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VOLUME XIII Winter 2021

## FOCUS on Research

### Taking on the Many Challenges of Alzheimer's Research

Dr. Michael Weiner is a highly accomplished scientist, garnering international acclaim for his more than three decades of research on Alzheimer's disease and other neurodegenerative disorders.

His body of work is broad and impactful. He developed and enhanced the use of magnetic resonance imaging (MRI), positron emission tomography (PET) and blood-based biomarkers to diagnose Alzheimer's. In addition, he has headed the most extensive and largest observational study in the world to understand how normal aging can take a biological twist and progress to dementia and Alzheimer's disease.

Notably, his work has laid a foundation for more scientists to build crucial Alzheimer's research that will lead to treatments for a disorder that now ranks as the third-leading cause of death for older people, just behind heart disease and cancer.

Weiner – who is a UCSF professor of radiology and biological imaging, and former and founding Director of the Center for Imaging and Neurodegenerative Diseases (CIND) at the SFVAHCS, which is currently known as the VA Advanced Imaging Research Center (VAARC) – has mentored more than 150 post-doctoral fellows and authored over 900 peer-reviewed research papers. He has been an advocate for sharing research data openly and promptly, counter to the traditional practice of embargoing information until publication.

In 2014, he launched the internet-based Brain Health Registry (BHR) to attract greater numbers of people to observe for cognitive changes associated with the progression of neurodegenerative diseases and brain aging. The large pool of



*Michael W. Weiner, MD  
Professor of Radiology and Biomedical Imaging, Medicine,  
Psychiatry, and Neurology, UCSF  
Radiology Service, SFVAMC*

participants – thus, a wealth of research data – informs and accelerates clinical trials of neurological diagnostics and treatments.

To date, over 90,000 people from around the world have participated in the BHR. Weiner recently has focused on developing inexpensive, scalable tools to identify normal elders at risk for cognitive decline and dementia and has provided the BHR software to facilitate the work of other scientists.

But even with more than 40 productive years as a researcher and academic, Weiner will not rest on his laurels. As long as there is a missing puzzle piece to find or a research gap to fill, Weiner will push for answers.

## Diversity Needed in Clinical Trials

Weiner has an urgent challenge now: enrolling many more people from underrepresented groups into clinical research. “The science is not capturing what’s going on with Alzheimer’s disease in diverse populations.”

“We all have much more to do,” said Weiner in July at the 2021 Alzheimer’s Association International Conference, where he received a Lifetime Achievement Award for his contributions to Alzheimer’s disease and dementia research.

“We need to work together to do a much better job at enrolling people with low education, low incomes, more comorbidities, people from all communities and underrepresented populations to ensure our results more generalizable,” he said. “This award renews my energy to continue the work.”

According to the Alzheimer’s Association, older Black Americans are about twice as likely to have Alzheimer’s or other dementias as whites; older Hispanics are one-and-a-half times as likely to have these disorders as whites.

By 2030, nearly 40 percent of all Americans living with Alzheimer’s will be Black or Latino, according to UsAgainstAlzheimer’s, an organization founded in 2010 to diversify Alzheimer’s research.

Even in his own large studies, 90 percent of research volunteers are white, and most have higher education and income than the average American, said Weiner. Also, those who volunteer for clinical trials enter through a health care system that still poses barriers for minorities and underrepresented groups.

Weiner aims to change those numbers. His goal is to eventually increase the number of minorities – including Blacks, Latinos, Asians, Native Americans and other underrepresented groups – in clinical studies from 10 percent to 50 to 60 percent.

It may seem like a lofty goal, but Weiner has lived up to previous research challenges. He plans to employ networks and models from his previous and successful research to demonstrate how this could be done.

### Alzheimer’s Disease Neuroimaging Initiative (ADNI)

ADNI, which began in 2004 under Weiner’s leadership, is the most extensive Alzheimer’s observational study globally and considered by many to be the gold standard for clinical trials for the disease. The study has attracted more than 2,000 subjects since 2004 at 60 sites across the U.S. and Canada.

It’s first phase, “ADNI-1” explored combinations of biomarkers – neuroimaging, cerebrospinal fluid and blood – to determine which are most powerful for diagnosing Alzheimer’s and monitoring treatments. Subsequent phases – ADNI-2, ADNI-GO (Grant Opportunities) and ADNI-3 – expanded biomarker exploration to include brain scans that detect tau protein tangles (tau PET), a known indicator of the disease. To date, the ADNI studies have received \$200 million in research funding, which includes grants and awards from the National Institute on Aging, pharmaceutical companies, and non-profit foundations.

Data derived from ADNI has led to more than 3,600 scientific papers, and it has been a model for numerous clinical trials around the world. For example, Biogen, which developed aducanumab – the first FDA-approved medication for Alzheimer’s in nearly 20 years – benefited from ADNI research data, said Weiner.

But the keys to ADNI’s success are its volunteer participants who agree to be monitored over years and literally give their blood for the good of research.

Weiner now has proposed an “ADNI-4” that will significantly alter the clinical trial participant pool to include larger numbers – the 50 to 60 percent goal for underrepresented groups that he has set. ADNI-4 will utilize its network of research centers across the country – including prestigious collaborators such as Duke, Stanford, USC, and others – to reach out to communities and break down some of the barriers that exclude people or make them reluctant to join clinical trials. For example, they hope to partner with neighborhood blood centers to recruit participants and educate them about Alzheimer’s disease and research.

Weiner has submitted a grant for ADNI-4 and hopes he will hear about approval in summer 2022 with the project starting by fall of that year.

### Brain Health Registry (BHR)

Weiner and co-researchers for the BHR are already piloting strategies to recruit underrepresented groups for Alzheimer’s disease and related dementias clinical research.

One project, funded by the California Department of Public Health Alzheimer’s Disease Program, employs internet advertising and culturally-tailored messaging to enroll participants in the BHR.

Use of custom audience targeting ads on Facebook and Google in California zip codes with large Latino populations is a technique being employed. Recruitment strategies,

including “look-alike” audience targeting, ad retargeting, simplification of the BHR enrollment process, and revamped email campaigns to individuals that did not complete enrollment to BHR also are employed. Future efforts include a Spanish-language BHR website, Spanish digital ads, and messaging to improve engagement and retention of Latino participants once they are enrolled.

“One of BHR’s overarching goals is to accelerate the search for treatments for brain diseases that can benefit all communities,” states the BHR website. “To do this, we need our participants to be representative and include people from all walks for life.”

## From Nephrologist to Neuroscientist

When Michael Weiner started his medical and research career he never imagined where his path would take him.

After earning his medical degree from SUNY Upstate Medical Center in Syracuse, New York in 1965 and finishing a residency in Medicine from Mt. Sinai Hospital in 1967, he completed fellowships in metabolism from Yale-New Haven Medical Center, nephrology from Yale University School of Medicine and biochemistry from the University of Wisconsin Institute for Enzyme Research.

From 1972 to 1980, he taught and practiced medicine at University of Wisconsin and Stanford. “In the 70s, I was a nephrologist running a hemodialysis unit,” said Weiner.

It was in 1980, after he came to UCSF and the San Francisco VA Medical Center, when his interest shifted to radiology and biomedical imaging. The SF VA had one of the first whole body MRIs, and he and other scientists were able to conduct groundbreaking MRI and Magnetic resonance spectroscopy (MRS) studies .

In 1980, Weiner was one of the first to perform MRS on an intact animal, and subsequently pursued his goal to develop MRI and MRS as a clinical tool. In 1988, his research group used MRS to show that the amino acid N acetyl aspartate (NAA), a marker of healthy nerve cells, is reduced in the epileptic focus in the brain. In 2004, his group reported that reduced NAA predicts development of Alzheimer's disease in mildly impaired elderly subjects.

That same year, he established ADNI. And the rest is Alzheimer’s disease research history.

Weiner is a hands-on researcher who stays heavily engaged with co-researchers, mentees and research volunteers. He even is a participant in ADNI studies, having undergone the same procedures as volunteers, including brain imaging scans and lumbar punctures. So, his own body, brain, and progression of aging is part of the data.

Whenever he receives awards and accolades, he acknowledges his colleagues at UCSF, SFVAHCS and collaborating centers around the world – site principal investigators, study coordinators, postdoctoral fellows, research assistants, and study participants.

He has a special appreciation for the staff at NCIRE who administer the large research grants. “Truly, they have been part of the team, offering vital support since day one.”

# Q and A: An Interview with Dr. Susanna Fryer



Susanna Fryer, PhD  
Assistant Professor, In Residence, Department  
of Psychiatry and Behavioral Sciences, UCSF  
Clinical Psychologist, SFVAHCS  
Associate Director, Brain Imaging and EEG  
Laboratory

## **Q: How did you develop an interest in neuropsychology?**

**A:** I became interested in science because of great teachers, I was lucky and very privileged to have. From a first-grade teacher who had us come back at night to look at the planets to the high school teachers and college professors who truly made time for me, they served as models of inquiry, ingenuity, and originality. I sometimes worry that we've all become so busy that we are forgetting to encourage our youth.

That early encouragement was crucial, along with the very seasoned professional mentoring I received during graduate school and my postdoctoral training. In addition, I am fortunate to have worked with stellar clinical neuroscientist "grandparents" and "parents" here at SFVAHCS, most notably Drs. Dan Mathalon and Judy Ford.

**Q: You're a scientist and a clinician. Why do you do both, and how does one role complement**

**the other?**

**A:** Payoffs in research are typically distal, and uncertain. The personal relationships inherent to clinical work help remind me of the humanistic roots that initially propelled my own interest in neuroscience, and of the palpable need in mental health treatment for new discovery and novel treatment development.

## **Q: Your research focuses on the brain reward system. Please explain how that system works, or doesn't work.**

**A:** When the brain's reward processing systems are working optimally, people find pleasure in experiences that they enjoy and are willing to work for those experiences. Whether that enjoyment stems from interactions with family or friends, professional achievement, a beautiful sunset, or a favorite meal or memory, it will vary based on individual preferences and values. But the elemental point is that the capacity for joy and pleasure as well as the willingness to put considerable effort into pursuing reward is there, and effectively drives the individual's behavior.

**Q: You specialize in cognitive-behavioral therapy and mindfulness-based techniques. Why may behavioral interventions work for some or many people with major depressive disorders or other conditions?**

**A:** How and why psychotherapy works (and for whom) are great, complex unknowns that the mental health field is eager to try to answer because we could then offer more individualized, optimized treatments. Clinically, I've always gravitated toward providing cognitive-behavioral therapy and mindfulness-based therapies (meditation is, after all, a behavior), because I find something inherently optimistic about behavioral change. The idea that we aren't inflexibly fixed as individuals offers the compelling possibility of growth and adaptation. As a clinician, I find that helping to create the context for that change for Veterans engaged in our care really is an honor.

## **Q: Who do you hope will benefit most from your research?**

**A:** I hope that the research I contribute, along with many others, will help people who do not, for whatever reason, find much day-to-day enjoyment in their experiences or do not find or pursue goals they value.

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

**A:** I am fascinated by all primates (even humans). As a college student, I used to volunteer with the Koko gorilla project, including such festive duties as preparing Koko's meals, tidying her room, and emptying her chamber pot (which was quite large).

# In the Helix



*Paul Betancourt*  
NCIRE Staff Research Associate III



*Andy Evangelista*  
NCIRE Science Writer



*Linda Huang*  
NCIRE Accounts Payable Specialist

## **Q: What was your favorite subject in school?**

**A:** I never really liked a specific subject or school itself, yet have always loved reading everything that was assigned. All the way back to first grade, my parents had to meet with my teacher because I was refusing nap time and trying to read instead. Replace “naps” with “studying for exams,” “writing papers,” or “being in class,” and reading always won out.

## **Q: What was your first job?**

**A:** My first few summers in high school I worked on a hog farm 6 days a week. I helped deliver over 200 piglets and cleaned many, many more pigpens than I care to remember, although thinking about it definitely helps me appreciate working in an office all day.

## **Q: What risks are worth taking?**

**A:** Anything you truly believe may improve life for others and you is a risk worth taking. Although from my experience, just as important as deciding to take the risk is having a plan for what comes next.

## **Q: What was your favorite subject in school?**

**A:** I’m assuming PE is not a subject. So, history. Up to this day, I can’t get enough history – ancient, world, U.S., medicine and more. It’s all fascinating and gives one perspective on how we all got here and why things are the way they are today.

## **Q: What was your first job?**

**A:** After high school and during college summers, I worked as a phone solicitor. They would call that “marketing” today, but the job really was to be irritating over the phone. In the early 70s, during the shopping mall boom, I offered department store credit cards to people all over California. You earned money as fast as you can dial a phone. Unfortunately, they still had some rotary dial phones. I came home with sore fingers.

## **Q: What risks are worth taking?**

**A:** Trying new things. That could be anything – skills, hobbies, food, whatever piques curiosity. The saying “you’ll never know unless you try it” is so true. If you miss or fail once in a while, so what? The more things you try or become involved in, the more opportunities for positive experiences and more people to meet. Better chance for a fuller life and good memories. Take it from an old guy.

## **Q: What was your favorite subject in school?**

**A:** I would say that my favorite subject was the coursework that focused on theories of race, ethnicity, and social movements while I was in an Ethnic Studies program. I enjoy subject matters that leave you with a wider understanding of the world.

## **Q: What was your first job?**

**A:** My first unofficial job was doing bookkeeping work for a friend of the family while I was in high school. After a roundabout journey through different fields, I came back full circle to accounting work.

## **Q: What risks are worth taking?**

**A:** If you think you’re going to look back on your life and wonder “what if” on an action, then I think the risk is worth taking.

# Department Updates

## NCIRE Core Office Welcomes New Members to the Team

Linda Huang, NCIRE's new Accounts Payable Specialist, joined the Accounting team in July 2021. Linda has more than 20 years of AP experience, and is responsible for reimbursement requests, vendor payments, ClinCard subject payments, and quarterly use tax filings. We are particularly impressed with Linda's detail-oriented skills and great customer service and wish her much success at NCIRE.

Juanita Kalif and Jessica Schmidt, NCIRE's new Contracts & Grants Specialist III, joined NCIRE's Contacts and Grants Team in September 2021. Both Jessica and Juanita have impressive backgrounds and experience administrating grants and contracts. With their addition, the Contracts and Grants Department has reallocated PI portfolios to ensure our Research Community receives the best response time. We are very excited to have them on our team!

## NCIRE Adds 'Floating Holiday' to Paid Holidays Schedule



We are pleased to share with you that NCIRE will be adding a floating holiday for all full-time and part-time regular employees, equivalent to eight hours. This is an additional paid day off for employees to use at their discretion by the end of the year. With the addition of the floating holiday, NCIRE will now provide 12 paid holidays.

In revising our holiday schedule to include one floating holiday, a key priority was providing employees the latitude to take time off for observances that are most meaningful to them. We acknowledge and honor the fact that members of our Research Community have a diverse array of cultural, religious, and personal commitments, which are deeply important. This holiday honors the diversity of our workplace and supports individual beliefs.

As a reminder, floating holidays must be used each year by December 31st. Employees must obtain supervisory approval for time off, as they do for vacation or personal time off.

## Acumatica Implementation Update

Our new financial system, Acumatica, has been online since October 1st, 2021. At the time of this writing, we have brought over the project transactions data for active projects, and we are working on verifying the numbers. Once this task is completed, we will begin sending login information to research groups that have returned the Acumatica System Access Authorization Form to us.

The final stage of the implementation is to bring the Requisition and Purchase Order modules online, and we anticipate the completion by the end of the year. If you have any questions about this new system, please contact Keith Chan at [keith.chan@ncire.org](mailto:keith.chan@ncire.org) or by phone at ext. 23143.



NCIRE 2022 PAY DAY SCHEDULE				
BI-WEEKLY				
PAY PERIOD	PAY PERIOD DATES		DUE DATE	PAY DAY
1	12/19/21	01/01/22	12/31/21	01/07/22
2	01/02/22	01/15/22	01/14/22	01/21/22
3	01/16/22	01/29/22	01/28/22	02/04/22
4	01/30/22	02/12/22	02/11/22	02/18/22
5	02/13/22	02/26/22	02/25/22	03/04/22
6	02/27/22	03/12/22	03/11/22	03/18/22
7	03/13/22	03/26/22	03/25/22	04/01/22
8	03/27/22	04/09/22	04/08/22	04/15/22
9	04/10/22	04/23/22	04/22/22	04/29/22
10	04/24/22	05/07/22	05/06/22	05/13/22
11	05/08/22	05/21/22	05/20/22	05/27/22
12	05/22/22	06/04/22	06/03/22	06/10/22
13	06/05/22	06/18/22	06/17/22	06/24/22
14	06/19/22	07/02/22	07/01/22	07/08/22
15	07/03/22	07/16/22	07/15/22	07/22/22
16	07/17/22	07/30/22	07/29/22	08/05/22
17	07/31/22	08/13/22	08/12/22	08/19/22
18	08/14/22	08/27/22	08/26/22	09/02/22
19	08/28/22	09/10/22	09/09/22	09/16/22
20	09/11/22	09/24/22	09/23/22	09/30/22
21	09/25/22	10/08/22	10/07/22	10/14/22
22	10/09/22	10/22/22	10/21/22	10/28/22
23	10/23/22	11/05/22	11/04/22	11/10/22
24	11/06/22	11/19/22	11/18/22	11/25/22
25	11/20/22	12/03/22	12/02/22	12/09/22
26	12/04/22	12/17/22	12/16/22	12/23/22
<b>**** TIMESHEETS ARE DUE ON UTM OR NCIRE BY 2:00 PM EVERY OTHER FRIDAY ****</b>				
HOLIDAYS	Friday	12/31/21	New Year's Day (observed)	
	Monday	01/17/22	Martin Luther King Day	
	Monday	02/21/22	Presidents' Day	
	Monday	05/30/22	Memorial Day	
	Monday	06/20/22	Juneteenth (observed)	
	Monday	07/04/22	Independence Day	
	Monday	09/05/22	Labor Day	
	Monday	10/10/22	Indigenous Peoples' Day	
	Friday	11/11/22	Veterans Day	
	Thursday	11/24/22	Thanksgiving Day	
	Monday	12/26/22	Christmas Day (observed)	
	8 hrs	1/1/22 - 12/31/22	Floating Holiday	

# Message from the Chief Executive Officer

I hope you enjoyed your Thanksgiving Holiday and that it was filled with happiness and warmth. After the last 19+ months, this quality time has never been more important. I am thankful for the consistent collaboration of everyone at the SFVAHCS campus, and the positivity they exhibit day after day.

Thank you for your support of the NCIRE 2021 Winter edition with remarkable contributions from Drs. Michael Weiner and Susanna Fryer. We recognize their willingness to share their research and provide their time. Additionally, you will find interesting details on three NCIRE staff members in our In the Helix section.

I am pleased to share that the preliminary fiscal year 2021 financial results reached a record high of \$2.7M, with impressive growth in the clinical trial research area this past year.

## Grant highlights of the Fiscal Year 2021:

### 120 total applications

- 60-Prime applications to federal sponsors
- 59-Subcontracts for federal awards
- 1-Foundation project

### 41 New Awards

- 15 NIH
- 1 CDC
- 4 DoD
- 21 Subcontracts on federal awards

### 10 New CRADA's (industry research/awards)

In the fiscal year 2022 financial planning, there are sixty-six active Investigators, compared to sixty-one in 2021. The number of awards has also increased from one hundred twenty-one in 2021 to one hundred thirty-three in 2022.

Thank you for taking time to read our Winter Newsletter and learn about recent NCIRE activities. Please let me know if you have any questions or comments. In these times optimism, generosity, and understanding are highly contagious. Remember, wash your hands, social distance, stay optimistic and remember to keep wearing a mask.

Our newsletter is created and edited by a hardworking group of volunteers. If you are interested in becoming a member of the newsletter committee, please contact me.



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.

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