BRAIN,
COGNITION
& LANGUAGE

UCONN
CONNECTICUT INSTITUTE
FOR THE BRAIN AND
COGNITIVE SCIENCES

2018–2019

SHAPING THE BRAIN: NEUROPLASTICITY

IN THIS ISSUE:

SCIENCE AND THE PUBLIC GOOD

The brain is an amazing organ that has the power to think, learn and compute. It has the ability to adapt and mold itself over time: During brain development, its cells (neurons) move from one place to another, forming connections that will later become stronger or weaker depending on the input that the brain receives and the behaviors it must control. Studying these changes, or *neuroplasticity* as it's called, leads to a better understanding not only of how brains work, but also of how they sometimes don't work as expected, perhaps when something goes wrong during development, or if later the brain suffers a physical injury. To what extent, and how, can the brain heal itself?

If researchers can pinpoint how positive, adaptive brain changes occur and what factors promote healthy growth, their research could enhance treatments, therapies, or strategies for learning. Furthermore, if researchers can understand what factors influence unhealthy changes in the brain or influence normal decline in brain function during aging, preventative measures might be developed to stem the decline.

The Brain, Cognition and Language Digest highlights UConn's unique, interdisciplinary approach to brain science. UConn's scientists study the brain from differing perspectives – from the lifecycle of a neuron growing from a stem cell into maturity, to how the brain communicates with other organs. They study the healthy brain, and they also study rare neurodevelopmental disorders and common ailments like hearing loss and urinary urgency. By understanding the way the brain changes over time, they hope to make discoveries that can improve quality of life for all.

STUDENT FEATURE

Derek Lee

Derek Lee recently graduated from the University of Connecticut with a Bachelor's Degree in Physiology and Neurobiology. His interests are in how we can use different species of animal to "model" neurological disorders in humans. As an undergraduate, Derek worked in Dr. Roslyn Fitch's lab in the Psychological Sciences department helping with various behavioral and motor tasks for rodents with neurological development disorders. Additionally, he worked in Dr. Geoffrey Tanner's lab in the Physiology and Neurobiology department investigating brain injury in Drosophila (commonly known as the fruit fly). Derek's research in these areas was funded by an Office of Undergraduate Research (OUR) Supply Award from UConn and an undergraduate research fellowship award from IBACS.

Derek is continuing his research in Dr. Tanner's lab as he pursues his master's degree in Physiology and Neurobiology. Traumatic brain injury (TBI) affects over a million people each year. These injuries can cause symptoms such as memory loss, aggression, and other debilitating conditions. The lab aims to use an organic chemical compound, beta-hydroxybutyrate, as a possible treatment for brain injury in a Drosophila model. The researchers are working toward understanding the ability of this compound to reduce symptoms, such as aggression, in Drosophila with substantial TBI.

BRAIN, COGNITION & LANGUAGE DIGEST

A publication for the CT Institute for the Brain and Cognitive Sciences

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TERMS TO KNOW

Neuroplasticity is the flexibility of the brain to change itself over time.

There are two major types of brain cells: **neurons** and **glial cells**.

- **Neurons** are a type of cell that communicate through electrical and chemical signals, and these signals are sent through axons (but received via dendrites).
- **Glial cells** provide structure and support for the nervous system. Glial cells include NG2 cells (see page 7) and oligodendrocytes, the latter which are responsible for producing myelin.

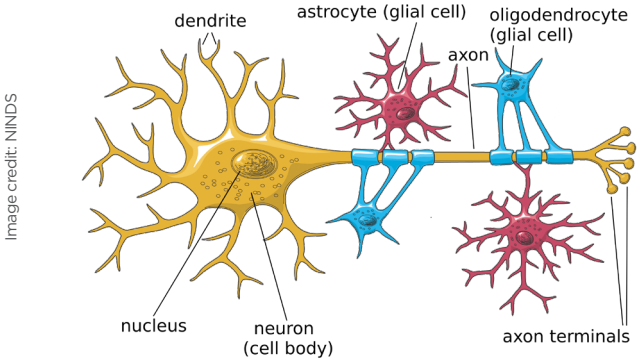


Image credit: NINDS

Myelin is a protective covering on axons, similar to insulation on a wire. Myelin helps signals be transmitted more effectively in the brain.

- **Multiple Sclerosis** is a disease in which myelin is destroyed by the body, limiting the brain's ability to communicate and leading to a wide range of symptoms, such as impaired movement.

Autism Spectrum Disorder can refer to a broad and varied set of behaviors, but its hallmarks are social and communicative impairments. Individuals who were diagnosed with autism but whose symptoms then improve to the point where they would no longer be diagnosed as such are referred to as **LADS (Loss of Autism Diagnosis and Symptoms)**.

Epilepsy is a brain disorder which causes seizures.

Chromosome 15q duplication syndrome (Dup15q) is a genetic disorder that can result in a wide range of symptoms, including behavioral disorders as well as atypical development of physical features, motor skills and speech skills.

Angelman syndrome (AS) is a genetic disorder that causes delayed development and can result in intellectual disabilities, impairments in speech and motor skills, and behavioral disorders. It often co-occurs with epilepsy.

Stem cells are cells which can develop into different kinds of cells with different functions. They don't necessarily come from fetal cells; they can often come from skin or blood samples donated by patients. These cells allow scientists to study rare genetic disorders because they come from patients who have these disorders. For instance, by reprogramming stem cells into neurons, scientists can study the brain basis of these disorders and ultimately develop potential interventions.

DR. JENNIFER TUFTS (LEFT) AND DR. ERIKA SKOE ARE AMONG THE MANY SCIENTISTS AT UCONN WHO STUDY HOW OUR BRAINS PROCESS AUDITORY INFORMATION.

THIS IS YOUR BRAIN ON SOUND

Think about the last time you went to a concert performance. You were probably able to perceive the music with relative ease, so you might not have given much thought to the physical and psychological processes that allowed you to perceive it. But figuring out exactly how we perceive sounds involves answering many complex questions: How is information about sounds processed in the ear and in the brain? How might the things you hear now shape the way you perceive sounds later? These are just a few of the fundamental questions being investigated by researchers in the Connecticut Institute for the Brain and Cognitive Sciences.

One of the challenges in understanding how sound is processed comes from the fact that our auditory systems have many processing stations. When sound enters the ear, it brushes up against tiny receptors in the cochlea, triggering a cascade of electrical signals within multiple places in the brain. Critically, different parts of the brain are specialized to respond to different aspects of sound – for instance, some regions respond more to high-pitched sounds than to low-pitched sounds.

Brain cells and neural models

But exactly which aspects of sound are processed at each auditory processing station, and how? It's a complex question that requires a combination of approaches. One approach is to record directly from brain cells and to measure their responses to sounds, as done by UConn researchers Dr. Douglas Oliver and Dr. Monty Escabi. In a recent study using this approach, Dr. Oliver and colleagues discovered a group of neurons in the brainstem that continue to respond to sounds even after those sounds have stopped. "Normally," Dr. Oliver said, "neurons respond while the sound is on and stop when the sound is off. [But when these brainstem neurons] hear a sound for more than a minute or two, they keep responding even when the sound goes off. We don't know why, but it is like they still hear a sound." Dr. Oliver noted that the action of these brainstem neurons might have something in common with the experience of tinnitus (see box); his team recently received a grant from the Department of Defense to explore this possible link and to develop an electrophysiological test for tinnitus.

In Dr. Escabi's lab, recent animal studies have demonstrated that different parts of the midbrain respond to how quickly a sound turns on or off, sort of like the flickering of a light. Some parts of the brain respond to very fast "beats" of sound, turning on and off several hundreds of times per second, while other parts respond to slower beating.

Dr. Escabi noted that being able to detect the beat of sounds is important both for music perception and speech recognition, since both involve sounds turning off and on.

"Think of the beat from the drum, or the pitch from a human voice," Dr. Escabi said.

Findings from animal studies are then used to build mathematical models, which Dr. Escabi hopes can provide a more precise understanding of how the auditory processing system works in humans.

Perception/Cognition

But it is not only different aspects of the sound signal that affect our perception – our expectations also play a fundamental role in how we perceive sounds. In a recent fMRI study, Dr. Edward Large and colleagues examined the role of expectations in how we perceive music. In the study, participants heard several pieces of music, each performed twice. One time, they were told the piece of music was performed by a professional; the other time, they were told it was performed by a student. In other words, half the time they were given an accurate label for a piece of music (for instance, a "professional" label when a professional was playing) but the other half, they were given an inaccurate label (for instance, a "professional" label when a student was playing).

In order to examine how expectations influence perception, the researchers looked at brain activity and how it related to whether participants said they preferred the "professional" or the "student." In listeners who preferred the professional performance (regardless of whether it was accurately labeled), there was increased activity within auditory centers of the brain – the researchers argued that these individuals, believing the professional would perform better than the student, devoted more attentional resources to areas involved in auditory perception. By contrast, listeners who said they preferred the "student" showed relatively increased recruitment of executive control areas, which may be involved in overcoming the biasing label they were given.

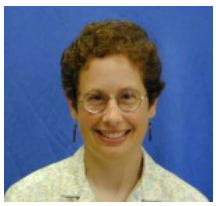
Individual experience

In addition to being guided by expectations, auditory processing can also be affected by our experiences with sound throughout our lifespan. Work in Dr. Erika Skoe's lab looks at how factors like loud noise exposure or musical training can influence auditory processing, both in the short term and in the long term. Such experiences might enhance processing of some sounds while reducing sensitivity to others.

Her lab's recent work, in collaboration with Dr. Jennifer Tufts, has revealed that noise exposure may reduce the hearing benefits that come from musical training. By studying diverse populations with distinct auditory experiences, Dr. Skoe and her team hope that scientists might get a better understanding of how the auditory system works in concert with other parts of the brain to perform complex cognitive tasks, such a following a conversation in a noisy restaurant.

TINNITUS is a sensation of hearing a noise or "ringing" in your ears when there is no sound present. It often occurs following exposure to loud noise, and more than 20 million Americans experience tinnitus each year, according to the National Institute on Deafness and Other Communication Disorders.

NEUROPLASTICITY RESEARCH AT UCONN

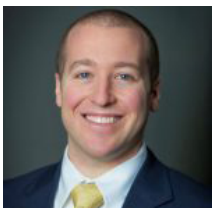


LETITIA NAIGLES

Children with autism spectrum disorder (ASD) vary widely in their language abilities, yet the underlying brain mechanisms related to this language variability remain unclear, especially early in development. It has been suggested that ASD diagnoses could be tied to atypical white matter development. White matter is in the center of the brain, connects different regions of the brain together, and communicates signals faster than the gray matter that makes up the outer regions of the brain. Dr. Letitia Naigles and colleagues used diffusion tensor imaging (DTI) to look at white matter in the brains of 104 preschool-aged boys with ASD. The boys were split into subgroups according to their vocabulary size (Low, Middle, High). Dr. Naigles' team found that the subgroups differed in fractional anisotropy (FA), a measure of the strength of the connections in white matter. This measure was correlated with the boys' language scores, but not the severity of their ASD diagnoses. This finding can help us understand how differences in brain communication and development may factor into differences in how children with ASD learn to talk.

INGE-MARIE EIGSTI

For reasons scientists don't fully understand, some children on the autism spectrum eventually move off of it – that is, they no longer show the symptoms required for an autism diagnosis. Researchers refer to these individuals as LADS because they have had a Loss of Autism Diagnosis and Symptoms. LADS individuals are often indistinguishable from their typically developing peers, doing just as well in school and in social situations. A team of UConn researchers led by Dr. Inge-Marie Eigsti hopes to figure out how this happens by studying the brains of individuals with current autism, LADS individuals, and typically developing individuals. In a recent fMRI study, the researchers examined what brain regions these groups used while reading sentences. While everyone recruited the same brain areas, the LADS individuals recruited them to a larger degree. The authors concluded that this increased brain activation may underlie a compensatory mechanism that allows the LADS individuals to adapt to their environment.



ADAM LEPLEY

Musculoskeletal injuries, such as a torn ACL or tendonitis, represent the leading cause of physical disability in the US. Even after rehabilitation, patients with joint injuries often suffer from muscle weakness. Research by Dr. Adam Lepley focuses on the often undiscussed role of the brain in these injuries, and in particular looks at how the nervous system is altered following joint injury and how that affects the ability of the nervous system to guide motor control.

After injury, an injured joint no longer communicates with the nervous system the same way it did previously. This leads the brain to rely more on other kinds of sensory input, such as visual information, and to decrease motor output, leading to muscle weakness. Dr. Lepley's research is one of the first to examine the neuroplasticity that follows joint injury and will assist in the development of improved rehabilitation techniques for these patients.

PHILLIP SMITH

Loss of bladder control has a tremendously negative impact on the quality of life and becomes increasingly common in later life. Standard diagnosis and treatment for these problems focus on abnormalities of bladder muscle action. However, even after decades of research, this approach has not achieved reliable results, especially for older adults. Dr. Phillip Smith's research is rooted in the idea that addressing urinary symptoms requires focusing not just on the bladder but also on its relationship with the brain.

As the bladder ages, it may become less responsive to signals from the brain, and this may in turn influence the way the brain works to control the bladder. Good bladder control is the result of a brain-bladder system being able to adapt to external and internal factors. As the brain-bladder system ages, the system becomes less adaptable; as such, older adults may find it difficult to maintain socially appropriate bladder control. Dr. Smith hopes that taking a more integrative approach to addressing urinary problems will lead to better evaluation, prevention, and treatment of urinary symptoms, particularly in older adults.

MASON YEH

Studying the development of human brain cells has been limited to single layers of cells in petri dishes, but Dr. Mason Yeh is leading a project to develop three dimensional "mini-brains" from human stem cells taken from blood samples or skin tissue. These mini-brains could allow Dr. Yeh and other researchers to study the molecular and cellular systems underlying neurodevelopmental disorders, such as autism, with the goal of identifying new therapeutic interventions that take advantage of brain plasticity. Dr. Yeh's team uses a bioreactor, which fosters natural biochemical reactions, to turn these cells into neurons that can then be used to grow a 3D, miniature brain. So far, Dr. Yeh and his lab have successfully created early versions of mini-brains with immature neurons, though more work is needed to refine the technique.

MIN TANG-SCHOMER

We don't yet know how neurons organize themselves to build a brain or why they can sometimes fail, leading to certain mental illnesses and intellectual deficits. Dr. Min Tang-Schomer has taken on the challenge of illuminating part of that process by growing neurons in a petri dish, creating a simple, single brain circuit.

In the brain, neurons communicate with each other using electrical signals that are converted to chemical signals. After some experimentation using electrodes to send electrical signals to the neurons in the petri dish, Dr. Tang-Schomer was able to get the neurons to fire in synchrony, an indication that the neurons are wiring together. In the brain, this wiring together is how different parts of the brain form connections, and these connections are reinforced the more neurons communicate with each other. Dr. Tang-Schomer has also been able to direct the growth of these connections and has plans to connect these cells to a synchronization program to see how the neurons will adapt. Using these technologies and others, her hope is that one day we can see how a brain grows, play with an artificial mind, and help those who don't have typical connections between neurons.

IBACS AND THE COMMUNITY

High School Students visit UConn's Brain Imaging Research Center (BIRC)

One of IBACS' goals is to provide education and outreach in the community. Therefore, IBACS was eager to reach out to high schools across CT and connect with instructors teaching Advanced Placement Psychology. The Institute hosted tours of UConn's Brain Imaging and Research Center for two visiting high schools, Middletown and Region 19. The students learned about technologies such as EEG (electroencephalogram), tDCS (transcranial direct current stimulation), and fMRI (functional magnetic resonance imaging), and how the tools are employed in research studies.

"I had no idea this research was being conducted at UConn," said one student.

"We all wanted to try it," said another. The Institute hopes to continue this outreach and to inspire young people to explore the brain and cognitive sciences.

Living Lab: A partnership between UConn and the CT Science Center

While many think of scientists as working in labs with microscopes and test tubes, a lot of researchers in the brain and cognitive sciences need to interact with people in order to achieve their research goals, and they are continually looking for people interested in participating in studies. It is helpful for researchers to have access to a wide variety of participants that are nearby in the community, but many universities are not located near large populations. Hence, the National Living Laboratory Initiative — the concept of using science museums as opportunities to conduct research in the community — was born.

The University of Connecticut has been partnering with the Connecticut Science Center in downtown Hartford to operate in their Living Lab space for nearly three years. Public visitors to the museum can become involved in studies that are designed to be fun, interactive and quick - but still offer researchers valuable information. IBACS proudly awarded some funding to help secure materials needed for researchers, like iPads, to make research successful at the Living Lab. Running participants in this setting allows for recruitment of a diverse group of people and also offers researchers a chance to share their science. Getting personally involved in research may also inspire young scientists. It's a win-win partnership!

GRADUATE STUDENT SPOTLIGHT

Each year, a large number of graduate students compete to receive national scholarships and fellowships. These prestigious awards provide funding for students to conduct research on a broad range of topics and often have direct application for clinical populations. This year, five students affiliated with the IBACS program have been supported by such awards.

JULIA DROUIN

Hearing loss is a common impairment affecting 360 million people worldwide. Cochlear implants (CIs) are a treatment option that may restore the sense of hearing. A critical challenge is accounting for differences in speech and language outcomes in CI users. Julia Drouin's research, with funding provided by a PhD scholarship from the Council of Academic Programs in Communication Sciences and Disorders, is aimed at examining factors that contribute to these differences in order to optimize user outcomes.

HANNAH MORROW

When you think about dogs, you might imagine what a dog looks like, or the bark sound that a dog makes. How can the shape, color, smell, and sound of a dog combine into the single concept of "dog" when each of these is processed by a different part of the brain? Hannah's research looks into how our brain integrates information into a single concept. She received a Graduate Research Fellowship from the National Science Foundation to support this work.

SAHIL LUTHRA

Everyone produces their speech sounds slightly differently, and Sahil is interested in how we learn to adjust to the particular styles of different talkers. Currently, Sahil is looking at whether our ability to predict the next word that a talker will say affects how well we can adjust to that talker's speech. He is thrilled to have received a Graduate Research Fellowship from the National Science Foundation that will support him while he pursues this research.

MEAGHAN PERDUE

Meaghan Perdue was selected as a National Science Foundation Graduate Research Fellow in spring 2017. Under the support of this fellowship, Meaghan aims to characterize relationships among brain structure and brain chemistry associated with reading disability. Through her work, Meaghan hopes to contribute to the understanding of causes of reading disability across levels of genes, brain, and behavior.

NICK MONTO

Nicholas Monto received the 2018-2019 Raymond H. Stetson Scholarship in Phonetics and Speech Science, awarded by the Acoustical Society of America. Under the support of this scholarship, Nicholas will examine how listeners adapt to the way different people speak and identify factors that contribute to individual differences in adaptation.

CAPCSD
Council of Academic Programs in Communication Sciences and Disorders

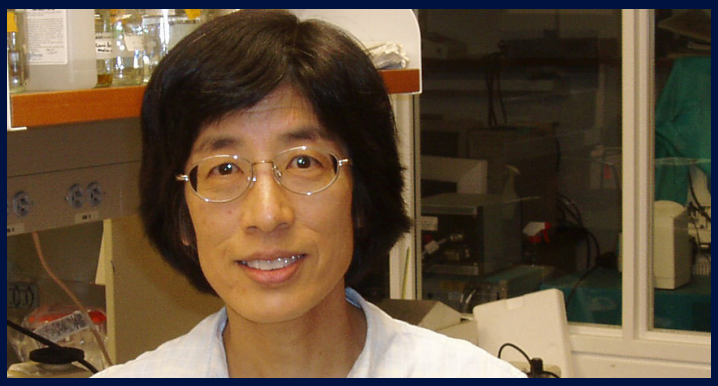
ASA
ACOUSTICAL SOCIETY OF AMERICA

GRFP
NSF GRADUATE RESEARCH FELLOWSHIP PROGRAM

NSF

FACULTY FEATURE

Dr. Akiko Nishiyama



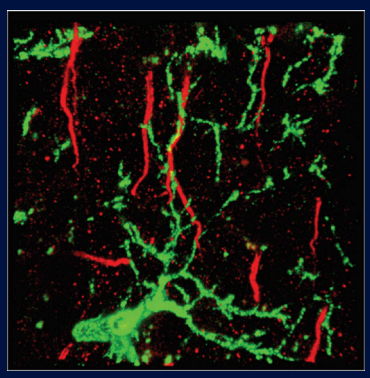
When people talk about brain cells, they are usually referring to neurons, the cells that send and receive information through chemical messengers and whose action ultimately allows us to interact with the world around us. However, neurons represent only about 10 percent of brain cells. The vast majority of brain cells are known as glial cells, or glia. However, relatively little is known about the function of these cells.

Dr. Akiko Nishiyama studies a class of glial cells known as NG2 cells (also called oligodendrocyte precursor cells). Early research has shown that these NG2 cells can mature into oligodendrocytes, which produce a fatty substance called myelin. Sheaths of myelin provide insulation for neurons, much in the same way that insulation covers electrical wires, and thus allow neurons to transmit signals faster. Damage to the insulating myelin sheaths can result in diseases like multiple sclerosis.

However, the fact that NG2 cells still exist in mature brains (after myelin is formed) suggests that they may also have other (yet unknown) functions. Based on the new observation that NG2 cells often wrap around the beginning of the nerve fiber (called the axon) where inhibitory neurons contact and modulate the activity of excitatory neurons, Dr. Nishiyama's lab is testing the hypothesis that NG2 cells may influence the degree of excitation of neurons in the brain. This could have important consequences for understanding a variety of medical conditions, as the balance between excitation and inhibition is altered in disorders ranging from epilepsy to schizophrenia.

Further reading:

Nishiyama, A., Komitova, M., Suzuki, R., & Zhu, X. (2009). Polydendrocytes (NG2 cells): Multifunctional cells with lineage plasticity. Nature Reviews Neuroscience, 10(1), 9-22.



Tissue analysis of NG2 cells (green) and axons (red)

ALUMNI FEATURE

Dr. Noelle Germain

Dr. Noelle Germain is an Assistant Professor in the Genetics and Genome Sciences Department at UConn Health. Dr. Germain received her PhD in Biology with a focus in Stem Cell Biology from Wesleyan University in 2012, then worked as a postdoctoral researcher in the lab of Dr. Stormy Chamberlain at UConn Health. In her research, Dr. Germain hopes to establish a collaborative research niche in the development and genetic manipulation of stem cell models of neural diseases.

Dr. Germain's doctoral research was geared towards creating models of neural development *in vitro* (in test tubes) using mouse and human stem cells. In an effort to develop these models for therapeutic applications, Dr. Germain worked to direct the development of the stem cells towards a particular subtype of neuron cells that are specifically affected in some forms of epilepsy. She developed methods to transplant these cells into mice, which allowed her to investigate whether these particular stem cell-derived neurons could integrate into the mouse brain effectively, and provided information that addresses the concern of tumors growing following stem cell transplants.

Dr. Germain then aimed to apply her cell culture models towards the study of neurodevelopmental disorders. She helped to develop several stem cell lines derived from two neurogenetic disorders: chromosome 15q duplication syndrome (Dup15q) and Angelman syndrome (AS). These stem cell lines have helped illuminate some of the neural mechanisms behind Dup15q and AS, and Dr. Germain's current objective is to use her human stem cell models of AS to develop new therapeutic approaches for the disorder, in hopes that this will someday lead to a cure for those suffering from Angelman syndrome.

Further Reading:

Fink, J., Robinson, T., Germain, N., Sirois, C., Bolduc, K., Ward, A., Rigo, F., Chamberlain, S.J., Levine, E. 2017. "Disrupted neuronal maturation in Angelman syndrome-derived induced pluripotent stem cells." Nature Communications 8 doi: 10.1038/ncomms15038. PMID: 28436452.

Banda, E., McKinsey, A., Germain, N., Carter, J., Anderson, N.C., Grabel, L. 2015. "Cell polarity and neurogenesis in embryonic stem cell-derived neural rosettes." Stem Cells and Development 24(8): 1022-33. PMID:25472739.

Germain, N., Chen, P-F., Plocik, A., Glatt-Deeley, H., Brown, J., Fink, J., Bolduc, K., Robinson, T., Levine, E., Reiter, L., Graveley, B., Lalande, M., Chamberlain, SJ. 2014. "Gene expression analysis of human induced pluripotent stem cell-derived neurons carrying copy number variants of chromosome 15q11-q13.1." Molecular Autism 5(44). PMID:25694803.

Germain, N., Banda, E., Naegele, J., Grabel, L. 2013 "Derivation and isolation of NKX2.1-positive basal forebrain progenitors from human embryonic stem cells." Stem Cells and Development 22(10):1477-89. PMID:23351095.

The CT Institute for the Brain and Cognitive Sciences publishes its Brain, Cognition & Language Research Digest for the purpose of community outreach. This issue includes research from Speech, Language and Hearing Sciences; Physiology and Neurobiology; Psychological Sciences; Kinesiology; Biomedical Engineering; and the UConn Health Center.

IBACS Stats

$198,000
Awarded in seed grants during 17/18 year

183
Affiliates across 23 departments

20
Graduate fellowships

13
Undergraduate fellowships

6
Research Assistantships in Neuroimaging

OUR RESEARCH COMMUNITY

WHO ARE WE?

The CT Institute for the Brain and Cognitive Sciences (CT IBACS) serves as an incubator for research across the brain and cognitive sciences at UConn and beyond, promoting and supporting the interdisciplinary science of the mind and its realization in biological and artificial systems. The Institute was conceived through cross-department discussion and collaboration fostered by the **Neurobiology of Language program (nbl.cogsci.uconn.edu)** and the **Cognitive Science program (cogsci.uconn.edu)**. It has since grown to encompass a broad scientific community across the UConn campuses.

WHAT DO WE DO?

Our goal is to further the scientific understanding of the mind and its biological systems through a cooperative and integrative approach. Since many problems arise from a multitude of factors, it makes sense to look for solutions with input from multiple perspectives. Working in an interdisciplinary fashion, researchers may learn and become familiar with the theories and methodologies of their peers from other disciplines. These methods include mathematical modeling, behavioral studies, electrophysiology, behavioral approaches, bench neuroscience, genetics, and animal models.

Neuroplasticity is an important area of research at UConn. Changes in the brain environment may play a role in many of the diseases and disorders that our faculty and student investigators are studying, such as Multiple Sclerosis, Epilepsy, Autism Spectrum Disorder and Schizophrenia. The changes can be dramatic, such as in the case of brain injury, or perhaps just subtle changes over time, but these scientists hope to understand how the changing landscape of the brain affects health and behavior. This issue aims to provide a brief summary of some that important, integrative research.

To Learn More

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