Fall 2010

UCLA Department of Neurology

# Partners *in* Discovery


Rehabilitation is changing. New technology enables UCLA neurologists to better monitor patients' physical activities and to measure outcomes in order to improve therapy and recovery. "To translate our basic neuroscience research into therapies for disabled patients, we need better ways to monitor the physical activities and measure the outcomes that we are hoping to improve in the home and community," says Dr. Bruce Dobkin, UCLA professor of neurology and director of the UCLA Neurological Rehabilitation and Research Program.

To improve these measurements, Dobkin has been collaborating for the past year with Drs. William Kaiser and Maxim Batalin from the UCLA School of Engineering and Applied Science to use accelerometers as sensors to detect purposeful movement. Signals from the gravity sensors are sent to a computer server where the complex motions are analyzed by mathematical algorithms into definable patterns of activity, such as walking, ascending or descending stairs, bicycling, or exercising. This system of acquisition of sensor data, analysis of the data, and sending to the clinician a summary of the type, quantity, and quality of movement-related activity is called the Medical Daily Activity Wireless Network (MDAWN).

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# Chair's Column

John C. Mazziotta, M.D., Ph.D.
Chair, Department of Neurology
Stark Professor of Neurology
David Geffen School of Medicine at UCLA

"The secrets to successful recovery and regeneration in the nervous system have to do with its very development."

Those of us in the fields of neurology and neuroscience were taught and believed that once the system—including both the brain and spinal cord—was damaged there was no hope of recovery or repair. This "fact" was completely wrong. Recent discoveries have demonstrated that the nervous system can repair itself and regenerate components, but the process is much more complicated than in other organs in the body that are more homogeneous in their composition and function. Nevertheless, this is great news for those of us who seek to find ways to help individuals with disorders of the nervous system or injuries to it.

The secrets to successful recovery and regeneration in the nervous system have to do with its very development. Genes and pathways in nerve cells are programmed to construct the nervous system during fetal development and soon after birth. When injuries occur, these programs are reactivated in an attempt to repair the damage and reestablish function. In the adult human, this process is, at best, incomplete. Nevertheless, if you've known someone who has had a mild stroke or traumatic injury, you most likely have seen that person recover. The recovery is due, in part, to this process.

Investigators in the UCLA Department of Neurology, as well as elsewhere, are developing ways to facilitate and enhance these natural processes. Strategies have included attempts to "turn on" developmental genes in the appropriate pathways, use stem cells to repopulate damaged portions of the brain or spinal cord, and to consider the use of nano-technologies to build artificial structures in the brain and spinal cord to guide growth and connections, among other things. As you will read in the article entitled, "Engineering Recovery," these activities are not only possible but they are becoming practical.

One final note: neuroscientists have, in general, been unsuccessful in developing approaches to protect the brain or spinal cord from injury. As a result, such injuries do occur and take their toll. Strategies designed at enhancing recovery and rehabilitation of the nervous system combined with renewed efforts at protection will likely result in the best possible outcome for individuals afflicted by diseases of the nervous system or trauma to it. Your support in helping us to achieve these goals is, as always, greatly appreciated.

# Functional MRI as a Window into Early Familial Alzheimer's Disease


"Researchers at UCLA play a critical role in learning how the brain responds to early changes of AD."

The changes in the brain caused by Alzheimer's disease (AD) begin to develop many years prior to the emergence of symptoms of the disease. What then determines the point at which a given person with such changes demonstrates symptoms? No one can provide a complete answer to this question, but investigators at UCLA have made some headway.

In a pioneering observation, scientists at UCLA demonstrated, using functional magnetic resonance imaging (fMRI), that non-demented persons carrying a genetic risk factor for AD (the APOE 4 allele) showed an increased amount of blood flow in certain brain areas during a memory task than did persons who did not carry this version of the gene. This may represent an increased amount of brain activity required to accomplish the task in persons in whom the earliest pathological changes of AD may already have begun. Based on this observation, John Ringman, M.D., and colleagues at the Easton Center for Alzheimer's Disease Research in the UCLA Department of Neurology, working with Dr. Susan Bookheimer, attempted to confirm this in persons inheriting different genes that determine the development of an aggressive form of AD that occurs at a young age (familial AD or FAD typically beginning at age 40 to 50). In a paper published this year, they indicated that, using a different mental task, they were unable to reproduce this finding of a "compensatory increase" due to the FAD genes, but found an independent effect of the APOE 4 allele.

Meredith Braskie, Ph.D., working with Dr. Ringman and Paul Thompson, Ph.D., of the Laboratory for Neuroimaging (LONI) at UCLA, has taken this a step further. In an article soon to be published, she reveals that cognitively normal persons carrying FAD mutations showed an increase in blood flow to a region of the temporal lobe as they were closer to the age of disease onset. Though this might represent a compensatory response, it also could be due to a less specific increase in blood flow related to inflammation or some other aspect of the brain changes of AD. More recent findings support the latter explanation. Dr. Braskie has found that an increase in memory-task related blood flow was seen only in FAD mutation carriers who were performing the task poorly. This suggests that the increase blood flow seen in normal persons at increased genetic risk for developing AD may be due to directly to detrimental changes in the brain rather than occur as the result of compensation for such changes.

There is still much to learn about how the brain responds to the early changes of AD and researchers at UCLA are playing a critical role in clarifying these issues—issues with tremendous implications in how the disease is diagnosed and, ultimately, treated more effectively. ■

## Easton Alzheimer's Disease Research Center Conducts Two Exciting New Studies

Two new studies are being conducted by the Katherine and Benjamin Kagan Alzheimer's Disease Treatment Development Program within the UCLA Mary S. Easton Center for Alzheimer's Disease Research. Joshua Grill, Ph.D., is the principal investigator for both studies.

1 One study, recently funded by the John Douglas French Foundation, will examine the brain metabolic effects of Axona®, a prescription medical food that represents the newest means of treatment for Alzheimer's disease. The study will enroll 22 participants with Alzheimer's disease who are able to undergo positron emission tomography (PET) scans.

2 The Kagan Program is also conducting a clinical trial of a drug called a gamma secretase inhibitor, believed to prevent the production of beta amyloid, the toxic protein that accumulates in the brains of patients with Alzheimer's disease. This trial, which is sponsored by Bristol-Myers Squibb, is unique in that it is not enrolling patients who have been diagnosed with Alzheimer's disease and dementia. Instead, the study aims to enroll persons with mild memory impairment who may have the earliest stages of Alzheimer's disease, although they do not yet meet clinical criteria for dementia. In order to enroll, participants must have memory impairment and be willing to undergo lumbar puncture (also called a spinal tap). This procedure is used to examine protein levels in the cerebrospinal fluid. Only those with protein levels that place them at increased risk for dementia will be enrolled. ■

For more information about either of these studies, readers can contact the UCLA Mary S. Easton Center for Alzheimer's Disease Research at **(310) 794-6039.**

THE NEW

# REHAB

RE-ENGINEERING

increased

movement

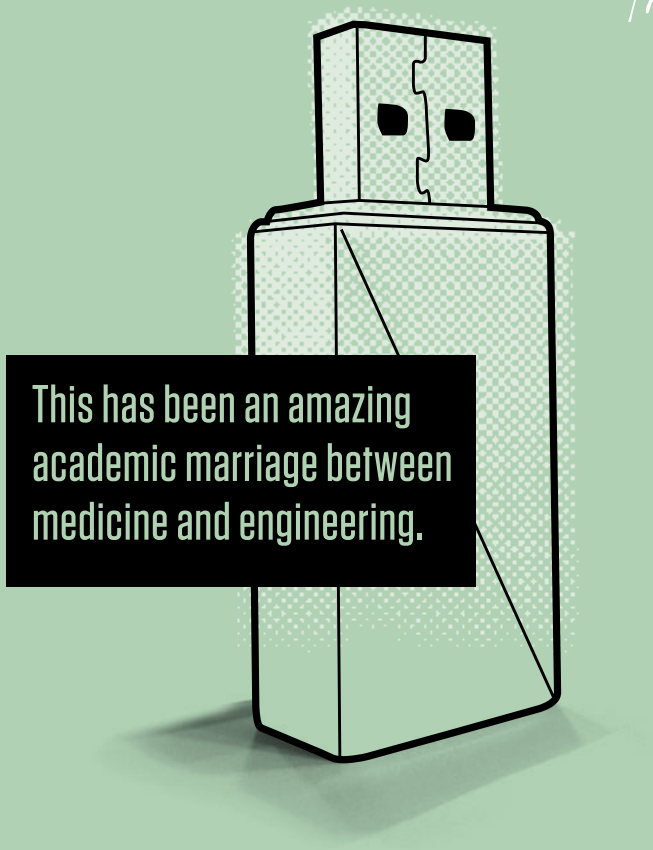
decreased

speed

distance

# RECOVERY

continued from cover



This has been an amazing academic marriage between medicine and engineering.

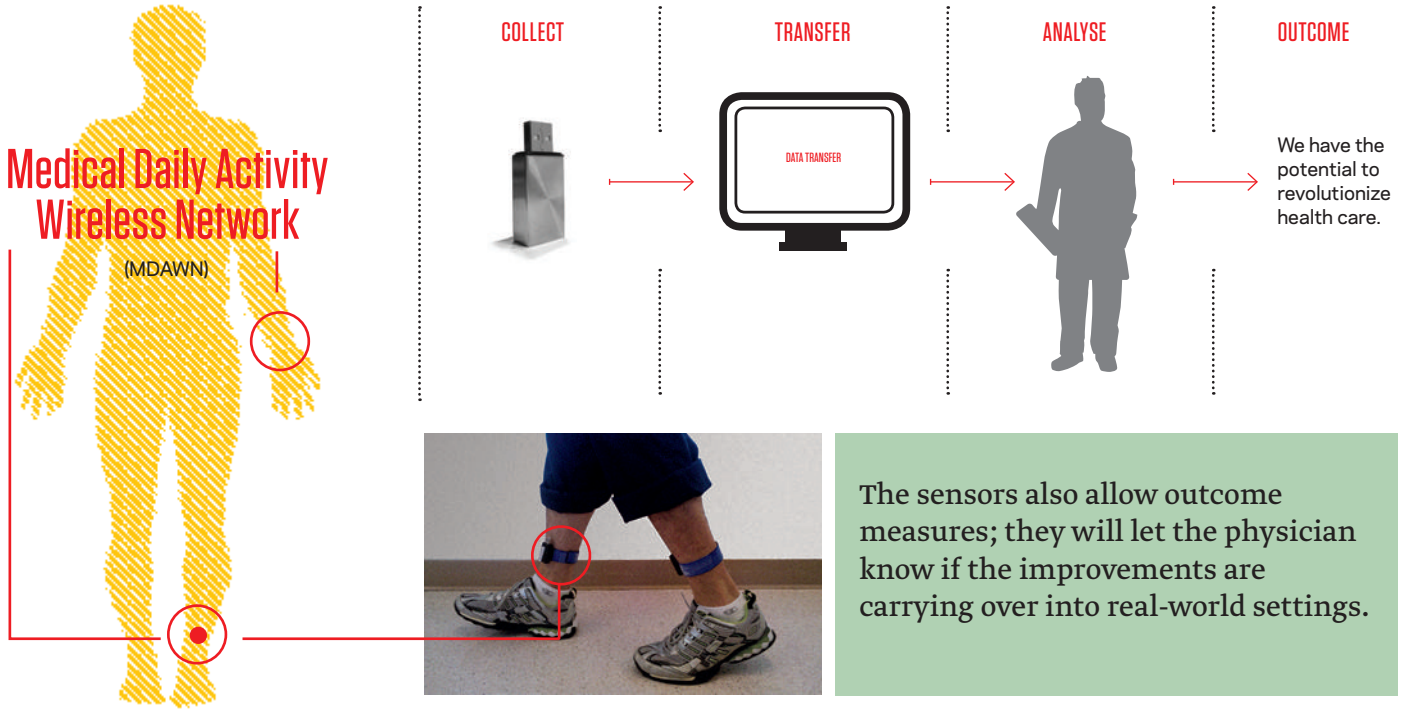
MDAWN can not only measure activities that patients want to maintain or recover, but it also can promote exercise and retraining of impaired skills, as well as guide rehabilitation. The low-cost wireless devices, which are the size of a wrist watch and are attached to elastic bands to fit around the wrists or ankles, record tiny accelerations, decelerations, and rotations as an arm or leg moves through space. The technology breakthrough is all about the trained machine-learning algorithms developed by engineers and computer scientists at UCLA. They can identify and characterize typical movements in real-world settings, such as exercising with each lower extremity, bicycling, climbing stairs, and walking. Most important, for the first time, MDAWN reveals how fast patients walk and describes the quality of walking under varying environmental challenges.

"By having continuous information about walking in the real world, as opposed to a laboratory or clinic setting, you can give patients much better feedback," says Dobkin.

The devices bring new, high quality measures into daily care to monitor activity as it increases or decreases in relation to a new medication or physical therapy. "We derive information about speed, distance, and quality of walking. The sensors become monitoring tools," he explains. They enable physicians and therapists to assess compliance with exercise and skills practice, and to test the utility of providing feedback to patients about the type and quantity of their daily skills practice and exercise.

According to Dobkin, what this measuring and collecting of data means is that when taking care of a patient with Parkinson's disease, for instance, neurologists could measure when a particular drug is having a peak effect or little effect on walking. They could also determine if patients are following instructions. "It will allow us to develop feedback systems."

"This will have a tremendous impact on clinical trials. We have spent $20 million over the past 12 years on clinical trials of different interventions for walking in people with stroke, spinal cord injury, and multiple sclerosis. Half that money paid to bring subjects back to the clinic and perform laboratory measurements. With the MDAWN, we can cut those costs dramatically by sending data from the accelerometers wirelessly over the Internet. In addition, our primary outcome measure was whether the rehab strategy could increase patients' walking speeds. We had patients walk 50 feet in a lab setting, and we






**The sensors also allow outcome measures; they will let the physician know if the improvements are carrying over into real-world settings.**

improved their speeds by 25 percent with our experimental therapies, but how do we know what that means if we have no measure of what the gains enabled people to do at home and in the real world?"

The sensors also allow outcome measures; they will let the physician know if the improvements are carrying over into real-world settings. "If we can monitor patients for a week before and after every 12 sessions, and then at completion of rehab one year later, we can take that 50-foot walk and decide if it really mattered," he says.

Dobkin is collaborating with electrical engineering professor William Kaiser and his team on the development of other powerful wireless devices, including restorators and canes, which will make rehab more personalized with real-time monitoring and data collection. He believes these devices have the potential to revolutionize health care.

"This has been an amazing academic marriage between medicine and engineering," Dobkin says. "Engineering developed these kinds of devices for athletes. They're also measuring the activity levels of the elderly and first responders. Now we are hoping to do work on disabled neurology patients." He believes that UCLA is a world leader in this arena, and that the University's real advantage is close collaborative interaction. "We're rubbing elbows with each other and across disciplines. Here, it's easy to share information and to problem-solve."

Remote monitoring devices have the potential to be cost-effective and wide-reaching in application, enabling neurologists to target large samples and access hard-to-reach groups, says Dobkin. He believes costs can be cut by half and that clinical trials that aim to prevent deterioration of activity or to lessen disabilities will have fewer drop-outs if patients can be monitored at home. He calls this an "ecologically sound measurement" as compared to an artificial measurement in a lab setting.

Dobkin is about to conduct two major studies. The first, scheduled to begin December, 2010, is the Stroke Inpatient Rehabilitation Reinforcement Activity Study (SIRRACT), involving 20 inpatient stroke rehabilitation sites around the world, including Korea, Nigeria, Italy, England, France, Australia, and Central America, among others, and about 200-250 patients.

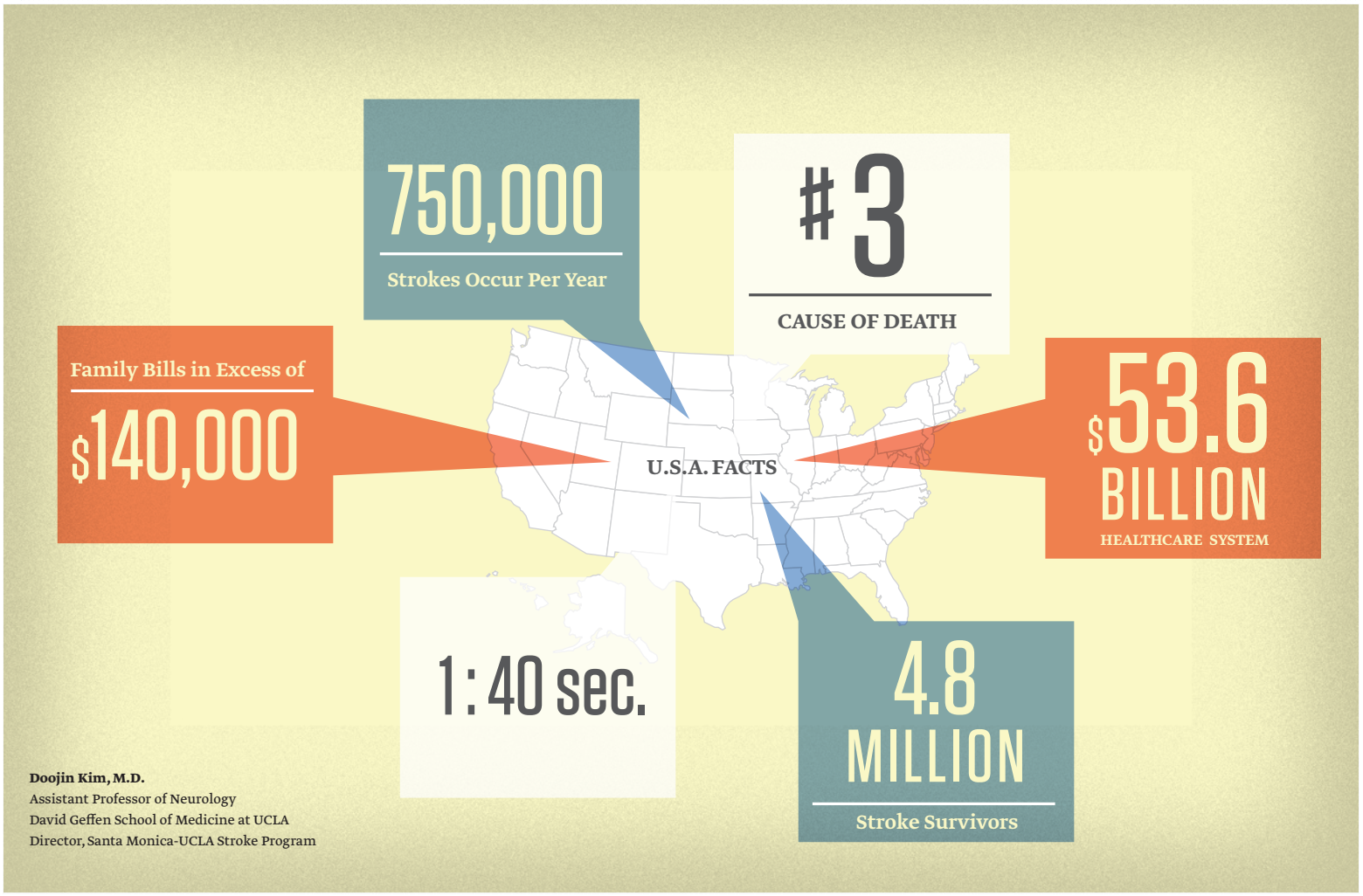
"We will randomize the inpatients to receive usual care from therapists or to also get feedback from the sensors about speed and distance walked during their therapies, how much exercise they are doing on their own, and how much time they are active. The feedback group, then, will get continuous measures of progress. We want to know if this incentivizes them to get better. They will also wear the accelerometers when they first get home, so we can learn how well they were prepared for home discharge. Then, they'll wear the device every two months to give us information on improvement," he explains. "It's a practical system and it will answer the questions, do people get enough therapy or the right kind of therapy and how much and how well do they practice?"

The second study starts in January, 2011. It involves the use of a small arm or leg pedaling device modified by UCLA engineers, so that it can be used by bedridden patients recovering from, for example, transplants. They call it the UCFit. The aim is to help hospital patients stay active and combat the muscle loss that comes from prolonged bed rest and illness. These patients now will be able to exercise their arms and legs to maintain some muscle strength. This device measures torque and repetitions and this will be used as feedback for patients and their families. The primary outcome, according to Dobkin, will be to see if they can walk independently upon discharge, and how well they walk. With preventive strategies, "We're trying to create a new culture in the hospital," he says.

The challenge for the engineers is cost, says Dobkin. "How inexpensively can you provide this information about activity to patients and medical staff? Can it be done without adding to the costs of healthcare and, overall, decrease the cost of care and of clinical trials?"

His excitement is palpable. "The applications are endless. Combine remote monitoring devices with telemedicine and it's possible that one therapist could manage a progressive program of rehabilitation by spending no more than 15 minutes 1-2 times a week with a patient who is on the Internet at home.

"Taking advantage of this type of technology will bring us into the 21st century," says Dobkin. "Each disability is different, and these new devices, by enabling us to look at individual activity patterns over time, will enable us to accurately analyze each patient's movement patterns to create a therapy specifically engineered to each person's disability." Patients will recover more quickly from customized therapy, and there will be a cost benefit, as well. They'll be able to get feedback about their performance without waiting for an office visit. ■




**Doojin Kim, M.D.**
Assistant Professor of Neurology
David Geffen School of Medicine at UCLA
Director, Santa Monica-UCLA Stroke Program

**Doojin Kim, M.D.**

# Stroke Prevention

The facts regarding stroke are sobering. In the United States alone, over 750,000 strokes occur per year. This means someone suffers a stroke every 40 seconds. Although stroke is the nation's third leading cause of death, the majority of stroke victims survive. There are 4.8 million stroke survivors in the U.S. today. It is estimated that stroke can cost a survivor's family in excess of $140,000. Stroke costs our healthcare system $53.6 billion a year and places a great burden on survivors, their families, and the U.S. economy.

Fortunately, there have been advances in the treatment of stroke after it has occurred. The time window for intravenous tPA, a clot-busting medication, has been extended to 4.5 hours. There are also multiple new devices that are used to help stroke victims. The best treatment, though, should be administered before stroke occurs. It is called prevention.

In order to prevent stroke, it is important that you identify and understand your risk factors. While some are non-modifiable—they can't be changed—others can and should be modified.

### Non-Modifiable Risk Factors

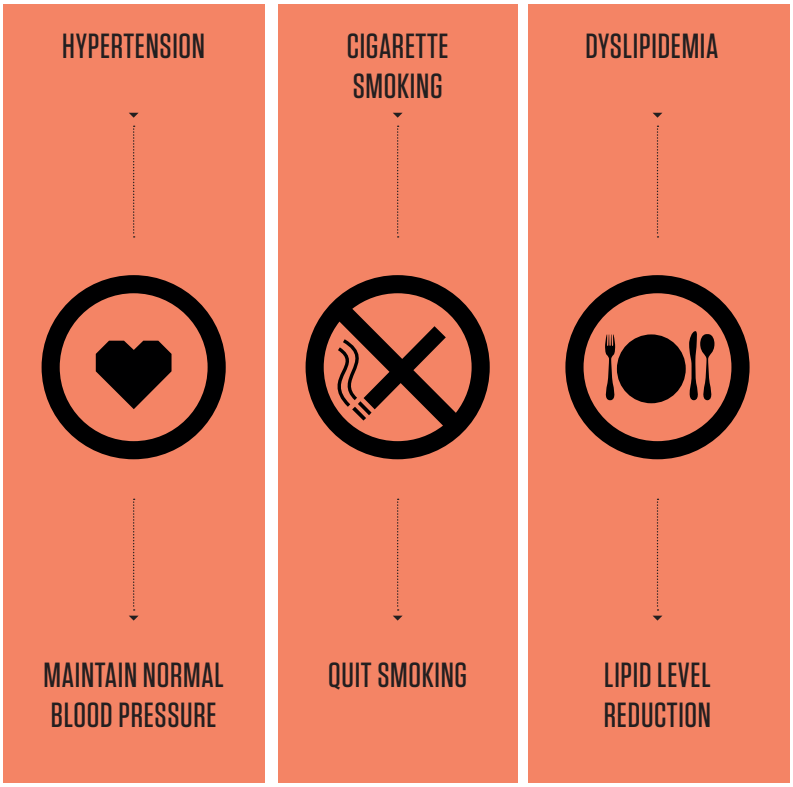
Non-modifiable risk factors for stroke include age, sex, and race/ethnicity. The risk of stroke doubles for each successive decade after age 55. Thus, a 75-year-old has four times the risk of stroke as a 55-year-old. Stroke is more prevalent in men than women. African Americans and some Hispanic American groups have a higher incidence of stroke mortality than Caucasian Americans. Some Asian American groups also have a high incidence of stroke.

### Modifiable Risk Factors

Many of the risk factors for ischemic stroke can be reduced with lifestyle changes and/or medication.

Hypertension (high blood pressure), a major risk factor for stroke, is modifiable. Blood pressure is the force of blood pushing against the walls of the arteries. High blood pressure causes the heart to pump harder to move blood through the body, which can weaken blood vessels and damage organs such as the brain. Treatment of hypertension with medications can reduce stroke risk by about 35 to

## Modifiable Risk Factors




45 percent. It is recommended that blood pressure should be reduced to under 140/90. Lifestyle changes can be paired with medications to achieve a normal blood pressure.

Cigarette smoking, which doubles one's risk of stroke, contributes to approximately 12 to 14 percent of all stroke deaths. Smoking reduces the amount of oxygen in the blood, causing the heart to work harder. There is growing acceptance that passive cigarette smoking is also a risk factor, perhaps of the same magnitude as active smoking. Although it can be difficult to quit, smoking cessation is associated with a rapid reduction in stroke risk.

Elevated cholesterol levels (dyslipidemia), which can lead to plaque build-up, are associated with a greater incidence of ischemic stroke. Reduction of lipid levels can dramatically lower stroke risk. Lifestyle changes, such as dietary adjustments and increased cardiovascular exercise, can be helpful, but are not always sufficient. Sometimes medication is needed to reduce total lipid and bad cholesterol levels. Certain cholesterol medications have been shown to reduce the risk of first stroke by 29%.

Hypertension, cigarette smoking, and dyslipidemia are only three of the many modifiable risk factors for stroke. Some others that, when treated, can reduce the risk of stroke include diabetes, atrial fibrillation, carotid artery disease, and the estrogen loss associated with menopause.

If you are worried about stroke and are interested in reducing your risk factors, it is important to discuss your concerns with your physician. He or she can evaluate your potential risk factors and make recommendations to address them through medical treatments and/or lifestyle changes. ■

**Charles C. Flippen, II, M.D.** / Associate Professor of Neurology/Headache Research and Treatment Program/David Geffen School of Medicine at UCLA/Physician Specialist/Coordinator of Adult Neurology Clinical Services/Olive View-UCLA Medical Center

### Charles C. Flippen, II, M.D.

# Why I Do This

"I get a lot of personal satisfaction from helping people," says UCLA neurologist Charles Flippen, II, M.D. Dr. Flippen wears two hats within the Department of Neurology. As physician specialist and coordinator of Adult Neurology Clinical Service at Olive View-UCLA Medical Center and associate professor, Headache Research and Treatment Program, David Geffen School of Medicine at UCLA, he treats a diverse patient population.

When asked about his motivation, he responds in two parts to what he terms a multi-level question. "To answer the first part of that question, why am I at Olive View, I've always worked in public health settings, and I go where I am needed most." (Olive View-UCLA Medical Center is a county hospital, located in the north end of the San Fernando Valley, which serves the needs of low income and indigent patients as well as the surrounding community.) Prior to joining UCLA in 1999, Flippen served as a clinical instructor for the Department of Neurology at Indiana University School of Medicine based at their indigent care hospital, Wishard Memorial. Previously, he served as a staff physician at Hurley Medical Center and McLaren Regional Medical Center in Flint, Michigan.

"I grew up in an urban setting with a large underinsured population," says the native Michigander. "I feel connected to patients in this setting." A graduate of University of Michigan Medical School, he interned at Henry Ford Hospital in Detroit and completed his residency at the University of Maryland School of Medicine.

As for the second part of the question, why he chose academic medicine, Flippen answers that he grew up in a teaching environment. "Both my parents were teachers, and they encouraged me to find answers on my own and then come and talk about it with them. They taught me to view each challenge from the aspect of what I could learn from it, and that's the way I'm raising my kids." He and his wife, a volunteer UCLA dermatologist who now practices at Kaiser, have two sons, who are 8 and 10 years old.

At Olive View, Dr. Flippen does three months of in-patient consultation and two weekly clinics, plus a seizure clinic every other week. He sees about 10 patients per clinic on average. His specialty at Westwood, where he practices twice a week, is headache, for which he treats between eight to 10 patients per day in clinic.

"Pain is one of the most poorly understood and treated disorders," he explains. "I like a challenge, and I like building relationships with patients. The Headache Research and Treatment Program affords me the opportunity to interact with a younger population. Plus, if I can help alleviate pain, patients are very grateful." ■


Dr. Flippen with his sons

Charity begins at home
but should not end there.

—Sir Francis Bacon

The late Katherine Kagan

The Power of Philanthropy

# A Passion for Giving

The back-story of the Sidell-Kagan Foundation is a lesson in philanthropy, according to the Foundation's administrator, Jerilee Nickerson, CPA. "My original client was Pescha Sidell, who was a pianist and the sister of Benjamin Kagan. I handled her estate. Pescha's husband, Nathan, had set up the Foundation, but it wasn't funded. That's how I became the accountant for the Kagans," Nickerson explains. She had a close relationship with the couple and dined with them weekly at their home.

Dr. Robert Kagan, who suffered from Alzheimer's disease (AD) and was treated at UCLA, died of an unexpected heart attack in 1997. He had founded and headed the Department of Pediatrics at Cedars-Sinai Medical Center, where he remained for over 30 years. A graduate of Johns Hopkins School of Medicine, he completed his residency at Columbia Babies Hospital in New York, served as a major in the U.S. Army, and then spent 10 years as head of pediatrics at Michael Reese Hospital in Chicago before moving to California in 1955.

Although there is no cure for AD, there are drug treatments that help slow the progression of the disease. Dr. Kagan was fortunate to have dramatically improved with the only approved drug for AD at the time. He maintained that improvement for three years until he died of an unexpected heart attack. Before he passed away, his wife, Katherine, made a commitment to help others who have AD. Mrs. Kagan was passionate in her desire to support the development of better treatments for AD. The Sidell-Kagan Foundation, which the Kagans headed, committed long-term funding for AD research and the Katherine & Benjamin Kagan Alzheimer's Disease Treatment Program was established.

An example of the gift that keeps on giving, the program provides access to the latest experimental therapies and offers eligible subjects participation in various research studies related to memory and dementia. All research-related procedures, including visits with UCLA neurologists, are free of charge to the study participants.

According to Nickerson and Jeannette Hahm, the attorney for the Foundation, Mrs. Kagan enjoyed seeing her support going directly to those for whom it was meant. She loved getting to know the people whom she helped, including doctors, researchers, and nursing staff, and once described it as "the gift I get. That in itself is so meaningful."

Mrs. Kagan's first priority was her husband—she was totally devoted to him, Nickerson recalls, as well as to raising their two sons, Chris and Robert—and to that end she undertook the project of building a home in Beverly Hills with features to accommodate a disabled person with diminishing mental capacity. Ahead of its time, the single-level home featured a wheelchair-accessible swimming pool, a bathtub designed for a disabled person, and even an independent power generator to support medical equipment in case of a power failure. The gates on the perimeter of the house could be electronically locked from inside to prevent wandering, a challenge raised by many AD patients. Dr. Kagan was able to enjoy a few months in the new home before he passed away.

"It's always nice if someone can have a passion for a certain cause and support it while they're alive," Nickerson says. That is certainly true In the case of Katherine Kagan. ■

## You Can Make A Difference!

The Department of Neurology at the David Geffen School of Medicine at UCLA is an academic department dedicated to understanding the human nervous system and to improving the lives of people with neurological diseases.

The Department of Neurology has many pressing needs to continue our mission. You can direct your charitable gifts of cash, securities, real estate, art, or other tangibles to our greatest needs, under the direction of Dr. John Mazziotta, Chair of the Department, or to specific research, training, laboratories, or programs of specific physicians or diseases. For more information please contact Patricia Roderick, Director of Development, UCLA Department of Neurology, **(310) 267-1837** or **proderick@support.ucla.edu**.

The late Katherine Kagan

Inspiring Philanthropy:

# A Bar Mitzvah Boy's Gift to Brain Cancer Research

"Since Pop Pop wasn't going to be at my bar mitzvah, I wanted him to be part of it."

Garrett Greller is 14 and a freshman at Mira Costa High School. His favorite subject is English, he loves going to the beach with his friends, and he has a passion for tennis and ping pong. A year ago, he donated 10 percent of the money he received as gifts for his bar mitzvah to UCLA's Dr. Timothy Cloughesy for brain cancer research.

* The bar mitzvah is an initiation ceremony in Judaism marking a boy's 13th birthday and signifying the beginning of religious responsibility.

Above: Garrett Greller

Left: Garrett with his late grandfather, Jerry Lushing

Garrett's beloved grandfather, Jerry Lushing, had recently passed away from the disease. Touched by Garrett's generosity, we sat down with him and his mother, Linda, to learn Garrett's thoughts about his grandfather, philanthropy, and what inspired him to make the gift.

"Since Pop Pop wasn't going to be at my bar mitzvah, I wanted him to be part of it," Garrett explained. "I knew right away that this was what I wanted to do. I could have given to an animal shelter—I love animals—but this came into my mind right away. I wanted the money to go to research to find a cure for Pop Pop's disease."

"My dad was an exceptional man," interjected Linda Greller. "Ironically, he was known for his brain. He was brilliant. Everyone went to him for everything, but love of family was the most important thing to him. It was family first.

To give you an example of his great spirit, the night before he started chemo, we were all at the hospital. It was 10:30 at night and he had markings all over his head. Still, he came out and said, 'Let's all go to Pink's for a hot dog.' That's the kind of man he was."

Jerry Lushing also loved to travel with his family—and it is a big family: his wife, Gloria; four children; their spouses and kids—20 people in all. "Our last trip before he got sick was a cruise to Europe. He loved to be with everyone and he loved planning that trip, down to the last detail," said Linda.

"I love all the cruises we went on, especially the last one. Pop Pop was the leader and he took us to fun places. Greece was really fun, and Venice," Garrett reminisced.

Lushing had a poker club and he taught all the grandkids—there are 12 of them—how to play. "All my cousins play poker. We still have sleepovers at my grandparents' house."

According to Garrett and his mom, the Lushings instilled philanthropic values in their children and grandchildren by example. "My grandparents always got awards; they were always giving, my Nana and Pop Pop," Garrett proudly boasted.

One of Garrett's friends, who recently learned about his gift, was incredulous. "My friend said, 'You mean you gave away your money?' I told him that it's not always about yourself. You don't always need another new thing. You might get sick of it in two weeks; but if you give to something, like a charity, that won't happen."

Garrett is involved with another local charity, "Lunches for Love," through the mother of a friend. Every three weeks, he is part of a group who make lunches and distribute them to the homeless in Downtown L.A. "It feels good to give,' he said.

What does Garrett's grandmother have to say about all this? "I am so proud and touched by my grandson, Garrett's, generous gift to Dr. Cloughesy," Gloria Lushing said. "It was given with love and with the hope that his gift, along with others, will make a difference in finding a cure for this devastating disease that killed a very important man in his life, his grandfather, Jerry, who was bigger than life to me, his wife, as well as to his 12 grandchildren, of whom Garrett is one."

Linda Greller agreed wholeheartedly and added another thought, "Dr. Cloughesy was our guardian angel for two and a half years, always with a smile on his face. He gave us hope, and it was a gift." ■

MEET
A
SCIENTIST

Ming Guo, M.D., Ph.D.
Associate Professor of Neurology and Molecular and Medical Pharmacology/Department of Neurology/David Geffen School of Medicine at UCLA

# Ming Guo, M.D., Ph.D.

To meet and chat with Dr. Ming Guo, you would never know that this charming, gentle young woman runs a lab at UCLA where her work is having a significant impact on advancing our insights into the two most common neurodegenerative disorders of the brain, Alzheimer's and Parkinson's diseases. Her work on Parkinson's disease has been internationally recognized as ground-breaking and field-defining.

"The brain is the essence of a human being. It's who we are."

"I chose to specialize in neurology because, really, life is brain," she says. "The brain is the essence of a human being. It's who we are. It contains so many mysteries and a lot of diseases. Also, neurology is a young profession. You can still contribute to the growth of the field."

Guo's goal is to understand the molecular mechanism—the function—of genes in the body in order to find a cure for Alzheimer's and Parkinson's diseases.

She is well on her way. Her lab has made important findings in the field of neurodegeneration using *Drosophila* (fruit flies) as a model. As the second most common neurodegenerative disorder, Parkinson's disease affects 5% of people over the age of 80, and no treatments can halt the progression of the disease. Dopamine replacement-based therapy only works well on the earlier stages of motor symptoms. Patients in the late stages and their non-motor symptoms usually do not respond well to this therapy.

Dr. Guo's lab studies recently identified genes which mediate familial Parkinson's disease, such as *PINK1, parkin,* and *LRRK2,* in order to understand the pathogenesis of the disease. Using the *Drosophila* model, her group was one of the first two in the world to report the function of the *PINK1* gene, and that *PINK1* and *parkin* function in a common genetic pathway to regulate mitochondrial integrity.

Her studies in *Drosophila* are key to understanding the fundamental cellular defects in Parkinson's disease patients. Mutations of the *PINK1* gene are common causes of autosomal recessive Parkinson's disease. Dr. Guo demonstrated that the loss of *PINK1* in *Drosophila* leads to defects in mitochondrial function in multiple tissues including dopamine neurons and muscle. The fact that *Drosophila* lacking *PINK1* could be rescued by human *PINK1* demonstrates that there is some functional conservation of the gene across species. The understanding of the cause of Parkinson's disease may significantly benefit the development of new therapeutic approaches for its treatment.

"If this model is correct, Parkinson's disease perhaps results from accumulation of damaged mitochondria. It suggests that the goal should be to develop pathway-specific therapies that would allow us to optimize the treatment potential and minimize side effects," says Guo.

Why *Drosophila?* According to Guo, 75 percent of human disease genes have *Drosophila* counterparts and the biological pathways are conserved. "They have a short generation time, and are easy to work with. From here, we will move into studying disease in humans."

She explains that Alzheimer's, Parkinson's, and ALS are all age-dependent diseases. "Our ultimate goal is to improve the quality of mitochondria to dial back the aging clock. Basically, we want to make fabulous mitochondria!"

A mentor, Guo directs a lab with five postdocs, five graduate students, four undergraduates, and a technician. The trainees in her lab have enjoyed outstanding success.

In addition, as a Board-certified neurologist, she spends 20 percent of her time caring for patients with neurological diseases. "My clinical work has provided me with a constant source of motivation and deep understanding of the diseases for my research," she says.

Guo currently holds several active grants, including four NIH grants. She is the recipient of prestigious private foundation awards, including the Alfred P. Sloan Foundation Award, the McKnight Foundation Brain Disease Award and the Klingenstein Fellowship. She was selected among the 10 fellows as the 12th Robert H. Ebert Clinical Scholar, outstanding physician-scientist of the year. She was 2009 recipient of the prestigious Derek Denny-Brown Neurological Scholars Award, given annually to a newly elected member of the American Neurological Association who promises to make a major contribution to the field of neurology. ■

## MEET OUR VOLUNTARY FACULTY

### Arthur Kowell, M.D., Ph.D.
### Co-chair, UCLA Neurology Voluntary Faculty Association (UNVFA)

**UCLA's voluntary faculty** comprises a dedicated group of physicians who help us ensure that UCLA Neurology residents receive the best medical education possible. Our voluntary faculty has grown from only a few neurologists in the 1950s and 1960s to 70 as of 2010. Many of them have been and are accomplished full-time academicians, and some have successful private practices. The commitment of these doctors in offering their clinical expertise and time without financial remuneration speaks to their generosity of spirit and is deeply appreciated.

"We learn from those we teach," explains Dr. Arthur Kowell, discussing his role as a voluntary faculty member and co-chair of the UCLA Neurology Voluntary Faculty Association (UNFVA). "I have a strong commitment to UCLA as a voluntary faculty member. I have taught medical students, fellows, and residents—even students from other medical schools. Being a voluntary faculty member means you're always in the educational process. It forces you to rewind back to the resident's level to approach problems. It's part of the educational renewal process. It forces you to be current, and to integrate and pass on older knowledge that computers don't access."

Kowell, who has a private practice, Encino Neurological Medical Group, with two other neurologists who are voluntary faculty, has been active clinically since 1978. He graduated from the University of Pennsylvania Medical School with combined M.D. and Ph.D. degrees; did his internship in Medicine at UCLA; and completed his residency in Neurology here. A clinical neurophysiologist, Kowell has an interest in dementia and a subspecialty in violent and aggressive behavior. His research at UCLA has been connected with PET scans and the molecular biology of brain DNA.

He feels fortunate to have spent his entire career in one place. "I feel a responsibility to UCLA to maintain the educational process, and I don't think they could run the system without voluntary faculty," he says. "I'm happy to be affiliated with an organization where people want to give back to the system."

Kowell continues to be educated by the teaching experience, not only in the microclimate of Los Angeles, but also within the larger reaches of medicine throughout the country. "It's one of the best ways to stay educated," he says. "It's a privilege to be on the voluntary faculty." ■

## Ride Ataxia to Benefit Research of Dr. Susan Perlman

Dr. Susan Perlman, after almost 30 years of studying and treating ataxias as well as Huntington's disease, has not only built the nation's largest clinical practice dedicated to those disorders, but also has given patients hope and optimism. In addition, her work has also inspired others to help raise awareness and funds.

One extraordinary example is Kyle Bryant, who founded Ride Ataxia in 2007. Stricken with Friedreich's Ataxia (FA), a debilitating, life-shortening, degenerative neuro-muscular disorder, Kyle had to give up many things he enjoyed, but he refused to give up his passion—cycling. He and the Ride Ataxia team have traveled over 3,500 miles in three years and have raised almost $1 million in research funds. This year, on December 4 and 5, Ride Ataxia SoCal will travel 80 miles along the coast from Long Beach to Dana Point and back. Proceeds will benefit Dr. Perlman's research.

Ride Ataxia is a program of the Friedreich's Ataxia Research Alliance (FARA). FARA is a non-profit organization dedicated to research and a cure for FA. To learn more about the ride visit **www.rideataxia.org.** ■



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MEET
OUR
ALUMNI

# Rohit Bakshi, M.D., F.A.A.N.

Dr. Rohit Bakshi, Professor of Neurology at Brigham and Women's Hospital and Harvard Medical School and director of the Laboratory for Neuroimaging Research at Partners Multiple Sclerosis Center in Boston, MA, completed a neurology residency at UCLA in 1995.

He has built a research program involving quantitative Magnetic Resonance Imaging (MRI) in MS and currently is principal investigator on an R01 grant from the National Institutes of Health, focusing on gray matter disease in MS. His work also has been funded by the National Science Foundation and National Multiple Sclerosis Society.

"UCLA was a great place for residency training," says Dr. Rohit Bakshi. "In the early '90s, Dr. John Mazziotta was the director of the program and he had a close relationship to the residents. I looked at him for a role model. I had followed his work—especially in imaging technology—and was impressed."

Bakshi, a native of Buffalo, NY, and graduate of Cornell University and University at Buffalo Medical School, completed a one-year neuroscience research fellowship at UCSF and a one-year internship at Massachusetts General Hospital and Harvard Medical School prior to his neurology residency at UCLA. He then completed a neuroimaging fellowship at Dent Neurologic Institute in Buffalo.

"I had the opportunity to learn a lot of neurology while I was at UCLA. Dr. Robert Collins (former chair) put together extraordinary faculty and I was able to learn from world experts in the field of MS, such as Dr. Jerome Engel in epilepsy, Dr. Robert Baloh in neuro-otology, Drs. Jeff Cummings and Frank Benson in neurobehavior, Dr. George Ellison in multiple sclerosis, Dr. Bruce Dobkin in neuro-rehab, Dr. Jeff Saver in stroke, and Dr. Susan Perlman in ataxia. UCLA is extremely well-organized in these subspecialties," Bakshi says.

"I trained directly with Dr. Mazziotta in his laboratory and he got me very interested in neuroimaging. I saw a tremendous variety of neurologic patients at UCLA, the Sepulveda VA, and Olive View. Plus, the other residents were very good to train with side by side. Many of them have gone on to do very important things."

Dr. Bakshi is one of those people. In addition to his teaching responsibilities, laboratory directorship, and research, he has delivered more than 200 invited academic lectures and authored more than 190 peer-reviewed articles. A member of the American Neurological Association and a Fellow of the American Academy of Neurology, he serves on the editorial Board of the Journal of Neuroimaging and as associate editor of the journal Neurotherapeutics. He is treasurer of the American Society for Experimental NeuroTherapeutics, past chair of the Neuroimaging Section of the American Academy of Neurology, and a past president of the American Society of Neuroimaging. ■