

2016

Brain Power

Sue DiBella

Raegen Pietrucha

Shane Bevell

Kevin Dunegan

Follow this and additional works at: <https://digitalscholarship.unlv.edu/innovation>

Repository Citation

DiBella, Sue; Pietrucha, Raegen; Bevell, Shane; and Dunegan, Kevin (2016) "Brain Power," *UNLV Innovation*: Vol. 9, Article 7.

Available at: <https://digitalscholarship.unlv.edu/innovation/vol9/iss1/7>

This Features is protected by copyright and/or related rights. It has been brought to you by Digital Scholarship@UNLV with permission from the rights-holder(s). You are free to use this Features in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s) directly, unless additional rights are indicated by a Creative Commons license in the record and/or on the work itself.

This Features has been accepted for inclusion in UNLV Innovation by an authorized administrator of Digital Scholarship@UNLV. For more information, please contact digitalscholarship@unlv.edu.

N

I

A

B

B

B

E

N

O

O



Through collaboration and innovation, UNLV researchers are changing the way we think about the brain.



PORTRAITS BY JOSH HAWKINS

Jeff Kinney chose to join the UNLV psychology faculty in 2007 for many reasons, but the one that clinched the deal was the opportunity to build out the neuroscience area.

"The prospect of building a program from the ground up was far more appealing to me than joining an already established group," says Kinney. "For me, carving out something new had great appeal."

Today, Kinney's hopes—and his efforts in his first several years here—are coming to fruition. In the last year, he led a UNLV research team that joined with the Cleveland Clinic Lou Ruvo Center for Brain Health to obtain an \$11.1 million grant from the National Institutes of Health for advanced study of both Parkinson's and Alzheimer's diseases. Additionally, the department now offers a Ph.D. area of emphasis in neuroscience, with plans to offer a stand-alone neuroscience doctorate soon. The department also recently launched a neuroscience minor, in which more than 100 undergraduates are currently enrolled.

"And now the department is approaching a critical mass of faculty in neuroscience, and faculty from other departments are collaborating with us as well," he says. "This will enable us to begin building a center of excellence in neuroscience that will dramatically help with securing research funding in the form of collaborative and individual grants."

One of the keys to the successful acquisition of research dollars, he notes, is the inclusion of collaborators, both on and off campus. Kinney and his team are working with several UNLV faculty members studying myriad topics. The following profiles offer a glimpse into the growing neuroscience research being conducted on the UNLV campus.

Patterns of Activity

As a 19-year-old education major, Rochelle Hines' career ambition was to work with schoolchildren who have special needs. Then she enrolled in an elective course called "Brain and Behavior."

"I was captivated," Hines says. "By the second week of this class, I had changed my major and started working in the lab of my professor."

The undergraduate research experience that followed enabled Hines to use various advanced technologies—electron microscopy among them—to gain a thrilling view of cerebral structures at the molecular level. From there, she recalls, she went on to explore sites of communication between brain cells, called synapses, falling "in love with their incredible intricacy."

"I became focused on wanting to understand how we build billions of these complex structures so reliably during normal development, and how a failure in this process may lead to developmental disorders like those that I observed working with children with special needs."

Her early fascination with neuroscience has spawned a career rich in research. Today, Rochelle Hines, along with her husband and collaborator Dustin Hines, is rapidly expanding our understanding of how, for better or worse, neuronal activity patterns guide human behavior and ultimately contribute to pathology.

"Patterned activity in the brain is achieved

through a balanced relationship between 'on' signals originating from excitatory cells and 'off' signals from inhibitory cells that act to modulate the activity of the excitatory cells," she says. Her focus, she adds, tends toward the inhibitory cells, cellular "dimmer switches" that finely tune levels of excitation in the brain.

"Rochelle and I have a common thread, in that we both study cells in the brain that modulate brain activity patterns," says Dustin, noting that he focuses more on the brain's abundant glial cells, which surround neurons and provide support for and insulation between them.

The couple, who recently moved to Las Vegas together to continue their research in UNLV's psychology department, shares an interest in this area of neuroscience for a number of reasons.

"The subject of modulatory cells has been attractive to us, as many studies are now pointing to this area as the most likely avenue for therapeutic advancement," says Dustin, noting that pharmaceutical companies have been interested in his research. "We also enjoy working in these areas because, to date, they are largely understudied in neuroscience. So it's exciting to work on topics where there are a lot of new discoveries and advancements to be made."

The two researchers, who met early in their careers, work synergistically. Both explore the functioning of these modulatory systems in the brain, but each has a specialty area. Rochelle uses a molecular and cellular approach to focus on interneurons, also called "relay neurons," cells that

modulate communication between other neurons. Dustin's work with glial cells, specifically astrocytes and microglia, involves a cellular physiological and behavioral approach to understand how glia modulate neuronal communication.

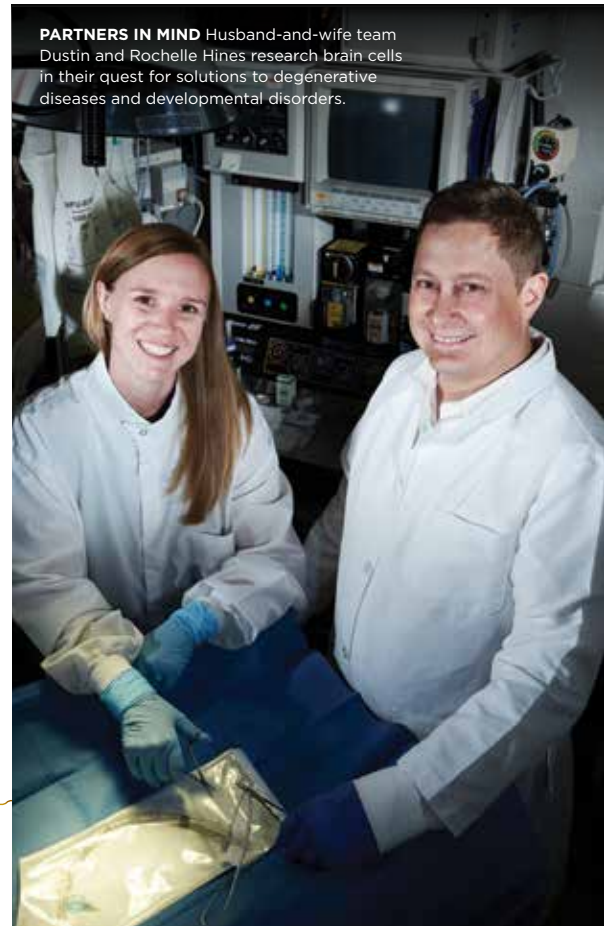
His research has implications for degenerative maladies such as depression and stroke. For example, one of his studies examined how the chemicals activated in sleep deprivation may be used to help diminish depression. His research team used an animal model to examine how a certain compound that affects adenosine receptors in the brain mimics sleep deprivation and improves mood and behavior.

He believes glial cells have been largely overlooked in brain research and provide an oasis for novel therapeutics.

"The tools that were needed to study glial cells were not available early on in neuroscience research," he says. "After World War II, many electrical technologies used to detect submarines, like oscilloscopes, drove the research; consequently, the electrical properties of neurons became the focus of the field. In the late 1980s, the development of new microscopes and genetic tools allowed us to see how glial cells contribute to brain function by modulating neurons."

Rochelle's research, meanwhile, examines how interneurons and inhibitory synapses affect neurodevelopmental disorders such as autism and schizophrenia. By investigating the activities of inhibitory cells in the brain—those "dimmer-switch" cells that finely tune

PARTNERS IN MIND Husband-and-wife team Dustin and Rochelle Hines research brain cells in their quest for solutions to degenerative diseases and developmental disorders.



levels of excitation—she seeks to learn more about the development of signaling in the nervous system.

“Excitatory signaling can be thought of as a typical light switch, either fully on or fully off,” she says, adding that inhibitory signaling modulates this activity, allowing for subtler variations of brain activity.

Like her husband, Rochelle chose to study a research area that has abundant potential for discovery.

“The role of inhibitory signaling is becoming increasingly apparent, and much of it is based on the symptoms associated with these disorders as well as studies in postmortem tissue from human subjects with these disorders,” she says.

She recently authored an article describing a study of inhibitory receptors in the brain and how certain inhibitory synapses might contribute to the symptoms of schizophrenia.

“These receptors are the target for many drugs that are in wide clinical use, including anesthetics and anti-anxiety and sleep drugs, so we know that they are a powerful target,” she says. Her work has also garnered the interest of pharmaceutical companies.

The couple has more than 50 scholarly journal articles between them. By the end of the year, they expect to submit their first jointly authored article emanating from their UNLV research. It will focus on how the brain regulates sleep.

—SUE DIBELLA

Smoking and Schizophrenia

You might be surprised to learn that the smoking rate for schizophrenic patients is 45 to 88 percent higher than the general population’s, according to “Co-Morbidity of Smoking in Patients With Psychiatric and Substance Use Disorders,” published in the *American Journal on Addictions*. And if you wonder what the underlying cause of such a pervasive habit might be, you’re not alone.

Xiangning Chen and Jingchun Chen of the UNLV Nevada Institute of Personalized Medicine (NIPM) are looking to genetics for the answer.

“Genetics actually influences everything we are and do,” Xiangning Chen says. “Genetics defines your potential or capacity, and how you reach that capacity depends on the environment you’re in.”

People with schizophrenia can experience delusions, hallucinations, dissociations from reality, abnormal social behavior, erratic speech and behavior, and the inability to focus and recall information. Although environmental factors may contribute to the development of schizophrenia, the disorder has been linked to specific genetic variants that predispose a



SMOKE AND PEERS Xiangning Chen (right) and Jingchun Chen (left) look at genes to clear the air on the link between schizophrenia and smoking.

person to developing the condition.

“Researchers have performed a lot of twin studies and family studies with respect to schizophrenia,” Jingchun Chen says. “The results show time and again that the more overlap people have in their genetic makeup, the greater their chances are for developing this disorder. For instance, if one twin sibling has schizophrenia, the other has a 50 percent chance of developing it as well. So there’s clearly a genetic component.”

Previous research has noted a strong correlation between heavy smoking and schizophrenia. A 2011 finding in the journal *Psychiatric Services*, for example, concluded that the “prevalence of smoking has remained alarmingly high among individuals with schizophrenia and bipolar disorder in routine psychiatric settings.” Although there is some dispute among researchers as to why, the most commonly cited explanation is that patients are attempting to “self-medicate.” In short, researchers have concluded schizophrenic patients smoke because it makes them feel better.

Xiangning Chen and Jingchun Chen wondered whether genetics might play a role in creating this analgesic effect.

Supported in part by separate grants from the National Institutes of Health, Xiangning Chen and Jingchun Chen examined genes associated with both schizophrenia and smoking to determine whether the disorder and nicotine dependence might be linked. Using sophisticated analytic techniques as well as data on the genetic components involved in the general population’s smoking behavior, the two discovered that while

there was likely a genetic predisposition to smoking in schizophrenics, the cause of schizophrenic patients’ excessive tobacco use was not entirely due to nicotine dependence or addiction, as is often the case with smokers in the general population.

“Schizophrenic patients have some unique behavioral factors that cause them to smoke, and smoke quite a bit,” says Xiangning Chen, a professor in both UNLV’s Department of Psychology and NIPM. “One of the challenges for schizophrenic patients is that they cannot remember things accurately, follow their thoughts easily, or concentrate effectively. Therefore, they use cigarettes to help them cope and overcome some of the symptoms caused by the disorder, as one effect of nicotine on humans is to improve cognitive function.”

Although schizophrenic patients are smoking for reasons that extend beyond what their genomes might predispose them to, the discovery of genetic liability between the schizophrenia and smoking has troubling implications.

“Schizophrenia and smoking are considered complex disorders, meaning that more than one gene contributes to them,” says Jingchun Chen, an assistant professor at NIPM. “Because we found some genes and pathways that are shared between schizophrenia and smoking, we now believe that smoking may actually increase the risk of schizophrenia developing in a person who has these genes, so the next step is to find out what the function of those genes are.”

The scientists say their work to pinpoint those genes could one day lead to personalized treatments aimed at improving patients’ quality

of life or even preventing the condition entirely. The two researchers indicate that their plan to take advantage of the capacity of UNLV's Cherry Creek II supercomputer, one of the fastest and most powerful supercomputers in the world, should enhance their ability to deliver results.

In the meantime, they say, they'll be looking at genes associated with other disorders and diseases to see if these might also be related to schizophrenia. At this point, for example, the researchers know that schizophrenic patients have an increased chance of developing an autoimmune disorder—and vice versa—and are working to determine what genetic liability might link the two.

Another project involves using Cherry Creek II to look for genetic ties between smoking and lung cancer—that is, whether a gene or set of genes might predispose a person to lung cancer, nicotine addiction, or both. Contrary to popular belief, Xiangning Chen says, the relationship between cigarette smoking and lung cancer is much more complicated.

"Smokers that develop or die of lung cancer are actually the minority," Xiangning Chen says. "If smoking directly caused lung cancer, you'd expect to see more of it."

Discovery of genetic roots in disease and disorder rests at the heart of NIPM's mission. If research can determine which genes cause a particular condition, a "personalized" treatment strategy can be established. This would eliminate expensive guesswork associated with treatments that patients may or may not respond to, while increasing the likelihood of an individualized treatment's success at the same time.

"I never expect that what I do will change the world," Xiangning Chen says. "But what I can do is give people something to think about from the information I can give them. If you find out you carry a gene that predisposes you to lung cancer, for example, maybe you won't smoke. That's what NIPM and researchers like me are here for—to try to find a way to better treat people and help them make more informed decisions."

—**RAEGEN PIETRUCHA**

A Powerful Protein

Cell and molecular biologist Nora Caberoy never thought that a protein she worked with years ago could potentially lead to new discoveries in the fight against Alzheimer's disease. But that's exactly what the protein, called "tubby" because it is encoded by the TUB gene, may offer scientists.

It all started in 2007 while Caberoy, now an assistant professor in UNLV's School of Life Sciences, was working as a postdoctoral fellow at the Bascom Palmer Eye Institute in Miami.

While occupied with a project related to macular degeneration—a retinal condition that causes a loss in central vision—she identified a tubby protein that is involved in the clearance of photoreceptor debris in the eye.

Photoreceptors are cells responsible for reception and processing of light as well as sending the signal to the brain. When old bits of cellular debris accumulate around the ends of photoreceptors, these need to be removed. Specialized cells make this happen, but they need proteins to guide the process.

This is where tubby comes in. Tubby proteins bind onto cellular debris while inviting another type of cell, phagocytes, to begin clearing it. Tubby serves, in other words, as a bridge between the cells that need to be consumed and those that are supposed to eat them.

So, what does all this have to do with Alzheimer's disease? Patients with Alzheimer's have an accumulation of amyloid beta, a protein that aggregates in the brain. Caberoy says that, for reasons that are not entirely clear, the amyloid beta deposits of those with Alzheimer's squeeze in between the brain cells, eventually killing them.

"We all produce amyloid beta, but in healthy individuals, the production of amyloid beta is somehow equal to the degradation," she says. "In those with Alzheimer's, the balance is not equal."

According to Caberoy, the body maintains this balance in part thanks to the work of debris- and pathogen-eating microglial cells that, in addition to gobbling up diseased cells, also have a taste for excess amyloid beta. But many scientists suspect that this microglial assault may have a serious side effect: an increase in inflammation that may hasten the disease's progress and the subsequent death of brain cells.

Caberoy noted from her research on photoreceptors that the tubby protein assisted in the removal of damaged cells in the eye without inflammation. Could they perhaps be repurposed for use in the brain?

"We know that the active receptor in the eye also is present in the brain, but for some reason, it is not the preferred receptor," she said. "We also know that the molecules that bridge that amyloid beta are not binding directly to the receptor."

In an attempt to encourage such binding, Caberoy is working to create a new type of molecular "bridge," one that could link amyloid beta to a less inflammatory protein that might neutralize it.

In the lab, her research team undertook screenings to discover proteins that could bind to amyloid beta. They were able to identify several. Caberoy then "optimized" these proteins by mutational analysis until she found one that could bind to the most toxic form of amyloid beta.

"I fused the amyloid beta binding protein to the part of tubby that recognizes the silent

receptor," she said. "Through testing, we were able to show that chimeric protein, which is created through the joining of two or more separate proteins, was able to bind to both the receptor and the amyloid beta. We also found that this process could reduce the production of inflammatory factors."

Over the next few months, Caberoy's research team will test this process on mice with Alzheimer's. She says they will first inject the affected mice with the chimeric protein, then see if it results in a reduction in the level of amyloid beta in the brain with the production of inflammatory factors in the blood.

If successful, this process will bolster the patent application Caberoy has submitted for this method of clearing amyloid beta.

Additionally, if the results are positive, the approach could eventually be used to develop therapies for human patients, although she cautions that there are still questions as to whether such treatment would need to be deployed before the disease develops or if it might help individuals already affected.

Regardless, she says, there is much to be hopeful about.

"There could be clinical applications where we would produce proteins that could be injected into an individual," she says. "You can imagine someone that has a family history of Alzheimer's disease taking a pill or getting an injection before the disease develops."

—**SHANE BEVELL**

Learning From Cancer

UNLV biochemist Ron Gary is deeply interested in physiological processes affecting human health, a fact that's not immediately obvious as one gazes down at the petri dishes positioned around his lab. But Gary's molecular-level work with the cells housed in these dishes continues to yield important cancer-related discoveries and, more recently, potentially game-changing neuroscientific findings related to Alzheimer's disease.

The Alzheimer's discoveries were an outgrowth of the cancer research. Gary and his laboratory team were working to learn whether inhibiting the aberrant activity of a particular "signaling" enzyme, glycogen synthase kinase-3 (GSK-3), might slow the explosive growth of cancer cells. Because the enzyme has also been implicated in the development of Alzheimer's, Gary's team soon found themselves thinking about the ways in which inhibiting GSK-3 might affect a key component of that disease as well.

There are two microscopic structures that are characteristically found in the brains of



EYES WIDE OPEN

Nora Caberoy discovered that her research on proteins in the eye might someday help us fight Alzheimer's.



DOUBLE TROUBLE

Ron Gary's enzyme research serves two purposes; cancer and Alzheimer's, beware.

"There could be clinical applications where we would produce [tubby] proteins that could be injected into an individual," says Caberoy. "You can imagine someone that has a family history of Alzheimer's disease taking a pill or getting an injection before the disease develops."

Alzheimer's patients: plaques and neurofibrillary "tangles." At the molecular level, neurofibrillary tangles are perhaps the illness's most distinguishing feature. The tangles are composed of tau—proteins that, when working normally, play a key role in transporting nutrients and other important materials throughout the cell. When tau proteins aggregate in the brain and form tangled clumps, the transportation system breaks down, cells begin to die, and Alzheimer's symptoms appear.

Gary, a professor in UNLV's Department of Chemistry and Biochemistry, suspects that GSK-3 may be inadvertently inducing tau tangling by accelerating a process called phosphorylation—a crucial metabolic step by which, under normal circumstances, cells regulate various molecular processes.

"Though we don't know why it becomes overactive and produces tangled tau, our thinking is that, if you could suppress or slow that phosphorylation activity of GSK-3, you could stop or slow the formation of tau tangles," Gary says. "Then maybe you could prevent or slow the progression of Alzheimer's."

In order to reduce GSK-3 and suppress the formation of tangles, Gary says, researchers would need to develop an inhibitor, a compound or drug that would depress its activity. Gary and his team of students are working to do just that.

"We take human cells of brain origin, treat

them with different drugs in a dish, and look at the molecular consequences of that treatment," he said. "You can't just eliminate the GSK-3 enzyme, because that would be problematic as well."

Gary says a handful of key questions are guiding his lab team's efforts. What are the consequences more broadly throughout the cell, and specifically, do different types of inhibitors do the same thing throughout the different areas where GSK-3 has a function? Or could different inhibitors have subtly different effects on GSK-3-related systems?

Gary says he's also interested in examining beta-catenin, another important molecule influenced by GSK-3. Beta-catenin plays a crucial role in the control of cell growth. If out of balance, it could potentially be a contributing cause of cancer.

According to Gary, when you inhibit GSK-3 with the goal of reducing tau tangles, it seems likely you would also reduce the phosphorylation of beta-catenin.

"You would initially assume that any inhibitor that suppresses GSK-3 enzyme activity would have a similar effect on beta-catenin, but we found that different inhibitors have different effects on beta-catenin," he says. "This is important because Alzheimer's work covers everything from treating patients to the other end of the spectrum, looking at molecular effects in isolated cells. But if we ever want to use this class of compound to

treat patients, we would want to know what else happens in the cell when you suppress tau phosphorylation by inhibiting GSK-3."

— SHANE BEVELL

Treatments in Balance

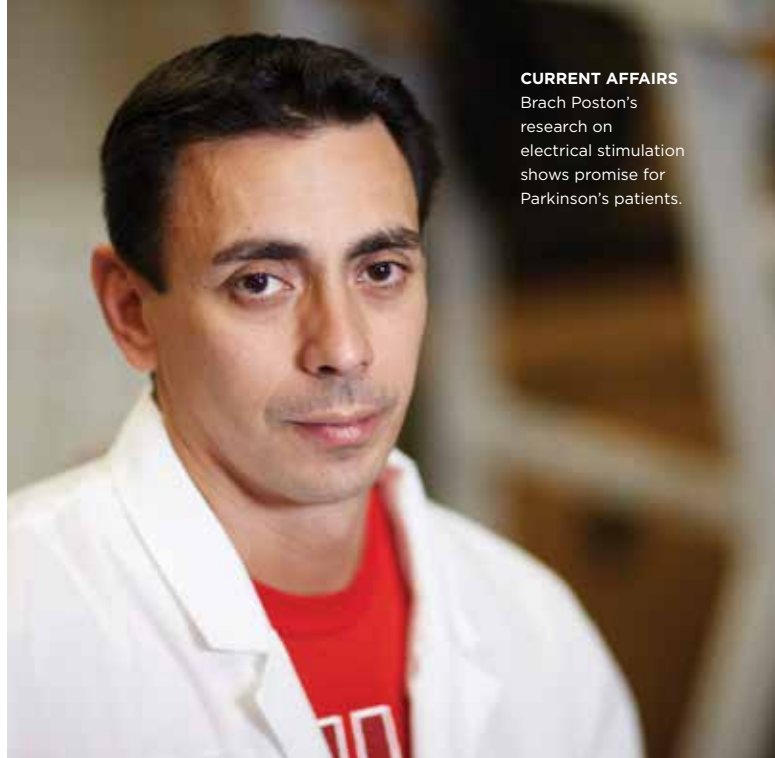
Much like other parents, Merrill Landers, a father of four who chairs UNLV's Department of Physical Therapy, often admonishes his children to go outside and play. Sometimes, he admits, he does this so that he and his wife have a moment's peace. More often, he says, it's to encourage his children to be more physically active. Landers knows that outdoor activities such as running around in the yard, kicking a soccer ball, or riding a bicycle are crucial to the growth and development of healthy young bodies.

And that may not be the only benefit. According to recent research findings, Landers indicated, an accumulation of steady physical activity during our youth and college years may generate a protective effect in the brain—one that could reduce the risk of, or even prevent, neurodegenerative diseases like Parkinson's disease.

Landers' research has focused on Parkinson's disease since he joined the UNLV faculty in 2001. His recent work involves examining how exercise might influence the disease's



BALANCING
ACT Physical activity can help protect us from Parkinson's, Merrill Landers says.



CURRENT AFFAIRS
Brach Poston's research on electrical stimulation shows promise for Parkinson's patients.

“Falling represents one of the two leading causes of premature death among people with Parkinson’s disease,” says Merrill Landers. “Falling can cause the domino effect of fractures to surgery to postoperative complications to other falls. For me, preventing falls is a big issue.”

course and determining whether patients’ physical activity might improve their balance and walking—work that has neatly segued into a broader set of findings on activity and neurodegenerative protective effects within the field, he indicated.

The four cardinal signs in Parkinson’s disease, Landers says, are bradykinesia (slowness of movement), rigidity, resting tremors, and postural instability (poor balance). The first three respond to and can be improved with medication. Postural instability does not respond to Parkinson’s disease medications; the only treatment approach that has been demonstrated to be beneficial is balance training.

“Falling represents one of the two leading causes of premature death among people with Parkinson’s disease,” says Landers. “The first is aspiration pneumonia. Falling can cause the domino effect of fractures to surgery to postoperative complications to other falls. For me, preventing falls is a big issue.”

One aspect of Parkinson’s disease that piques Landers’ curiosity is how falls affect people with the disease. Healthy adults typically evaluate the circumstances of a fall in two ways. If it’s a fluke, they forget about it. If there is a reasonable chance the fall could happen again, they seek ways to prevent future tumbles.

For people with Parkinson’s disease, it’s more complicated. A fall may cause anxiety or fear, emotions that may result in an unhealthy avoidance of normal activities. They may limit

visits to friends, attending church, or venturing out in public. Some become reclusive, a condition that can initiate a spiral of declining health. When fall-averse people with Parkinson’s disease seldom leave their homes, they tend to lose strength, coordination, and balance. These deficits, in a cruel irony, make them more susceptible to falling in their homes as they move from room to room.

“Some level of fear is good and can be protective, but too much can become harmful, especially in this disease population,” says Landers. “Those who shouldn’t be going out can be coached to become more careful and trained to improve their balance. Those who have high levels of fear need additional help.”

During a study involving older adults, Landers first measured “balance characteristics,” or participants’ ability to balance, while asking them to self-report their “balance confidence.” He followed the study participants for one year, noting when and how often they fell. The results indicated the self-assessments were the best predictors of future falls. The next best predictor was fall-avoidance behavior.

Using data obtained from another study, Landers helped rebuild the confidence of those who reported lower levels of balance and stability. Balance training became a key prescription.

As with his own children, Landers says, adults need exercise to maintain and strengthen muscles. Most people with Parkinson’s disease are

prescribed a regimen of low-intensity exercise—a level so low, Landers says, it’s ridiculous.

“When we look at someone with Parkinson’s disease and see the poor posture and the slow movements, we assume he or she can’t handle exercise. I think this is a big misconception and became something I wanted to test.”

In 2015, Landers led an “exercise boot camp” study to evaluate the ability of people with Parkinson’s to handle high-intensity exercise, which comprised three components: strength exercises at greater than 70 percent of the person’s one-repetition maximum, endurance exercises at 70 to 75 percent of the person’s estimated maximum heart rate, and exercises using dynamic and challenging balance-coordination tasks.

The results were clear: Those with high-intensity workouts responded well to the increased level of activity, and they did not experience more falls than the low-intensity group. What’s more, they enjoyed it—even more so than the low-intensity group enjoyed their activity.

Landers next sought to determine whether such intense exercise might act as an inhibitor of the disease’s progression. Many studies among laboratory animals had previously indicated that exercise can protect the brain from the disease. Some of the results even showed small animals actually recovering from the disease.

Landers then found results from five or six studies that indicated exercise during a person’s early adult life could have a cumulative effect and protect against the disease—that is, the risk

for Parkinson's decreased with an increase in physical activity in early adult life. Those results, he says, stimulated his curiosity further.

"As scientists, we know exercise benefits many different body systems, but the evidence strongly suggests that exercise also benefits our brains," Landers says. "Physiologically, exercise—particularly aerobic exercise—increases a chemical called brain-derived neurotrophic factor, or BDNF, which stimulates neuronal growth and helps potentiate neuroplasticity.

"BDNF is present when the brain learns a new skill or motor task. It also protects neurons, including the dopaminergic neurons that are affected by PD. So, presumably, having greater quantities of BDNF will protect more of those neurons, thereby slowing the progression of the disease."

Landers and his team are currently exploring how BDNF (known to increase with aerobic exercise) and anti-inflammatory enzymes influence disease progression and response to exercise, and whether the successes with laboratory animals might apply to human beings. If successful, the study could further validate exercise as a neuroprotective strategy against Parkinson's disease, either preventing its onset or slowing its progression.

Landers plans to present his findings during the World Parkinson Congress in Portland, Oregon, this October. He hopes his results will help convince those working with Parkinson's patients that high-intensity exercise is not only safe but more effective than low-intensity workouts.

In the future, Landers says his plans include studying the effects of exercise during midlife and later. He'll also explore related genetic information, which might allow scientists to gain additional insights into gait and balance function in those with Parkinson's disease.

As for his children, Landers expects them to make exercise a regular part of their lives. And he plans to join them.

— KEVIN DUNEGAN

Stimulating Parkinson's Research

UNLV's Brach Poston is exploring how low levels of electrical stimulation may contribute to improved motor performance in people with neurodegenerative diseases such as Parkinson's disease.

And how did he choose this scientific path? Foresight.

After earning a master's degree in exercise physiology from UNLV and a doctorate at the University of Colorado, Boulder, Poston began a postdoctoral program at Arizona State University. There he learned about brain stimulation, immediately recognizing its potential as

the next "big thing" in his field.

"I was introduced to the methods of transcranial magnetic stimulation [TMS] and transcranial direct current brain stimulation [tDCS]," Poston says. "I saw tDCS as a promising [way] to help people, and I was fortunate enough to be admitted to a postdoc program at the National Institutes of Health [NIH], where I was able to learn about this type of stimulation."

Poston spent the next year and a half studying how to use multiple noninvasive brain-stimulation techniques. After reviewing studies from other scientists, he became convinced that, as he puts it, "tDCS was most likely to be the best noninvasive stimulation option for aiding those with Parkinson's disease."

Parkinson's is a disease of the basal ganglia, an area of the brain that is vital to motor control and the production of dopamine. Dopamine is more known for its involvement in reward mechanisms and reinforcement learning in the brain, but it also plays a crucial role in mobility. When a person completes a complex movement, action, or task, dopamine is required to enable the basal ganglia to assist his or her motor cortex with movement planning, execution, and learning.

When using tDCS to treat Parkinson's patients, clinicians connect saline-soaked sponges to rubber electrodes that are distributed across the scalp. They then pass a weak electric current from one electrode to the other. The idea is to use the current to excite or inhibit activities that are thought to originate in specific areas of the brain. For Parkinson's disease patients, these areas often include the motor cortex, a part of the brain's cerebral cortex associated with muscular activity.

Preliminary findings by Poston and others have shown promise: tDCS does appear, in fact, to improve performance of simple motor tasks performed by hands and arms. These tasks can include using a pinch-grip movement to generate force against an object, retrieving small objects like buttons or coins, or performing an arm movement to a target.

The electric current doesn't cause the action to happen, Poston explains; it simply augments the normal increase in the "excitability of cortical neurons" when a task is practiced. When someone wants to lift an object—picking up a glass, for example—cortical neurons become excitable and act to execute that movement. When you practice a particular action, such as throwing a ball, the neurons become more excitable over time. This leads to improved accuracy and efficiency of movement.

The lower levels of dopamine common among Parkinson's patients cause impairments

in the communication between the basal ganglia and the motor cortex, a breakdown that reduces cortical neurons' excitability during movement execution—thus the slower movements, reduced muscle activity, and less accurate movements experienced by Parkinson's disease patients. By augmenting excitability among cortical neurons when tasks are being attempted, tDCS boosts motor control in the short term.

Although tDCS today is used only on outer areas of the brain, Poston believes—based on study results involving animal models—the technique might one day be used to elicit effects within deeper brain structures.

Poston's first studies at UNLV sought to identify the optimal method for one-time tDCS treatment among people with the disease. His findings helped identify optimal placements of electrodes, correct electric current strengths, and optimal durations for stimulation.

With these parameters established, Poston moved on to explore using daily stimulation to treat patients during a two-week period. "During a single treatment, we and other research groups have typically seen a 10 to 15 percent performance improvement, with the effects lasting up to 90 minutes," he says. "Daily application could produce a cumulative effect, and we hope to be able to elicit performance improvements of approximately 30 percent, which were seen in studies among young adults, when we apply stimulation over a two-week period."

Poston also broke some new ground last summer by using tDCS on the cerebellum. This hasn't been done in Parkinson's disease before but has been shown to increase motor performance in both younger and older adults. The rationale for this is that, because the cerebellum has been shown to compensate for impaired basal ganglia activity in Parkinson's disease, applying tDCS to excite the cerebellum may enhance this compensation.

Poston's previous and current studies focus exclusively on the hands and arms, but he says he now has the funding that will enable him to test tDCS while a person is walking. Doing this will involve Parkinson's disease patients walking on a treadmill. The goal is to determine how tDCS treatments affect patients' stride length, velocity, and movement variability.

So far, Poston says his results are positive and that, in the future, he expects the treatment to become a more widely used adjunctive therapy. He also says that affordable, wearable tDCS devices have a realistic potential to become available for home use, a place where patients or caregivers could easily apply the stimulation as needed.

— KEVIN DUNEGAN