NEWSLETTER

INSTITUTE FOR SUCCESSFUL LONGEVITY

FLORIDA STATE UNIVERSITY

MUSCLES MATTER

AN ISL RESEARCHER LOOKS AT THE ROLES SKELETAL MUSCLES PLAY IN LONGEVITY — PAGE 4

How to read ads aimed at fooling older consumers

PAID ADVERTISEMENT PAID ADVERTISEMENT

Leading Acid Reflux Pill Becomes an Anti-Aging Phenomenon

Clinical studies show breakthrough acid reflux treatment also helps maintain vital health and helps protect users from the serious conditions that accompany aging such as fatigue and poor cardiovascular health

Stewart Blum
Health Correspondence

Seattle, WA – A clinical study on a new acid reflux pill shows that its key ingredient relieves digestive symptoms while suppressing the inflammation that contributes to premature aging in men and women.

And, if consumer sales are any indication of a product's effectiveness, this 'acid reflux pill turned anti-aging phenomenon' is nothing short of a miracle.

Sold under the brand name *AloeCure*, it was already backed by clinical data documenting its ability to provide all day and night relief from heartburn, acid reflux, constipation, irritable bowel, gas, bloating, and more.

But soon doctors started reporting some incredible results…

"With *AloeCure*, my patients started reporting less joint pain, more energy, better sleep, stronger immune systems… even less stress and better skin, hair, and nails" explains Dr. Liza Leal; a leading integrative health specialist and company spokesperson.

Doctors are calling AloeCure the greatest accidental health discovery in decades!

AloeCure contains an active ingredient that helps improve digestion by acting as a natural acid-buffer that improves the pH balance of your stomach.

Scientists now believe that this acid imbalance is what contributes to painful inflammation throughout the rest of the body.

The daily allowance of *AloeCure* has shown to calm this inflammation which is why *AloeCure* is so effective.

Relieving other stressful symptoms related to GI health like pain, bloating, fatigue, cramping, constipation, diarrhea, heartburn, and nausea.

Now, backed with new clinical studies, *AloeCure* is being recommended by doctors everywhere to help improve digestion, calm painful inflammation, soothe joint pain, and even reduce the appearance of wrinkles – helping patients to look and feel decades younger.

FIX YOUR GUT & FIGHT INFLAMMATION

Since hitting the market, sales for *AloeCure* have taken off and there are some very good reasons why.

To start, the clinical studies have been impressive. Participants taking the active ingredient in *AloeCure* saw a stunning 100% improvement in digestive symptoms, which includes fast and lasting relief from reflux.

Users also experienced higher energy levels and endurance, relief from chronic discomfort and better sleep. Some even reported healthier looking skin, hair, and nails.

A healthy gut is the key to a reducing swelling and inflammation that can wreak havoc on the human body. Doctors say this is why *AloeCure* works on so many aspects of your health.

AloeCure's active ingredient is made from the healing compound found in Aloe vera. It is both safe and healthy. There are also no known side effects.

"ACCIDENTAL" ANTI-AGING BREAKTHROUGH: Originally developed for digestive issues, AloeCure not only ends digestion nightmares... it revitalizes the entire body. Some are calling it the greatest accidental discovery in decades.

Scientists believe that it helps improve digestive and immune health by acting as a natural acid-buffer that improves the pH balance of your stomach.

Research has shown that this acid imbalance contributes to painful inflammation throughout your entire body and is why *AloeCure* seems to be so effective.

EXCITING RESULTS FROM PATIENTS

To date over 5 million bottles of *AloeCure* have been sold, and the community seeking non-pharma therapy for their GI health continues to grow.

According to Dr. Leal, her patients are absolutely thrilled with their results and are often shocked by how fast it works.

"For the first time in years, they are free from concerns about their digestion and almost every other aspect of their health," says Dr. Leal, "and I recommend it to everyone who wants to improve GI health without resorting to drugs, surgery, or OTC medications."

"I was always in 'indigestion hell.' Doctors put me on all sorts of antacid remedies. Nothing worked. Dr. Leal recommended I try *AloeCure*. And something remarkable happened… Not only were all the issues I had with my stomach gone - completely gone – but I felt less joint pain and I was able to actually sleep through the night."

With so much positive feedback, it's easy to see why the community of believers is growing and sales for the new pill are soaring.

THE SCIENCE BEHIND ALOECURE

AloeCure is a pill that's taken just once daily. The pill is small. Easy to swallow. There are no harmful side effects and it does not require a prescription.

The active ingredient is a rare Aloe Vera component known as acemannan.

Made from of 100% organic Aloe Vera, *AloeCure* uses a proprietary process that results in the highest quality, most bio-available levels of acemannan known to exist.

According to Dr. Leal and several of her colleagues, improving the pH balance of your stomach and restoring gut health is the key to revitalizing your entire body.

When your digestive system isn't healthy, it causes unwanted stress on your immune system, which results in inflammation in the rest of the body.

The recommended daily allowance of acemannan in *AloeCure* has been proven to support digestive health, and calm painful inflammation without side effects or drugs.

This would explain why so many users are experiencing impressive results so quickly.

REVITALIZE YOUR ENTIRE BODY

With daily use, *AloeCure* helps users look and feel decades younger and defend against some of the painful inflammation that accompanies aging and can make life hard.

One AloeCure Capsule Daily

- Helps End Digestion Nightmares
- Helps Calm Painful Inflammation
- Soothes Stiff & Aching Joints
- Reduces appearance of Wrinkles & Increases Elasticity
- Manages Cholesterol & Oxidative Stress
- Supports Healthy Immune System
- Improves Sleep & Brain Function

By buffering stomach acid and restoring gut health, *AloeCure* calms painful inflammation and will help improve digestion… soothe aching joints… reduce the appearance of wrinkles and help restore hair and nails … manage cholesterol and oxidative stress… and improve sleep and brain function… without side effects or expense.

Readers can now reclaim their energy, vitality, and youth regardless of age or current level of health.

HOW TO GET ALOECURE

This is the official nationwide release of the new *AloeCure* pill in the United States. And so, the company is offering our readers up to 3 FREE bottles with their order.

This special give-away is available for the next 48-hours only. All you have to do is call TOLL-FREE 1-800-753-2014 and provide the operator with the Free Bottle Approval Code: AC100. The company will do the rest.

Important: Due to *AloeCure's* recent media exposure, phone lines are often busy. If you call and do not immediately get through, please be patient and call back. Those who miss the 48-hour deadline may lose out on this free bottle offer.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease. All doctors mentioned are remunerated for their services. All clinical studies on AloeCure's active ingredient were independently conducted and were not sponsored by the American Global Health Group.

FROM THE DIRECTOR

Neil Charness, Ph.D., is the William G. Chase Professor of Psychology at Florida State University and director of the Institute for Successful Longevity.

Our local newspaper, the *Tallahassee Democrat*, like many other newspapers, has struggled to survive the shift of advertising revenue from print to online sources. As a result, it is prey for what can truly be called "fake ads," those aimed at selling questionable products, mostly "nutraceuticals" that are not regulated by the Food and Drug Administration.

Nutritional supplements such as vitamin pills have a dismal record in scientific studies, almost never showing benefits in gold-standard clinical trials (and sometimes showing harm), yet they have become a booming business aimed at the so-called "worried well" consumer. For rather strange historical reasons (and intense lobbying by politicians who directly profit from associations with these companies) such nutritional products are not subject to overview by regulatory bodies such as the Food and Drug Administration. That is, the products are not required to be tested for efficacy. And as long as they don't make claims that are blatantly unsubstantiated they mainly evade regulation, even by the Federal Trade Commission that watches over such claims. An example of such an ad (July 24, 2019) is shown at left.

So, how can you avoid being duped by these paid advertisements? The first clue to be on your guard is the small print at the top saying "PAID ADVERTISEMENT." Presumably the FTC requires such ads, which tend to present themselves as health news stories, to display that warning prominently. Similarly, at the bottom in relatively small print is the disclaimer "These statements have not been evaluated by the Food and Drug Administration…." But you'll notice that your attention is drawn away from the paid advertisement statement at the top by the large type header "Leading Acid Reflux Pill Becomes an Anti-Aging Phenomenon."

The second clue is the weasel phrase "A clinical study on a new acid reflux pill shows that its key ingredient relieves digestive symptoms while suppressing the inflammation that contributes to premature aging in men and women." I'll bet you were tempted to conclude that this particular advertised supplement had a clinical trial conducted and showed beneficial effects. Careful reading suggests that there was a clinical trial on something else (but no reference given to that clinical trial) that probably shares an ingredient (acemannan) with this product.

I did a little hunting on pubmed for clinical trials for acemannan and most seem to be for treatment of teeth, with mixed results, some favoring acemannan, some favoring other agents. The one study that looked at it for a condition often found in immobile older adults, healing of pressure ulcers, found no benefit relative to

a saline dressing control. The rest of the claims in the article based on "scientists believe" and "Dr. Leal recommends" don't have any evidence provided. Claims quickly escalate: "… will help improve digestion … soothe aching joints … reduce the appearance of winkles [sic] and help restore hair and nails … manage oxidative stress … and improve sleep and brain function … without side effects or expense."

Presumably the pills cost nothing??? They state that there is a free bottle, but on the phone they try to upsell to months of treatment (least expensive is $50/month). Their sales tactics are quite interesting, too.

Finally, always be on your guard for the term anti-aging (highlighted in the ad). Although "anti-aging," too, is becoming a growth industry, the evidence for slowing down the aging process is pretty weak for humans. The most recent study, the CALERIE clinical trial, showed benefits for cutting down calories in non-obese younger to middle-aged people. The goal was a 25-percent reduction but people achieved about half that reduction (12 percent) over a two-year period. Benefits were seen for risk factors such as cholesterol, blood pressure, C-reactive protein (a measure of inflammation), insulin sensitivity, and metabolic syndrome. Of course, the study was unable to track longevity increases as it ran for only two years.

If you happen to be a calorie-restricted monkey, mouse, rat, fruit fly or worm, research seems convincing that caloric restriction slows down metabolism and leads to greater longevity.

Of course, having a longer life-span is only part of the puzzle. You want to have an *enjoyable* longer life-span. Unfortunately, those organisms showing increased longevity can't be queried about their quality of life on a restricted diet.

The CALERIE clinical trial experienced fairly low dropout over the two-year interval with about 82 percent completing the treatment condition, compared to 95 percent in the passive control condition, but even these very keen participants couldn't keep to a 25-percent calorie reduction. Although 82 percent is a high retention rate for a two-year study, it seems very unlikely that many people could keep up with this diet for 40 years (mean age at entry was 38 years) to really track longevity effects.

Nicholas Gray joins ISL as post-doctoral researcher

Nicholas Gray, Ph.D., has joined the Institute for Successful Longevity as a post-doctoral researcher. He will support ISL's mission, including community outreach, and become involved in research related to successful longevity.

Gray earned his doctorate in psychology from Florida State University in 2019. His research has centered around understanding long-term memory, the impact of spontaneous memory retrieval, and making associations between the past and the present.

His other research interests include the impact of different environmental and emotional contexts on memory and the formation of false memories.

I know of only a few cases of humans who tried to cut down their caloric intake over long periods of time. The most famous case, a scientist who pioneered research on the effects of restricting caloric intake, Roy Walford, tried to do this himself, and died of a rare disease, ALS, at age 79. Anecdotally, another gerontologist I knew who also tried to cut back on food intake in later life also died of a rare disease, at age 75. So I wouldn't advise this approach to increasing longevity.

When it comes to ads in your local newspaper (or on Facebook) that boast magical "anti-aging" ingredients, it should be a case of *caveat emptor* (buyer beware) particularly for any product not evaluated for efficacy by the Food and Drug Administration (all neutraceuticals). Save your money for activities that you truly enjoy (but don't lead to obesity) and that boost your quality of life. Trying to find hope in a bottle is usually hopeless. ■

ISL researcher finds disruptions to molecular clock threaten mass and health of muscles

Dr. Bradley Gordon, assistant professor in the Department of Nutrition, Food and Exercise Science in the College of Human Sciences and a Faculty Affiliate of the Institute for Successful Longevity, conducts research into how stimuli such as nutrients, hormones, and physical activity regulate changes in skeletal muscle mass and muscle function in diseased and non-diseased conditions. In 2018, Gordon was awarded an ISL Planning Grant. Here we talk to him about his work.

Do our muscles play a role in our longevity?

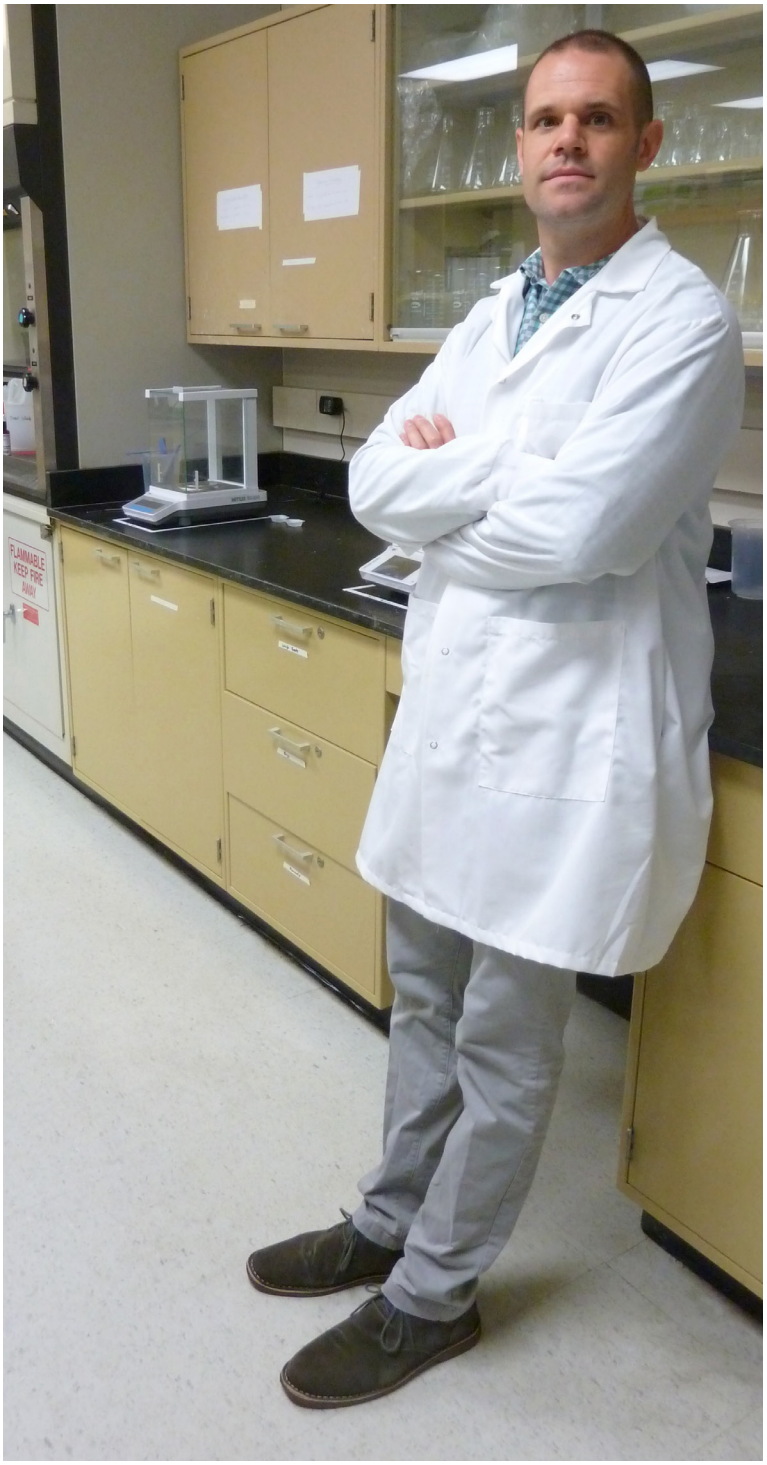
Under various pathological conditions, most notably aging, we lose our muscle mass. This not only has significant consequences on the physical function, but it also has a lesser appreciated role in the ability to prevent morbidity and mortality. So the more muscle mass that you lose, the more likely you are to have metabolic complications, and your risk of death increases.

What is the connection between muscle mass and metabolic behavior?

Well, muscle controls a lot of processes other than just physical function — thermoregulation, glucose homeostasis, are all mediated in large by skeletal muscle. Your skeletal muscle is also one of the largest storage tanks for proteins within your body. So if your body needs to mobilize amino acids for use as protein building blocks elsewhere in the body, skeletal muscles can provide those amino acids. Without the skeletal muscle, your ability to sustain life through these processes are compromised.

When you say skeletal muscle, is that distinct from some other muscle groups in the body?

Yes. A muscle is not a muscle is not a muscle. Muscles have similarities in terms of structure and function, but they do have differences. For instance, there are differences between the muscles of the legs, of the arms, and of the thoracic cavity. Our lab focuses on what regulates muscle mass, particularly mass of the limb skeletal muscles, and this is what the Institute for Successful Longevity funded our lab to study. In particular, we are interested in how



Bradley Gordon, Ph.D., in his lab at FSU. Gordon received a Planning Grant from the Institute for Successful Longevity to support his work on skeletal muscle mass and function.

androgens regulate mass of the limb skeletal muscles. Interestingly, nobody really has any idea how that actually happens. We know that it happens — if you give bodybuilders super physiological concentrations of testosterone, their muscles get bigger. Conversely, in an aged male, testosterone production declines. If you give them back testosterone to a value that is equivalent to roughly a young, middle-aged male, their limb muscles will grow back, but nobody has any idea how that actually happens.

This is kind of a surprise to me because of what we know testosterone does to skeletal muscle. And the reason why we think this is important to understand is because there are conditions where males can't get testosterone replacement, which is a big, trendy therapy right now.

There is potential carry over to females as well. But in males, the use of testosterone-replacement therapy has gone sky high. A couple issues with that is we don't really know how it works, and the long-term uses are literally unknown. So maybe what we find out in the future is that giving that testosterone back is bad for the overall health of a person despite increasing muscle mass. There are also groups that are contraindicated from using testosterone. So if you have an established cancer tumor, typically under those conditions, the male will become hypogonadal [decrease in normal production/bioavailability of primary sex hormones such as testosterone]. A first-line defense for prostate cancer may even be to stop the normal production of testosterone as a means to inhibit growth of the tumor.

But even though the loss of testosterone might slow the tumor growth, it's going to have the off-target effect of inducing the muscle to atrophy. This is important because under conditions where there's some type of pathology, like cancer, holding on to skeletal muscle mass is really, really important.

Is there some other way to regain muscle mass without taking testosterone supplement?

Yes, there is a variety of ways. The most effective

German researcher meets with ISL experts

Anna Schlomann, Ph.D., of the University of Cologne in Germany came to Florida State University this summer to learn more about the work of the CREATE project.

Schlomann's research involves the oldest of the old, those 80 years or older, and how these individuals engage digital technology. This age group is growing in numbers but has not been the focus of many studies.

Anna Schlomann, Ph.D., of the University of Cologne

Schlomann has studied older adults and their attitudes toward digital technologies and has looked at relationships between the use of technologies and sense of well-being. She has just started work with a new project on assistive and digital technologies, such as smart walkers, designed to improve mobility in old age.

While at FSU she gave a presentation of her work to interested faculty and graduate students and met with CREATE researchers to learn more about how the project develops and evaluates interventions and design solutions to promote successful technology adoption among older adults.

CREATE — the Center for Research and Education on Aging and Technology Enhancement — is a multidisciplinary and collaborative center that involves researchers at FSU, the Weill Cornell Medical College, the University of Illinois at Urbana-Champaign, the University of Miami and Georgia Tech. The center works to ensure that the benefits of technology can be realized by older adults to support and enhance the independence, productivity, health, safety, social connectedness and quality of life of older people.

Walter Boot, Ph.D., a Faculty Affiliate of the Institute for Successful Longevity, and Neil Charness, Ph.D., ISL's director, are two of the principal investigators on the CREATE project.

You can learn more about CREATE at http://www.create-center.org/.

way that we found to increase muscle mass is resistance exercise. Aerobic exercise may protect against muscle atrophy. A diet that contains sufficient amino acids can also blunt muscle atrophy. There is evidence though, that in the absence of testosterone, these may not be as effective.

If you looked at what regulates muscle mass, there are many pieces of the pie. Disrupting any sliver of the pie can contribute to the loss of muscle mass. We're trying to understand one particular sliver with the overall goal of being able to target any piece of the muscle-mass pie to help maintain muscle mass. I think natural ways such as diet and exercise should be a first-line treatment, but if there's some way to enhance the regrowth of muscle, then that would also be a benefit of our work.

How are you conducting this work?

In rodents. We can perturb the system a little bit more in rodent models to help us understand how the system works.

And do you have any findings from that?

Yes, yes. We started down this avenue of research [androgen regulation of muscle mass]with very little background because there's not really anything consistent out there about androgens and skeletal muscle. We really had no idea where to start. So I did one study as soon as I became an assistant professor, and from that study we started branching out based off the findings.

One of the findings we found was that androgen depletion appeared to alter something in the limb muscle called a molecular clock. You can almost think of it as a machine that cycles over a 24-hour period of time to regulate various processes. So over the course of the day, the clock activity will go up and then it will come down, and then the next day it will go up and come back down. And this muscle clock has been shown to be important for regulating various aspects of muscle health. One of those aspects is mitochondrial quality. If you were to physically disrupt the clock in skeletal muscle, the quality of the mitochondria is impaired. And in some of our early work we found that indices of mitochondrial quality were decreased in the limb muscle when testosterone was depleted, and this was related to the degree of muscle atrophy.

We kind of lucked out and found this, this alteration to the molecular clock within the skeletal muscle, and that's where the Institute for Successful Longevity's support came in. We wrote a grant to try to characterize what disruption to the clock is doing under conditions where testosterone is there and not there. Essentially, what we found is that the normal cycling of the clock is disrupted in the muscle when you take testosterone away from these animals. We also found that this disruption to the clock coincided with changes in the signals that regulate mitochondrial quality. The clock normally regulates expression of genes that contribute to mitochondrial health, and when we take testosterone away expression of those genes is disrupted.

OK, that sounds like a pretty important finding.

It was a great way to dive into a new field that I had never been exposed to. ISL's support gave me the opportunity to form some collaborations, both here at Florida State University and at other universities. It's really a lot of serendipity that we got into that avenue because there's a guy over in the FSU medical school, Choogon Lee, who is an expert in circadian biology. There's also Karyn Esser at the University of Florida, who studies circadian biology, specifically in the skeletal muscle, and she really is the pioneer of that area. Being so close to her and being right next door to Choogon has been completely serendipitous, and they have been really helpful for this project. We have submitted this work for publication, and we only have very minor revisions for the work. The reviewers thought it was a timely and novel finding.

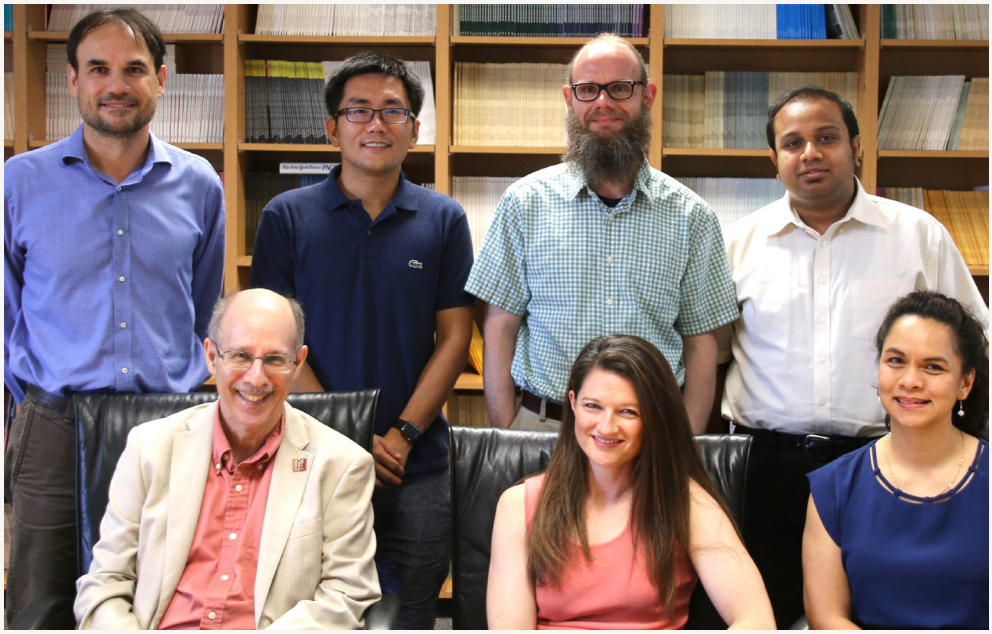
So, what's next?

Basically, everything that I've done in my prior training related to skeletal muscle biology has nothing to do with the avenues that I'm now investigating, which is a good thing and a bad thing. It's a good thing, because, you know, if you pigeonhole yourself into one thing the rest of your life, it might get kind of boring. I now have to learn a variety of new techniques and topic areas. And biology is not just one avenue; everything integrates together. So what I'm starting to find is that I need to integrate these new areas into my research program to keep moving forward. ■

Walter Boot and FSU team win $2.9 million NIA grant

The National Institute on Aging has given an R01 grant to ISL Faculty Affiliates Walter Boot, Ph.D., the principal investigator, and Shayok Chakraborty, Ph.D., the co-PI, along with an interdisciplinary team of FSU researchers, for their project: The Adherence Promotion with Person-centered Technology (APPT) Project: Promoting Adherence to Enhance the Early Detection and Treatment of Cognitive Decline.

The total award is for $2.9 million.



The research team, front row: Neil Charness, Dawn Carr, Mia Lustria; at top: Antonio Terracciano, Zhe He, Walter Boot, Shayok Chakraborty.

The Institute for Successful Longevity served as a crucial resource for the formation of this interdisciplinary team. In addition to Dr. Boot of the Department of Psychology and Dr. Chakraborty of the Department of Computer Science, the team includes ISL affiliates Zhe He, Ph.D., of the School of Information; Dawn Carr, Ph.D., of the Department of Sociology; and Antonio Terracciano, Ph.D., of the College of Medicine, as well as ISL Director Dr. Neil Charness. Dr. Mia Lustria of the School of Information is also a team member.

The aims of the project are to promote early detection and treatment of age-related cognitive decline and dementia. The significance of the project is highlighted by Boot, who said, "As the population in the United States and around the world ages, it will be important to understand ways to detect cognitive change as soon as possible so individuals experiencing these changes can be treated and supported. This project will help develop effective methods through which cognitive changes can be monitored over time in someone's own home, using technology."

Although mobile cognitive assessments and training are available, Boot said, these are only part of the solution. People need to engage with assessment and training over a long period of time for benefits to be observed. This project will develop Artificial Intelligence (AI)-based reminder systems to help ensure long-term engagement with home-based cognitive assessment and cognitive training protocols. AI reminder systems will learn about the user and adapt based on their history and their preferences.

"This project involves fundamental AI challenges such as learning from multiple sources of heterogeneous data, learning from data on-the-fly in real-time, as well as learning in the presence of weak supervision and noisy annotations," said Chakraborty. "This research will result in the development of next generation AI-based assistive aids for the elderly, with the potential to improve their health and well-being, as well as promote independent living."

The ability to detect that someone is on the cusp of cognitive decline has large implications for how dementia is studied. Treatments and interventions can be tested before large changes in brain structure and function that may be hard to reverse have occurred. ■

ISL researcher finds connection between job complexity and cognitive function in retirees

Retiring from your full-time job might not be the best thing for your brain as you age, according to a new study out of Florida State University.

A team of researchers led by FSU Associate Professor of Sociology Dawn Carr, a Faculty Affiliate of the Institute for Successful Longevity, found that people in so-called low-cognitive-complexity jobs, such as truck drivers and food prep workers, lose cognitive function more rapidly once they leave their 9-to-5 compared to people in high-cognitive-complexity jobs, such as financial managers or accountants. The study was recently published in *The Gerontologist*.

Dawn Carr, Ph.D., is an associate professor in the Department of Sociology in FSU's College of Social Sciences and Public Policy.

"Our study supports a growing body of research that shows that challenging our brains is really good for us," Carr said. "As our population ages, there's a growing need for older people to stay in the workforce longer. It's important to examine the benefits and consequences of longer working lives for the people who want to work well past the traditional retirement age of 65 ... or need to delay their retirement."

The research team used longitudinal data from the Health and Retirement Study to examine people over the age of 50 who went from working full time to completely retiring, partially retiring, or returning to work within a few years. They compared individuals who made these retirement transitions with their counterparts who kept working full time.

They found that workers who retired from high-cognitive-complexity jobs had cognitive function that was just as good as their continuously working counterparts regardless of which retirement pathway they chose. In fact, those who retired from high-cognitive-complexity jobs and then returned to work experienced slightly improved cognitive function.

"This result might mean that when these individuals started a new position after leaving their career jobs, they were able to learn new things and challenge their brains in beneficial ways," Carr said.

However, not everyone benefitted from leaving work and then returning. Those who retired from low-cognitive-complexity work, even if they returned to work, experienced significant cognitive decline. Those who remained employed full-time maintained their level of cognitive function.

"It seems that for individuals in this low-cognitive-complexity group, the type or amount of post-retirement activities they engaged in were insufficient for maintaining cognitive function," Carr said. "Our work and non-work lifestyles both influence how we use our brains over our entire lives."

Carr and her team encourage stakeholders to consider the groups that are more vulnerable to losing their cognitive function and identify interventions that may help them better maintain their cognitive health.

The research was supported by the Alfred P. Sloan Foundation and the National Institute on Aging.