Important Alzheimer's Risk Factors via Imaging Transcript

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Introduction and Summit Welcome

Welcome to the Reverse Alzheimer's Summit. I'm your host, doctor Heather Sanderson, and I'm so excited to have doctor Rob Lufkin here today. He's a full professor at a leading medical school and chief of neurology at a large medical network in Southern California.

In addition to being a practicing physician, he is author of over 200 peer reviewed scientific papers, 32 book chapters, and 13 books that are available in six languages.

Doctor Lufkin is good at getting the word out. He is also hosting a Prevention and Alzheimer's Prevention Summit, and so he and I share a lot of the same passions and, you know, goals for making Alzheimer's a rare disease.

Doctor Lufkin, thank you so much for taking the time to join us today. Oh, it's great to be here, Heather. I'm really excited about participating in your summit, and I can't wait to hear the other speakers too.

I'm really looking forward to it. Thank you. And thank you also. Doctor Lufkin and I are collaborating on some science and research that we're both in Southern California, and so we feel very, very fortunate to be able to send some of our study participants up to get imaging from him.

So he really is on the cutting edge of the research and science around getting the best imaging for Alzheimer's patients and dementia patients. So I want to dive right in.

So imaging is one part of our our workup in an Alzheimer's patient because we can see not only the brain but other anatomy through the pictures that we take as they see it.

Pictures tell us how a picture says a thousand words. And so I want to understand more about what imaging can and can't do. Can we rule Alzheimer's in or out based on a picture of the brain?

Okay. Yeah, that's a very, very good question. Because any time we we do any imaging study and my background is, as you mentioned, I'm a neuro radiologist.

So I specialize in imaging.

Why Brain Imaging Matters in Cognitive Decline

And that's what I do all day. But any time we, do an imaging study for a patient, it's important to consider the question and why we're doing it. So, for example, a patient with who comes in with new cognitive impairment.

And we're trying to diagnose what might be the cause of that. There are a number of conditions that, are rapidly treatable. Some are even emergencies that can cause cognitive impairment.

So the very first thing with a patient with cognitive impairment is to do an imaging study that will exclude immediately treatable causes of, dementia and cognitive impairment.

So, that can either be a CT scan or an MRI scan. Either one of those allows us to look at the brain and, find treatable things like, if the patient was involved in an accident, they may have, bleed in the brain, something called a hematoma, where blood accumulates and pushes on the brain gradually.

And that can, with the increased pressure, will cause cognitive impairment that will occur over, over a short period of time. But that's something that can be treated with a with a drill hole in the brain by a neurosurgeon.

And, and the patient's completely resolved. Other causes of cognitive impairment in the brain also can be recognize things like, brain tumors, like a glioblastoma or meningioma.

These grow more slowly and the cognitive impairment can come on over a much more gradual period. But again, these are things that can be addressed, with surgery or other types of treatment.

And the, the treating the tumor will in most cases treat the cognitive impairment as well. So first thing we want to do is exclude all those immediately treatable conditions.

Then once we've done that, then the next thing is to look at the, look at the brain and look at the other causes of dementia that may not be immediately treatable, but it's important to recognize them because they may be slightly different than Alzheimer's disease.

So the the types of long term treatment or lifestyle modifications that we make for them may be slightly different. So when we are talking about Alzheimer's, that one of the things that we've talked a lot of the other summit, interviewees about is that it's not always one thing.

And oxygen, especially at night, airway is a really, really big piece of, one of the big contributors to cognitive decline. And so you have shared with me that you can actually see when you do these studies, you can actually see part of the airway and get a lot of great information about that as well.

Can you, can you speak to how you're doing that? Sure. Absolutely. And that's one of the very exciting things about Alzheimer's disease, because, you know, for many years, there was the amyloid hypothesis for Alzheimer's disease.

And, and still many investigators are looking for a single drug that will somehow work on that. There's now growing and very compelling evidence that, Alzheimer's disease may be based on, I have a multifactorial origin.

Things like it can involve airway problems that can involve insulin resistance, inflammation, metabolic syndrome, trauma history, and as well as toxins, which I'm sure your other speakers have been, have been addressing.

But to the point about imaging studies with with an MRI scan of the brain, we're able not only to look at, images of the brain itself and identify specific biomarkers for Alzheimer's disease that we can talk about.

Alzheimer's Biomarkers Visible on MRI

But as you as you asked about, we can also see other areas on that image of the brain, which covers essentially from the neck up through the top of the head, which includes the brain.

But we also get a view to your point of the airway. So, we can look for signs anatomically that would predispose for obstructive sleep apnea, which, you know, sleep disorders are a huge risk factor for Alzheimer's disease.

And and that can be done as part of the the Misr imaging of the Alzheimer's, of the brain Alzheimer's study. So I want to go into that. You mentioned other biomarkers of Alzheimer's that would be readily visible on these pictures that you're getting.

What are they? Okay, well, the the classic, biomarker for Alzheimer's disease is, atrophy in a part of the brain that is the basis for memory, and that is the hippocampus and and the hippocampus.

There's a bilateral structure and studies have shown that, in patients with Alzheimer's disease, it's not all of them, but a significant portion of them will show hippocampal atrophy or loss atrophy, meaning loss of volume of that structure.

And the interesting thing about it that that really surprised a lot of people when this was just discovered a few years ago, was that hippocampal atrophy can happen before any sign of cognitive impairment, which is the usual, usual

thing that that brings a patient to the doctor thinking they have Alzheimer's disease.

The this hippocampal atrophy can occur 10 or 20 years before the onset of cognitive impairment. This creates a great window for therapy, especially these lifestyle interventions and other things that can be done because, research has shown that the earlier these things are started, these therapeutic interventions, the more successful they are.

So if you can wait before you have any cognitive impairment at all and, and begin these things, these treatments, then you can, you can have much better results than if you wait until the brain is actually damaged and, and, and the memory occurs.

So, the hippocampal atrophy is the key finding. And many people are now recommending in patients who have risk factors for Alzheimer's disease, such as, the ApoE e4 carrier stage in the gene, or else if they have a family history of Alzheimer's disease, that it's worthwhile going back 20 years from the date of the onset of your Alzheimer's disease in your in your relative, for example, you know, God forbid, if you're if your parent had Alzheimer's disease and it arrived it it began at age 70, then it's probably worthwhile at age 50 to begin thinking about evaluating risk factors in yourself for possible Alzheimer's disease, because we're already seeing the changes starting to occur.

And that's when ideally, you would start the lifestyle management and the treatment to make it better. So so hippocampal atrophy is the is really the the key finding for Alzheimer's disease.

But there are a bunch of other biomarkers that we can see on the scan. If you'd like I can I can talk about those if you want. Sure. Yeah. Yeah. So in addition to the hippocampal atrophy we can also see evidence of vascular disease in the brain which Alzheimer's disease and vascular causes of dementia are the two main causes of dementia.

So there there are classic findings of vascular changes in the brain that can be recognized on an MRI scan. And quite honestly, vascular dementia overlaps with Alzheimer's disease.

So it's it's not a clear finding there. But you can you can find the vascular disease signature as well. Going outside of the brain, in addition to the hippocampus and the vascular structures, we can look at the airway, as we already mentioned, looking for signs of obstructive sleep apnea.

And that can then indicate the patient might benefit from a sleep study or, or, looking at their blood oxygenation, while they sleep. And doing that. Other things we can look at are, the sinuses.

It's interesting. Chronic sinus disease is an independent risk factor for Alzheimer's dementia and treating patients. Sinus disease has have improved the cognitive impairments in these patients.

It's it's interesting to think that the the sinuses are separate from the brain. Yet they can have the effects. But if we think about inflammation we think about some of these other factors that we know now cause Alzheimer's disease, it it all sort of makes sense.

So the sinuses can be beautifully evaluated on the imaging study. And it's important to note that patients can have sinus disease visible on the EMR without symptoms.

So these can it can be asymptomatic. And it's just there. And possibly contributing to their Alzheimer's disease. But they're not even aware of it because they don't have symptoms of sinusitis.

When we're looking at the sinuses on the MRI scan, another thing that we can look at specifically is there are specific hallmarks of fungal sinus disease, which is a particularly troublesome, biomarker for Alzheimer's.

Fungal infections at various locations in the body. Can can contribute to risk for Alzheimer's disease. So there are specific imaging findings of the sinuses that indicate a fungal sinus infection.

And the EMR scan can pick that up. And like conventional chronic sinusitis, this fungal sinusitis may be clinically silent also. In other words, the patient may not be aware that they that they even have it.

So in addition to the sinuses and the brain structures, if we go down one step lower, the scan will also include the teeth, the the mandible, the, the maxilla, and and all the dentition.

And, as as we're learning now, inflammation in the teeth, interestingly, can predispose a patient to a risk for a heart attack, but also for Alzheimer's disease.

So you don't want to get Alzheimer's disease, brush your teeth every day. The, the the things on the scans that we can look at the markers for teeth is, we can see periodontal disease, we can see end of Donald disease that in some cases may be clinically silent, that the patient may not be aware of.

But, we can also detect abnormalities of the teeth and then, you know, suggests that they, they might benefit from a, from a thorough, dental exam as well on the, on the scans, the the MRI scan is also very sensitive to metal.

It just detects it it distorts the magnetic field when the images are obtained. So metal anywhere in the head and neck area will show up on the scan.

Practical Benefits, Costs, and Scan Limitations

So patient may have had surgery in the past, and they may not even remember that metal was put in or they may not know it, or they may have, you know, dental work with with metal embedded.

And while a good a good dentist should be able to see it with the EMR, we can we can immediately detect metal and at least raise the possibility that that metal is there.

And and some researcher, some researchers are even advocating removal of certain types of metals that may contribute more to Alzheimer's disease. In addition to, the sinuses, the brain, the airway and the teeth.

The other area we can look is, just the overall facial structure of the bones in the skull. Trauma is a risk factor and independent risk factor for Alzheimer's disease.

And it may not be it may not be immediate trauma that the patient even remember said may have been something that occurred ten, 20 years ago. We're even seeing, you know, a career in high school football with relatively minor head injuries.

Even no concussions or loss of consciousness may contribute and and is a known risk factor for dementia later on in life. So the the imaging studies in some cases will provide evidence of, of trauma such as, a nasal bone fracture or facial fractures that the patient forgotten or, you know, doesn't remember any more that they occurred.

And so it can basically begin the conversation with the patient about about the history of trauma. And, and also if, depending on what their lifestyle is or their current employment, they may want to be counseled about, you know, not being in a position where they have continued head trauma, if they're at a risk for Alzheimer's disease or have other biomarkers.

So as our listeners, and yours may imagine, when I heard that we could get all of this from one image, I was ecstatic. I mean, this changes the game because so many patients, I'll ask a little bit about, you know, their dental history or did you ever hit your head?

And as you mentioned so many times, these things are not showing up clinically. Patients will not complain of a toothache or even remember that they hit their head.

And so they're not they're not always making the connections that can often be there. And being able to rule these and rule these out, or at least consider them is really, really, really important.

So I of course, I was thrilled when you told me that you do this. And my next question was, well, can everyone get this? Do they need contrast? You know, how long does it take?

What if they're claustrophobic and they can't sit in the MRI machine? How long do they need to be in there for? You know, what are some of these these barriers to entry.

Sure. And it doesn't cover it. I can certainly speak from a clinician standpoint that I've done neuro, you know, volume metrics. And the information I get is very simply, how big are the different, regions of the brain, including the, the campus.

But it really doesn't go beyond that. It's not looking at airway, which we know is so important. It's not looking at bones. It's not looking at the sinuses as you've mentioned.

So you are unique in in terms of radiology, as a radiologist, that you are considering all of these things. So I wanted listeners to know how they can access, you know, your interpretation of these pictures.

Yeah. Just just to be clear, yeah, all the information is on the scan. But many radiologists, based on their training, if they're if they're not focusing on Alzheimer's disease or don't have an interest in it necessarily, the average radiologist doesn't pay attention to the airway and, and may not may not make an effort to comment on some of the other areas that I mentioned.

So, I, I'm, very excited about Alzheimer's disease and the possibility of how this can help people. Maybe I'll, later on, I'll give you some information about a website that we're setting up that they could send us, the scans for that.

We can put that in in the show notes if you want. Specifically, the questions you asked is very good about, what are the barriers for these types of studies and everything because, the great thing about Mr.

Magnetic Resonance, other than things like CT scans, computed tomography or Pet scanning, which have been used and are used for Alzheimer's disease. The problem with these is those two types in particular, they when they're expensive and they also, use radiation, you know, as, as your listeners probably may know, any exposure to radiation, X radiation from a CT scan or Pet scan raises the possibility of developing cancers later on in your life.

So it limits the ability to do repeat scans for follow up. And the great thing about magnetic resonance is there's no x rays, there's no ionizing radiation, so there's no known harm to the patient.

The other thing that, we're working on is coming up with a tailored Mr. Scan that is, relatively inexpensive, that omits a lot of the unnecessary things, and that's unnecessary charges so that it would be something that would be affordable, that the patient could actually, have done more than once and even as a follow up to monitor their treatment, because, amazingly, even things like brain atrophy in the hippocampus have has been shown to be reversible by lifestyle and other treatments in as short a time as six months.

So this would be a tremendous, driving factor for the patient to be able to see. I'm actually fixing my brain and fixing the part of the brain that controls memory.

And I can see it on this follow up scan that I do in maybe a year or something like that. And of course, the airway and the sinuses would also you could see the improvement there.

So, the, the great thing about magnetic resonance is that it there's no radiation with it. We're keeping the costs down very low with this, with this, limited, very limited scan.

And then also there is no injection. You asked about contrast material, which, usually involves putting a catheter or a needle into a vein and then injecting things.

We don't do any of that with the Mr. scan. So it's it's completely noninvasive. I even, having my 12 year old daughter doing this to look at her brain for a science project, but so it's, it's an ideal imaging study for this, for this

type of evaluation.

Yeah. When you mention that somebody should be looking at this 20 years before the onset of symptoms, that's exactly what I started wondering. Well, if if we're measuring hippocampal volume, that area of the brain that's so associated with memory, and if we measure it when someone's already got symptoms, how do we know if maybe they're not just there?

They maybe were born with a little bit smaller hippocampus on the, you know, the curve, the standard deviation. And so what if that's part of what's going on if we don't have a baseline from before when they had symptoms, then we don't really know what's caused it.

So yeah, I'm just curious, like if in an ideal world, how often would somebody who has risk factors be getting one of these images? Okay, that's a very, very good question.

Tracking Risk Over Time and Research Questions

And this this technology is literally just developed in the last ten years or so. It's involving, large amounts of computing power. And actually it involves deep learning and artificial intelligence with the, you know, convolutional neural networks that everyone is talking about.

But to your point about, how do we know if the hippocampal volume is not some preexisting thing or how do we know it's even abnormal? Well, the first thing that is done when these these volumes, these brain volumes are, calculated.

So patient gets an MRI scan of their head and the first thing you do is we measure the size of the head on the scan. And I may have a big head, but. And my hippocampus will be big, or I may have a very small head, and my hippocampus will be small. So we need to account for that.

So the first thing we do is we we take the size of there. We either shrink it or we enlarge it to a normal, a normal atlas, sort of a normal volume. But that's that's really not enough because the hippocampus changes in size with aging.

It gets bigger as you younger, and then it gets smaller as you get older. And those changes actually are different in men and women. So both of those things have to be taken into account.

So in addition to the shrinking the or expanding the head to the normal atlas, then the next thing we do is we we map it on to an age matched and gender matched, normal atlas for that person.

So we look at, you know, 50 year old man and we, we compare it with that. So that does that that does the comparison. But your point about follow up scans is very important because, if I do one scan and my hippocampal volume is let's say it's low normal, it's still normal, but it's, it's low normal.

I could still be at risk for Alzheimer's disease because six months ago or a year ago, it may have been high normal, but from that single study it's still within the normal range.

So the real advantage and many investigators are advocating this is it's not a single scan, but it's a change over time. So do a repeat scan in one year.

And I could be low normal. The first scan and then the second scan I could be very low normal but still normal. But the fact that it has a downward trajectory is very concerning.

And that in effect is a positive biomarker for Alzheimer's disease. So, having at least two scans is valuable to assess the essentially the, the velocity of the change rather than a static point in time rate.

That change over time is what's more important than even maybe that number itself. And that that number is

formalized, you know, so that we know what is normal and what's not in the age your sex.

And hopefully compared to previous, because it does sound like a baseline, would be very, very helpful, particularly if you have high genetic risk or other factors.

And it's it's been shown that, people who are ApoE, e4, homozygous, which means they have both alleles or ApoE e4, they, they genetically have smaller hippocampal volumes than do normal people.

And we're still trying to we're still gathering data and understanding, if they increase their hippocampal volume, what the does the risk and, and and as you might expect the homozygous ApoE4 is have a smaller volume.

The heterozygous with one ApoE4 and 188.3 or 2, have a have a slightly larger hippocampal volume, but work is being done on this and with more and more experience will hopefully be able to understand this better and make better recommendations for people trying to manage their risk.

That's fascinating. Yes, I'm excited to collaborate. And hopefully it leads me to the question. I'm curious if you could design any study. You know, we're working on some research together.

If you could design any study and answer any question, there is, you know, there's no constraints financially or otherwise. You have all the participants. You want, and all of the money you need to finish it.

Well, what question would you ask? What would what is the burning question in your mind that we don't know about the subject yet? Well, I think the the real exciting question for me is the one that many investigators are beginning to address like, like Dale Bredesen and the work that you're doing and in your clinic.

And that is how these, how these long term risk factors, can contribute to Alzheimer's disease and how, how we can how we can, manage the risk factors through lifestyle changes and other other management and thus prevent developing Alzheimer's disease later on.

And the tools that I would offer for that would be, imaging to take a look at the brain and the other areas and just do it as inexpensively as possible to make it affordable.

And and of course, with no radiation. I think one other question you asked about, insurance, payment for these, and this varies according to insurance companies and varies according to different things.

But my my general experience is if the patient has a diagnosis of cognitive impairment or dementia, significant clinical finding there that most insurance companies and Medicare will pay for an imaging study.

At least one imaging study, like we talked about earlier, to rule out other immediately treatable causes of dementia. It's been my experience. They won't pay necessarily for follow up ones unless the patient changes, unless something happens that they, they really, change their, their pattern that way.

Hope, Prevention, and Closing Remarks

But, and then as far as prevention patients who don't have, any cognitive impairment yet, but let's say they have a family member who developed it or they're able for positive.

It's been my experience that the insurance companies won't cover, imaging studies for this, which is which is really sad because just from a financial perspective, Alzheimer's disease is incredibly expensive in the health care system.

I mean, just aside from the cost to the families and everything, but the financial costs are very high. You'd be much better off beginning lifestyle management and changes early on and preventing Alzheimer's disease than waiting till people actually have cognitive impairment, which, as we've said, is really a late finding in Alzheimer's disease.

Although it's for most people, the first finding that they that they detect to acknowledge they even have it. It really is so heartbreaking that I think you and I now are, we feel strongly that this is preventable, that there are interventions you can take.

We can we can get the information early enough that we can prevent Alzheimer's and even reverse it. We're seeing lots of that in my clinic. And I think we want to share that information.

And what you were doing creates so much hope. And so you seen that picture I think is really, really, really valuable. We can talk about lifestyle changes and we can talk about the genetics.

And I think they they tend to be a little nebulous for people. It's not as it's not is tangible as seeing a picture of their brain and going, wow, that is shrinking.

And I've got to do something about it. So I think in a, in a very real way, you give people not only the motivation they need, but also the hope that these things can change that you've watched the images change, that you've watched the symptoms change, that you've seen people do this successfully, and that there is a way to avoid this heartbreak.

Like you described. You know, it's Alzheimer's is so destructive financially, but also it robs as of this generation that has so much wisdom and so much to offer us.

It's almost in my mind it's the squandered resource, right? The the height of their wisdom and experience. Our elders are being removed from society because of dementia.

That is predictable. Yes. Thank you for doing the work that you're doing. Well, thanks. It's it's such an exciting area. And the changes that are happening now with the possibility of treatment, which wasn't there a few years ago, the possibility of prevention that was there a few years ago.

The work you're doing in your clinic, the work that researchers like Dale Edison and others are doing, it's it's really revolutionary. And and it's so exciting to be involved with this and to try and get the message out to help as many people as we can.

Yeah, very, very hopeful and exciting time. Thank you again, Doctor Rifkin. It's just an absolute pleasure not only to get to have these conversations with you, to get to share them, but also to be collaborating in other ways to advance this field and give more and more families hope and an answer so that they don't have to suffer.

Great. Well, thanks a lot, Heather, and I'm really looking forward to your summit and hearing the other speakers. It's going to be very exciting. Can you give our listeners, you have Pro-health, is your your business, is there a website or other places where they can find out more information about what?

Yeah, if I could, if I could pass it to you afterwards in the show notes, if that's possible. We have a website that they can go to and get more information.

We're just putting it together now. Perfect. Wonderful. We'll have that in the show. Notes.