FOCUS on Research

Solving the Inequities of Stroke

As a clinician and neuroscientist, Dr. Bruce Ovbiagele sees first-hand the devastating effects of stroke on individuals and families. In severe cases, stroke can cause long-term damage affecting mobility, speech, and how one thinks and feels. Unfortunately, stroke also kills millions of people per year.

But as a global health scholar concerned about high-risk populations, Ovbiagele looks beyond the physical symptoms. He eyes a variety of societal ills and health disparities that target vulnerable people, such as racial and ethnic minorities, military Veterans, disabled, elderly, rural dwellers, and the poor.

Ovbiagele – who is Chief of Staff at the San Francisco VA Health Care System (SFVAHCS), and an Associate Dean and Professor of Neurology at University of California, San Francisco (UCSF) – aims through his research to reduce the massive burden of stroke. He has led several National Institutes of Health (NIH) studies focused on improving outcomes for those at risk of stroke in the U.S. and Sub-Saharan Africa. Still, he understands there are significant challenges ahead.

Consider the daunting data: Globally, more than 13 million people suffer a stroke each year, and an estimated 5.5 million die as a result, according to the World Stroke Organization. According to the CDC, the disease is a leading cause of long-term disability – 795,000 will suffer a stroke, and 140,000 will die each year in the U.S.

Stark facts like the following continue to stoke Ovbiagele’s research passion: The risk of stroke is nearly twice as high for African Americans as for Whites, and African Americans have the highest death rate due to stroke. In addition, although some progress has been made over the past few decades in stroke-related death among various races and ethnicities, Hispanics have seen an increase in deaths as a result of a stroke since 2013.

“This has been pervasive for five decades in the U.S.,” said Ovbiagele. “We know about some inequities. For example, that African Americans either at risk for stroke or who have had a stroke do not get timely treatment, or even the best evidence-based treatments, compared to non-Hispanic Whites.”

“In 50 years, we have pinpointed some disparities, but there is a dearth of evidence of why they exist,” he said.
Thus, Ovbiagele is working with fellow concerned scientists at the NIH, the American Academy of Neurology (AAN), and other organizations to develop a framework for researching and understanding the effects of racial disparities in stroke cases, including how racism plays a role. This research is urgent. “We know that the population is getting older and the incidence of stroke and other neurological conditions correlate with rising age,” said Ovbiagele. “And the demographics in this country are changing in terms of race ethnicity. So, we could be seeing a wider gap in disparities between non-Hispanic Whites and many minorities if this issue is not addressed.”

“I see patients at the point when they already have neurological disease,” he said. “But really the best way to try and potentially breach these disparities is to look at those social determinants of health – whether it’s where a person lives or what a person’s income is like – all those discrepancies between minorities and non-Hispanic Whites.”

Grow the Force

A key objective of Ovbiagele and his HEADS-UP collaborators is promoting the careers of individuals – of any professional or scientific discipline – with an interest in addressing inequities in stroke cases, but especially people from groups underrepresented in medicine (UIM).

“We want to train and develop these future scientists and health professionals because we know they are much more likely to serve the populations that are disproportionately affected by stroke and other diseases.”

That, too, is a challenge. Ovbiagele noted that while African Americans make up about 13 percent of the U.S. population, only 3 percent of neurologists are African American. Latinos comprise 18 percent of the American population, yet only 6 percent of U.S. neurologists.

But there is headway. Ovbiagele is program director of Training in Research for Academic Neurologists to Sustain Careers and Enhance the Numbers of Diverse Scholars (TRANSCENDS), a partnership between the NIH and the AAN.

Established in 2016, the program includes an online graduate research degree program, monthly webinar conferences, and special interaction sessions at the annual AAN meeting. A study of TRANSCENDS published in July of 2021 found that so far, it is a feasible program for supporting UIM neurologists towards careers in research and academia.

The study found that of the 23 program scholars, 56 percent were women, 61 percent Hispanic/Latinx, 30 percent Black/African American, and 30 percent were assistant professors. To date, 48 percent have graduated from the TRANSCENDS program, and participants have already published 180 peer-reviewed research articles.

“But I think grooming more researchers of all stripes – it doesn’t have to be just people of color, who are interested in health inequities to consider studying the issue of racism and inequities in health – is critical,” said Ovbiagele. “We need more training programs to help people develop their careers in stroke disparities research. We need all hands-on deck if we are actually going to successfully tackle this issue.”
An Affinity for Gulf War Veterans

Linda Chao was a college student at UC Davis when on the other side of the world, men and women around her age were fighting in the Gulf War.

She recalls watching the developments of Operation Desert Storm on the news in 1991, a campaign that impacted the health of hundreds of thousands of troops deployed to Kuwait after neighboring Iraq invaded the country.

More than 30 years after the Gulf War, Dr. Linda Chao – a Research Biologist and Neuroscientist at SFVAHCS and UCSF Adjunct Professor of Radiology & Biomedical Imaging and Psychiatry – feels a kinship with Gulf War Veterans (GWVs), many of whom are now in their fifties.

“They’re kind of a forgotten group when it comes to Veterans’ health,” she said. “They’re between Vietnam War Veterans, who are now aging and prominent in VA hospitals and clinics, and the younger Veterans of the Afghanistan War, which lasted 20 years.”

The GWVs with whom she works are more research partners than subjects. “I’m impressed by their active participation, fortitude, commitment to scientific research, and understanding that research will benefit many others probably more than them individually,” Chao said.

Sick from War

An estimated 250,000 Veterans suffer Gulf War illnesses, a cluster of chronic symptoms that include fatigue, respiratory disorders, headaches, joint pain, insomnia, dizziness, and memory problems.

Since 2004, Chao has followed some 200 GWVs at the VA Advanced Imaging Research Center (VAARC), formerly known as the Center for Imaging of Neurodegenerative Diseases (CIND). Chao conducts neuropsychological and cognitive testing of Veterans and analyzes the most precise MRI images of their brains. Her various research projects focus on how the Gulf War has affected their brain health. She’s published many significant findings.

Chemical Weapons

In a series of studies on the nerve gas Sarin, Chao found that GWVs exposed to even low levels of the chemical weapon showed long-term adverse effects to their brain structure and memory function.

GWVs exposed to the infamous 1991 Khamisiyah plume – when U.S. demolition of an Iraqi munitions depot carried low levels of the nerve agent downwind – showed a decreased volume of the hippocampus in their brain MRI scans compared to nonexposed Veterans, Chao reported in 2017.

Moreover, smaller hippocampus volume correlated with lower scores on a test of verbal learning and memory. Because memory problems and smaller hippocampal volumes are linked to risk of late-life dementia and Alzheimer’s disease, Chao and co-researchers suggest that Veterans exposed to Sarin should receive regular follow-up examinations as they age.

That study is often cited by GWV advocacy groups, who have been at odds with the Department of Defense and the National VA regarding the effects of Iraq bombing munitions on Veterans exposed to toxic chemicals. GWV advocacy groups say these agencies have downplayed the long-term impacts on Veterans’ health after being exposed.

MCI Now, Alzheimer’s Risk Later

In a study of 202 GWVs at SFVAHCS, Chao found that 12 percent had mild cognitive impairment (MCI). The median age of those with MCI was 48 years. Compare that with the MCI prevalence rate in the general population, where it is 6.7 percent for people aged 60-64 years and 10 percent for those 70-74 years of age.
Chao also found that GWVs with MCI had higher rates of posttraumatic stress disorder and major depressive disorder compared to GWVs without MCI. Moreover, they had smaller hippocampal volume and a thinner parietal cortex – two hallmarks for Alzheimer’s disease pathogenesis.

“GWVs are aging at a faster rate than the general population,” said Chao. Because individuals with MCI develop dementia at higher rates, “it may portend higher rates of future dementia in deployed GWVs,” she warned.

### Parkinson’s Disease

Interestingly, many symptoms of Gulf War illness are similar to non-motor symptoms in Parkinson’s disease (PD). Those include fatigue, pain, gastrointestinal and sexual dysfunction, sleep disturbances, anxiety, depression, and cognitive dysfunction such as difficulties with memory and concentration. Moreover, some of these symptoms persist many years before diagnosis of the disease and before some of its classic motor symptoms manifest.

In a study led by Chao, GWVs with Gulf War illness reported PD-like symptoms and more Gulf War-related exposures, while healthy GWVs reported few of these symptoms. The Veterans with Gulf War illness also had lower volumes of basal ganglia, the clusters of neurons in the brain responsible for motor control.

Now, Chao is studying some GWVs who were exposed to toxicant chemicals. Researchers will obtain clinical, behavioral and MRI measures in GWVs and compare them to matched healthy controls, PD patients and people with early symptoms of PD. They will explore if there is any link between toxicant exposures during Gulf War deployment and the early signs of Parkinson’s disease.

“The precise diagnosis of PD in GW Veterans with high-levels of deployment-related exposures could facilitate the targeted delivery of neuroprotective therapies when they become available,” she said. At-risk Veterans may also be counseled to adopt lifestyle changes that may lower their risk of PD.

### Part of the Solution

Chao’s expertise in neuropsychological testing and her analysis of sophisticated brain images are crucial in understanding illnesses and diseases among Veterans. She has stepped into the frontlines of Veterans health research.

“I got tired of documenting problems and analyzing data,” said Chao. “I felt like I wasn’t doing enough, and I wanted to be more involved in looking for solutions.”

Her research thus has taken a wider path. She has partnered with clinical researchers at the SFVAHCS and around the country to uncover diseases and their causes and has worked on potential therapies for Veterans whose illnesses are rooted to their time in the war.

With a variety of NIH, VA, and Department of Defense-funded research grants, Chao still utilizes her expertise in cognitive neuroscience, neurodegenerative processes and brain imaging, but she also heads clinical trials that could lead to a better quality of life for Veterans.

Insomnia, for example, is among the cluster of symptoms in Gulf War illness. In a study with 85 GWVs reported earlier this year, Chao and a team of researchers found that cognitive-behavioral therapy for insomnia (CBT-I) delivered by telephone improved both sleep and non-sleep symptoms of Gulf War illness.

Chao is also a Principal Investigator of Preventing Loss of Independence Through Exercise (PLIÉ) in Persons with Mild Cognitive Impairment (MCI). The project incorporates Eastern and Western exercise modalities and builds the capacity to perform basic functional movements while increasing mindful body awareness and enhancing social connection.

A pilot study of the program at an adult daycare center in San Francisco found that PLIÉ improved cognitive function, physical performance and quality of life among participants, and reduced caregiver burden when compared with the usual care at the facility.

A goal of the project is to investigate whether PLIÉ for four months will result in neurobiological changes that improve cognitive and physical function and quality of life. Chao will employ MRI to track changes in the brains of participants over the four months.

If the program is successful, researchers will work with VA and community-based organizations to implement PLIÉ more broadly, said Chao.

After all, what Gulf War Veteran – or anyone else – couldn’t use a good night’s sleep, some independence, and a healthier body and mind?
Q: How and why did you become a medical geneticist and decide to pursue research in this important field?

A: In high school, I had a phenomenal biology teacher (Mrs. Robinson) who opened my eyes to the world of genetics. She assigned me special reading on genetic engineering happening at the University of Michigan. I was hooked for life! As I pursued my education, I saw the value in using genetic information to inform diagnoses, influence management decisions, and assess risk for diseases that can be prevented or have better outcomes if detected early.

Before medical school, I trained as a genetic counselor at the UCLA School of Public Health. My public health education was crucial to my interest in health services research. Mentors along the way solidified those interests. But perhaps most importantly, throughout my medical training, first in internal medicine and then medical genetics, I saw a tremendous need to better integrate genetic services into clinical practice – and that need has continued to grow with the ever-increasing discovery of genetic underpinnings of health and disease.

Q: What is your role as Director of Clinical Genetics at the SFVAHCS?

A: I work part-time as a clinical geneticist, receiving consults for a variety of health concerns from primary care and specialty clinicians at the San Francisco VA and the Southern Nevada VA Health Care Systems; and there are plans to expand services to other VA facilities. The types of conditions referred to the genetics clinic cover the spectrum of conditions seen in internal medicine practice – clinical geneticists have been described as the most specialized generalist.

I provide comprehensive care that starts with assessing the possibility of a genetic diagnosis. Next, I define the genetic risk, which is often informed by genetic testing, and based on the diagnosis and risk assessment. I make recommendations for management, surveillance, and prevention; and when indicated, describe implications for family planning. I sometimes co-manage high-risk patients with other specialists and primary care, providing updates on what is known about their genetic diagnosis, specific genetic test results, and how best to manage associated disease risks.

My research focuses on health services and implementation research as it relates to the integration of genetic services (i.e., genetic consultation, genetic testing) into the clinical practice of frontline clinicians. Areas of focus include: care coordination for genomic medicine in the VA; delivery models for clinical genetic services; outcomes of genomic medicine and their value; clinical validity and utility of family history tools in risk assessment and disease prevention; genetic testing technologies and communication processes between the laboratory and ordering provider; and the intersection of health information technology and genomic medicine.

Q: Please give an example of how patients are benefiting from therapy interventions rooted in genetics.

A: Caring for patients with advanced-stage cancer is a clinical area where therapies are available that target specific gene variants that are either inherited (i.e., germline) or acquired (i.e., somatic). For example, patients with pathogenic variants in a DNA damage response gene (e.g., BRCA1, BRCA2, ATM, ATR) may benefit from PARP inhibitors. And for patients with pathogenic variants in mismatch repair genes (e.g., MSH2, MLH1, MSH6, PMS2, EPCAM), PD-1 blockade may be prescribed to treat their cancer.

In addition, the VA’s National Precision Oncology Program has recently published a new clinical
pathway that calls for offering both germline and tumor genetic testing for all patients with metastatic prostate cancer. With funding from VA QUERI and working with our operational partners in the Precision Oncology Program, we are evaluating various delivery models available in the VA to ensure access to the germline genetic testing for these patients.

Q: Why is the SFVAHCS an ideal place for your research?

A: The VA oversees the most extensive integrated healthcare system in the U.S., and the electronic health records system and the supporting Corporate Data Warehouse allow for examination of structured and text-based data within patient medical records. This is a rich source of data to address health services and implementation research questions.

But perhaps the greatest strength for conducting research in the VA is working with VA patients – they are volunteers by nature and are very willing to participate and work collaboratively in research efforts aimed at improving their health and health care, and that of their fellow Veterans and the community at large.

Q: Genetics seems to be a field in which discovery has been exciting and rapid; yet implementing genetics into the clinic has been slow. Is this true?

A: There are too few genetics professionals to ensure access to genetic testing, and frontline clinicians are under-prepared to use genetic tests in their practice. This is true in the VA and in the community. Currently, in the VA nationally, there are only six clinical genetics programs staffed by 25 genetics professionals, including six clinical geneticists (most with only part-time appointments in genetics), one genetic nurse, and 18 genetic counselors serving the nine million VA patients enrolled nationwide. This equates to about 0.3 genetics professionals per 100,000 patients, which is about two- to three-fold fewer genetics professionals than genetics programs in the community that primarily serve adults.

The demand for genetic services is outstripping the current capacity within VA, and the demand will be accelerated by the VA precision oncology programs and the VA Tele-Oncology initiative.

Last summer, with funding from VA QUERI, we conducted a survey of front-line clinicians at 20 VA facilities characterized as centers of excellence for precision oncology practice and research. Only 21 percent of the 909 respondents (physicians, nurse practitioners, physician assistants, and pharmacists) feel prepared to use genetic tests in their practice.

Only 22 percent of front-line clinicians currently order genetics tests with only 8 percent having ordered at least one cancer genetic test (germline or somatic) in the past year. Among clinicians (n=72) who had ordered cancer genetic tests, only about two-thirds were confident in knowing the indications for testing; discussing the potential benefits, harms and limitations of testing; understanding the test report; and implications of results on disease management and prevention. Many (44 percent) believed improving knowledge of genetic testing would alter their practice, and 30 percent were unsure.

Clinical genetics providers were rated as the top choice for the best way to update VA clinicians about genetics. Thus, genetics professionals are needed in the VA not only to deliver genetic consultation but also to inform and educate frontline clinicians about how to best utilize genetic information.

Q: What would you like the field to look like 10 years from now?

A: It would be great to see an increase in the genetics workforce in the U.S. that meets the growing demand, including more clinical geneticists, genetic counselors, and genetic nurses. I also hope that the integration of clinical genetics becomes more routine in the practice of frontline clinicians. I believe this is the only way we will more fully realize the health benefits of genetic information.

Q: What would most people be surprised to know about you?

A: I love the water. I love swimming in it – pool, lake, river, or ocean – and rowing, kayaking, and boating on it. Perhaps this is because I was born and raised in Michigan, the Great Lake State. Living near a body of water is almost a must for me. It gives me a sense of peace and perspective that restores me.
Q: If you could spend a day in someone else’s shoes, whose would they be, and why?
A: I would love to spend a day in my daughter’s shoes (or bare feet). She just turned two, and her outlook on the world is so awe-inspiring. She lives purely in the moment, is amazed by the smallest of experiences, and expresses herself so naturally. I would love to see the world from her eyes and remember how it felt to be so free-spirited at that age.

Q: What does success mean to you?
A: To me, success means having the confidence to be my authentic self while positively impacting others. Being able to let your light shine and bring out the light in those around you is truly rewarding.

Q: What energizes you and brings you excitement?
A: I am enthusiastic about and energized by anything to do with health optimization! Whether it’s physical activity, nutrition, sleep, metabolic health, and mental wellness, I am constantly seeking to learn more about these topics and put them into practice.
Department Updates

NCIRE Wellness Challenge
August 16, 2021 - September 10, 2021

In the April 2021 NCIRE Employee Survey, wellness was ranked as one of the top three perks important to employees. Company wellness programs have been able to provide:

- An increased sense of camaraderie among employees participating in wellness challenges
- The growth of a health and wellness culture
- Improved employee health

On August 16th, NCIRE started a four-week companywide Wellness Challenge to engage and promote healthy living for our employees. The purpose of the challenge was to motivate employees to develop personal/individual healthy habits, while having fun and competing with their colleagues for prizes.

The challenges were designed for all fitness levels; an NCIRE Wellness Group was created on the Microsoft Teams page to track progress. Points are assigned to each activity completed, and employees are encouraged to post their activities and pictures that bring joy or highlight their day on the MS Teams Page.

The Wellness Challenge has been well received, and NCIRE will continue to promote wellness initiatives to keep employees healthy and happy!

Acumatica is coming to NCIRE

NCIRE is transitioning to a new Enterprise Resource Planning (ERP) system called Acumatica. While the system configuration is still in progress at the time of this update, we anticipate the system will be ready for all users in October/November 2021.

Why did NCIRE decide to change the system?

Currently, we have three systems (Solomon, ReQlogic, and NCIRE Reports Portal) serving different functions, and these systems have been in place for more than 15 years. While they work fine, a new system provides an opportunity to streamline and improve our operations. Acumatica is an integrated platform, and it replaces all three systems by using a single system. It also allows for easy access to information, and is accessible anywhere with internet connectivity.

Why did NCIRE choose Acumatica over other well-known systems in the market?

Though there are many ERP systems on the market, we chose Acumatica because it provides the functions and performance we need at a reasonable cost. One of the key considerations is the unlimited user license model which allows for a consistent and sustainable annual system operation budget. In addition, this company invests heavily into product development and has major system updates twice a year.

What can we expect to see in this new system?

At the very beginning of the system rollout, we will try to mirror the functions we have in the current systems to ease the transition. One of the core components of Acumatica is its robust Business Intelligence module. We plan to rollout dashboards and other data retrieval queries in the first half of calendar year 2022.

Will there be training available?

Yes, once the system configuration is completed, we will schedule training sessions. In addition, user guides will be available.

Who should we contact if we have questions/concerns about this new system?

You may contact Keith Chan at keith.chan@ncire.org or by phone at ext. 23143 if you have questions or concerns about the new system.
CRADA IDC Increase

Effective October 1, 2021, the Indirect Cost Rate (IDC) for Industry Sponsored projects (CRADAs) will change from 35% to 37%. The moderate change is necessary to account for increased costs associated with managing these studies and is in line with market comparison for other similarly situated research institutes.

CRADA agreements negotiated prior to October 1, 2021 will remain unchanged at their existing IDC rates. The new rate will apply to new/unexecuted agreements. If there is a research agreement in-process, please contact NCIRE with questions.

Message from the Chief Executive Officer

The past weeks have been filled with devastating news about the California wildfires, Hurricane Ida, the resulting storm, and the recent developments in Afghanistan. As we navigate these tumultuous transitions, may we also remember to take time for self-care to bolster our physical and mental health. As such, thank you for taking the time to read the NCIRE fall edition with exceptional contributions from Drs. Chao, Ovbiagele, and Scheuner. We appreciate their willingness to share their research and appreciate their time.

NCIRE is currently considering implementation of a Grants Management System and is engaged in reviewing systems to determine feasibility. Once in place, the system will streamline existing processes and support ever-increasing sponsor compliance.

In May, NCIRE sent out a Satisfaction Survey to Principal Investigators and their teams. In July, the results indicated a forty-three percent response rate. The satisfaction survey will be conducted annually. Next year, we hope to see the response rate increase to sixty percent. Every comment and note were considered. To review the full survey results, see here.

Notable Survey Results:

Q: NCIRE provides appropriate staff support.
   • 46% of respondents strongly agreed
   • 40% of respondents agreed
   • 2% of respondents disagreed

Q: Overall, I am satisfied with NCIRE as my grant administrator.
   • 58% of respondents strongly agreed
   • 35% of respondents agreed

On June 28th, 2021, NCIRE's Paycheck Protection Program (PPP) loan was forgiven in full. The ~$1M supported thirty-eight Principal Investigators and one hundred-nineteen employees in FY 2021. As we approach the end of Fiscal Year 2021, we will be closing the accounting records. NCIRE is preparing the Fiscal Year Budget for 2022. Please review requests for information, so that our projections can be accurate.

In this issue, we are excited to feature details on NCIRE employees, take a look at the In the Helix. Get to know your colleagues. If you have any questions or comments, please feel contact me at Rebecca.Rosales@ncire.org.

Rebecca Rosales, MBA, CRA
Chief Executive Officer

About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support over 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

NCIRE is a 501(c)3 nonprofit. (Tax ID #94-3084159). Visit NCIRE at www.ncire.org

The DNA Newsletter is an NCIRE Publication.
Editor-in-Chief: Rebecca Rosales, Chief Executive Officer
Staff Contributors: Tai Arceneaux, Lydia Blednyh, Andy Evangelista, Theresa Gio, Newton Ong

Please send comments to dna@ncire.org