personal medical advice, or give referrals. So, again, just have it be something broad enough that's of interest. So we'll go one at a time. I'm going to do like the Academy Awards and pull you off if you go too long. Sorry. (Laughter) I'm going to apologize beforehand. Go ahead.

B: Hi. My name is Bess. A lot of our veterans are coming back with severe PTSD, and there are many people who have severe PTSD from childhood difficulties. What is the effect of severe PTSD on the brain and aging?

RR: (Inaudible)?

JM: Yeah, I was actually very involved with a research effort for a long time funded by NIH to get at the brain's circuitry that's affected by PTSD. Now, the aging element that you brought into it is very interesting, and we don't know a lot about that, about how aging will impact PTSD. I don't think those studies have been done. But it's very clear that PTSD in animal models as well as humans changes brain circuitry, it really does, and it changes brain circuitry primarily in a triangle of connections from prefrontal cortex, hippocampus, and amygdala. Raj and I haven't talked about amygdala at all. Amygdala essentially confers emotional tone on what's going on around you. And there is no doubt from human studies and animal studies that the amygdala circuitry has been altered in PTSD. Now, how do we change it back? It comes back to this notion of plasticity. We need to retrain the amygdala through behavioral therapies and through drug therapies so that the person either forgets the events that bring on PTSD, but that's probably not going to work. What you really have to do is learn something new. It's really a matter of learning to repress that reaction to those stimuli. And I actually think we're

going to make good progress in that area.

SW: Okay, we're going to go on. There was a gentleman out here in the middle of the audience that couldn't get up.

JM: Oh, my God, look at this (Inaudible).

M: Okay. Is there a hereditary aspect to Alzheimer's, and can amyloids be measured in spinal cord fluid?

RR: Yeah.

JM: You want to start?

RR: Yeah, so there is a hereditary aspect to Alzheimer's disease. There are a number of early onset Alzheimer's disease that involve mutations in different genes that regulate the production of this toxic A beta substance. Many of you have heard of ApoE. It's a gene involved in cholesterol metabolism. If you have ApoE4, your risk of Alzheimer's goes up by 5 percent. If you have two alleles of ApoE4, remember you have two copies of every gene, your risk goes up by greater than 10 percent, so it is the most significant general risk factor, and if you have ApoE2 on the other hand, you are protected. At this point, knowing that can help you to understand whether you're at

risk, but there is no specific intervention if you have that. But there are a series of familiar Alzheimer's disease, and A beta can be measured in the spinal fluid. It's a complicated ... the test is not a simple one, it's a ratio of what's called A beta with another protein called "tau" that can tell you whether you have Alzheimer's.

SW: Thank you so much. Ma'am?

W: I was going to ask a similar question. Do you think hereditary plays a role in getting Parkinson's disease?

SW: Very good.

RR: Right. There also are familiar forms of Parkinson's disease, but like Alzheimer's disease, these are less than 5 percent of the total, and you can be tested for a number of these genes. There is one important risk, genetic association and that's people who have mutations in a gene called glucocerebrosidase, and if you have two copies of that you have what's called "Gaucher's disease". That has a much higher risk of Parkinson's disease. But again, the vast majority of Parkinson's and Alzheimer's is what we call "sporadic". It has no familial (Inaudible).

SW: Thank you. Ma'am?

W: Yes, good afternoon. Good morning, good afternoon.

SW: (Laughs)

W: I appreciate the county, and the doctors, and Shannon White for hosting this very important topic. As you can see, the room is filled, it's very important, so I want to thank all of you for that. I do want to say I sort of respectfully disagree with when you said about supplements. I think if you really work with your doctor with the supplements, I think they could be beneficial. They've been quite beneficial to me and members of my family, and Shannon and I appreciate you talking about meditation. It's a wonderful form of healing the brain, and keeping the brain very healthy. And I'm also going to go on another side as far as, you know, going to your church, going to your synagogue.

SW: Mm-hm.

W: Those are all forms of meditation and support ...

JM: Yeah.

W: ... like you said about having some sort of support, emotional support. Okay, those are great ways of getting

some kind of support.

SW: Do you have a question?

W: Could you please talk a little bit about Lewy dementia?

RR: Right.

JM: About what?

RR: Lewy body dementia.

JM: Oh, Lewy body dementia.

W: Lewy body dementia, sorry. Mm-hm.

RR: Right. So Lewy body dementia is actually a combination of Alzheimer's disease and Parkinson's disease, and it's characterized most by the accumulation of these protein (Inaudible) structures in the brain called "Lewy bodies". The manifestations of Lewy body disease primarily are usually psychosis and dementia first, and what will happen is somebody will present with, you know, either having fixed false beliefs, or being very aggressive, and they'll come into the hospital, they'll get treated with a drug that normally is meant to calm people who are psychotic, and those drugs will cause them to get stiff and Parkinsonian. So the mental aspects of the disease, the dementia,

is prominent, and the movement disorder aspects of Parkinson's seem to be much later.

W: Okay, thank you.

RR: And the other thing is it's not treated with dopamine-supplementing agents like Sinemet or other things. It has a different class of treatments than Parkinson's.

SW: Thanks for your question. Next, ma'am.

W: Hi. I sort of have a two-part question, even though you said we could only have one. The impact on Ambien on the study that came up that said that Ambien is correlating to Alzheimer's, and then if you could recommend some computer games. People have talked about Luminosity and the impact of that, and are you familiar with them, or are there any other ones that you could provide?

SW: Just one question.

JM: I can take the computer game. Which one would you rather have answered? (Laughs)

SW: We have one question. Which is your (Inaudible)?

W: The computer game.

SW: Okay.

JM: So the two key people who are working on this are Michael Merzenich, who is at UCSF, and Adam Gazzaley, who is also at UCSF, and they're taking slightly different approaches. So rather than give a longwinded answer, I would suggest you Google them.

SW: How do you spell that, do you know?

JM: Merzenich is M-e-r-z-e-n-i-c-h . And he actually has a company that's developed several of these games, and has had quite a lot of success, particularly with elderly people.

W: Are you familiar with Luminosity as ... ?

JM: Which one is that one?

W: It's called "Luminosity".

SW: Luminosity.

JM: I don't know the trade names for them.

SW: Okay, we need to move on.

JM: Those are two key ... especially Merzenich.

W: Merzenich, okay.

SW: Simon, you had somebody back there.

W: Thank you.

W: Yes, I'm a cancer ...

SW: Wait, we can't hear.

W: Oh, sorry. I was a cancer victim, and I had chemotherapy, and I developed chemo brain, and that was about ten years ago, but I still have some cognitive issues. But I'm also a familial ... my grandmother and all her siblings had Alzheimer's, so I'm concerned about the combination of the two things. Is there any way of reversing or limiting any more damage than what I've already got?

JM: Oh, wow.

RR: You know, my recommendation would be to exercise 30 minutes a day, do a lot of the things that we've talked about here that are social engagement, mental activity. I think those are probably the safest things to do that might provide improvement. But the other thing is this is an important thing to discuss with your physician obviously because, as you point out, chemotherapy can have effects on stem cells in the brain, and thereby decrease the threshold at which other diseases might manifest. So I think I would see a doctor.

SW: Thank you. Ma'am?

W: I believe you said that an accumulation of metal in the brain causes problems? Where did these metals come from?

SW: Great question. (Laughter)

RR: Yeah. Excellent, excellent question.

SW: I wondered that, too. (Laughter)

RR: I'm glad you mentioned it. So one thing that many people are not aware of is that a multivitamin contains iron. Unless you are iron deficient, you should not be taking a multivitamin with iron, okay?

W: Oh ...

RR: Because it will cause overload. The second thing is that it's thought that what happens is is that when the A beta comes together, it polymerizes, it binds, it sequesters metals that are actually good ...

JM: Right.

RR: ... from the neurons and pulls them out of the neurons where they can't perform their function. So it's actually stealing metals from areas of the brain where they're actually needed. It's more of a redistribution than an accumulation. And

the drugs that ... PDB2, in particular, the one I mentioned that was in phase II trials, it has the ability to take the metal from the plaque, move it back into the neuron, and that's the theoretical way in which it's beneficial.

SW: And again, people need to check with their doctors to see if they're iron deficient to see if they need to take the (Inaudible).

RR: Right.

JM: And zinc, of course, is an important metal.

SW: And zinc.

W: Well, since you raise this ...

SW: I'm sorry, we've got to go on to the next person. But you had a great question. Thank you so much.

W: (Inaudible)

RR: It's very difficult to increase zinc by taking it as a supplement.

SW: Okay, thank you, ma'am.

W: Thank you.

SW: Uh-huh?

W: Thank you all for the wonderful panel

discussion. And my question is what role does music have as a function of positive ...

SW: Great question.

SW: ... play for people who need an uplift mood?

JM: Yeah. Well, music ... what a great question.

SW: Mm-hm.

JM: Music, again, is a very demanding task. It's mostly sensory, but as you know, it taps into memory very, very rapidly, and you can hear a song that reminds you of your wedding day, or anything. So music is great, great therapy for not only people, but Alzheimer's patients appreciate music way, way into severe Alzheimer's, and Parkinson's patients for some reason can dance.

W: Fantastic. (Laughter)

JM: So even if they have difficulty moving, if they hear familiar music, they can dance. So there's something about music and dance that gets them past all the motor difficulties of the disease. So, yeah, and playing music. If you are a musician yourself, my gosh, what a great thing to do.

SW: And I'll add to that real quickly, the

importance of ritual. So in houses of worship I have served as a chaplain in a nursing home, and there was a woman who had long-term dementia, but the moment that she started in the Catholic mass, she stopped rocking and she joined in the Our Father. It was amazing. Anyway.

(Applause)

SW: So that was good.

W: Thank you very much.

SW: Okay, yes, right over here.

W: You mentioned ...

W: I'm just thrilled with what you said.

SW: Okay. (Laughs)

W: Absolute (Inaudible).

SW: Okay. Go ahead, ma'am.

W: You mentioned the oxygen and glucose when necessary for the brain.

RR: Yes.

W: Do you find any relationship with the increase in diabetes and the restrictions that's on glucose in your diet affecting the brain at this point?

SW: Good.

RR: It's a fantastic question.

JM: Yeah.

RR: So an emerging theory about Alzheimer's disease, so a very early consequence of Alzheimer's disease is that you have decreased glucose uptake in the specific areas of the brain. So there are a number of groups, including group at Burke that's exploring the idea that Alzheimer's is kind of diabetes to the brain, that you have a resistance of the brain to insulin in taking up glucose and utilizing it appropriately. So I think that's a ... and there are a number of treatments that you might use for diabetes that actually might ultimately be beneficial for Alzheimer's disease.

SW: Great. Next question, sir.

M: This has been an excellent session, but you only mentioned alcohol in passing. How bad is alcohol for the brain, and in what quantities?

SW: Thank you for that. Mm-hm.

JM: Well, again, you might get two different answers. There is actually quite good evidence that moderate

doses of alcohol are good for the heart, and in turn good for the brain. It's also an anxiolytic, so it can help with stress. Now, of course, higher doses of alcohol, I mean, very, very high doses of alcohol can actually cause degeneration of certain parts of the brain, but you've got to be really drinking a lot for that to happen. Interesting link with alcohol is to a receptor called the NMDA receptor, which is a receptor very important for forming memories, and so alcohol consumption beyond moderate consumption can disrupt memory through its interaction with that particular receptor. So it's, you know, moderation in everything.

SW: Yeah. Great ...

RR: Just to add to that, so alcohol distributes into membranes in the brain for reasons that John mentioned. The membranes are where the lipids, but there are lots of receptors there, so in toxic doses it has global effects. The other thing is it gets back to this issue of excessive alcohol is sometimes associated with malnutrition, particularly thiamine deficiency ...

JM: Right.

RR: ... and that can be bad for the brain.

SW: I'll say, too, I've turned(?) as an alcoholism

counselor. Aging and alcoholism, people who are aging process alcohol differently than people who are younger, and that sometimes alcohol can mask other functions in the body. So it can make a person look like they have dementia when they don't. I actually address that in the book, too. So thank you so much for your question. Yes, ma'am?

W: Good morning. I just want to say first thank you. It's been an excellent panel. But I'm still not clear on the difference between dementia and Alzheimer's.

SW: Perfect, thank you. Go ahead.

JM: There is no difference. Alzheimer's is the leading cause of dementia, but there are other causes of dementia. So dementia is a set of symptoms that you see in the person's behavior. And as we talked about earlier, there are many potential causes of it. Some are temporary and if treated can go away. So I would just say that Alzheimer's is the leading cause of dementia, but dementia is, in fact, what has gone wrong with the brain, and it results from the degeneration of certain brain circuits.

W: I'm sorry. Dementia is a symptom?

SW: Everyone who has Alzheimer's has dementia

...

JM: Right.

SW: ... but not everyone who has dementia has Alzheimer's.

W: (Inaudible) I'm totally confused.

RR: Exactly. See, it's this way. So here are all the people with dementia. Alzheimer's is within that circle, but dementia itself, it's the simple word for decreased cognitive function below a threshold that's considered ... that is defined, operationally defined as abnormal. And so not being able to speak, not being able to plan, not being able to remember, all of those are symptoms of dementia. But there are many reasons why those things can develop, and Alzheimer's is one of them.

SW: I hate to tell you this, we have time for one more question.

W: Oh, okay.

SW: I'm so sorry. Okay, go ahead, sir.

M: It's a short question. Is there an age that you reach and you haven't got it and you're safe from it? (Laughter)

SW: Great question!

M: Male and female?

SW: When are you in the clear?

(Applause/Laughter)

JM: That's a very ...

SW: Maybe it's who cares after that point.

(Laughter)

JM: There is actually a lot of data on that, and there is an age at which you're probably safe from early onset Alzheimer's disease. (Laughter) Early onset Alzheimer's disease would be in the 50s or 60s, and often has a genetic link, and it's more severe, and it progresses more rapidly. And if you get to ... you probably have a different age, but I would say 75 or 80 without Alzheimer's, you probably won't get it, or at least you won't get it in any dramatic fashion.

SW: Wow.

JM: Now, I would add to that that there are centenarians, people who live to be 100 without Alzheimer's who have very interesting brains. Their brains actually are cleaner of pathology than most people in their 70s and 80s. So, yeah, if you're 75 ... how old are you sir?

M: I'm not telling. (Laughter)

JM: I think you're fine.

M: Is it the same with men and women?

JM: Women have a higher risk of Alzheimer's than men.

M: High a higher ...

JM: And one of the enduring questions is is that related to menopause or not, and can hormone treatments soon after menopause protect against Alzheimer's onset later on? There are some data that suggest that it can, but it's very controversial.

SW: And did you have a response to that?

RR: John and I have agreed so much, I think it's only fitting that at the end we would completely disagree. (Laughter)

SW: Oh, you're going to leave us on a hard note. (Laughs)

W: I'm depressed now.

RR: Yeah. I'm sorry. But I think that the risk of Alzheimer's after ... actually up after 80 or 85 goes up to 1 in 2,

very, very common, and beyond 100, you know, 95, 100, then it starts to taper off, probably because you're protected from other things.

JM: (Inaudible)

RR: I think that this is the ... as we talked about before, the health cliff that we're looking at because the population is aging. We're going to see an increase in the incidence of Alzheimer's if we don't stop it. So remember to call your politicians. (Laughter)

SW: Very good. That's a great way to end it.

M: Thank you.

SW: So I would like to say thank you ... I'm so, so sorry ...

(Overlapping Voices/Inaudible)

SW: I need guidance here from the Dana folks.

M: Is there a way of identifying positively whether someone has dementia or not?

JM: Well, the neuropsych assessment. I mean, if a person is demented, it's fairly easy for a physician to determine that. What's much more difficult is to determine the early cognitive

decline that might lead to dementia. That is much more difficult. As you pointed out ...

M: So there is none.

RR: No, no, no. If you see, there are many trained neuropsychologists who perform tests that usually take several hours, and after those tests in consultation with your doctor, they can tell whether you have dementia or not.

M: Right. Right. Thank you.

RR: Even early dementia.

SW: All right, we've been asked to take two more questions. Just two more, I'm sorry, and then we've got to cut it. Go ahead, sir.

M: I was under the impression that stressful situations are bad for you, and you said there was good stress and bad stress. Give me an example of good stress, please.

SW: Good stress.

JM: Great question. Great question. Good stress, in a sentence, good stress is stress that you were able to respond to successfully. So you felt stressed, but you were able to do something that relieved that stress and achieved your goal.

That would be what we refer to as good stress. Bad stress, and it's usually more chronic, are stressful conditions that are overwhelming, that no matter how you respond, you can't relieve the stressful condition, and you can't solve the problem.

SW: Okay, and we're going to cut there. And then last question, sir.

M: I haven't heard anything about concussions. I know that particularly in the NFL and in college, in the NCAAs ...

RR: Yeah.

M: ... they're very concerned about concussions as in all other major sports.

RR: Right.

M: What does concussion have to do with either Alzheimer's ...

SW: Great question.

M: ... or with dementia?

SW: Go ahead.

JM: Yeah, this is a really good question.

RR: So, yeah, I'm sorry we didn't cover this.

SW: That's right.

RR: It’s a really important issue.

SW: Hang with us for just a minute, please. Okay, thank you.

RR: Traumatic brain injury, which is what concussion usually comes from, is a risk factor for Alzheimer's disease. There appears to be a convergence in the same things that cause the problems after a traumatic brain injury and that cause Alzheimer's. So traumatic brain injury causes an increase in this toxic A beta peptide in the brains that ultimately probably lowers your threshold for getting Alzheimer's disease.

JM: And when you look at these athletes, these football players, when you look at their brains, they have tangles, as plaques and tangles in Alzheimer's. They have tangles in all the same circuits that area effected by Alzheimer's, and they’re causing the dementia. Just as one comment, you know, I played sports, I played contact sports. I will be amazed if football ten years from now is the same as it is right now.

SW: Can you hang out five more minutes to answer the question? Okay, so for the people that were in line before, these two gentlemen are going to stay to answer your

questions. I want to say thank you to Dr. Morrison and Dr. Ratan.

(Applause)

JM: Thank you.

SW: Excellent, excellent information. Again, thank you to the Dana Alliance, AARP, MetLife Foundation, thank you so much for having us here today, and the Westchester County Office of Aging. Thank you so much.

(Background Conversation)

(END OF TAPE)