Nutrition and Cellular Aging

Insights from the GSA Publication, What's Hot: Cellular Nutrition and Its Influence on Age-Associated Cellular Decline

GSA Momentum Discussion, a podcast from The Gerontological Society of America

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Welcome to The Gerontological Society of America Momentum Discussion podcast series, where researchers, educators, and practitioners stimulate dialogue on trends with great momentum to advance gerontology. The content of the podcast today was developed by GSA, and this program has received a grant from Nestle Health Sciences.

Dr. Fielding:

Welcome to the podcast. My name is Roger Fielding. I'm the Associate Director of the Jean Mayer USDA Human Nutrition Research Center on Aging, and I lead a research team in the Nutrition, Exercise Physiology, and Sarcopenia lab. I'm excited to be your host for a series of podcasts that are based on the GSA What's Hot publication, *Cellular Nutrition and Its Influence on Age-Associated Cellular Decline.*

Researchers have identified several molecular pathways at a cellular level, including defects in mitochondrial function that appear to influence both aging and age-related chronic disease. These cellular changes associated with aging are cumulatively referred to as age associated cellular decline or AACD. Identifying AACD risk factors and intervening with cellular nutrients earlier in the aging process, before major mobility disabilities and disease-driven limitations emerge, could help improve overall healthy aging.

Today we will focus specifically on nutritional interventions that have the potential to extend human health span, as well as those that may slow age associated cellular decline and may impact longevity. I'm pleased to introduce Dr. Sai Das a Scientist I, and part of the Energy Metabolism Team here at the Jean Mayer, USDA Human Nutrition Research Center on Aging. Sai is also an Associate Professor at the Friedman School of Nutrition Science and Policy here at Tufts University

Sai's research focuses on the role of diet composition and energy metabolism in body, weight regulation, metabolic health, and aging. She was a co-investigator on the landmark, multi-site /Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy/ (CALERIE) trial which was the first study to examine the impact of calorie restriction on biomarkers of aging in humans. She is currently leading the efforts to conduct a follow up of CALERIE participants to examine potential legacy effects of exposure to caloric restriction in early-to-mid adulthood on hallmarks of health and aging. Welcome Sai.

Dr. Das:

Thank you, Roger. It's a pleasure to be here.

Dr. Fielding:

Well, let's, let's start it off and just give me your sense, Sai, how do you think about defining biological aging?

Dr. Das:

Sure. Biological aging refers to the accumulation of diverse forms of molecular and cellular damage over time. Some examples of biological aging include age-related mitochondrial dysfunction and damage to

tissues and cells resulting from oxidative stress. And as you mentioned, Roger, these changes are sometimes referred to as age associated cellular decline. Now an individual's biological age may differ from their chronological age, or their time since birth. And this is primarily how age is defined. Researchers who study aging use markers of biological age to essentially distinguish between individuals who are of the same chronological age and who may have very different rates of biological aging or very different biological ages. So, essentially, biological age is an indicator of cellular health status.

Dr. Fielding:

That's great. Now, for some of our listeners that don't swim in this space all the time, are there links between biological aging and health and disease?

Dr. Das:

Sure. The short answer, Roger is yes. There's a direct link between aging and health and disease. Aging is the greatest risk factor for the majority of chronic diseases, including cancer, diabetes, cardiovascular disease, and neurodegenerative diseases. However, as I mentioned, chronological age does not necessarily correlate with health. Instead, declines in function and development of chronic diseases appear to be associated with biological aging. Many chronic diseases are also associated with molecular and cellular processes that are implicated in biological aging, including those involving the mitochondria.

Now a number of physical and environmental risk factors can also have a marked impact on trajectories of biological aging--rates of cellular damage accumulation among these. The most important factors that have been identified include smoking, obesity, sedentary lifestyles, persistent physical or psychological stress, chronic disease, and unfavorable genetics. Essentially, it is the combination of genetics and lifestyle really.

And, Roger, there are clinical indicators for identifying the impact of adverse biological aging on impairments in health. These clinical indicators include fatigue, low quality of sleep, low mood, lack of motivation, subjective memory complaints, and poor exercise tolerance. These are essentially biological indicators of health status and can easily be detected from both clinical and biomarker studies.

Dr. Fielding:

That's really important. Having been in this area for a long time now--I grew up thinking about aging in terms of longevity--but as you know, we've been hearing a lot about health span recently. What's the difference between how we think about health span versus lifespan or longevity?

Dr. Das:

Yes, health span is very popular these days in terms of usage and also research focus, including debating whether it's one word or two words. But, with regards to the difference between lifespan and health span, I think of lifespan or longevity as a measure of how long someone may live. Lifespan only takes into account the cumulative years in the life of a human. On the other hand, health span refers specifically to the period of life in which people are disease and disability free. In other words, health span is the length of time older adults are able to live independently and carry on their activities of daily living.

Now, there have been remarkable improvements in life expectancy or lifespan in part the result of medical advances that has resulted in an unprecedented growth of the population of older adults. However, chronic diseases are now the leading cause of morbidity and mortality worldwide. A critical need is, therefore, to improve health span. And much of the research is focused on health span improvements with a goal to reduce healthcare burden and improve quality of life for older adults.

Dr. Fielding:

This is a really key issue as we move forward, Sai. As I talk to older people, while they want to live longer, the most common thing I hear is that they want to live better and live well. So, I think this has a lot of resonance with this concept of health span.

Dr. Das:

Absolutely.

Dr. Fielding:

So, let's talk about things that we can do about this. Are there lifestyle interventions that can improve some of these biomarkers and potentially modify a person's health span?

Dr. Das:

Absolutely. This is the focus of my research. And research has clearly shown that behavioral factors and lifestyle interventions are important for healthy aging. Adoption of healthy eating patterns and exercise have been shown to improve markers of age-associated diseases and attenuated biological aging.

While many dietary interventions can improve health span and prevent chronic disease, calorie restriction is the only intervention that has been shown to increase longevity in animal studies. Calorie restriction may modulate cellular functions directly at the cellular level to slow the aging process and age-related cellular decline. Calorie restriction, when combined with exercise, has some beneficial synergistic effects such as improving insulin sensitivity, lowering systemic inflammation, and improving body composition. That is the amount of fat and fat-free mass, or the lean mass that one's body composed of however studies and animals suggest that exercise may not provide an additive or an additional benefit for longevity or lifespan when added to calorie restriction. So this is where the science in the field of interventions is.

Dr. Fielding:

When we're talking about calorie restriction in people, what do some of the studies do when to make people calorie restricted? Are we talking about a 50% reduction in energy intake? What's typically used?

Dr. Das:

In animal studies, 50% is typically the rate of reduction in calories from what one would be habitually eating. In human calorie restriction studies, a target of 20 to 25% is what has been attempted—up to a 30% calorie restriction. But if you look at the findings from our calorie restriction trials, the human calorie restriction trial for a two-year period, the average level at which calorie restriction could be sustained was around 12 to 15%. So that's what has been found to be feasible. And there are a lot of research efforts looking at how a higher percentage of calorie restriction can be achieved and sustained for the longer term.

Dr. Fielding:

And obviously people lose weight when they do this. Correct?

Dr. Das:

That is correct. Yes. By reducing calories, there is weight loss that always accompanies what's called a negative energy balance condition.

Dr. Fielding:

And it's generally safe, is that right?

Dr. Das:

At the 12 to 15% levels that we did observe, it was found to be safe and tolerable, and people were able to sustain it over the two-year period.

Dr. Fielding:

Really important information. So, what does this research mean for the future of dietary interventions for improving health span and longevity? What are some of the key questions researchers are focusing on now?

Dr. Das:

Calorie restriction appears to improve markers of disease risk in humans. There were system-wide beneficial effects that were observed both for physiological as well as quality of life measures. But the acceptability and long-term sustainability or feasibility is really a challenge and continues to remain a challenge. Researchers are looking at promising alternatives to continuous calorie restriction or following a 25% or 30% caloric restriction for life. The alternatives include various forms of intermittent fasting. By that, I mean time-restricted eating or eating within a narrow window of time within the day and typically eight hours since or six hours is the recommendation. Or alternate day fasting--or every other day fasting, as it's sometimes called. Or the five and two fasts, which is five days of the week of normal intake, and two days of fasting. These two days of fasting can either be continuous or non-consecutive.

These are approaches that have been recommended, or are being examined, for sustainability over the long term, and for obtaining hopefully the benefits from such interventions. All these forms of intermittent fasting have been shown to improve markers of health span, or reduce risk for chronic disease, over the short term in humans. More research is needed to fully characterize not only the impact of calorie restriction, which needs longer study, but also these alternative nutrition and lifestyle approaches for their impact on biological aging in humans over the long term. Those are the key characteristics that I want to emphasize—looking at these things over the long term and making sure that they're sustainable and feasible. And, as always, being safe and tolerable without any risk to humans is key. However, the preliminary data is highly encouraging, and it suggests that this is a very promising field of study.

Dr. Fielding:

And, given the increasing prevalence of overweight and obesity in our older population—people over the age of 60 or 65 years—it seems to me that the study of these interventions, particularly in those older people where there's always been this tension about whether weight loss or energy restriction is advised for older individuals. You know, I think we need to learn a lot more about this. What are your thoughts about the prevalence of obesity among older adults? Because a lot of those listening to the podcast probably take care of older patients and what do we tell them now? And, and what do we still not know about this in terms of caloric restriction, or do we need more information?

Dr. Das:

Absolutely. You point out one of the major concerns and public health needs that is important with older adults, alluding to the quality of life. That is the most important focus—not just extending lifespan but improving health span. Weight loss is recommended as a beneficial intervention for reducing chronic disease risk. However, it is important that calorie restriction, which improves biomarkers of aging and reduces risk of chronic disease, is studied very carefully in older adults to ensure that health span is improved.

There are caveats to calorie restriction and, Roger, I want to point out that there is actually research that is currently underway looking at the older adult population. Specifically looking at calorie restriction and alternative approaches to calorie restriction, which include the forms of fasting, plant-based diets, and other diet composition-related research, and seeing how older adults respond to it.

CALERIE, as you mentioned was in the younger adult age group, 20-to-50-year-olds. And there were systemwide benefits, but we do not know if this is sustained in older adults as well. And this research will be very timely and inform not only the aging field, but also individuals who want to practice this lifestyle in their older adult years.

Dr. Fielding:

It's so important and so exciting. Really understanding the underlying biology and whether there's impact on age-associated cellular decline is going to be really important. Thank you, Sai, for a really terrific discussion today.

This podcast is one of three on the topic of cellular nutrition and its influence on age-associated cellular decline. The other two podcasts focus on mitochondria and aging with Anthony Molina and cellular aging in everyday practice with Nathan LeBrasseur for more in-depth information on the topic, please refer to the GSA what's hot publication, Cellular Nutrition and its Influence on Age-Associated Cellular Decline. Thank you and have a good day.