The Cellular Cleanup That Could Change How You Age Transcript

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Introduction to Autophagy

Hello, my name is Renee Fitton. I am a longevity dietitian and the vice president of growth at El Nutra, the makers of prolon. I am here to talk today about Authophagy.

For those of you who are a little from. I hope that I'm able to add a little bit more color to this incredible innate mechanism that lives within us and is able to do some pretty powerful stuff.

And for those of you who are not familiar, we are going to start at the very beginning and give you a little insight into what this is. And this is really timely because there have been some incredible advancements in the science and understanding of this process that is happening within our bodies.

You know, in the very recent past. So we are going to dig into that. And so, without further ado, I'd love to share my screen with you all and share a few slides.

So let's go here. Here we have it. So let's go ahead and get kicked off. Right now your cells are eating themselves. That doesn't necessarily sound like a good thing, but let me tell you it is.

It is one of the most incredible things and most important things that your body can do. And it's essentially a clean up system. So. What we have seen over the last several decades is this advancement in our understanding of how ourselves clean themselves from the inside out.

In 1963, Christian de dove coined the term autophagy, which we will discuss in a moment. But essentially it just means to self eat.

How Autophagy Works in Cells

In the 90s, Doctor Yoshinori Shumi identified how our body is able to run this incredible clean up process in yeast. In 2016, he finally won the Nobel Prize in Physiology and Medicine for the.

This discovery of this gene identification. And now, just last year, we were able to find the measurement of autophagy in humans for the very first time through a randomized clinical trial showing how diet specifically can impact this in humans.

And we'll come back to that in a moment. So what we're going to talk about today is what autophagy is, why it matters how it switched on, how to activate it.

And we'll dig into that first study that really was able to show in humans autophagy through nutrition. So what is it. I mentioned this a little earlier with the Christian to do definition and naming of autophagy, which is to self eat auto is self faggy or faggy is to eat.

And so together it is self eating. Now again this is incredibly positive. It is a beautiful scientific process that allows our cells to take out the trash.

So this is kind of like honestly a whole recycling plant that is happening within your cells. And importantly, our whole body is made up of cells. There is not a single part of who we are.

That is not made up of cells. And so you can imagine that as we age these cells, they kind of start breaking down. Some of the components don't work as well as they used to.

And it's really important that when that starts to happen. Not only do we replace it with newer and healthier

components that aren't broken, but also take the parts that are not functioning as well, consume them and get rid of them and ideally recycle them.

And that is exactly what's happening here in a. What happens is, is our body in its infinite wisdom goes in and it finds the components of our cells that are no longer working as well as they should.

And they give it like a little stamp, a little tag that says, this guy's got to be taken out to trash. From there they go and collect it. They wrap it through something that we call the a tall, fat gazelle.

So a tough egg is that is the kind of envelope or the trash bag, if you will, that we put around the components that need to be thrown away. Then in that little vessel, they transport it to the lysosome.

That is where we're able to actually start breaking things down. So inside the lysosome, we are taking all of the components and we're breaking them into subcomponents.

And then all of those pieces of this potentially protein or compound or, you know, cellular component that no longer is working. That was all made up of all these wonderful building blocks that we can go reuse again.

And so that's what we do. We go and we recycle all of those subcomponents so we can build up new machinery that is working better than it ever did before.

So that is kind of the whole process of autophagy.

Why Autophagy Matters for Aging

And as you can see really important so that our cells can be clean so that they can function at their optimal capacity. Now really quickly I'll mention that there are a bunch of different types of autophagy that happen within our body when we talk about autophagy.

And when you hear a most people are talking about macro autophagy. That is when our cells are going and they're taking whole chunks that are broken down of the cell.

And that can be misfolded proteins or broken down cellular components or organelles. That is macro autophagy. And this is like bulk cleanup. Then we have another very selective cleanup and known as mitos.

And this one has gotten a lot of press these days. It's really starting to be quite popular because our mitochondria are specifically being cleaned. When we talk about mitotic and our mitochondria are the energy kind of centers of ourselves.

And so when we can have our mitochondria nice and clean and optimally functioning because of that cleanup happening or that might be happening, then we are able to again, just be able to power all of these wonderful reactions and processes in our cells that then power all of the wonderful things that we can do as human beings. So then there's the last one and is chaperon mediated.

That's super targeted. It's really very specific components that are being engulfed and then broken down in that lysosome. So why does this matter? Well, it is, you know, I think pretty evident that it's nice to have a clean cell that's not accumulating a bunch of waste when we've accumulated a bunch of waste.

The cell itself can no longer function as well. And also that waste, it also can create damage elsewhere in the cell. So it's not even just kind of taking up space.

It can also be damaging and in impact some of the other cellular components, almost like a virus in that way. So in fact, in 2023, they updated the hallmarks of aging, which is a kind of the areas that scientists recognize as some of the biggest factors that cause us to age more rapidly.

And macro autophagy being disabled. So the poor functioning of autophagy was one of the new hallmarks of aging. And so this is really critical, as you can see in ages and healthy aging and ensuring we can optimize our longevity.

And that's because healthy autophagy is able to clean out our dead damage proteins and organelles. It keeps our mitochondria those power sources in our cells working well.

It can help our immune system. And it can also keep our inflammation in check. And you've probably heard inflammation is not so great. It impacts our whole system.

And it really is very damaging to so many, not just our organs, but even, you know, pretty much every single component of our cells, including our vascular, our muscle, our I mean, you name it, inflammation is really having a very dangerous and damaging impact on our bodies.

So if autophagy can help across all of these places is really making an impactful difference to our health. So when that damage accumulates, where do we see challenges again, as given our cells are really across our whole body.

What Turns Autophagy On and Off

We see it all over the place, but it can impact our brain and increase risk of neurodegenerative disease, things like Alzheimer's, etc.. Metabolism so linked to insulin resistance and fatty liver, which are of course leading causes of type two diabetes, we see damage to the immune system which can be associated with autoimmune conditions or chronic inflammation and then cancer.

Of course, our cellular damage and cellular malfunctioning is the root cause of cancer. And therefore or in fact, the definition maybe of cancer is a better way to put it.

And so, as you can imagine, poor Lee functioning autophagy can lead to all of these things. So these are certainly not a diagnosis or a guarantee. But it is what we are seeing as associated from the research that we've been seeing come out to date.

Now is a rhythm and not a switch that you can just turn on and off. But it is really interesting to see how our body is able to kind of increase or decrease or kind of lean in or lean out of it.

And really what we see is it's kind of a balance. You're not really you're ether focusing on the cleanup, which is that a being turned on or you're focusing on building which is off and nutrients in.

So that's really what your body is balancing between when we are fed, when we are eating nutrients, our body is using those nutrients to build and grow.

And when we do not have very many nutrients present, our body is going to shift into repair, clean up, rejuvenation, and a is going to increase. So you are really juggling between those two back and forth.

And importantly, we do need both of these right. So we can't just be in a all of the time and always focusing on cleanup. We eventually have nothing left to clean, and our body would start breaking down things that it doesn't need to.

But we can't always be in building phase because then the trash will accumulate. So really critical that we kind of live in both phases and cycle between the two.

So it is worth noting that especially in midlife, and this is both for men and for women, I should say, even though this slide really does call out women's health in midlife and through aging in general, our body will increase in its cumulation of waste.

Autophagy also declines in its efficiency and its effectiveness as we age. And so that is really kind of like a double whammy that's happening around that midlife time, because our bodies aren't functioning as well as they should

and could.

There's rising insulin resistance. There's metabolic shifts, there's increase in weight. There's low grade inflammation. This is just the beginning of the list.

As we age, these things become more difficult to resolve. And we also see that a toffee isn't as easily turned on. And it is oftentimes not working as well as we age.

So that combination is certainly something that we have to push back against. The good news is, is that we do have some great solutions to really kind of pull the throttle on autophagy even as we age, which then again supports the gradual decline.

And as we see with age in the function of our bodies and ourselves. So how is a G turned on? Well, your cells are always listening. They are always looking to see.

Are we at a place where nutrients are low enough? Where we have not enough food, that we should stop focusing on this building phase and start focusing on that cleanup phase?

They are looking for actually very specific nutrients in specific amounts for the alarm bells to be raised. And so when we are eating, we will see an increase in insulin.

We'll see an increase in amino acids. We'll see an increase in sugar blood sugar glucose. Right. Well and that will increase something called IGF one as well.

So all of those signals, all of those going up when we eat food we'll turn on something called enter. Mature is something that we call a nutrient sensing pathway.

But I like to think of it as the alarm bell as this, the sounder of the alarms saying, hey guys, there's food here and we should grow. And so when M Tor turns on and it sounds the alarm, autophagy turns off.

Now the opposite is true. When we are in the fasting signal phase when insulin is down, amino acids are down, IgG4 one is down, blood sugar is down, and ketones go up.

And all of those things kind of happening simultaneously will turn off mTOR and turn on Ampk. And that combination will turn a toffee G on. So this is, again, kind of that balancing act that is happening in the body that is happening based off of opposing things that could happen in the body.

But depending on whether or not there is the nutrients that are activating these pathways or not.

Fasting, Ketosis, and Timing

So here's a quick myth check. With the way that we described it, we were explaining and seeing that autophagy really turns on when our nutrient sensing pathways, or the alarm bells that sense nutrients are not being turned, are not being flagged, the alarms are not going off, there is no food present.

So the real question then becomes, okay, so when does that alarm sound? How long do nutrients have to be gone for the alarm bells to sound? And what we do know is that ketosis generally starts to turn on.

Or I should say when our body has run out of sugar, it switches to ketosis, meaning it will start using fat for fuel, fat for energy. And when it does that, it creates something called ketones and our body can use those for energy.

Now that process usually starts around the 12 hour mark and starts gradually increasing. And you know, given that though, that's kind of one of those hallmarks for the repair phase, what we a lot of people make the assumption that a toffee G is going to start around that same time.

But what we are really seeing is that it seems to take a little bit longer than that. And generally we see that autophagy is activated closer to the three day mark.

And so while intermittent fasting and fasting for, you know, 12 to 16 hours can have some benefits, especially for that ketosis and that fat burning that is likely being activated at least in some amount around that time, we don't really see that statistically significant boost in a toffee until around the 72 hour mark.

So that's pretty interesting. Now, that being said there, I do throw in a couple of caveats here, which is a lot of the research out there around autophagy, especially in humans, are coming from animal and cell studies.

And it's it can be tricky to measure autophagy in living cells. And so until recently, there's just not really been a lot of trials on a G in humans. But note that says until recently.

So based off of the strength of the human evidence, how is it turned on? Well, we know without a doubt that periodic fasting, meaning fasting for a certain amount of time, of typically three days or more, or fasting mimicking which we'll talk about in a moment, is able to achieve some very statistically significant autophagy.

And this has now been shown in humans. So importantly, yes, fasting for three plus days, certainly with water only. But don't worry, I'm going to share a solution that doesn't require only water or water, only fasting.

There is other answers here where we can add in food, and your body will still believe that you're in a fasted state and still turn on a while you eat.

And so that's really the magic of the fasting mimicking protocol. Now, there is also some research that suggests that very strenuous exercise can for a period, a short period of time, increase autophagy.

The research around time restricting eating is much smaller, as we showed, where there hasn't really been any research in a topic in humans with time restricted eating.

And so it's hard to say that you would actually activate autophagy with any certainty, or certainly any notable or statistically significant level without extending that fast for several days.

And then, of course, sleep and circadian rhythms can. Your body does a lot of really wonderful repair as you sleep. But this is kind of what I would call baseline autophagy or just kind of baseline cleanup crew.

What we really want when we're doing this deep cleanup this spring cleaning is notable increases in a G. Not just like bare bones baseline.

Fasting-Mimicking Diet and Human Trial

We need to give our body time to really increase and activate and turn on autophagy periodically, right. So that our body can do that deep spring cleaning.

So there are also some interesting compounds that have been studied around that increase or kind of pulling of the throttle of a your life. And a has probably the most researched date.

It is. You know, it's interesting there are some human trials that have shown some improvement in some markers of autophagy, but it's still very, very early and hard to say the extent to which something like that could support autophagy as sperm is another one.

Even less research. And then coffee, green tea. Or is there very, very, very minimal research there. But all interesting in terms of supporting autophagy increase.

But at the end of the day, none of these are going to replace or beat out what you're eating. And that especially when we're doing these fasting, mimicking and fasting protocols of three plus days, that's where we move the

needle.

That's where we see the true, you know, the true benefits of what our body has been able to achieve through evolution. Now, I mentioned I was going to come back to the fasting mimicking diet, which we know is the most well researched way to really pull the throttle on atop the fasting mimicking diet is a five day plant based food and nutrition program where you are getting breakfast, lunch, dinner, snacks every day for five days, but your body will believe that it is in a fasted water only state, and for that reason, turn on which will go into the study in a moment.

But it's really incredible. Is backed by about 25 years of research that started at USC with Doctor Walter Longo, and it has really taken this science to the next level in really understanding the pathways that are within our body to turn on or off autophagy and to turn on or off that fed versus fasted state so that it goes into this fasted state.

It's figured out the pathways, it's figured out what turns on and off the pathways, which nutrients in which amount, and then kind of worked our way backwards into the very specific nutrients, foods, ingredients that would need to come together to produce the results that we're looking for.

So the combination then becomes lower protein. That's actually one of the biggest ways to kick yourself out of the fast is to eat high protein, because our body uses that as a very notable and obvious growth signal.

And remember, we want to live in the repair mode. So we want low protein, low sugar, high fiber, high plant based fats and high micronutrients. And that's really just for the nourishment component, the added ease and safety of the protocol. Now, I've been talking about and hinting to the most recent human clinical trial that was done measuring autophagic flux in humans through diet.

So we'll talk a little bit about what the heck that mouthful of words means in just a second. But just to look at the study design, what the researchers did was they asked some healthy adults to either do the prolonged five day fasting mimicking kit or follow a control just regular diet.

So one or the other, they did this out of Cedars-Sinai Medical Center and the UT Health in San Antonio, in partnership with doctor and L Neutra. And they measured all of these incredible metrics that give us a sense of improvements in health, but also measures of G at baseline.

So before they started the five day nutrition or the control diet on day four, on day six, and then on day eight, and what they were measuring specifically when they were looking at autophagy is they were looking for those kind of trash bags, right, that we were talking about before the autophagosome.

Right. And so we were when we see them going through the cells, they're typically just like kind of like chugging along. And if it is happening faster, we're going to see more of them kind of going through.

And so think about this as like cars on the highway, those are going down the highway. And they're kind of like chugging along. And then what we do and we're trying to measure the flux, how quickly it's happening.

We actually block the highway with something called chloroquine. When that is given, it blocks the highway. And all of those cars or those autophagosome are piling up, and then we're able to count them all.

And so that is how we assess how quickly autophagy is going through and how quickly we are seeing the process of a in the cell. I hope that that analogy makes sense.

I know it's it can be a little bit confusing, but it is the most incredible way to measure autophagy as we have it today. And we can do so in humans. And with this, in this study, where we compared the prolonged five day fasting mimicking protocol to a control diet, so regular eating, we were able to see that the fasting mimicking protocol decreased body weight, improved fasting glucose, improved insulin, improved our insulin resistance and increased ketones, meaning that the individuals were in fact in a fasted state.

Now they. So we were able to see that by the end of the that sixth day, the body had shifted to from fed to repair.

And that means that we expected autophagy to be turned on.

And that's exactly what we saw. If you look at that red line that is prolongs impact on autophagy, the autophagic flux was dramatically higher on that V3, which is on that day six.

You can see notably statistically significantly higher upon completion. And then we also even see that upon completion of the trials, even when individuals were completing their fast and had resumed regular eating, we still saw a marginal increase in a G at that point.

Research Results and Health Benefits

So there was about a two times better improvement, or a two times better rate of autophagic flux happening at that day six mark. Now, what we can also see is that nutrition in general can improve autophagy in humans.

And so that's exactly what this study has shown. It's showing that fasting and fasting mimicking dramatically notably increases autophagy in humans. And also which nutrition can really turn it off.

Right. So that higher protein, higher sugar can turn it off. Now let me just qualify, because sometimes when I say high protein is bad for a G, people start getting a little concerned because we keep hearing that it's important to consume enough protein to support our muscles and our health and our immunity and all these other wonderful things.

And that is absolutely true. It is important to consume adequate protein. But when we are in these periodic longer fasts, we want to be lower in protein.

We are only doing this for about five days, maybe 3 to 4 times a year. That's it. So it should be not done all of the time, but periodically just so that we can get that clean up.

So it is important to note that yes, this was a pilot study. It's a smaller study. It's only using one five day cycle. So it wasn't done a multiple times.

We took all of that and did a shorter follow up. So the trial was done after the eighth day instead of, you know, seeing what happens, maybe on day 30 or at the end of a year.

What have you, the peripheral blood cells that were used to pull the markers to measure the autophagy were blood cells and not the rest of our body cells.

So that's something to be mindful of. You know, different levels of autophagy could have been happening in different areas. Perhaps fasting actually would have had an even bigger impact in other cells, or it could have had less.

So what we were looking at here was the blood cells. So that's the easiest one for us to be able to pull and measure from. But it is worth noting and it is a strong first signal but not the last.

And there are many more studies coming our way. We are certain this one was run in partnership with El Neutra, so it is worth noting that all of this, you know, means that there is so much more to come in the research, and I'm certainly very much looking forward to seeing that.

There is a lot of other research on fasting mimicking protocols. And this is really important because there are not just 1 or 2 more, which I'm going to call out a couple here, but there are now over 45 clinical trials that have been published showing the benefits of fasting, mimicking oftentimes really coming from the benefits of a.

Certainly not the only reason why these benefits are being seen, but many of those benefits are coming from that activation of a G. So we were able to see that in 2017, in a human trial with 100 adult, that there was the fasting mimicking diet was able to improve weight management, improved body composition.

So muscle was protected even though weight was lost. Improvements in blood pressure. Improvements in a lot of the markers that are associated with aging.

In fact, when we look at a study that was published in 2024. We also see a reversal in biological age of two and a half years. So an improvement in your biological age by two and a half years with just three cycles.

So that's once a month, five days for three months in a row. And then you see a two and a half year younger age on your biological score. That's pretty impressive.

Now taken together, we can really see that this is just really, again, still just scratching the surface when we look at the body of evidence that is now available.

If the 47 plus trials that are now available around passing mimicking, we really start seeing that picture that it all ties in together and that with the addition of just oftentimes 15 to 20 days a year, we can see some really outstanding benefits to that deep cellular cleanup that will kind of waterfall down to other benefits for our health.

Who Should Be Cautious and Final Takeaways

So fasting mimicking I mean, honestly, we generally I oftentimes will say it's all for almost everybody, whether you're a healthy individual or not. You can find some benefits here.

Healthy individuals might use this to optimize to prevent. And those who may have higher blood pressure cholesterol, triglycerides, blood sugar, prediabetes.

I mean, there are incredible ways that fasting mimicking can and has been leveraged to support in seeing improvements there. Now, it's really important that you do talk to your clinician first.

Of course, especially individuals who are pregnant or breastfeeding, have a history of disordered eating, have type one diabetes, or take glucose lowering medications, are underweight or frail, so very low muscle density or bone density and then manage a serious medical condition or take prescription medication.

All of those things should be absolutely discussed and cleared with your physician before proceeding with any sort of fasting, mimicking, or even fasting protocol.

And it you know, it's worth noting that, yes, fasting is an incredible tool. It is not. It doesn't need to be this test of willpower. It can be this enabler of our health and our longevity.

And it can be so much easier when we add in nutrition, and we add in meals throughout the day that are going to make it supported and safer and all around healthier in achieving those goals of a.

So really quick roundup here at is your built in renewal system. It declines with age. It responds to signals you control. So what you eat, when you eat, how you move and how you sleep, all of those things can impact autophagy, the biggest one in the most important and best studied is going to be when and what you eat.

So ideally, getting in these longer fasts of 3 to 5 days and even more, preferably with food through fasting, mimicking. And this has now, for the very first time, been shown in a randomized clinical trial in humans through diet using the fasting mimicking protocols.

So we are so grateful that you joined us to listen a little bit more about autophagy. I hope that you learned something new. And if you have any questions, please don't hesitate to reach out to me directly on any sort of social platforms.

LinkedIn, Instagram. I'm on a ball, and if you are interested in learning more about longevity science with Prolon, please join me on the Almost Forever podcast, which I co-host with another longevity dietitian, Melanie Murphy.

Every other week, anywhere you listen on YouTube, it's a vodka. And on Apple's Spotify and all the wonderful places. So I hope to see you there. And thank you again for listening to us today.