Brain Plasticity:
IHSI and the Beckman Institute launch new Center for Brain Plasticity, p. 13
**NeuroMatters**, a publication of IHSI at Illinois, covers clinical and translational neuroscience topics relevant to University of Illinois at Urbana-Champaign investigators and the university’s clinical partners.

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## On the Cover

“A Clear Mind,” created by Chris Seward, UI graduate student in cell and developmental biology. The image depicts a whole mouse brain using a technique that Seward has helped develop, called CLARITY. Learn more at http://news.illinois.edu/view/6367/481607

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Thank you for reading this issue of NeuroMatters newsletter. Here, our goal is to begin telling the story of the breadth and depth of neuroscience research and engagement activity happening on the Urbana-Champaign campus. Through NeuroMatters, we hope to introduce you to investigators doing important work in neuroscience, and perhaps catalyze connections and collaborations along the way.

Clinical and translational neuroscience at Illinois is an ever-changing and evolving realm of research, with Illinois’ investigators at the forefront of many new insights, discoveries, and technological advances. IHSI keeps the neuroscience community at Illinois current on the latest news, events, and funding opportunities through our monthly Neuroscience News email newsletter. I encourage you to send an email to me at gcooke@illinois.edu or healthinstitute@illinois.edu to subscribe.

At IHSI, I work directly with Illinois faculty, staff, and students—and our clinical partners—to manage the various aspects of collaborative clinical and translational neuroscience research activities. I stay closely connected to the entire clinical and translational research resources landscape at Illinois, and have developed a Health Sciences Research Guide that includes information on research set up, administration, and tips for success for investigators at Illinois. I also work in tandem with the Illinois Biostatistics Core at IHSI to assist faculty and staff with data-driven research and funding-related projects. Visit healthinstitute.illinois.edu/research-resources to learn more.

To discuss new or existing opportunities in research, education, or engagement within the IHSI clinical and translational neuroscience program area, contact me at gcooke@illinois.edu or (217) 300-6709.

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The research in Dr. Sadaghiani's CONNECT Lab involves neurocognitive networks, neural communication and connectivity, and cognitive control. She and her team focus on how distant brain regions communicate with each other—called functional connectivity—and how that connectivity is organized and ordered to flexibly process internal and external (sensory) information, called flexible cognition. They use various imaging technology, including functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and simultaneous EEG-fMRI, and genetic analyses to study healthy younger adult brains with the goal of better understanding flexible cognition.

Recently, Sadaghiani and one of her graduate students, Richard Oliver Bido-Medina, traveled to a conference in the Dominican Republic, where Bido-Medina was born and raised. There, she was struck by reports about severe effects of Zika virus on the adult central nervous system in certain rare cases. Until now, the majority of Zika virus-related research has focused on perinatal Zika transmission and infants diagnosed with microcephaly and a host of other severe fetal birth defects. Working with a small grant from the Center for Latin American and Caribbean Studies (CLACS) at Illinois, Sadaghiani and Bido-Medina undertook one of the first longitudinal group case-control neuroimaging studies of Zika virus-infected adults presenting severe neurological complications.

Pilot work in Zika virus-infected adult population

Working with Salvador B. Gautier hospital in Santo Domingo, D.R., Sadaghiani and Bido-Medina began studying a small group of nine adult patients, reviewing their functional and structural MRI scans and spinal fluid samples to track changes in the brain, over several months, post-Zika virus exposure.

Sadaghiani’s lab is measuring the brain’s gray matter volume changes in these Zika patients—specifically, long-term shrinking and expanding of the gray matter due to inflammation. She is further studying the effects on functional connectivity. Even with a small patient group compared to most imaging studies, her lab at the Beckman Institute has a paper in progress that reports significant findings with respect to functional networks. Additionally, IHSI research development manager Gillian Snyder identified that Sadaghiani’s work with neurologically-affected adults with Zika virus matched an NIH funding opportunity. The lab wrote and submitted a grant, with Snyder’s support, and is awaiting NIH council decision with a promising score.

As unique as studying the brain scans of Zika-infected adults is, Sadaghiani is extremely grateful for being connected to helpful clinical and translational neuroscience resources a bit closer to home.

"The Carle Illinois Collaborative Research Seed Grant I received a couple of years ago really gave me the ability to even begin working with neurological patients. Just working alongside Carle neurologists has been so valuable, even more so than the funding. Getting to do research collaboratively with psychologists and clinicians would have been pretty much impossible without IHSI facilitating this," says Sadaghiani.
According to their website, research in Dr. Jefferson Chan’s lab group "lies at the interface of chemistry, biology, and medicine." There are several research interests his lab group explores; summarized, they include the development of small-molecule and protein-based sensors for non-invasive molecular imaging, the preparation of new diagnostics and therapeutics for infectious diseases, and synthetic organic chemistry.

The first of these interests—development of small molecular and protein-based sensors—looks to have applications to impact several different neurological medical conditions.

**Non-invasive photoacoustic imaging for acute hypoxia**

Hypoxia, which happens when tissue is oxygen-deprived, is indicative of blockages or narrowing in blood vessels, which often lead to stroke or peripheral artery disease. Chan and his team have developed an oxygen-sensitive molecule probe that emits ultrasound signals in response to light—a process called photoacoustic imaging. The imaging technique can be done in real time, non-invasively, at a higher resolution and lower cost than the current clinical standard.

“In a clinical setting, you would take a regular ultrasound machine and equip it with a light source—you can buy LEDs for around $200 that are powerful enough and safe for clinical applications,” says Chan. Physicians would administer the photoacoustic molecules to the patient by injection, then use the ultrasound machine to get a visual of the hypoxic tissue area.

The oxygen-detecting molecular probe has been tested on cell cultures and in mice, so far. Chan and researchers have found that their photoacoustic technique can find hypoxia mere minutes after a mouse’s artery was constricted, showing promise for quickly finding stroke sites or blood clots in tissue.

Additionally, neurodegenerative disorders such as Alzheimer’s disease (AD) are characterized by a decline in cognitive abilities that result from neuronal cell death. Hypoxia, oxidative stress, metal ion signaling, and neurotransmission are all believed to play a role in the neuropathology of AD. Chan says their interplay is inadequately studied, especially in the context of in vivo biological systems, so his group plans to modify and further design these chemical and protein-based probes to discover the mechanisms underlying AD. His group has also applied photoacoustic imaging to tumor tissue.

“We know that a lot of tumors are hypoxic, so many new treatments have been developed that become activated in low-oxygen conditions. But these treatments have been inconsistent in clinical trials, because not all tumors are hypoxic,” Chan says. “This gives scientists and physicians a way to non-invasively look inside tumors and determine whether a patient’s tumor is hypoxic and they would be a good candidate for a certain drug, or should go with a different treatment plan.”

For more details on this research, see the paper “A bioreducible N-oxide-based probe for photoacoustic imaging of hypoxia” available in the online journal Nature Communications.

**Know an Illinois investigator doing neuro-related research?**
Nominate them to be highlighted in the next issue of NeuroMatters. Email Gillian Snyder at gcooke@illinois.edu with your suggestion and a few details, and IHSI will follow up.
Nutrition has been linked to cognitive performance, but researchers have not pinpointed what underlies the connection. A new study by University of Illinois researchers found that monounsaturated fatty acids—a class of nutrients found in olive oils, nuts and avocados—are linked to general intelligence, and that this relationship is driven by the correlation between MUFAs and the organization of the brain’s attention network.

The study of 99 healthy older adults, recruited through Carle Foundation Hospital in Urbana, compared patterns of fatty acid nutrients found in blood samples, functional MRI data that measured the efficiency of brain networks, and results of a general intelligence test. The study was published in the journal NeuroImage.

“Our goal is to understand how nutrition might be used to support cognitive performance and to study the ways in which nutrition may influence the functional organization of the human brain,” said study leader Aron Barbey, a professor of psychology. “This is important because if we want to develop nutritional interventions that are effective at enhancing cognitive performance, we need to understand the ways that these nutrients influence brain function.”

“In this study, we examined the relationship between groups of fatty acids and brain networks that underlie general intelligence. In doing so, we sought to understand if brain network organization mediated the relationship between fatty acids and general intelligence,” said Marta Zamroziewicz, a recent Ph.D. graduate of the neuroscience program at Illinois and lead author of the study.

Studies suggesting cognitive benefits of the Mediterranean diet, which is rich in MUFAs, inspired the researchers to focus on this group of fatty acids. They examined nutrients in participants’ blood and found that the fatty acids clustered into two patterns: saturated fatty acids and MUFAs.

“Historically, the approach has been to focus on individual nutrients. But we know that dietary intake doesn’t depend on any one specific nutrient; rather, it reflects broader dietary patterns,” said Barbey, who also is affiliated with the Beckman Institute for Advanced Science and Technology at Illinois. The researchers found that general intelligence was associated with the brain’s dorsal attention network, which plays a central role in attention-demanding tasks and everyday problem solving. In particular, the researchers found that general intelligence was associated with how efficiently the dorsal attention network is functionally organized using a measure called small-world propensity, which describes how well the neural network is connected within locally clustered regions as well as across globally integrated systems.

In turn, they found that those with higher levels of MUFAs in their blood had greater small-world propensity in their dorsal attention network. Taken together with an observed correlation between higher levels of MUFAs and greater general intelligence, these findings suggest a pathway by which MUFAs affect cognition.

“Our findings provide novel evidence that MUFAs are related to a very specific brain network, the dorsal attentional network, and how optimal this network is functionally organized,” Barbey said. “Our results suggest that if we want to understand the relationship between MUFAs and general intelligence, we need to take the dorsal attention network into account. It’s part of the underlying mechanism that contributes to their relationship.”

Barbey hopes these findings will guide further research into how nutrition affects cognition and intelligence. In particular, the next step is to run an interventional study over time to see whether long-term MUFA intake influences brain network organization and intelligence.

“Our ability to relate those beneficial cognitive effects to specific properties of brain networks is exciting,” Barbey said. “This gives us evidence of the mechanisms by which nutrition affects intelligence and motivates promising new directions for future research in nutritional cognitive neuroscience.” This work was conducted through a partnership between the University of Illinois and Abbott Nutrition at the Center for Nutrition, Learning and Memory.
Specially tailored, ultrafast pulses of light can trigger neurons to fire and could one day help patients with light-sensitive circadian or mood problems, according to a new study in mice at the University of Illinois.

Chemists have used such carefully crafted light beams, called coherent control, to regulate chemical reactions, but this study is the first demonstration of using them to control function in a living cell. The study used optogenetic mouse neurons – that is, cells that had a gene added to make them respond to light. However, the researchers say the same technique could be used on cells that are naturally responsive to light, such as those in the retina.

“The saying, ‘The eye is the window to the soul’ has some merit, because our bodies respond to light. Photoreceptors in our retinas connect to different parts in the brain that control mood, metabolic rhythms and circadian rhythms,” said Dr. Stephen Boppart, the leader of the study published in the journal Nature Physics. Boppart is an Illinois professor of electrical and computer engineering and of bioengineering. Boppart also is a medical doctor and a professor in the Carle Illinois College of Medicine.

The researchers used light to excite a light-sensitive channel in the membrane of neurons. When the channels were excited, they allowed ions through, which caused the neurons to fire. While most biological systems in nature are accustomed to the continuous light from the sun, Boppart’s team used a flurry of very short light pulses – less than 100 femtoseconds. This delivers a lot of energy in a short period of time, exciting the molecules to different energy states. Along with controlling the length of the light pulses, Boppart’s team controls the order of wavelengths in each light pulse.

“When you have an ultrashort or ultrafast pulse of light, there’s many colors in that pulse. We can control which colors come first and how bright each color will be,” Boppart said. “For example, blue wavelengths are much higher energy than red wavelengths. If we choose which color comes first, we can control what energy the molecule sees at what time, to drive the excitement higher or back down to the base line. If we create a pulse where the red comes before the blue, it’s very different than if the blue comes before the red.”

The researchers demonstrated using patterns of tailored light pulses to make the neurons fire in different patterns. Boppart says coherent control could give optogenetics studies more flexibility, since changing properties of the light used can give researchers more avenues than having to engineer mice with new genes every time they want a different neuron behavior.

Outside of optogenetics, the researchers are working to test their coherent control technique with naturally light-responsive cells and processes – retinal cells and photosynthesis, for example.

“What we’re doing for the very first time is using light and coherent control to regulate biological function. This is fundamentally more universal than optogenetics – that’s just the first example we used,” Boppart said. “Ultimately, this could be a gene-free, drug-free way of regulating cell and tissue function. We think there could be ‘opto-ceuticals,’ methods of treating patients with light.”

The National Institutes of Health and the National Science Foundation supported this work.
Fan Lam is developing and applying advanced magnetic resonance (MR)-based techniques to more accurately map the molecular information in the brain. The ability to map and quantify molecular fingerprints of neural tissues would have significant impact on the study of the physiological basis of brain functions and neurodegenerative diseases, early diagnosis of central nervous system disorders, as well as accurate monitoring of treatment efficacy on these diseases.

MRSI has been established as an essential tool to probe the brain’s anatomy and function by imaging the water molecules, but Lam is working to extract additional information from the MR signals, and enable researchers to visualize detailed spatial and temporal variations of many different molecules in the brain, which are involved in various important physiological functions and are altered in specific diseases and their subtypes.

“There are many molecules in the brain, such as metabolites and neurotransmitters, which are very important in terms of brain function, and provide abundant information in characterizing different types of diseases,” Lam said.

“My research focuses on developing imaging tools to visualize these molecules in the brain non-invasively,” Lam said. “Specifically I’m developing a set of MR spectroscopic imaging (MRSI)-based technologies which will allow us to detect and quantify these molecules without the need of injecting any contrast agents into the body.”

MRSI has been used to study metabolic changes in the brain as well as other organs. “The main challenges for achieving such label-free molecular imaging using MRSI lie in the facts that these molecules typically have three to four orders of magnitude lower concentrations than water molecules—existing imaging methods to acquire their information are very slow, preventing them from being practically useful,” Lam said.

To address these challenges, he has dedicated his research to the development of new models, data acquisition strategies, and quantitative analysis and computational tools to address the speed, resolution, and sensitivity challenges for MRSI—and its integration with other neuroimaging technologies to study brain functions at normal and diseased states. Lam, who earned his master’s and doctoral degrees in electrical and computer engineering (ECE) at Illinois, was named a Beckman Graduate Fellow in 2012, working with Zhi-Pei Liang, a professor of ECE, and Brad Sutton, a professor of bioengineering—both members of the Bioimaging Science and Technology Group (BST). As a Beckman Institute Postdoctoral Fellow, Lam is able to continue these collaborations, but has greater autonomy.

“The Beckman Postdoctoral Fellowship provides me with a lot of flexibility in choosing the projects that I am interested in, and also opportunities to seek collaborations with colleagues from different disciplines,” Lam said. “I am really excited about brain mapping, both for its scientific importance and the technological challenges. Beckman has the Biomedical Imaging Center (BIC), an amazing facility, and a lot of people working on neuroscience and neuroimaging, so it turned out to be very easy to realize ideas and establish collaborations, by leveraging the campus’ strength in engineering and neuroimaging expertise in Beckman.”

With Liang and his students, Lam has already contributed to the development of what is considered an important advance in MRSI technology: SPICE (spectroscopic imaging by exploiting spatiotemporal correlation). In development by Liang’s group for more than a decade, the new approach addresses fundamental technical challenges in MRSI using novel signal generation, encoding and decoding methods developed within a subspace imaging framework.

“Fan is an outstanding researcher; he is one of those rare talents that a professor may encounter once in every 10 years or so,” Liang said. “I was very pleased to have recruited him to my group and he has exceeded all my expectations, making important contributions to our solution of the long-standing problems associated with MRSI.”

Through his postdoc fellowship, Lam has elevated SPICE even further and established a new technological framework for achieving rapid, ultrahigh-resolution MRSI. “Now we are able to achieve whole brain mapping of a number of metabolites in just five minutes with resolution matching that of a standard functional MRI scan. This is already more than an order of magnitude improvement over any existing methods,” Lam said. “My goal is to make simultaneous metabolite and neurotransmitter mapping, and comprehensive metabolic profiling of neural tissues into reality. I believe that with our recent progress these goals are within reach. Accomplishing them would lead to early diagnosis of diseases, better and more efficient treatment, and more importantly, move us toward the goal of better understanding the molecular basis of brain function and diseases.”

Lam is devoted to his research at Illinois and values the collaborative relationships he has developed that help further his goals and find new applications for these imaging techniques. He is excited about the continued opportunities he will have as a faculty member in the Department of Bioengineering at Illinois, beginning this fall, (pending approval by the U of I Board of Trustees). “I’m very excited that I will be able to continue some of these collaborations, and I want to establish a new collaboration with the Carle Illinois College of Medicine to develop and translate new molecular imaging technologies to study specific neurodegenerative diseases and assess the effectiveness of treatments.” Lam said.

“I have no doubt that he will become a key technical leader of our field. I excitedly look forward to continuing our collaboration after he assumes his faculty position with the Department of Bioengineering,” Liang said.
Preterm babies born early in the third trimester of pregnancy are likely to experience delays in the development of the auditory cortex, a brain region essential to hearing and understanding sound, a new study reveals. Such delays are associated with speech and language impairments at age 2, the researchers found. The findings are reported in eNeuro, a journal of the Society for Neuroscience.

“We have a pretty limited understanding of how the auditory brain develops in preterm infants,” said University of Illinois speech and hearing science professor Brian Monson, who led the study. “We know from previous research on full-term newborns that not only are fetuses hearing, but they’re also listening and learning.”

Ultrasound studies reveal, for example, that, beginning at least as early as 25 weeks into gestation, fetuses will blink or move in response to externally produced sounds, he said. Other research shows that newborns prefer to listen to sounds—such as music or speech—that they were exposed to in the womb over unfamiliar sounds. And electroencephalogram studies of the brains of preterm infants show electrical activity in the auditory cortex in response to sound.

From these types of studies, we know that fetuses in the third trimester of gestation are hearing, learning and creating memories,” Monson said. “It’s pretty remarkable that such an immature system already has the ability to start distinguishing and learning.”

To better understand how the auditory cortex matures in the last trimester of gestation, Monson and his colleagues turned to a large dataset collected at the St. Louis Children’s Hospital Neonatal Intensive Care Unit between 2007 and 2010. The 90 premature infants in the study had undergone magnetic resonance imaging one to four times in the course of their stay in the NICU. Another 15 full-term babies were recruited from the Barnes-Jewish Hospital in St. Louis and scanned within the first four days of life. These scans were used as examples of uninterrupted fetal brain development, for comparison with the preterm babies. The team used diffusion neuroimaging to study development of the auditory cortex in the infants’ brains.

“This technique measures the diffusion of water in the brain tissues, which can tell you a lot about the development of neurons and axons,” Monson said. As brain structures grow and mature, water diffusion in the gray matter and white matter also changes in recognizable patterns, allowing researchers to track how the tissue is developing, and at what rate, he said.

The team focused on the primary auditory cortex, which is the first cortical region to receive auditory signals from the ears via other parts of the brain, and the nonprimary auditory cortex, which plays a more sophisticated role in processing those stimuli.

“We wanted to know: What is the relationship between these two regions? Do they mature at the same time, but at different rates? Do they mature at different times but similar rates?” Monson said. “A different rate of maturation may render one tissue more vulnerable to injury or disruption associated with preterm birth.”

The analysis revealed that by 26 weeks of gestation, the primary auditory cortex was in a much more advanced stage of development than the nonprimary auditory cortex. Between 26 weeks and about 40 weeks—the latter the equivalent of full-term birth—the nonprimary auditory cortex in the preterm infants matured quickly, partially catching up to the primary auditory cortex. Both regions appeared less developed at 40 weeks in the preterm infants than in the full-term babies.

The team also found an association between the delayed development of the nonprimary auditory cortex in infancy and language delays in the children at age 2, suggesting that disruptions to this part of the brain as a result of premature birth may contribute to the speech and language problems often seen later in life in preemies, Monson said.

“It’s exciting to me that we may be able to use this technique to help predict later language ability in infants who are born preterm,” he said. “I hope one day we also will be able to intervene for those infants who may be at greatest risk of language deficits, perhaps even before they begin to use words.”

The research team also included scientists and physicians from Harvard Medical School, University College London and Washington University School of Medicine in St. Louis.

The National Institute of Child Health and Development, the National Institute of Neurological Disorders and Stroke and the National Institute of Mental Health supported this research.
The National Science Foundation (NSF) recently granted the University of Illinois $3 million for an interdisciplinary graduate student training program to help form new insight on the brain—and to expand participation in the field of brain science itself. Sixty graduate students from across campus will participate in the five-year NSF Research Traineeship, led by Martha Gillette, a professor of cell and developmental biology and director of the Neuroscience Program at Illinois.

The project’s primary goal is to provide students with an immersive research experience that blends techniques from multiple disciplines to better understand the many aspects of the human body’s most complex organ. The program will teach students to use and understand miniature brain machinery critical to examining and regulating brain activities. It’s also designed to increase the participation of women, underrepresented minorities, and students with disabilities in the field of brain science. A third goal is to improve scientists’ communication skills with the public.

“This is a training initiative between neuroscience and engineering. It’s building on some of the new technologies in engineering, but it’s focused on better understanding the brain,” Gillette said. “It’s exciting because it’s going to let us do new things and train graduate students in new ways.”

Students will come from several departments across campus, including neuroscience, cell and developmental biology, molecular and integrative physiology, chemistry, psychology, chemical and biomolecular engineering, bioengineering, and electrical and computer engineering.

The training program will bridge two research paradigms about the brain: cognitive and behavioral studies, including the use of bioimaging and computational tools to understand adaptation, decision-making, psychology, and learning of an individual; and cell and tissue studies, with a focus on altering cell activity through a variety of methods. To meet these goals, the program will guide graduate students through specialized courses to broaden their knowledge beyond their own specific fields. Training courses will address behavior and the development of the nervous system as well as engineering, biological, and psychological perspectives on how brain activity can be modified.

The U of I project was one of only three proposals aimed at understanding the brain selected for this particular NSF project, out of a large national competition. Co-directors on the project include Rashid Bashir, professor of bioengineering and electrical and computer engineering, and the Department of Bioengineering; Neal Cohen, professor of psychology; and Jonathan Sweedler, professor of chemistry.

Students also will have opportunities to visit and work with the laboratories of international partners, including the Institute of Bioengineering and Nanotechnology of ASTAR (Singapore), the Biomedical Research Institute of the Korean Institute of Science and Technology (S. Korea), the University of Tokyo (Japan), the University of Okayama (Japan), the University of Birmingham (U.K.), and the Johannes Gutenberg-University at Mainz (Germany).

While the funding mainly contributes to a training program for graduate students, the project also has a research component. Gillette expects the project to advance a relatively new field of study regarding how, through cross-talking, groups of cells behave differently than the entity that they’re part of.

“The idea of using these self-organizing neuron preparations is new,” Gillette said. “It’s new enough that over the five years of the grant and training period, it will really develop a lot, especially with the technologies we have.”

The U of I’s interdisciplinary approach fits with the NSF’s focus for the training program.

“Integration of research and education through interdisciplinary training will prepare a workforce that undertakes scientific challenges in innovative ways,” said Dean Evasius, director of the NSF Division of Graduate Education. “The NSF Research Traineeship awards will ensure that today’s graduate students are prepared to pursue cutting-edge research and solve the complex problems of tomorrow.”
Mesial temporal lobe epilepsy was never something that Hillary Schwarb, IHSI research scientist in neuroscience, imagined her day-to-day work would revolve around. Schwarb, who arrived at Illinois in 2012 as a post-doctoral researcher in Prof. Neal Cohen’s Memory Systems Lab, has a PhD in Cognition and Brain Sciences and her research had been focused on the mechanics of memory, cognition, and brain plasticity.

After attending a talk by former Beckman Institute research scientist Curtis Johnson on magnetic resonance elastography (MRE), Schwarb became interested in how the imaging technology could be applied to hippocampal composition with regard to cognition. She familiarized herself with the Biomedical Imaging Center’s MRE tools and capabilities. Almost concurrently, Carle Health System neurologist and epileptologist Dr. Graham Huesmann, also a research assistant professor of molecular and integrative physiology at Illinois, began asking important questions about MRE applications in mesial temporal lobe epilepsy. The most common form of human epilepsy, it is often misdiagnosed as anxiety or presents as a mood or memory disorder. Seizures happen from one side of the hippocampus, and if untreated, they spread to both sides of the brain.

With an interest in using MRE to study the tissue structure of the hippocampus as their common thread, Schwarb and Huesmann began working together on a clinical and translational project.

What are the potential clinical impacts or outcomes of using MRE for epilepsy patients, besides just scientifically evaluating the composition of brain tissue?

“Since this particular form of epilepsy becomes increasingly resistant to treatment by medication, over time, surgery is often a better long-term treatment,” said Schwarb. “Identifying good surgical candidates has been the challenge, because it takes years of seizures to detect damaged, scarred tissue. MRE is more sensitive to hippocampal tissue integrity than previous imaging modalities, so it can help earlier detect microstructural changes in the hippocampus related to epilepsy. It can help determine the severity and make surgery more successful, ultimately leading to better quality of life for patients.”

Have you experienced any challenges with your project, and if so, what?

“As I think is usual, one challenge is identifying a large number of patients who want to participate and who qualify to be scanned in our study; then, we have folks who travel great distances to just get scans here for research—not even to see a doctor,” said Schwarb. “There’s recently been a resurgence in participation in our project, so we’ve been reviewing more scans. It can be tough to be clear with patients that this research may not benefit them directly, but could help others in the future—so it’s very selfless of them to be a part of this.”

Describe your research progress from studying MRE scans of Carle patient participants?

“In addition to developing markers or baselines for brain tissue viscoelasticity (stiffness) measurements as they relate to epilepsy, we have other exciting preliminary results from data collected so far,” said Schwarb. “We have been able to determine that the affected side of the hippocampus is much stiffer than the unaffected side, in patients. Unexpectedly, we have seen that the unaffected side of the hippocampus is significantly softer than the microstructure of the healthy control brain. Based on older imaging technology, this tissue would read as normal and healthy. But with MRE, we may help identify people at risk of epilepsy earlier, by the unaffected hippocampus. It may be an even earlier indicator than the scarred tissue side of the hippocampus.”

In your opinion, what are must-haves for a successful clinical research collaboration?

“Both sides of the collaboration need to be committed to the success of the project. Having a clear understanding of what each party can feasibly bring to the collaboration is vital,” said Schwarb. “Also, having an enthusiastic physician in Graham (Huesmann) has been vital. Doing this work wouldn’t be possible without a collaboration; on the university side we bring expertise in the technology and its application; the Carle side obviously gives us access to patient data, but also physicians who are asking the right clinical questions.”

What are your goals for the future of this project with Dr. Huesmann on MRE and epilepsy?

“First, we’d like to grow the size of our patient population and sample to validate the interesting preliminary findings we’ve seen. We’d also like to start probing some of the unanticipated findings to find their relevance and potential for clinical treatment solutions,” said Schwarb. “We also have plans to apply for two NIH grants and other funding in the near future.”

Other team members working on the MRE and epilepsy project with Schwarb and Huesmann include Curtis Johnson, Biomedical Imaging Center Director Tracey Wszalek, and Brad Sutton, bioengineering professor.

Two MRI scans, compared with an MRE scan of a 29 year old female, experiencing one seizure/week; one aura/day; 10+ years of seizure activity. The right and left sides of the hippocampus are circled, with arrows pointing to seizure-affected areas of stiffer tissue.
Both new research findings and familiar, friendly collaborations were celebrated at the Clinical and Translational Workshop last spring, hosted by IHSI at Illinois and Carle Neuroscience Institute. The day-long agenda focused on the topics of neurological disease, sleep, and rehabilitative and restorative neuroscience, featuring experts from Champaign-Urbana, and beyond, presenting their research in these areas.

Jeffrey Kleim, associate professor at Arizona State University, delivered the workshop’s keynote lecture on “Neurorehabilitation: Encouraging the Brain to Change.” Dr. Kleim is an Illinois alum, having completed his master’s degree and PhD in psychology from the University of Illinois, doing his graduate work under the late professor Bill Greenough, a pioneer in the study of brain plasticity. In addition to his clinically-geared keynote lecture, Kleim gave a more informal talk the evening before the workshop to a smaller audience at the Beckman Institute. He spoke on “Neural Plasticity: where did we come from, where are we, and where are we going?” and recalled his days as a graduate student at the Beckman Institute.

“Jeff is an incredible researcher and part of the academic family tree of brain plasticity research here at Illinois,” said Neal Cohen, professor of psychology and IHSI at Illinois director, who introduced Dr. Kleim. “We are thrilled to have him share with us his work with patient populations in the neural substrates underlying motor skill recovery after stroke and during Parkinson’s disease.”

Following Dr. Kleim’s keynote, University of Illinois at Urbana-Champaign associate professor of molecular and integrative physiology Hee Jung Chung spoke about her collaborative research with Carle neurologist Dr. Graham Huesmann. The two are studying certain potassium channels as key players various forms of seizures in epilepsy. Next up, Andrew Steelman, assistant professor of immunophysiology and behavior in the UI’s department of animal sciences gave a talk about the connections between upper respiratory infections and multiple sclerosis.

After lunch, Carle Neuroscience Institute’s Dr. Charles Davies provided workshop attendees insights into new technology—wireless biomedical sensors—being developed to non-invasively and more accurately detect sleep disorders in the clinic. Ken Paller, director of the Cognitive Neuroscience Program at Northwestern University (Evanston, IL) continued the conversation about sleep, but with an emphasis on his work in aspects of human memory, including contrasts between conscious and non-conscious memory expressions, and memory consolidation during sleep.

The final talks of the day addressed rehabilitative and restorative neuroscience, again—but this time in the context of aging and hearing loss, audiovisual speech perception in persons with hearing loss, and cochlear implants and executive functioning.
New for 2017, the Clinical and Translational Neuroscience Workshop included a poster session and reception at the end of the day. Several neuroscience-focused graduate students participated in the poster session, getting the opportunity to share their research with faculty, staff, and clinicians. We spoke with a few of the students to get an idea of the broad range of research happening at Illinois.

Kathleen Roeing studies cognitive motor interference rehabilitation in multiple sclerosis (MS) patients, in the Motor Control Research Lab, under the direction of Dr. Jacob Sosnoff. Roeing’s research focuses on improving patients’ multitasking ability through two different training methods. The first method involves online cognitive brain training. The second test is a dual training, requiring participants to conduct physical exercises and a cognitive test at the same time. Through analyzing gait speed and measures of cognition, the studies show that the dual task training helped improve participants’ cognitive abilities and capacity to multitask, compared to the computerized cognitive training. Continuing the research, Kathleen and her lab mates are now investigating the impact of virtual reality training, which can target cognition, gait, and balance simultaneously.

Lydia Nguyen, a third year PhD student in the Neuroscience Program working with Professor Raksha Mudar in the Department of Speech and Hearing Science, presented a poster focused on characterizing electroencephalographic (EEG) differences between early and late stages of amnestic mild cognitive impairment (aMCI), a population that is at high risk of developing dementia, especially of the Alzheimer’s disease type. EEG is recorded while subjects completed visual Go/NoGo tasks involving semantic categorization. The results showed that alpha power differentiated the early and late aMCI groups, particularly during NoGo trials which involved inhibitory processing. These preliminary findings suggest the potential utility of alpha power in differentiating severity of cognitive deterioration at the pre-dementia stage.

“As a cheaper and less invasive examination method, the long-term goal of the study is to determine if EEG can be used as a clinical marker of cognitive decline,” says Nguyen.

Matthew Biehl is a graduate student in the lab of Dr. Lori Raetzman researching the hypothalamus, a part of the brain which controls all homeostasis functions of humans, and links the nervous system to the endocrine system through the pituitary gland. The Raetzman lab hopes to learn more about signaling pathways and how different stem cell molecules develop in this dynamic area within the brain. Biehl treats a pure stem cell population from mice with various signaling molecules and observes how they differentiate into neurons and other cell types of the brain. They are curious about what specific type of stem cells can become after being manipulated. Through isolating, expanding, and categorizing the different markers these cells express, they are able to detect the cells’ differentiation trajectory. Their current work is not yet published, but papers are in the works.

Several other students also had the chance to present their work at the poster session, and received suggestions from senior researchers and clinicians. Gillian Snyder, research development manager of the clinical and translational neuroscience program at IHSI, hopes to expand the poster session for future workshops.
The University of Illinois at Urbana-Champaign has a rich history of plasticity-related research, much of it stemming from the pioneering work of researcher William Greenough, which revealed experience-related plasticity within the mammalian brain. Current research at the university has built upon and extended this work—investigating the ability of physical exercise, cognitive training, mindfulness meditation, and nutrition, among other factors, to promote neural plasticity.

As part of the university’s sesquicentennial celebration, researchers gathered to initiate a dialogue about the future of brain plasticity research on campus. The day-long symposium, focused on ‘Revolutionizing Brain Plasticity through Advanced Science, Engineering, and Medicine,’ brought together scientists, clinicians, and community partners to lay the groundwork for interdisciplinary research aimed at understanding and enhancing brain plasticity. The technological and behavioral approaches to measuring plasticity featured in the symposium presented an incredible opportunity for researchers to assess the impact of these interventions in ways that have not yet been possible.

Keynote speakers of the symposium included Jocelyn Faubert, a professor at Université de Montréal and the creator of the NeuroTracker brain-training program; Peter Bandettini, the Chief of the Section on Functional Imaging Methods and director of the Functional MRI Core Facility at the National Institute of Mental Health; David Van Essen, the Alumni Endowed Professor of Neuroscience at Washington University in St. Louis; and Sanmi Koyejo, assistant professor of computer science at the University of Illinois at Urbana-Champaign.

Throughout the day, panel discussions facilitated an open dialogue between keynote speakers and members of the audience and raised several issues that will be of utmost importance for plasticity researchers going forward. Paramount among them is the question of the scale at which scientists should examine neural plasticity—whether at the level of synapses or entire sub-regions of the brain. It is likely that understanding the ever-changing nature of the brain will require a multidisciplinary approach to plasticity-related research at all scales, harnessing the full breadth of the technological expertise for which Illinois is renowned.

The symposium coincided with the recently announced launch of the University of Illinois’ Center for Brain Plasticity, supported by the IHSI and the Beckman Institute for Advanced Science and Technology. Many of the featured talks highlighted the ways in which the technological expertise encompassed by the Beckman Institute, particularly within the realms of structural and functional neuroimaging, can be leveraged to create a sophisticated set of tools with which to characterize plasticity within the brain.

“Our hope for this event was to provide a catalyst for research at the intersection of neuroscience, engineering, computer science, and medicine, aligning with the priorities of the new Center for Brain Plasticity. We wanted to hear from researchers who are actively engaged in cutting-edge research, with whom our faculty and students would want to collaborate. After hearing some of the discussions on the day, I believe we were very successful!” said Gillian Snyder, who emceed the symposium.
A new center is taking shape, championed and supported by both the Interdisciplinary Health Sciences Institute and the Beckman Institute for Advanced Science and Technology. Led by co-directors Aron Barbey and Neal Cohen, the Center for Brain Plasticity brings together researchers, university-wide, with the aims of advancing understanding of the brain and the power of the brain to be changed by experience and other external influences.

“The study of brain plasticity has a long historical connection to the Beckman Institute, and we are pleased to partner with IHSI to establish this center of excellence,” said Jeff Moore, director of the Beckman Institute.

Brain plasticity, or neural plasticity, is the ability of the brain to change throughout an individual’s life—synapse strengthening or weakening, grey matter changes, cortical remapping, and more. The notion of the brain having the capacity to reconfigure itself is a hallmark of modern neuroscience, transforming prior scientific consensus that the brain develops during a critical period in early childhood and remains largely static. This contemporary area of research has the potential to transform much of how we understand the nature of human intelligence, learning, and memory, and how we characterize and treat traumatic brain injury and neurological diseases. The new center provides a hub for basic and translational research at Illinois that aims to measure, model, and elicit brain plasticity through scientific discovery and technological innovation.

“The Center for Brain Plasticity aims to promote interdisciplinary studies of the neurobiological foundations of brain plasticity, innovative methods and technologies to drive neural plasticity through the application of cognitive training, non-invasive brain stimulation, physical fitness training, mindfulness meditation, and nutrition, among others,” said Barbey, who is associate professor of psychology, neuroscience, bioengineering and full-time Beckman Institute faculty. “The center will also encourage clinical trials that investigate science and technology that aims to mitigate or reverse the effects of cognitive aging, traumatic brain injury, stroke, and neurological disease.”

The Center for Brain Plasticity builds upon the incredible wealth of plasticity research and data at the University of Illinois at Urbana-Champaign to provide a nexus for long-term interdisciplinary collaborations. It brings together a community of like-minded investigators, drawing on the strengths of work already being conducted at the Beckman Institute (especially its newly-formed Intelligence, Learning, and Plasticity research group), the Interdisciplinary Health Sciences Institute’s (IHSI) Clinical and Translational Neuroscience program area, many other centers and initiatives on campus, the Carle Neuroscience Institute, and with clinical partners. IHSI Director Neal Cohen spoke to the advantages of aligning efforts and resources in this particular area of health sciences research.

“There is tremendous strength and interest in brain plasticity across multiple campus units at Illinois, and a long history here of significant advances in this field. The new center provides a hub for basic and translational research that aims to measure, model, and elicit brain plasticity through scientific discovery, technological innovations, and clinical application,” said Cohen.

Visit the new Center for Brain Plasticity website at brainplasticity.illinois.edu to learn more. For more information and to collaborate, email brainplasticity@illinois.edu.
As the uniting institute for health sciences and technology on the Illinois campus, IHSI is rooted in research and grounded in tech. IHSI supports faculty-driven research at Illinois by organizing our campus around health challenges, team-building, coordinating projects, and managing grant efforts. IHSI makes a point to fuse technological advances with health science research.