NEUROSCIENCE
Interdisciplinary Graduate Program

THE UNIVERSITY OF IOWA
www.uiowa.edu/~neuro/
MISSION

The past two decades have witnessed spectacular conceptual and methodological advances in the biomedical/biobehavioral sciences, and especially in Neuroscience. Developments in molecular biology, developmental and cell biology, neuroimaging, computer modeling, and the cognitive sciences have offered unprecedented insights to fundamental problems in the neurosciences. Significant steps are now being taken toward elucidating genetic and environmental disease mechanisms. New areas for fruitful investigation are developing, and scientists from a variety of backgrounds and disciplines meet at the frontiers. The neuroscience community is poised for a quantum leap in the understanding of the biological substrates of phenomena that have provoked philosophical and scientific inquiry for thousands of years, including language, memory, emotional processing, social conduct, personality, decision-making, planning and judgment.

The University of Iowa has a long tradition as a leading center for study of the nervous system and behavior, and for the training of graduate students in this area. Research training in Neuroscience at Iowa has received continuous federal support for over 25 years. Building on this foundation, the Iowa Neuroscience Graduate Program, established in 1984, formalizes the long-standing, interdisciplinary commitment of a diverse faculty. The Program promotes interaction among faculty, post-doctoral fellows, and graduate students, and fosters a congenial and collaborative environment for investigating the structure and function of the nervous system and its role in determining behavior. Research and teaching in the neurosciences at Iowa are consolidated in three partially overlapping tracks: molecular/cellular; developmental/systems; and cognitive/behavioral.

The Program enrolled its first graduate students in the fall of 1985 and awarded its first Neuroscience Ph.D. degree in May, 1989. Nearly fifty graduate students are currently enrolled in the Neuroscience Graduate Program at various levels of training.
Curriculum

The curriculum for the Neuroscience Program is designed around a three track system. Specifically, students can select and specialize in one of three offered tracks: molecular/cellular; developmental/systems; cognitive/behavioral. To some extent, the curriculum for each student will be tailored to meet their needs, depending on the track they select and their background. A set of Core courses are required irrespective of the specific track a student is in. Then, students in different tracks will focus on different types of courses.

The curriculum is designed to provide a multidisciplinary foundation in the conceptual and methodological approaches to study of the nervous system, emphasizing original, independent student research. It is anticipated that most students will complete the program in four to five years (in fact, the average time to degree currently is right at 4.5 years). The first two years emphasize formal instruction, laboratory rotations, and directed research; the final two to three years emphasize research and the writing of the Ph.D. dissertation. The Comprehensive Examination is typically taken in the Summer of the second year.

Financial Aid

Full-time Program students receive stipend and full tuition scholarship support through fellowship and research assistant awards. Awards are renewed annually, based on continued satisfactory progress and availability of funds. University of Iowa Presidential Fellowships, awarded on a competitive basis to incoming UI graduate students. Cheap, subsidized health, dental, and vision insurance are provided to graduate students.

The Neuroscience Program is committed to supporting its graduate students for their entire training period. The first year of support is normally provided by the Neuroscience Program, either from a block allocation from the Graduate College, or from the Neuroscience Program Training Grant. Thereafter, students are expected to be supported by their primary research mentor. On some occasions, advanced students will be supported by teaching assistantships. In all cases, students will have their tuition paid.

The Neuroscience Program is supported by a Training Grant from the National Institutes of Health (NIH). The Training Grant provides stipend and tuition support for a select number of first- and second-year graduate students.

Information on other forms of financial aid, including student loans, may be obtained by writing to:

Office of Student Financial Aid
Room 208 Calvin Hall
The University of Iowa
Iowa City, Iowa 52242
Teaching

During the course of their graduate studies, students are expected to establish their credentials in teaching excellence. Opportunities are available for students to organize and present lectures and seminars and to assist in laboratory instruction of undergraduate and health professions students. Teaching duties of Neuroscience Program students are primarily centered in the home departments of their faculty research advisors. Typically, a limited number of teaching assistantships are available either through the Neuroscience Program directly, or through related Departments (e.g., Psychology, Biology, Anatomy & Cell Biology). Students normally pursue teaching assistantships after they have completed the comprehensive examination.

Participation In Scientific Meetings

The Neuroscience Program is committed to providing regular opportunities for graduate students to attend national and international neuroscience meetings, and participation in such meetings is viewed as an important aspect of graduate student training. The principal meeting, which all neuroscience students are encouraged to attend, is the annual meeting of the Society for Neuroscience. All students are encouraged to participate in this meeting, even though students may not have work to present (e.g., as a poster or platform presentation) until their second year and thereafter. Presenting a poster (or giving a platform presentation) at the Society for Neuroscience Meeting is a valuable learning experience, and the Program will make every effort to support students in this endeavor. Other annual meetings (e.g., the Cognitive Neuroscience Meeting; the Neurobiology of Drosophila Meeting in Cold Spring Harbor) also provide good forums for students to present research work to other scientists.

The Neuroscience Program sponsors a booth at the annual Society for Neuroscience meeting, which promotes graduate student study in neuroscience at the University of Iowa. The booth is staffed by graduate students and faculty, and it has proved to be a valuable recruiting mechanism for potential graduate student applicants. The Neuroscience Program also hosts a social gathering at the Society for Neuroscience meeting, at which University of Iowa neuroscience students, faculty, and alumni have the opportunity to exchange news.
How to Apply

Students interested in neuroscience have the following two options:
1- Apply directly to the Neuroscience Graduate Program
2- Apply to the Biosciences Program, which is an umbrella program that includes the Neuroscience Graduate Program, as well as other programs in the biological and biomedical sciences.

A completed applicant file must contain the following: an application to the Graduate College directed to the Neuroscience Graduate Program, official transcripts of all undergraduate and graduate course work undertaken, at least three letters of recommendation from individuals familiar with the applicant's scientific aptitude and qualifications, and the Graduate Record Examination (GRE) scores. In addition, for individuals whose native language is not English, the test of English as a Foreign Language (TOEFL) examination score is required. The letters of recommendation do not need to be in a specific format. However, they should be addressed to the Admissions Committee, and be sealed and signed on the envelope flap.

The Program requests that applications be complete by January 1st.

Applicants are encouraged to visit The University of Iowa to meet with Neuroscience students and faculty. Neuroscience Graduate Program participants are available to discuss the program with interested individuals. Applicants whose qualifications are competitive, and who demonstrate a strong interest in the University of Iowa, will be invited for on-campus interviews in connection with a common biosciences recruiting weekend generally held in February. Expenses for this visit are underwritten by the Neuroscience Program.

For further information and application materials, contact:
Anita Kafer
Neuroscience Graduate Program Office
Room 1178 Medical Laboratories
The University of Iowa
Iowa City, Iowa 52242

Email: neuroscience@uiowa.edu
Telephone: (319) 335-9968
or (800)-551-6787
Fax: (319) 353-5330
Paul Abbas, Ph.D.
paul-abbas@uiowa.edu

-Professor of Speech Pathology & Audiology

Our research is primarily in auditory physiology with emphasis on electrical stimulation of the ear. Studies include the application of electrophysiological measures in cochlear implant users as well as basic research on the response properties of the auditory nervous system to electrical stimulation. One response measure that we use is the electrically evoked compound action potential which can be measured in both human cochlear implant users as well as experimental animals. A second is the use of microelectrodes to record activity in single neurons of the auditory nerve.

Specific studies that are currently underway include assessment of interaction between acoustic stimulation and electric stimulation of the ear with surviving functional hair cells. Other experiments are involved with assessment of the spatial selectivity of electrical stimulation in the cochlea. Others involve the measurement of adaptation in response to electrical stimulation.

Selected Publications:


François Abboud, M.D.
francois-abboud@uiowa.edu

- Edith King Pearson Chair in Cardiovascular Research
- Professor of Medicine and Molecular Physiology and Biophysics
- Director, Cardiovascular Research Center
- Associate Vice President for Research

Research interests are directed toward the neural regulation of the circulation in pathologic states such as hypertension and heart failure.

Specific studies examine the cellular and molecular mechanisms of mechanical activation of baroreceptor neurons and the role of mechanosensitive ion channels in the generation of baroreceptor nerve activity in transgenic mice. Integrated control of sympathetic activity during sleep apnea and hypertension has been the focus of studies in humans.

Dr. Abboud is Edith King Pearson Chair of Cardiovascular Research. He directs an interdisciplinary cardiovascular research training program and a Program Project Grant on Integrative Functions in Neurovascular Control, now in its 32nd year. He has been director of the Cardiovascular Research Center since 1974.

Selected Publications:

Acid-Sensing Ion Channels 2a and 3 Heteromultimerize to Form pH-Sensitive Channels in Mouse Cardiac Dorsal Root Ganglia Neurons.
Hattori T, Chen J, Harding AM, Price MP, Lu Y, Abboud FM, Benson CJ.
PMID: 19590043 [PubMed - as supplied by publisher]

Acid-sensing ion channels interact with and inhibit BK K+ channels.
Petroff EY, Price MP, Snitsarev V, Gong H, Korovkina V, Abboud FM, Welsh MJ.
PMID: 18287010 [PubMed - indexed for MEDLINE]

Acid-sensing ion channels contribute to transduction of extracellular acidosis in rat carotid body glomus cells.
Tan ZY, Lu Y, Whiteis CA, Benson CJ, Chapleau MW, Abboud FM.
PMID: 17872465 [PubMed - indexed for MEDLINE]

Mechano- and chemosensitivity of rat nodose neurones--selective excitatory effects of prostacyclin.
Snitsarev V, Whiteis CA, Chapleau MW, Abboud FM.
PMID: 17478531 [PubMed - indexed for MEDLINE]

NAD(P)H oxidase-induced oxidative stress in sympathetic ganglia of apolipoprotein E deficient mice.
Ma X, Zhang HJ, Whiteis CA, Tian X, Davison RL, Kregel KC, Abboud FM, Chapleau MW.
PMID: 16584925 [PubMed - indexed for MEDLINE]
Research in my laboratory is aimed at understanding fundamental physiological properties of the eye and the pathophysiological mechanisms underlying a variety of complex eye diseases. Of primary interest are the glaucomas, a leading cause of blindness that affects approximately 70 million people worldwide. Glaucoma typically involves three types of events: molecular insults compromising the anterior chamber, increased intraocular pressure, and neurodegenerative retinal ganglion cell loss. Not surprisingly, the biological relationships linking these events are complex. Our approach for studying these events is founded in functional mouse genetics and supplemented by a variety of molecular, cellular, immunological, and neurobiological techniques. The premise for this approach is that stringently performed genetic studies offer great potential for overcoming the natural biological complexity of glaucoma. Current projects in the lab involve mouse models of pigmentary glaucoma and are testing the hypotheses that aberrant melanosomal processes and inflammation are potent contributors to this form of glaucoma. We are also interested in new mouse models of glaucoma and are developing mouse ES cell based genetic strategies for fostering the discovery of new glaucomatous mechanisms. In the long term, these studies will contribute to an increased understanding of eye diseases such as glaucoma, and ultimately to improved human therapies.

Selected Publications:

Local control of Ca(2+)-induced Ca(2+) release in mouse sinoatrial node cells.
Chen B, Wu Y, Mohler PJ, Anderson ME, Song LS.
J Mol Cell Cardiol. 2009 Jul 15. [Epub ahead of print]
PMID: 19615376 [PubMed - as supplied by publisher]

Role of calcitonin gene-related peptide in light-aversive behavior: implications for migraine.
PMID: 19587287 [PubMed - in process]

CaMKII and a failing strategy for growth in heart.
Anderson ME.
PMID: 19422097 [PubMed - indexed for MEDLINE]

Preclinical models of HPV+ and HPV- HNSCC in mice: an immune clearance of HPV+ HNSCC.
Williams R, Lee DW, Elzey BD, Anderson ME, Hostager BS, Lee JH.
PMID: 19283850 [PubMed - in process]

Calmodulin kinase II is required for fight or flight sinoatrial node physiology.
Wu Y, Gao Z, Chen B, Koval OM, Singh MV, Guan X, Hund TJ, Kutschke W, Sarma S, Grumbach IM, Wehrens XH,
Mohler PJ, Song LS, Anderson ME.
PMID: 19276108 [PubMed - indexed for MEDLINE]
My research interests are in human cognitive neuropsychology, with emphases in frontal lobe dysfunction, language processing, and cognitive/behavioral rehabilitation. The primary methods involve application of experimental cognitive and behavioral paradigms in patients with circumscribed brain lesions defined by MRI. Current projects are directed at delineating impairments of social behavior and executive function associated with adult- and childhood-onset damage to prefrontal cortex, evaluating the validity of the classical aphasia classification scheme, and investigating the potential of preserved procedural memory for rehabilitation of amnesia. I am particularly concerned with the interface of ongoing developments in basic neuroscience with clinical application, including development of new methods of treating cognitive and behavioral impairments acquired as a result of brain damage.

Selected Publications:

Chromatic Pupil Responses Preferential Activation of the Melanopsin-mediated versus Outer Photoreceptor-mediated Pupil Light Reflex.
Kardon R, Anderson SC, Damarjian TG, Grace EM, Stone E, Kawasaki A.
Ophthalmology. 2009 Jun 4. [Epub ahead of print]
PMID: 19501408 [PubMed - as supplied by publisher]

Predictors of driving safety in early Alzheimer disease.
Dawson JD, Anderson SW, Uc EY, Dastrup E, Rizzo M.
PMID: 19204261 [PubMed - indexed for MEDLINE]
Related Articles

Consistency of neuropsychological outcome following damage to prefrontal cortex in the first years of life.
Anderson SW, Wisnowski JL, Barrash J, Damasio H, Tranel D.
PMID: 19051128 [PubMed - indexed for MEDLINE]

Right ventromedial prefrontal cortex: a neuroanatomical correlate of impulse control in boys.
Boes AD, Bechara A, Tranel D, Anderson SW, Richman L, Nopoulos P.
PMID: 19015086 [PubMed - indexed for MEDLINE]

The effects of voluntary regulation of positive and negative emotion on psychophysiological responsiveness.
Driscoll D, Tranel D, Anderson SW.
PMID: 18845192 [PubMed - indexed for MEDLINE]
Nancy C. Andreasen, M.D., Ph.D., is Andrew H. Woods Chair of Psychiatry at The University of Iowa College of Medicine. She is actively involved in neuroimaging research, which involves the use of structural MR imaging, functional MR, and positron emission tomography. In addition, she leads a team working on three-dimensional image analysis techniques to integrate multi-modality imaging and to develop innovative methods for analyzing structural and functional imaging techniques in an automated manner. She has been given a Research Scientist Award from NIMH for her work in this area, directs a Mental Health Clinical Research Center and a training program that emphasizes neuroimaging, and conducts several investigator initiated projects in the area. Dr. Andreasen is past president of the American Psychopathological Association and the Psychiatric Research Society, as well as a member of the Institute of Medicine and the American Academy of Arts and Sciences. She won the President's National Medal of Science for 2000. She has received the American Psychiatric Association Prize for Research and the Dean Award from The American College of Psychiatrists, as well as the Distinguished Service Award of the latter organization. Dr. Andreasen is Editor-in-Chief of The American Journal of Psychiatry. She has written a book on neuroimaging (Brain Imaging: Applications in Psychiatry), as well as more than 500 articles and seven books on other related topics.

Title of Research: The primary emphasis of her research is on the development and application of novel neuroimaging tools, the study of normal cognition and emotion, and the study of major mental illnesses such as schizophrenia, schizophrenia spectrum disorders, schizoaffective disorder, schizophreniform disorder, and schizotypal personality.

Selected Publications:


Our laboratory is interested in understanding the basic mechanisms underlying both normal and disordered development of the nervous system. Our approach to these issues includes investigating the genetics of human neural tube defects (NTDs) and familial epilepsies, and elucidating the biology regulating neural stem cell development. The techniques used in our laboratory include genome wide linkage analysis (GWA), association studies, comparative genomic hybridization (CGH), copy number variation (CNV) analysis, transgenic mouse production, and cell culture. As part of our studies we have collected DNA samples from over 2000 patients and family members with congenital nervous system malformations, and several large families with autosomal recessive epilepsy syndromes.

Selected Publications:


Dr. Benson's research interests include the study of ion channels involved in sensation. We have focused on a class of ion channels called Acid-sensing Ion Channels (ASICs), which play a role in responses to nociceptive, taste, and mechanical stimuli. We have discovered that ASICs are highly expressed in cardiac sensory neurons and we believe they are particularly important as pH sensors in the setting of myocardial ischemia. In addition, we are interested in how cardiac afferent activation might trigger deleterious neural reflexes in cardiac disease states. Our lab is also interested on the general physiology of ASIC channels, and has discovered several proteins and signaling pathways that modulate ASIC function. Our research methods utilize electrophysiology, whole animal recordings, molecular and cell biology, and protein biochemistry techniques.

Selected Publications:


Sleep, like waking, is a complex phenomenon comprising fluctuations in many neural and physiological systems. When we fall asleep, our skeletal muscle loses tone, the electrical activity in our cerebral cortex (i.e., the EEG) changes, and, during active sleep, our eyes dart around and our limbs twitch. The challenge of studying infant sleep is that these various components, which have been studied extensively in adults, do not always present themselves clearly in infants. For example, the EEG of infant rats before eleven days of age does not exhibit the clearly differentiable activity upon which researchers rely so heavily when judging adult sleep. These and other factors mean that we must assess infant sleep on its own terms rather than judge it against an adult standard.

One of the goals of our research is to identify the role that sleep plays in the development of the nervous system. We view sleep as essential to the process by which sensory and motor systems establish the topographic relations (or somatotopic maps) that make normal function possible. This process is particularly critical during early development but also continues throughout life. We believe that sleep, especially active sleep, is critical to this process because it provides a period of relative quiescence when discrete signals can be sent and received by the nervous system.

Perhaps the most interesting developmental changes in sleep and wakefulness relate to the temporal organization of these states. For example, we have documented seminal developmental changes in the temporal organization of sleep-wake bouts and are seeking to identify the neural mechanisms that underlie these developmental changes in Norway rats. Developmental analyses can also be helpful for exploring evolutionary issues pertaining to sleep-wake organization. We are currently adopting a developmental comparative approach to understand circadian rhythmicity using nocturnal (i.e., night-active) Norway rats and diurnal (i.e., day-active) Nile grass rats. By tracking the development of sleep and wakefulness across early development and exploring their neural control, we are identifying the key components that have been evolutionarily altered to produce the phenotypes associated with these different species.

**Selected Publications:**


This laboratory investigates the biological mechanisms underlying neurologic birth defects. We are specifically interested in the brain injuries induced by lymphocytic choriomeningitis virus (LCMV) and by alcohol (fetal alcohol syndrome). In our studies of congenital LCMV infection, we utilize a rat model of the infection to study the cellular and molecular mechanisms underlying the virus-induced neuropathology. We are investigating the immune cell types and the cytokines involved in virus-induced neuronal death. In the developing brain, LCMV specifically infects certain neuronal populations and leaves others completely uninfected. We are studying the mechanisms by which LCMV spreads through the brain and are attempting to identify the metabolic and molecular characteristics of neurons that render them vulnerable to infection. Following infection with LCMV, both humans and the rats in our model system develop epilepsy. We are investigating the pathophysiology underlying this virus-induced epileptic condition. In our studies of fetal alcohol syndrome, we utilize animal models of the syndrome to study the mechanisms of alcohol-induced brain injury and the anatomical, histological and behavioral consequences of alcohol exposure. We have recently developed a mouse model of fetal alcohol syndrome, in which we utilize knock-out mice to study the importance of specific genes in influencing the pathological and behavioral effects of alcohol exposure.

Selected Publications:


Timothy Brennan, M.D., Ph.D.
tim-brennan@uiowa.edu

-Professor of Anesthesia

Uncontrolled pain continues to be a problem for patients. Pain management after surgery is one aspect of difficult to control acute pain. Because most pain models have not translated well to human postoperative pain, we have developed rodent models of postoperative pain undertaking a translational approach to acute pain mechanisms. Our more recent efforts have been aimed toward determining the role of particular pain transmitting substances like lactic acid and nerve growth factor in our experimental incisions. We are using a variety of techniques to assay these pain mediators that may activate or sensitize nociceptors in several tissues. Primary afferent fiber recordings using in vitro skin nerve preparations indicate unique mechanisms for primary afferent sensitization. Mediators measured in vivo that may contribute to sensitization will be studied in vitro. Further studies using knockout mice will examine pain related behaviors and sensitization using in vitro recording techniques.

Selected Publications:


Banik RK, and Brennan TJ. Spontaneous discharge and increased heat sensitivity of rat C-fiber nociceptors are present in vitro after plantar incision. (Submitted).
Work in this laboratory is primarily directed at delineating the microcircuitry of brain systems involved in emotion. Of particular interest are the input-output relationships of the amygdala and how they interact with the nucleus accumbens-ventral pallidum system thought to govern appetitive and goal-directed behaviors. Current work is focused on testing the hypothesis that the central extended amygdala is not the principal output structure of the amygdala, as currently thought, but is an integral part of the basal ganglia macrosystem. Rather than linking the amygdala with endocrine and autonomic structures, we believe the central extended amygdala may strongly influence emotive and appetitive behavior by controlling the flow of "sensory" information related to appetite and emotion into the other motor-related components of the basal ganglia. We are currently using anatomical methods in rodents to determine whether the extended amygdala participates in the same types of circuit networks as the rest of the basal ganglia, whether the neurochemical compartments of the extended amygdala mirror those in the nucleus accumbens system, and determine from following single axons what the likely sequence of sensory information flow is through the amygdala. We hope that by developing a new, network model of the amygdala and its external relationships, we can offer new insights into understanding the brain mechanisms behind emotion and how disruptions in these mechanisms lead to psychiatric disorders.

Selected Publications:


Course Participation 060:234 Medical Neuroscience (Spring)
Dr. Chapleau’s research program focuses on neural mechanisms that regulate arterial blood pressure and cardiovascular function. The baroreceptor reflex is a key mechanism of blood pressure regulation. Major goals of the research program are to define the molecular mechanisms influencing mechanoelectrical transduction and neuronal excitability in baroreceptor neurons, and to delineate mechanisms responsible for excessive sympathetic nerve activity and decreased baroreflex sensitivity in pathological states (e.g., hypertension, hypercholesterolemia, atherosclerosis) and in aging.

Ongoing projects in the laboratory address the following topics: The role of specific K+ and Na+ channels in modulation of excitability of baroreceptor afferent neurons; the role of reactive oxygen species in mediating autocrine activity-dependent inhibition of baroreceptor activity; the contribution of chronic oxidative stress to impairment of baroreflex/autonomic function in hypertension, atherosclerosis, and aging; and the ability of angiotensin and other humoral/autocrine factors to modulate sympathetic nerve activity through direct actions on neurons in sympathetic ganglia.

Experimental approaches include: 1) recording of baroreceptor activity and reflex changes in sympathetic nerve activity in genetically-modified mice in vivo; 2) long-term recording of blood pressure and heart rate in conscious unrestrained mice using radiotelemetry; 3) recording K+ and Na+ currents from isolated baroreceptor and sympathetic neurons in culture (sharp electrode and patch-clamp techniques); 4) fluorescent imaging of reactive oxygen species and calcium in baroreceptor and sympathetic neurons; and 5) manipulation of gene expression in baroreceptor and sympathetic neurons using adenoviral-mediated gene transfer.

Selected Publications:


Current projects focus on the effects of old age on grasp control, and the memory mechanisms underlying the advance specification of fingertip forces during dexterous grasp and manipulation. Loss of upper limb function in old age is predictive of living dependency, yet extant theories of age-related hand impairment were developed nearly exclusively through the study of healthy, community dwelling elders. Hence, the relationship between these specific changes in hand function and disability is unknown. We are particularly interested in determining the mechanisms of age-related impairment of hand function by correlating performance on specific laboratory tasks with severity of impairment on functional tests of daily living skills in a broad sampling of elders who span the range of performance on activities of daily living involving the hand. Elder subgroups with comorbidities of diabetes mellitus (Type II) and hypertension are of special interest given evidence for systemic alterations in central nervous system function that may affect hand control through a variety of mechanisms (cognitive, motor, and sensory). Our behavioral studies in humans employ multidimensional force/torque transducers embedded in objects that permit us to analyze the fingertip force vectors used to handle objects. We also have the capacity to record muscle action potentials intramuscularly from the intrinsic and extrinsic hand muscles. Servo-controlled torque motors allow us to inject controlled load or position disturbances to assess the neuromuscular system responses in health and disease.

Selected Publications:
Quaney, B., Nudo, R.J., Maletsky, R.A. and Cole, K.J. (submitted) Predictive control of fingertip forces for grasping and lifting an object: do we learn the object or the task? J. Neurophysiology
Robert Cornell, Ph.D.
robert-cornell@uiowa.edu

-Associate Professor of Anatomy & Cell Biology

Work in the Cornell lab focuses on identifying genetic pathways that regulate early events, including survival, lineage specification, growth, differentiation and migration, in embryonic precursor cells. Defects in these pathways underlie birth defects and cancer. These same genetic pathways regulate the progression of stem cells. We are motivated by the belief that knowledge of these pathways will improve the ability of clinicians to diagnose and treat birth defects and cancer, and to exploit the therapeutic potential of stem cells.

We focus on neural crest, a population of embryonic precursor cells with the potential to adopt diverse fates, including pigment cells, sensory neurons, muscle, cartilage, and autonomic neurons. We study neural crest because its broad developmental potential makes it a good model for the embryo in general, and because a variety of debilitating diseases affect neural crest derivatives.

Please visit http://www.anatomy.uiowa.edu/pages/directory/faculty/cornell.asp for a list of current projects and recent publications.

Selected Publications:
Semin Cell Developmental Biology (in press)
"The fate of human malignant melanoma cells transplanted into zebrafish embryos: assessment of migration and cell division in the absence of tumor formation."
Michael Dailey, Ph.D.
michael-e-dailey@uiowa.edu

-Associate Professor of Biology

We are studying cellular and molecular mechanisms regulating synapse formation and plasticity in CNS tissue. Our current focus is on the development of the major postsynaptic specialization, the dendritic spine. Using time-lapse confocal fluorescence microscopy, electron microscopy, immunocytochemistry, and physiological and molecular perturbations in rat hippocampal tissue slices, we are working to: (1) better define the spatiotemporal relationship between synapse formation and dendritic spine development, and (2) determine how cell-cell contact and synaptic activity regulate the morphological and molecular development of spines. We are also using the in vitro hippocampal slice system to examine the relationship between abnormal patterns of neural activity, such as occur during epilepsy, and alterations in dendritic spine structure.

In a separate project, we are studying cell proliferation and migration in developing brain tissue. Specifically, time-lapse imaging is being used to define the morphological and physiological (Ca++) dynamics of activated microglia within live hippocampal slices. Together, these studies are aimed at understanding how neural physiology regulates the cellular development and organization of the mammalian brain.

Selected Publications:
Research in my laboratory is focused on inherited genetic diseases that cause central nervous system dysfunction, with a focus on (1) recessive, childhood onset neurodegenerative disease, in particular the lysosomal storage diseases such as the mucopolysaccharidoses and Battens disease; and (2) dominant genetic diseases for example the CAG repeat disorders, Huntington’s disease and spinal cerebellar ataxia type I.

Our research on childhood onset neurodegenerative diseases is focused on experiments to better understand the biochemistry and cellular trafficking of proteins deficient in these disorders, and to develop gene and cell-based medicines for therapy. Our gene therapy studies are focused on vector development, emphasizing the study of novel envelopes for cellular targeting of lentivirus vectors, or non-traditional capsid proteins for encapsidated vectors (AAV and adenovirus). In recent work we demonstrated that the application of these vectors to animal models of storage disease could reverse CNS deficits. Molecular correlates, examined using gene chip arrays, corroborated the beneficial effects of gene therapy.

For cell based therapies, experiments are directed towards understanding the early signaling events required for differentiation of progenitor cell populations using microarray studies coupled with bioinformatics. The proteins revealed are then studied for their roles in development, and for their ability to induce differentiation of endogenous progenitor populations.

Therapies for dominant disorders are an exciting challenge and require that the dominant disease allele be silenced. To approach this, we have developed vectors expressing small inhibitory RNA, or siRNA. These small RNAs lead to the degradation of the targeted sequence. We have shown that siRNA reduces expression of the target in cell culture models of CAG repeat diseases, leading to an improved phenotype. Current studies are determining the effectiveness of in vivo delivered siRNA to correct disease manifestations in relevant models.

http://www.healthcare.uiowa.edu/labs/davidson/index.html

Selected Publications:


The organizing theme of my empirical work is the study of developmental changes in cognition. My main line of research involves the study of aging cognition. I am particularly interested in how attention and emotion impact cognitive functioning, such as memory and executive functioning, in both healthy and clinical populations of older adults. Utilizing an experimental gambling task that is designed to mimic real-world decision-making, we found that a sizeable subset of older adults failed to demonstrate appropriate risk-aversiveness, and instead continued to select from the disadvantageous decks in a manner reminiscent of patients with bilateral ventromedial prefrontal lobe lesions. Such findings may explain why older adults are at an increased vulnerability to advertising fraud (American Association of Retired Persons, 1996). We are currently investigating the neuroanatomical underpinnings of such disadvantageous decision-making, using structural MRI studies and psychophysiological measurement. Related interests include real-world decision-making abilities (e.g., medical and financial decision-making), recovery of cognitive function following stroke, and the relationships among aging, cancer, and cognition.

Presently funded grants:


Selected Publications:


Memory, communication, and social interaction

Concomitant impairments in memory and social functioning are the hallmarks of numerous neurological (e.g., traumatic brain injury, Alzheimer’s disease) and psychiatric (e.g., schizophrenia, depression) diseases. Not only are deficits in memory and social functioning common in such individuals and diseases, they are considered among the most handicapping of cognitive impairments. The research in my lab is designed to integrate the study of memory, communication, and social interaction so as to better understand the interactions and interdependencies of these domains in human behavior.

Specifically, our research is aimed at: 1) investigations of the interdependent relationship between memory and language and the contribution of declarative memory to social functioning; 2) characterization of preserved and impaired memory, communicative, and social abilities following acquired brain damage; and 3) development and validation of effective intervention approaches for individuals with disorders of memory and social functioning. Our work seeks to inform theoretical and neurobiological frameworks of memory and social functioning and to translate scientific knowledge into clinical application, helping to improve the lives of individuals with impairments in memory and social functioning.

Presently funded grants:


Selected Publications:


We are combining genetics with behavioral and electrophysiological, and cell biological methods to dissect auditory molecular mechanisms, using Drosophila as a model organism. The Drosophila male, when courting a female, vibrates one wing to sing the "love song" (figure). The female and male both hear the love song with their antennae and respond in a sex-specific manner. We have recovered several auditory mutants that represent genes involved in different molecular processes essential in hearing or responding normally to the love song. One of these mutants, beethoven, disrupts the normal neuronal electrophysiology (figure) of Johnston's organ, the ciliated mechanoreceptive organ in the antenna responsible for hearing. Identifying the gene product of beethoven and other such genes and examining their functional roles in hearing will provide new insights into auditory molecular mechanisms, not only in Drosophila, but perhaps in humans as well. Another goal is to further understand how organisms decipher the meaning in auditory information, and how different individuals, for example males and females, can respond differently to the same sounds. Thus we want to elucidate the neuronal circuitry by which sensory firing patterns are decoded in the brain. Genetically engineered Drosophila strains that express marker genes in specific subsets of neurons will facilitate this approach. For example, we can express a GFP-tagged n-synaptobrevin molecule in the auditory neurons to visualize their projections into the brain (figure). In our auditory mutant collection, we expect to find disruptions in genes required for the normal development of neurons in the auditory circuit, or disruptions in genes required for these neurons to function properly in a sexually dimorphic manner.

Selected Publications:
Carrie Figdor, Ph.D.
Carrie-figdor@uiowa.edu

Assistant Professor of Philosophy

My research focuses on theoretical issues in philosophy of mind, cognitive science and neuroscience, including the nature of mechanistic explanation of the mind, the relation between cognition, behavior and the brain, and neuroethics.

Selected Publications:

MIND AND METAPHYSICS


Neuroscience and the Multiple Realization of Cognitive Functions (2010). Philosophy of Science vol. 77 no. 3 (July), 419-456.


MEDIA ETHICS


Homeostasis is a robust form of regulation that allows a system to maintain a constant output despite external perturbations. In the nervous system, homeostasis plays a critical role in regulating neuronal and synaptic activity. Yet the molecular basis of this form of neural plasticity is generally unknown. We address this problem using the fruit fly, Drosophila melanogaster. This model allows us to combine electrophysiology with powerful genetic and pharmacological techniques. The overall goal is to define conserved signaling mechanisms that direct synapses to maintain stable properties, like excitation levels.

It is generally believed that molecules controlling the balance of excitation and inhibition within the nervous system influence many neurological diseases. Therefore, understanding synaptic homeostasis is of clinical interest. This area of research could uncover factors with relevance to the cause and progression of disorders such as epilepsy, which can reflect a state of poorly controlled neural function.

Selected Publications:


Our research examines the neural mechanisms of associative learning. Current projects are examining ontogenetic changes in the neural mechanisms of eyeblink conditioning. We are also investigating the cellular mechanisms of memory formation in the cerebellum.

**Selected Publications:**

1. Molecular Basis of Ear Development
Research on the molecular basis of ear development analysis, various mutations (knockouts, knockins, transgenic misexpression) of transcription factors (bHLH, Lim homeodomain, GATA, Pax, Eya), or diffusible factors (Fgfs, Wnts, Erbs). This mutational analysis provides in vivo data that help resolve, in collaboration with other laboratories nationally and internationally, the molecular interactions of normal ear development as well as aberrant development underlying congenital ear defects. Superimposed on this proximate analysis is the ultimate question: resolving evolution of the mammalian ear as a transformation of embryonic developmental programs to generate an improved system for sound perception.

2. Molecular Basis of Inner Ear Efferent and Brainstem Motoneuron Formation
The research on brainstem motoneurons is aimed to understand the evolution of novel motor outputs of the brainstem such as the evolution and development of eye muscles and their innervation and the evolution and development of the inner ear efferent system that modifies neurosensory information acquisition in the ear. These novelties are embedded in a fairly rigid framework of rhombomeric hindbrain development governed by the highly conserved homeobox genes as well as other transcription factors.

3. Molecular Basis of Hair Cell Proliferation, Maintenance, and Regeneration
Research on hair cell development and regeneration can be formally divided into two aspects: molecular basis of proliferation regulation and molecular basis of maintenance and differentiation of hair cells.

4. Improving Multicolor Dye Tracing Techniques
Research on improvement of lipophilic dyes as well as other tracing techniques is focusing on multicolor labeling techniques in combination with in situ and immunocytochemical analyses to maximize data collection from single mutations for optimized high-throughput phenotypic characterization of mutants. Current work focuses on the various aspects of carbocyanine dyes with the ultimate goal in mind to generate multiple (up to eight) dyes that allow independent labeling of various neuronal populations to investigate simultaneously the interactions of multiple neuronal processes to develop synaptic connections.

Selected Publications:


Oligodendrocytes in the central nervous system (CNS) serve to synthesize and maintain myelin sheaths, which are highly complex, multilamellar membrane structures. CNS myelination is a tightly regulated process that must occur during perinatal and early postnatal development in vertebrates. At the present time, our knowledge is very limited as to how oligodendrocytes elaborate their extensive array of architectures - including a spherical cell body, slender elongated processes, and the spiral wrappings that comprise the compacted myelin sheath itself. Our research efforts focus on issues of cell polarity and membrane targeting in oligodendrocytes. In particular, two membrane proteins, myelin/oligodendrocyte glycoprotein (MOG) and proteolipid protein (PLP), target to mutually exclusive compartments - uncompacted membrane domains vs. compact myelin sheaths. We are pursuing structure-function analyses to determine how this differential targeting is effected. We are also interested in identifying both extracellular and intracellular molecules that interact with these proteins at the plasma membrane. The long term goal of our research program is to define and understand some of the molecular communications that are necessary to synthesize and maintain normal myelin in the CNS. By gaining a better understanding of these processes, we can design improved therapies for immune-mediated demyelinating diseases (i.e., multiple sclerosis) and developmental neurological disorders.

Selected Publications:


The major goal of my laboratory is to understand the biological basis of neurological disorders caused by dysfunction of the basal ganglia and to develop novel therapies for this group of neurological diseases. Currently, my studies focus on a disease known as DYT1 or Oppenheim’s dystonia, the most common form of inherited dystonia. DYT1 dystonia, a dominantly inherited, incurable disease, is caused by a three-nucleotide deletion in the gene TOR1A that causes the loss of a glutamic acid in the protein torsinA. TorsinA is a AAA protein (ATPases Associated with diverse cellular Activities) that resides primarily in the endoplasmic reticulum. However, torsinA carrying the disease-causing mutation accumulates in the nuclear envelope generating cytoplasmic membranous inclusions known as spheroid bodies. Analyses of dominant negative mutants suggest that torsinA normally functions within the perinuclear space of the nuclear envelope.

Selected Publications:


Jean Gordon, Ph.D.

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-Associate Professor of Speech Pathology & Audiology

My research focuses on the process of word retrieval in normal speakers, and in speakers with acquired neurogenic language disorders (particularly aphasia). I am interested in exploring the factors which make words easier or harder to retrieve, and how these factors influence the production of speech errors. To investigate these questions, I use a combination of behavioural experimentation and computational modelling approaches.

Selected Publications:


We study the molecular and cellular mechanisms by which neuronal survival and synaptogenesis are regulated by neural activity. For studies of survival, we principally use spiral ganglion neurons (SGNs) in the cochlea. SGNs are dependent on their presynaptic input, the hair cells, for their survival. The death of SGNs in vivo after hair cell loss is reduced by electrical stimulation and SGN survival in vitro can be similarly maintained by depolarizing the neurons to stimulate activity. We conduct parallel investigations of SGNs in vivo after loss of hair cells and of depolarized SGNs in vitro to dissect the complex intracellular signaling pathways involved in neuronal death and in the ability of neural activity to prevent neuronal death. Our experimental approaches include the use of intracochlear infusion and transgenic mice to study SGNs in vivo and gene transfer and molecular / cell biological techniques to study SGNs in vitro. We have identified the intracellular signaling pathways that mediate the prosurvival effect of membrane depolarization: Ca2+/calmodulin-dependent protein kinase II (CaMKII) and CaMKIV, and cyclic AMP-dependent protein kinase (PKA). We have further determined the subcellular location at which they act and some of their key targets.

The intracellular signals that link neural activity to survival also link neural activity to stabilization and remodeling of synapses. In collaboration with other groups at the University of Iowa, we are investigating the roles of CaMKII, PKA and peptide neurotrophic factors in synapse formation and stabilization in the developing brain, focusing on the auditory cortex and consequences of deafening.

These studies are relevant to the use of cochlear implants, currently the only effective treatment for sensorineural deafness. These implanted electrode arrays provide direct electrical stimulation to SGNs. Understanding how electrical stimulation affects SGN survival and axon growth will lead to improved implants. Moreover, study of how deafness affects auditory cortex development is relevant to understanding and enhancing the ability of a deaf person to adapt to the use of a cochlear implant.

We are also investigating synaptogenesis in the cochlea, focusing on the disruption of synapses and their regeneration that occurs as a consequence of noise trauma. Synaptic regeneration in this circumstance fails to accurately recover the elegant and precise normal innervation of hair cells by SGNs. This may have adverse long-term implications for the viability of SGNs, which are known to be more susceptible to age-related hearing loss even long after noise exposure in youth. We are investigating the reasons for this imprecise reinnervation using a culture system that recapitulates the SGN to hair cell synaptic connections (see figure).

Selected Publications:


Jeremy Greenlee, M.D.
jeremy-greenlee@uiowa.edu

-Associate Professor of Neurosurgery

I study human language, audiovisual, and vocalization physiology using electrophysiological recordings from human subjects undergoing surgical treatment of intractable epilepsy.

Selected Publications:


This laboratory is interested in the neuroanatomy, neurophysiology and neuropharmacology of the central nervous system (CNS) pathways that convey pain, as well as the bulbospinal pathways that mediate the production of analgesia. Our studies emphasize a systems-level approach in which many different methodologies are used in concert, including behavioral pharmacology in normal, transgenic or knockout animals, neuroanatomical tract tracing, immunocytochemical labeling of neurons, and electrophysiological recordings from neurons in slices of the spinal cord or brainstem. We are particularly interested in the role that inhibitory neurotransmitters, such as gamma-aminobutyric acid (GABA) or the endogenous opioid peptides, play in the modulation of nociception. Our early studies focused on how these neurotransmitter systems dictate responses to acute pain. More recently, we have focused on their role in the response of the CNS to peripheral injury. Our results indicate that persistent pain can lead to long-term changes in the pharmacology and physiology of both the afferent pathways that convey pain, as well as the efferent pathways that suppress pain. These changes have significant consequences for the ability of drugs to produce analgesia and for the body to invoke its own homeostatic mechanisms for the control of pain. The plasticity of CNS pathways in response to persistent neuropathic and inflammatory pain will continue to be a focus of our future work.

Selected Publications:


N. Charles Harata, M.D., Ph.D.
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Assistant Professor of Molecular Physiology & Biophysics

My laboratory focuses on the study of synaptic transmission in the mammalian central nervous system. Synapses are the sites at which electrical signals in presynaptic neurons are converted to chemical signals (neurotransmitter release), and the released neurotransmitter induces postsynaptic responses in the form of electrical and chemical signals (such as an increase in the intracellular Ca2+ concentration). The efficiency of this two-step information flow during synaptic transmission is important to the control of neural network activity. The long-term goal of our research is to understand how the efficiency of synaptic transmission is regulated, and how its disruption contributes to neurological and psychiatric disorders. We are currently focusing on two major aspects of synaptic transmission. In one project, we are analyzing fundamental parameters of neurotransmitter release: the amount of neurotransmitter loaded into synaptic vesicles, the likelihood of neurotransmitter release under particular conditions, and variability in the amount of released neurotransmitter. A second focus is on Ca2+ dynamics in postsynaptic neurons. In the dendrites of these neurons, the Ca2+ concentration rises locally and transiently in response to neurotransmitter, and the resulting highly concentrated Ca2+ can propagate as a wave along the dendrites toward the cell body. We are investigating the precise roles of such Ca2+ waves, as well as the mechanisms that underlie their generation and propagation. Through these studies on both pre- and postsynaptic components of synaptic transmission, we expect to reveal the basic mechanisms of neural signaling, and the modes of their modulation under physiological and pathological conditions. For these studies, we are using live, cultured rodent neurons as a model system, and the fluorescence imaging and electrophysiology techniques in combination with electron microscopy.

Selected Publications:


Eliot (Richard) Hazeltine, Ph.D.
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-Associate Professor of Psychology

The main focus of my research has been on response selection, the set of cognitive processes that enable us to transform sensory information into goal-directed actions. I have approached this topic from a variety of perspectives, including motor learning, bimanual coordination, and dual-task interference using a range of cognitive neuroscience methodologies. Although this work represents a diverse set of findings, a central theme is that response selection processes act on flexible representations based on codes that incorporate action goals. These codes are abstract in the sense that they are determined by task demands rather than movement parameters. Therefore, interactions among possible responses, whether they are manifest in performance benefits derived from sequence learning or performance costs derived from response competition, are mediated by the individuals’ goals and their conceptualization of their actions.

Selected Publications:


My research investigates decision making. I focus on instances when people make decisions that violate standard economic assumptions or that are otherwise suboptimal. I use a range of techniques from simple paper and pencil surveys to functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), response time recording, and eye-tracking in an effort to document and explain why these behaviors occur.

Selected Publications:
Matthew Howard, M.D.
matthew-howard@uiowa.edu

Professor of Neurosurgery

Matthew A. Howard, III – Joined the Department of Neurosurgery in 1993, following his residency and neurosurgical training at the University of Washington, Seattle, and was appointed as the Head of the Department of Neurosurgery at the University of Iowa in July, 2001. Doctor Howard holds a joint appointment with the Department of Neurology and specializes in epilepsy surgery. His research interests include studies of hearing impairment, clinical research in epilepsy treatments, clinical models of Alzheimer's disease, magnetic stereotaxis for the treatment of focal neurological disorders, and investigations of the mechanical properties of brain tissue. He is the principal investigator of an NIH-funded research group studying the functional organization of human auditory cortex.

Selected Publications:


Steinschneider M, Volkov IO, Fishman YI, Oya H, Arezzo JC, Howard MA. Intracortical responses in human and monkey primary auditory cortex support, a temporal processing mechanism for encoding of the voice onset time (VOT) phonetic parameter. Cerebral Cortex (in Press)
Richard Hurtig, Ph.D.
richard-hurtig@uiowa.edu

-Professor of Speech Pathology & Audiology

Examination of invariant properties of human perception and information processing across visual, auditory and tactile modalities, with an emphasis on the underlying neural mechanisms. Studies include work on pattern recognition in speech perception and on the role of attention and feedback mechanisms. The lab also is working on micro-processor based assistive technologies for individuals with developmental and acquired disabilities which limit mobility and speech.

Selected Publications:


Research currently ongoing in Dr. Johnson's laboratory is concerned with the integrative role of the nervous system in the maintenance of body fluid and cardiovascular homeostasis. Three major projects are under active investigation: 1) brain targets, pathways and nuclei involved in the control of body fluid balance and of the cardiovascular system, 2) mechanisms involved in the "translation" of physiological challenges and environmental stressors into cardiovascular pathology (e.g., hypertension; heart disease), and 3) neural and endocrine mechanisms of hemorrhagic shock.

The brain constantly receives information about the disposition of body fluids and about the status of the cardiovascular system, integrates this input and then activates one or more effector systems to correct or minimize any disruption of homeostasis. The major efferent pathways or effector systems involved in body fluid and cardiovascular regulation include behavioral mechanisms associated with thirst and sodium appetite, the autonomic nervous system, and hormonal systems such as vasopressin, natriuretic hormone and renin-angiotensin. Information reaches the brain through circumventricular organs which sample the ionic, osmotic and hormonal content of blood and by way of afferent peripheral nerves. We use functional, neuroanatomical, neurochemical, molecular and electrophysiological methods to investigate the pathways and brain regions involved in sensing and processing the information that signals the state of body fluid balance and distribution.

Cardiovascular disease has been hypothesized to result from the interaction of one or more precipitating factors with a genetic predisposition for the particular disorder. Environmental stressors which are noxious or which are perceived as threatening have been implicated as one such set of precipitating factors. In the case of hypertension and heart disease, it has been hypothesized that stimuli or situations which result in repeated or sustained activation of a neural and humorally mediated defense response may be responsible for chronically elevated blood pressure and the progression of heart failure. For hemorrhagic shock, the degree of blood loss triggers different efferent autonomic and neural patterns that have consequences for the viability of different bodily tissues. To pursue questions on the role and mechanisms of environmentally-induced cardiovascular adjustments in the pathogenesis of hypertension, heart failure and shock, we record sympathetic nerve activity and measure hormonal and hemodynamic changes in rats in standardized behavioral paradigms and use physiological and pharmacological methods to determine the autonomic, immune and hormonal systems responsible for mediating such cardiovascular responses.

Selected Publications:


Wayne Johnson, Ph.D.

wayne-a-johnson@uiowa.edu

-Professor of Molecular Physiology & Biophysics

Somatosensory signaling is the process by which we become aware of external sensations such as touch, temperature or pain. Despite the importance of these sensory modalities to our everyday existence, we know relatively little about their molecular mechanisms. These sensations would appear to be quite different, however, recent work has shown that they may be separated by only a fine line at the molecular level. Two large ion channel families, the TRP channels and the ENaCs, appear to have been evolutionarily selected for a variety of physiological functions ranging from thermosensation and osmosensation to pain and touch. We have developed a genetic model system in Drosophila to examine the molecular components of somatosensory signal transduction in type II multiple dendritic/md) sensory neurons. We are applying a variety of techniques including electrophysiology, behavior, molecular biology and genetics to identify and characterize evolutionarily conserved signaling components.

Selected Publications:


A high concentration of free ionic zinc in synaptic vesicles is a prominent feature of some of the excitatory pathways in the mammalian forebrain. Despite the wealth of information on its distribution, and role in metalloenzymes and proteins, the role of vesicular zinc remains enigmatic, and serves as one of the foci of our research. Zinc is co-released with glutamate during synaptic transmission and fluorimetric Zn-probes could thus be used to follow glutaminergic neurotransmission.

An additional focus of our research is on the development of new techniques for exploring the neurophysiology of the cerebral cortex. We have given particular attention to developing methods for imaging neuronal activity, because it provides a possible way of visualizing the choreography of ensembles of neurons during activity, and it is the spatio-temporal pattern of neuronal activity that is probably at the heart of mental activity.

Toward these ends we use an array of techniques: electrophysiology (current and voltage clamp) in brain slices, acutely dissociated neurons & frog oocyte, fluorescent spectroscopy and imaging, nanochemistry and nonlinear dynamics.

Selected Publications:


Toshihiro Kitamoto, Ph.D.
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 Associate Professor of Anesthesia; Neurology

How does the nervous system control complex behavior? How do experience and genetic variation modify it? The goal of our research is to answer these fundamental questions in neuroscience. We use the fruitfly, Drosophila melanogaster as an experimental animal, and integrate knowledge of the nervous system at the molecular, cellular, systemic and whole animal levels. The current focus is on male courtship behavior. This behavior consists of a highly stereotypical sequence of activities that are genetically determined, but also shows considerable experience-dependent plasticity called “courtship conditioning”. By examining the behavior of various genetic variants, we study the function of particular genes in different aspects of courtship. In addition, using a recently developed strategy that allows one to perturb synaptic transmission rapidly and reversibly in a spatially restricted manner, we investigate the significance of particular neuronal subsets in sexual orientation, courtship initiation, and courtship memory. Our multidisciplinary research is expected to provide new insights into the basic mechanisms underlying higher-order brain functions that control complex behavior.

Selected Publications:


**Ryan T. LaLumiere, Ph.D.**

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- Assistant Professor of Psychology

**Neurobiology of drug addiction.** My research focuses on the neurobiology underlying cocaine-seeking behavior in rats. We use a drug self-administration model in order to understand the relapse back to drug-seeking behavior. Rats undergo cocaine self-administration in which rats receive cocaine infusions for pressing a lever. After a few weeks of self-administration, rats undergo extinction training in which lever presses no longer produce cocaine infusions. The rats’ lever pressing can be reinstated using triggers known to induce relapse in people. Using this model of drug-seeking, we investigate the neural systems that drive this behavior, with a particular focus on the medial prefrontal cortex. In particular, our recent work has examined how extinction training creates a neural circuit that suppresses drug-seeking and competes with the neural circuit that drives drug-seeking. It appears that divisions within the prefrontal cortex control these competing circuits and ultimately determine the behavior of the animal.

**Selected Publications:**


My lab is interested in understanding the neural mechanisms that regulate circadian rhythms, the daily patterns of physiology and behavior that are prominent in many species. We study the model system Drosophila, which exhibits robust daily rhythms in several behaviors, including locomotor activity. Genetic approaches in Drosophila have led to the identification of a number of key circadian rhythms genes, including several with conserved function in mammals. Much of this research has focused on understanding the molecular circadian clock, the cell-autonomous transcriptional feedback loops and post-translational modifications that generate ~24 hour molecular oscillations. In Drosophila and mammals, the central circadian clocks that control rhythmicity are located in neuronal groups within the brain. Yet, little is known about how the molecular clock regulates the output of these neurons to promote rhythmicity. We are interested in understanding the processes that occur downstream of the molecular clock to mediate circadian neuron function. I have previously demonstrated that a putative sodium leak channel, narrow abdomen (na), is an important component of circadian neuronal output in Drosophila. We are now using this system to further characterize the function and regulation of this unique channel, with a particular interest in determining whether NA is subject to circadian regulation. In addition, my lab is utilizing the molecular and genetic tools of Drosophila in order to identify new circadian rhythms genes, with a focus on genes likely to function in circadian neuronal output.

Selected Publications:


Our research centers on voltage-gated (Cav) Ca2+ channels and their roles in the nervous and cardiovascular systems. We view Cav channels as macromolecular complexes, the components of which regulate their properties and involvement in cellular transduction cascades. One focus is on Cav1 L-type channels at sensory “ribbon” synapses in the retina and inner ear, where Cav protein interactions transform presynaptic Ca2+ signals required for high-throughput neurotransmitter release. A second focus is on protein interactions regulate Cav1 channels involved in spontaneous firing (pacemaking) in the heart and brain. Our approach is multidisciplinary: we use patch-clamp electrophysiology for studies of Cav channel modulation and exocytosis; molecular biology, protein chemistry, and immunocytochemistry for analysis of Cav protein interactions; and gene silencing methods (siRNA, targeted gene disruption) and in vivo electrophysiology to evaluate the physiological consequences of Cav protein interactions in the context of hearing, vision, and cardiac rhythmicity. Our long-term goal is to develop pharmacological strategies to target cell-type and tissue-specific Cav regulatory mechanisms, which may prove more selective than current Cav agonists and antagonists in the treatment of neurological and cardiovascular disease.

Selected Publications:

Ca2+-dependent facilitation of Cav1.3 Ca2+ channels by densin and Ca2+/calmodulin-dependent protein kinase II.

Compensatory regulation of Cav2.1 Ca2+ channels in cerebellar Purkinje neurons lacking parvalbumin and calbindin D-28k.

Characterization of Ca2+-binding protein 5 knockout mouse retina.

The best disease-linked Cl- channel hBest1 regulates Ca V 1 (L-type) Ca2+ channels via src-homology-binding domains.

Ca(v)1 L-type Ca2+ channel signaling complexes in neurons.

Ultrastructural evidence for pre- and postsynaptic localization of Cav1.2 L-type Ca2+ channels in the rat hippocampus.
Our laboratory studies tau protein, a microtubule associated protein that is also the primary component of the neurofibrillary tangles of Alzheimer's disease. A few years ago, we discovered that tau interacts with non-receptor src family tyrosine kinases. We are currently identifying and investigating new functions acquired by tau as a consequence of this interaction. Our hypothesis is that tau has a role for in signal transduction in neurons. We are also investigating a possible role for this interaction in the neuropathogenesis of Alzheimer's disease and other age-related neurodegenerative diseases.

Selected Publications:


Models of human judgment and decision making

The effects of inference and information frame on judgments and decisions;

Individual differences in children's and adults' decision making;

Decision Neuroscience;

Applications in areas such as consumer behavior, risky decision making, medical decisions, and social judgments

Selected Publications:


Levin, A.M., & Levin, I.P. Packaging of healthy and unhealthy products for children and parents: the relative influence of licensed characters and brand names. Submitted for publication.

I am interested in the development of novel imaging approaches and analysis strategies to better understand psychiatric and neurological brain disorders. My work in image acquisition focuses on diffusion tensor imaging and chemical shift imaging. I am also working on methods to automate the analysis of brain morphology and incorporating these tools into diffusion tensor and chemical shift imaging.

Selected Publications:


Laurie McCormick, M.D.
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Assistant Professor of Radiology

My primary research interests are to better understand the pathophysiology of eating disorders, specifically in regard to anorexia nervosa and obesity. Additional research interests include investigating the clinical utility and mechanisms of action of brain stimulation technology for the treatment of depression, anxiety, and psychosis including electroconvulsive therapy (ECT), deep brain stimulation (DBS) and repetitive transcranial magnetic stimulation (rTMS). My current research projects include a longitudinal study of patients admitted for the treatment of anorexia nervosa, which uses neuroimaging methods and neuropsychological assessment to investigate symptom correlation with regional brain abnormalities and their relationship to outcome. Additional projects include: the developmental trajectory of the anterior cingulate cortex in schizophrenia and healthy controls; mirror neuron dysfunction in schizophrenia; limbic system abnormalities in psychotic depression; effects of acute estrogen depletion on mood and memory in women; glutamatergic NMDA receptor blocking agents with ECT for the treatment of major depression.

Selected Publications:


Bob McMurray, Ph.D.
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-Associate Professor of Psychology

My research broadly concerns how people recover the meaning of spoken language as it unfolds in real-time, and in particular how they cope with the vast amount of variability in the speech signal. To this end, we use techniques like head-mounted eye-tracking, event-related potentials and inter-cranial brain recording to examine some of the earliest sensory representations of speech. I apply both developmental and individual differences approaches to this question examining typically developing infants and children, as well as those with language or hearing-impairments, particularly children with specific language impairment or who use cochlear implants. Finally, in order to understand possible mechanisms I construct computational models using statistical learning, neural network and dynamical systems approaches.

Selected Publications:


My lab develops RNA-based technologies to understand and treat disorders of the nervous system. We are using RNA aptamers (structural, artificial RNAs) that bind cell surface proteins expressed in the nervous system to directly activate signaling pathways, and to deliver siRNAs to specific cell types. We will apply these tools to elucidate mechanisms of disease in animal models and to develop novel therapeutic approaches. As part of this work, we are also developing novel RNA aptamer identification methodologies, including cell-based and whole animal-based aptamer screening approaches.

Selected Publications:


The intrinsic excitability of mammalian neurons reflects the complex interplay between the inward and outward membrane conductances that underlie each neuron’s unique electrical activity pattern, and are governed by the expression, localization and activity of voltage-gated ion channels. These processes are homeostatically regulated during development and aging, and in response to short- and long-term changes in neuronal activity in the face of altered synaptic stimulations, which otherwise could drive the neuronal activity towards extreme excitation or quiescence. Altered expression and/or modulation of localization and function of voltage-gated sodium (Nav) and potassium (Kv) channels mediate these homeostatic processes in response to altered neuronal activity and nerumodulations.

Increase in the intracellular Ca\textsuperscript{2+} concentrations in neurons as a result of altered neuronal activity or neuromodulations, lead to the activation of a variety of protein kinases and phosphatases, which modify the phosphorylation state of a large variety of neuronal proteins including ion channels. These post-translational modifications often alter the localization and/or voltage-dependent biophysical properties of ion channel proteins. Since Kv channels are the key regulatory components of membrane excitability in neurons, modulation of their functional properties by post-translational modifications play a critical role in the regulation of intrinsic excitability during altered neuronal activity and neuromodulations.

We have recently shown that robust and sustained increase in the intracellular Ca\textsuperscript{2+} levels, and subsequent activation of the protein phosphatase calcineurin in mammalian central neurons in response to increased excitatory activity, epileptic seizures, and cholinergic neuromodulations, leads to rapid dephosphorylation of the major somatodendritic delayed rectifier Kv channel Kv2.1. Dephosphorylation of Kv2.1 leads to redistribution channel localization and alterations in the voltage-dependent gating properties of neuronal delayed rectifier K\textsuperscript{+} currents, which plays a neuroprotective role by suppressing the neuronal firing frequency under conditions of altered excitability.

We are interested in studying how the membrane excitability in mammalian central neurons are intrinsically regulated by modulation of localization & function of different Kv channels in response to diverse neuromodulatory stimuli acting through specific G-protein coupled receptor (GPCR)-mediated intracellular signaling pathways.

We are also interested in studying molecular organization, activity-dependent modulation and regulation of trafficking, localization, and functional properties of Kv & thermo-TRP channels and their signaling complexes in sensory neurons, in response to diverse pain-producing chemical, thermal, and mechanical stimuli.

We combine upto-date molecular/cell biological, biochemical, proteomic, fluorescence immunocyto-/histochemical, confocal imaging, and electrophysiological methods to answer these questions. These studies will certainly contribute significantly to the development of therapeutic interventions for a number of neuronal disorders like epilepsies, ischemia, and neuropathic pain.

**Selected Publications:**


Basic science collaboration with Dr. Kevin Campbell, Department of Physiology and Biophysics involves the pathologic characterization of genetic mouse models of muscular dystrophy. Our most recent basic science collaborations use Cre-lox methodology to selectively knock out brain or peripheral nerve dystroglycan. These mice model congenital muscular dystrophy. Clinical diagnostic work in the general area of muscular dystrophies has expanded into basic and clinical research projects in collaboration with Drs. Jerry Mendell (Department of Neurology, Ohio State University), Kevin Campbell, and Kathy Mathews (Department of Pediatrics, The University of Iowa). Current clinical studies involve: (1) a multicenter study of limb-girdle muscular dystrophy (LGMD) aimed at characterizing genotype/phenotype relationships in this diverse array of muscular dystrophies and (2) a gentamicin treatment trial in Duchenne and sarcoglycan-deficient muscular dystrophy patients with mutations that lead to stop codons.

Selected Publications:


David Moser, Ph.D.
david-moser@uiowa.edu

-Professor of Psychiatry

My primary research interest involves vascular disease, how this contributes to cognitive decline in the elderly, and how to develop strategies for early identification of those individuals at greatest risk for such decline. Additional research interests include decision making and capacity for informed consent in vulnerable populations, and neuropsychological and emotional functioning in the following populations: post-stroke patients, schizophrenia and other mental illness, eating disorders.

Selected Publications:


Our lab studies the structure and function of the brain using imaging tools such as MRI and cognitive / behavioral assessment. In the healthy brain we study topics such as brain development over the lifespan, gender differences and social cognition Disease populations that we work with include patients with schizophrenia, Huntington's Disease, and children with clefts of the lip/palate.

Selected Publications:


Nervous system tumors are the most common cause of death from pediatric malignancies and rank second only to accidents as a cause of death in this age group. These cancers arise in the developing nervous system during fetal growth or infancy. Neuropeptides are both neurotransmitters and important modulators of neurodevelopment. Vasoactive intestinal peptide is both a differentiation factor and a neuroprotective agent. Somatostatin is a potent modulator of growth factor release and also modulates the signal transduction pathway for multiple growth factors. We are studying the role of vasoactive intestinal peptide and somatostatin in neural development using transgenic and knock out mice. This new understanding of the role of neuropeptides in neural crest development should allow us to develop new diagnostic and therapeutic options for children with neuroblastoma and medulloblastoma.

Selected Publications:


Current research explores the neural basis of the cognitive abnormalities that characterize schizophrenia, and the cognitive and blood flow changes caused by marijuana. Both areas of research involve both behavioral cognitive assessments and structural and functional neuroimaging. We have ongoing positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies of schizophrenic individuals, as well normal volunteers and occasional and chronic users of marijuana.

Selected Publications:


Jane Paulsen, Ph.D.
jane-paulsen@uiowa.edu

-Professor of Psychiatry

Research in this laboratory uses tools of neuropsychology and cognitive psychology to examine behavioral correlates of brain dysfunction. Topics of current interest include subtypes of Alzheimer's disease, preclinical cognitive deficits associated with gene-carriers of Huntington's disease and clinical/imaging correlates of cognitive measures. Functional MR and PET are used to examine frontal-striatal circuitry dysfunction in these disorders.

Selected Publications:


My laboratory has been interested in the pathogenesis of murine coronavirus infections for several years. Now, we will also study three respiratory human coronavirus infections: SARS-coronavirus, human coronavirus-OC43 and human coronavirus-NL63.

Mice infected with mouse hepatitis virus develop a demyelinating disease with many similarities to the human disease, multiple sclerosis. Research in my laboratory is aimed at determining the immunological and viral factors involved in the demyelinating process. Previously, we determined the CD4 and CD8 T cell epitopes recognized in the central nervous system (CNS) of infected mice. We showed that in mice infected chronically with the virus, cytotoxic T cell escape mutants arise. These mutations completely abrogate recognition by CD8 T cells and thereby facilitate persistence. We have developed a reverse genetics system for introducing mutations into the murine coronavirus genome. We have developed a model to determine the role of individual effector molecules in demyelination, using immunodeficient mice infected with the virus. The ultimate goal of these experiments is to develop a system whereby we can introduce changes into immunologically important epitopes within the virus and study the effects of these changes on virus replication and persistence in the infected CNS.

The SARS-coronavirus causes the most significant disease of any of the human coronaviruses. Our goal is to understand the mechanism of disease. For this purpose, we are developing animal models of SARS. We are also analyzing individual OC43 and NL63 proteins for their roles in pathogenesis, both as isolated proteins and in the context of infectious, recombinant viruses.

Selected Publications:


Robert Philibert, M.D., Ph.D.

robert-philibert@uiowa.edu

-Professor of Psychiatry

The Psychiatric Genetics Laboratory is located on the first-floor of the Medical Education Building. It is fully equipped for translational genetics. Major pieces of equipment include an epifluorescence microscope capable of 3-D imaging, a Biomek 3000 liquid handling robot and an Applied Biosystems 7900 HT real-time machine, two cell culture hoods, and a number of state-of-the-art thermal cyclers, incubators and centrifuges.

The laboratory is headed by Rob Philibert M.D. Ph.D., an Associate Professor of Psychiatry and a member of both the Neuroscience and Genetics Program. The laboratory personnel are an eclectic mix of full-time research assistants, graduate students, database managers and work-study students.

The laboratory group has three major foci. The first is the role of the MED12 gene in human health and behavior. MED12 is one of the essential members of the Mediator complex and was first genetically characterized in 1998 by Dr. Philibert. In the past five years, we have developed compelling evidence that sequence variation in MED12 increases vulnerability to unique endophenotype of schizophrenia. In order to exploit these findings, our laboratory is using clinical genetic, transgenic cell modeling and systems biology approaches to discern the exact genetic mechanisms through which variation at this locus increases propensity for psychosis and to design new therapies for certain types of positive symptoms.

The second is the role of genetic variation and gene-environment interactions in the genesis of behavioral disorders. Dr. Philibert is a principal investigator with the Iowa Adoption Studies, the largest longitudinal adoption study of gene environment interactions in the United States. Using genotyping and gene expression techniques, our group which includes internationally known collaborators, is dissecting the roles of genetic variation and gene environment interactions in the initiation and maintenance of substance use disorders, depression and antisocial personality in this large cohort of subjects.

The third is the development of transcriptional profiling as a method for dissecting the etiology of complex behavioral illnesses and as a diagnostic aid for psychiatric illness. Over the past several years, it has become apparent that the majority of the genetic complexity underlying differential vulnerability to behavioral illness is manifested by differential gene expression and not by differential protein sequence. In a series of groundbreaking papers, we have detailed the development of a new set of techniques to exploit these findings and using one of the largest private collections of cell lines in the United States, we are actively working with academic and commercial collaborators to bring transcriptional profiling to the bedside as a diagnostic and prognostic tool.

Selected Publications:


The goal of our research is to understand how the central nervous system performs the complex functions underlying learning and memory by mapping metabolic and electrical activity within and between functional groups of cells. Is there one central learning circuit for sensory information or are there several circuits depending on the type of learning and/or the sensory modality? Our laboratory group is identifying the neural functional maps underlying various types of learning including delay nonmatching to sample (DNMS), classical and operant conditioning using auditory and visual stimuli. By using whole brain metabolic mapping techniques such as 2-deoxyglucose (2-DG) autoradiography and cytochrome oxidase (C.O.) histochemistry, the neural circuit differences between using auditory versus visual stimuli, classical and operant conditioning, learning by reward versus punishment, acquisition vs. extinction, and the temporal-spatial resolution of acquisition vs. maintenance, of behavioral patterns using a variety of sensory cues are being delineated. The neural circuits that are identified with metabolic mapping techniques are then verified and refined in rodents and primates through permanent lesion and temporary inactivation studies as well as neuronal recording studies.

Selected Publications:


Genetics and epigenetics of mood disorders. I am interested in the genetic variation and DNA methylation variation that confer susceptibility to depression and bipolar disorder. Family, twin, and adoption studies have made it abundantly clear that these disorders are substantially heritable, but only a very small proportion of that heritability has thus far been explained molecularly. Similarly, the environment clearly plays a role in the etiology of depression, but the molecular basis of that role remains undefined. I have an R01 grant from the NIMH to perform next-generation exome sequencing in about 3,000 bipolar disorder cases and controls, and examine the data searching for rare variants associated with this illness. I also have an R01 grant from the NIMH to assess genome-wide DNA methylation variation in a mouse model of stress and depression. Both of these projects involve bench work including DNA sequencing, bisulfite pyrosequencing, and gene expression assays. They further involve bioinformatics and statistical genetics assessment of large data sets.

Selected Publications:

Association study of serotonin pathway genes in attempted suicide.

Co-morbid anxiety disorders in bipolar disorder and major depression: familial aggregation and clinical characteristics of co-morbid panic disorder, social phobia, specific phobia and obsessive-compulsive disorder.

Data mining approaches for genome-wide association of mood disorders.

Adaptation of the CHARM DNA methylation platform for the rat genome reveals novel brain region-specific differences.

Genome-wide linkage analysis of 972 bipolar pedigrees using single-nucleotide polymorphisms.

Genome-wide association of bipolar disorder suggests an enrichment of replicable associations in regions near genes.
We combine behavioral, physiological, functional neuroanatomical, and cellular approaches to unravel the neural circuitry that underlies adaptive neuroendocrine responses to stress. Recently we have identified a locus in the basal forebrain that serves as a neural hub for integrating and relaying information between the limbic forebrain and neuroendocrine effectors in the hypothalamus. We now use this system to examine the cellular and circuit-induced alterations that contribute to chronic stress-induced neuroendocrine dysfunction.

Selected Publications:


My research focus is on the cardiovascular and neurophysiologic consequences of obesity with particular focus on obesity induced hypertension. My work in the lab has been focused on the renin-angiotensin system of the adipose tissue. I am pursuing several experiments to test the hypothesis that the adipose renin-angiotensin system is a new player in obesity-associated hypertension.

Selected Publications:


Research Interests

We are studying the role of serotonin neurons in mediating the effects of acidosis on brain function and behavior. We have shown that serotonin neurons are exquisitely sensitive to changes in pH. They are close to large arteries in the brain and contribute to the increase in breathing induced by increased CO2 levels (which indirectly decreases pH). They are also essential for the arousal from sleep that is induced by high CO2. We are using a variety of transgenic mice, brain slices and tissue culture to understand the mechanisms and significance of these responses, and a variety of techniques including patch clamp recordings, whole animal behavioral studies, confocal imaging and molecular biology. These experiments are also aimed at understanding the role of these effects in human conditions in which sudden death occurs, such as infancy (SIDS), epilepsy (SUDEP) and Parkinson's disease.

GABA transporters and tonic inhibition

We are also studying the role of GABA transporters in controlling the level of extracellular [GABA] at both the synapse and at extrasynaptic sites. We have shown that GAT1 reverses easily and the resulting nonvesicular GABA release can support synaptic transmission after blocking vesicular GABA release

- Neural control of breathing
- Sleep physiology
- Sudden death in epilepsy (SUDEP) and infants (SIDS)
- Serotonin effects on brain function
- GABA mechanisms in epilepsy
- Non-motor symptoms of Parkinson's disease

Lab website:
http://www.healthcare.uiowa.edu/labs/richerson/

Neurology website:

Selected Publications:


Matthew Rizzo, M.D.  
matthew-rizzo@uiowa.edu  

-Professor of Neurology-

Matthew Rizzo is a Professor in the Department of Neurology in the University of Iowa Carver College of Medicine. He is Director of the Division of Neuroergonomics and is a senior member of the Division of Behavioral Neurology and Cognitive Neuroscience. Dr. Rizzo also holds University of Iowa appointments in the Department of Mechanical and Industrial Engineering, Public Policy Center, Iowa Injury Prevention Research Center, and in the Neurosciences Program. Dr. Rizzo's research focuses on cognitive impairments caused by aging and neurological diseases such as stroke, Alzheimer's disease and traumatic brain injury. He has a special interest in vision and cognition, including their role in real-world tasks. The latter research uses an interactive driving simulator and an instrumented vehicle. Dr. Rizzo's research is supported by the National Institutes of Health and the Centers for Disease Control and Prevention.

Selected Publications:


Andrew Russo, Ph.D.
andrew-russo@uiowa.edu

Professor of Molecular Physiology & Biophysics

My research interest is the control of neuronal gene expression. The long-term goal is to develop gene therapy and diagnostic strategies for neurovascular disorders and neural crest-associated birth defects. There are two major projects in the lab involving the neuropeptide CGRP in neurovascular headaches and the PITX2 homeodomain protein in Rieger Syndrome.

CGRP neuropeptide levels are elevated during migraine headaches and lowered by serotonergic drugs. Importantly, a CGRP receptor antagonist has recently been found to be effective in treating migraineurs in clinical trials. We have found that the CGRP gene is up-regulated by MAP kinases and repressed by antimigraine drugs. We have recently shown that these drugs act via an unusually prolonged calcium signal. We are currently investigating these mechanisms and have initiated studies using adenoviral-mediated gene transfer to therapeutically regulate CGRP levels. The strategy involves a combination of culture and in vivo studies using reporter genes. We are currently using retrograde delivery of viral luciferase vectors to the trigeminal ganglion followed by light detection from the animal.

We are studying the human PITX2 protein and its regulation of GABA neurotransmitter synthesis. Interestingly, PITX2 can complement a mutation in the nematode C. elegans by restoring expression of GABA. We are characterizing the functional consequences of Rieger mutations in model systems, including C. elegans. In a new project, we are studying its possible role in palate morphogenesis via a novel involvement of nonneuronal GABA biosynthesis. In parallel, we are testing the role of interacting partners of PITX2 that we have identified by yeast two-hybrid screens.

Elucidation of the molecular genetic mechanisms that regulate PITX2 activity should provide insights into Rieger syndrome and related birth defects.

Selected Publications:


Peroxisome proliferator activated receptors (PPAR's) are ligand activated transcription factors which have a pleiotropic role in many physiological processes. PPARγ is the molecular target of the thiazolidinediones class of drugs which are used to treat patients with non-insulin dependent diabetes mellitus (NIDDM). Endothelial dysfunction, which develops in patients that are diabetic or chronically hypertensive, is thought to contribute to the progression of carotid artery disease, cerebral vascular dysfunction and stroke. PPARγ is expressed in vascular endothelium and smooth muscle and therefore is a potentially important factor in the regulation of vascular function and blood pressure. PPARγ has been reported to inhibit responses to vasoconstrictors such as endothelin, stimulate the release of vasodilators, and increase expression of CuZn-SOD in vascular muscle and endothelium. Importantly, patients carrying dominant negative mutations in PPARγ exhibit early onset type II diabetes and hypertension. Current data suggests that PPARγ exerts a protective effect in the vessel wall and we hypothesize that PPARγ plays an important role in the regulation of vascular function and blood pressure. We are currently testing this hypothesis using a variety of genetic, computational and Bioinformatic tools. We are: 1) using adenoviruses over-expressing wildtype and dominant negative mutations of PPARγ in blood vessels from normotensive and hypertensive mice to test whether they can alter endothelial function, 2) developing novel transgenic mice with expression of the wild-type and dominant negative mutants of PPARγ targeted specifically to vascular muscle and endothelial cells using cell-specific promoters, 3) using microarrays to determine the transcriptional targets of PPARγ, and 4) using computational and Bioinformatic tools to scan genomic sequences for PPARγ response elements (PPRE).

Selected Publications:


My research focuses on the spinal cord mechanisms involving the control of musculoskeletal pain. We use animal models of acute and chronic musculoskeletal pain that produce behavioral signs such as limping and guarding of the limb and an increased response to heat or mechanical stimuli, hyperalgesia. Our laboratory is particularly interested in the intracellular pathways and ion channels in chronic musculoskeletal pain. Experimental approaches include measuring behavioral responses to noxious stimuli (hyperalgesia), recording activity of dorsal horn neurons, measuring release of neurotransmitters (microdialysis/push-pull perfusion and HPLC), and anatomical localization of mediators of hyperalgesia (immunohistochemistry).

A second area of research has focused on deciphering the neurobiological mechanisms behind how transcutaneous electrical nerve stimulation (TENS) reduces pain. TENS is commonly used clinically as a non-invasive, adjunct therapy for pain control. Recently we began to decipher the pharmacological and anatomical pathways involved in the analgesia produced by TENS. Current projects include:

1) musculoskeletal pain: ion channels, intracellular pathways
2) neurophysiological mechanisms of action of TENS.

Selected Publications:


My primary research interests involve cognition in neurodegenerative diseases affecting the white matter and the contribution of depressive symptoms to cognitive impairment in neurodegenerative disorders (specifically Huntington disease and multiple sclerosis). Additional research interests include the contribution of extra-test factors on cognitive test performance, awareness of cognitive deficits in neurological populations, and cognition in deep brain stimulation for obsessive-compulsive disorder.

Selected Publications:


Long-Sheng Song, M.D.
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Associate Professor of Internal Medicine

Our laboratory is focused on understanding the role of highly spatio-temporal localized Ca2+ signals, namely Ca2+ sparks, in normal cell function and diseases (e.g., heart failure, arrhythmias and other diseases). We use state of the art techniques such as patch-clamp and laser scanning confocal microscopy in combination with genetic mouse models to investigate the cellular mechanisms of Ca2+ regulation and dysregulation. Specifically, we are studying 1) the structure-function relationship between t-tubule system and Ca2+ handling in normal and diseased hearts. In this project, we are testing our hypothesis that t-tubule remodeling plays critical role in Ca2+ release instability and therefore Ca2+-dependent arrhythmogenesis in cardiomyopathies; 2) Local Ca2+ signaling and sinoatrial node automaticity. In the second project, we are testing our hypothesis that Ca2+ sparks are highly locally controlled in sinoatrial nodal cells and that dys-regulation of local Ca2+ signaling in SAN cells contributes to pacemaker dysfunction. Our research projects are funded by National Heart, Lung and Blood Institute.

Selected Publications:


**Developmental Mechanisms in Retinal Degeneration**

My research interests center on the fundamental physiologic mechanisms of neurologic diseases affecting the visual system, and on the role that central nervous system (CNS) plasticity may play in the pathogenesis and potential treatments for such disorders. Ongoing investigations aim to better understand electrophysiologic changes that occur in hereditary retinal degeneration, the most common inherited cause of blindness, and also a central feature of many neurodegenerative disorders in children and adults, including those that cause severe mental retardation, motor disability, and seizures.

Currently proposed therapies for these disorders hinge upon the assumption that even after photoreceptor degeneration, remaining retinal neurons would be able to normally process signals from rescued or replaced photoreceptors, or from direct electrical stimulation. In fact, significant anatomic reorganization of the inner retina occurs, and recent work in my laboratory has identified corresponding physiologic changes that may involve mechanisms of developmental plasticity. The lab uses state-of-the-art multielectrode recording to monitor spontaneous and light-evoked activity simultaneously from 30-90 retinal ganglion cells in normal (wild type, w/t) mice or those of the well-studied rd1 mouse model of retinal degeneration. Surprisingly, as the animal becomes blind, retinal ganglion cells do not simply drift into silence as might be expected. Rather, they develop striking hyperactivity (~10 times normal firing rate) that is sustained for many weeks. In fact, ganglion cells pass through at least three stages of activity: 1) normal spontaneous "waves" of correlated firing in early development; 2) increasing spontaneous activity with temporary preservation of light-evoked responses, selective for the OFF pathway; then 3) sustained hyperactivity that lasts for months, well beyond the loss of virtually all photoreceptors and light-evoked responses.

These striking alterations in inner retinal physiology tell us that in the rd1 mouse: 1) blindness occurs in the face of sustained ganglion cell hyperactivity; 2) these cells remain viable, thus amenable to various treatments, for an extended time despite this activity; 3) ON and OFF responses are differentially affected in early stages of degeneration. Since photoreceptor loss begins early and progresses rapidly in rd1 mice, it overlaps substantially with a normal developmental period of highly active synaptic plasticity. Thus, the lab now is comparing several transgenic mouse lines to explore the possibility that developmental plasticity may play an adaptive role in resculpting specific inner retinal circuits such as the ON and OFF pathways. Other avenues of investigation include dissecting changes in the neural code that rd1 ganglion cells use to communicate with the brain, exploring circuit-level and cellular mechanisms that underlie the alterations in their physiologic activity, and determining how widespread these changes are among other neurodegenerative diseases such as neuronal ceroid lipofuscinosis (NCL) and tuberous sclerosis (TS).

**Recent Publications**

Stasheff, SF and Andrews, MP. Emergence of ganglion cell hyperactivity and loss of light-evoked responses follow distinct developmental time courses in retinal degenerate mice. (under review, J Neurophysiol).

Thompson, S, Stasheff, SF, Sheffield, VC, Stone, EM. Seeing bright light as dim light: in Rpe65 based visual cycle dysfunction, vision indirectly determines circadian phase. (under review, Inv Ophthalmol Vis Sci).


Cues in the extracellular microenvironment govern neuronal cell body migration, growth cone motility, and synapse formation by triggering changes in migration speed or direction. The cell surface receptors that interpret these cues engage cytoplasmic partners to transduce signals, but recent work reveals that many receptors also interact laterally with cell surface proteins that can be critical for proper receptor function. Thus, a more sophisticated understanding of cell migration will require a “cell surface interaction map” describing the connectivity of receptors and their cell surface partners. To begin to build such an interaction map, we are studying members of the tetraspanin family of cell surface adaptor proteins. Tetraspanins organize complexes containing integrins (major receptors for extracellular matrix proteins), Ig superfamily (IgSF) proteins, growth factor receptors, membrane-bound growth factors, and novel proteins. By targeting tetraspanins, which lie at the center of these complexes, a large number of new cell surface interactions can be uncovered at once. One major focus in the lab is on the tetraspanin protein, TM4SF2, a molecule responsible for one form of X-linked mental retardation. We are trying to unravel the mystery of TM4SF2 involvement in mental retardation by identifying its molecular partners and studying the effect of naturally occurring TM4SF2 mutations on TM4SF2 trafficking, localization, and molecular interactions. A second major focus is on alpha-5 integrin, a receptor for the extracellular matrix protein, fibronectin. We are studying the ability of transgenic alpha-5 integrin to support regenerative neurite outgrowth in CNS neurons. Wild type and modified forms of alpha-5, with different sets of interacting proteins, are being tested for their ability to support neuronal regeneration.

Selected Publications:


Reversible phosphorylation of key proteins, such as ion channels and neurotransmitter-synthesizing enzymes, regulates synaptic transmission and other aspects of neuronal physiology and development. While the enzymes that add phosphates to proteins, protein kinases, have been studied extensively, much less is known about the equally important enzymes that catalyze the reverse reaction, protein phosphatases.

My laboratory is interested in the roles of one of the major serine/threonine phosphatases, protein phosphatase 2A (PP2A) in normal and pathological brain function. PP2A is a diverse group of multi-subunit enzymes consisting of a constant catalytic (C) and scaffolding (A) subunit and a third variable, or regulatory (B) subunit. Regulatory subunits control enzymatic activity and substrate specificity and target PP2A holoenzymes to different parts of the cell. Research in the lab focuses on PP2A regulatory subunits that are highly expressed in brain, since they are likely to regulate specifically neuronal functions. One of these neuronal PP2A subunits, Bβ is mutated in a human neurodegenerative disorder, spinocerebellar ataxia type 12 (SCA12), implying that this subunit is essential for neuronal survival. Current studies focus on structure/function analyses of PP2A holoenzymes, regulation of signal transduction cascades and neurotransmitter synthesis by PP2A, and restructuring of neuronal mitochondria by kinases and phosphatases.

Current Projects:

1) Role of PP2A in nerve growth factor signaling and neurite outgrowth. Expression of the neuronal By subunit promotes differentiation of neuronal PC12 cells by stimulating the mitogen-activated protein kinase (MAPK) cascade. The Bα subunit, conversely, inhibits MAPK signaling, indicating that this important signal transduction cascade is regulated both positively and negatively by PP2A. Using RNA interference and pharmacological approaches, we are in the process of identifying the molecular targets of PP2A/Bγ and Bα.

2) Regulation of mitochondrial function and neuronal survival. We have recently discovered a novel alternative splice variant of the neuronal Bβ PP2A subunit that is mutated in the SCA12 disorder. The divergent N-terminus of Bβ2 targets PP2A to mitochondria to promote neuronal cell death by apoptosis. An outer mitochondrial cAMP-dependent protein kinase (PKA) holoenzyme opposes the death-inducing activity of PP2A/Bβ2. Using Bβ2 knockout mice and primary hippocampal cultures, we are identifying the physiological functions and molecular targets of outer mitochondrial PP2A and PKA.

3) Structure-function analysis of PP2A holoenzymes. Using site-directed mutagenesis and a variety of in vitro analyses, we are investigating how regulatory subunits interact with the A and C subunit to determine substrate specificity. The B’ family of PP2A subunits are heavily phosphorylated in cells, and we are studying the effect of phosphorylation of specific residues on catalytic activity and subcellular localization.

4) Regulation of catecholamine biosynthesis by PP2A. We found that tyrosine hydroxylase (TH), the rate limiting enzyme in the synthesis of dopamine and (nor)epinephrine, is dephosphorylated and inactivated by a neuron-specific PP2A holoenzyme containing the B’β subunit. We are exploring the regulation of PP2A/B’β activity in dopaminergic neurons with the eventual goal of developing new Parkinson’s disease therapies.

Selected Publications:


William Talman, M.D.
william-talman@uiowa.edu

-Professor of Neurology

My laboratory examines 1) the role of parasympathetic nerves in regulating cerebral blood flow and the influence of those nerves on neural protection during stroke; 2) the role of nitric oxide in transmitting cardiovascular signals in the brain; and 3) the mechanisms underlying cardiac damage secondary to lesions of the central nervous system.

Selected Publications:


Daniel Tranel, Ph.D.
daniel-tranel@uiowa.edu

-Professor of Neurology

My research is aimed at understanding brain-behavior relationships in humans, at systems level. Two main approaches are used: (1) the lesion method, in which brain-damaged patients are studied with neuropsychological procedures to determine how certain lesion sites are related to certain cognitive and behavioral deficits; and (2) functional imaging, including PET and fMRI, in which the brain activation in normal subjects is measured while the subjects are performing various tasks. Specific topics that I am working on currently include: retrieval of conceptual knowledge; retrieval of words and lexical knowledge; emotion and decision-making; face processing; nonconscious processing; acquired disorders of social conduct; memory; psychophysiology. My research has been continuously and fully funded for two decades. I have about a thousand square feet of laboratory space in the Department of Neurology in the University of Iowa Hospitals.

Selected Publications:


Retinal degenerative diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are currently the leading cause of incurable blindness in the western world. These diseases are characterized by death of the light sensing photoreceptor cells of the outer neural retina. As the intrinsic regenerative capacity of the mammalian retina is extremely limited, the only viable treatment option for people suffering from photoreceptor cell loss is cellular replacement. Although a range of data suggests that the use of stem cells to achieve such a goal is now feasible, two major hurdles blocking establishment of a viable cell based clinical therapy exist. These are 1: generation of a suitable cell type, and 2: development of an optimal cell delivery/transplantation system. For instance, much of the focus in the stem cell field has been placed on the use of cell types that, although potentially effective, for one reason or another are not entirely suitable for clinical application (i.e. immune compatibility, inability to obtain sufficient cell numbers and ethical concerns relating to cell source). Similarly, current delivery methods typically result in massive cell loss and limited cellular integration. Thus, regardless of the cell type chosen, this prevents progression toward clinical trial and successful development of a restorative cell-based therapy. To circumvent these issues, my lab is focused on combining state-of-the-art patient-specific stem cell and biodegradable tissue engineering technologies to develop outer retinal equivalents, de novo, to be used as a means of retinal regeneration following transplantation.

Selected Publications:


Our laboratory is working on the topic of speech perception by normal and hearing-impaired listeners. This work also involves basic psychophysical capabilities of normal and impaired listeners. In addition to the theoretical contributions of this work, we also see applications in the design of a new generation of hearing aids and cochlear implants as well as improved speech recognition by machines. Our goals are to identify the types of speech cues that are (mis)perceived by hearing-impaired listeners, as well as to design digital signal processing algorithms to assist their communication abilities. We have also participated in studies of the human auditory cortex.

Selected Publications:


Interdisciplinary Graduate Program in NEUROSCIENCE
Ergun Uc, M.D.

-Associate Professor of Neurology

Certain conditions and illnesses can drastically affect a person's driving capabilities. However, determining if an illness-related impairment makes someone an unsafe driver is a complicated decision. Ideally, that decision should be based on an ability to accurately predict how certain aspects of a disease contribute to risky driving.

Using a five-year, $1.6 million grant from the National Institute of Neurological Disorders and Stroke, a team of University of Iowa researchers will study how Parkinson's disease affects driver safety. The team, led by principal investigator Ergun Uc, M.D., (left) assistant professor of neurology in the UI Roy J. and Lucille A. Carver College of Medicine, and co-principal investigator Matthew Rizzo, M.D., UI professor of neurology, engineering and public policy, aims to generate data that will help predict driver safety for individuals with this condition.

"Parkinson's disease affects people in many ways that can have an impact on their ability to drive," Uc said. "Most people know about the motor effects of the disease -- the tremors and difficulty walking -- but the disease affects lots of systems in the brain and the body. Mental functions -- including the ability to think and make decisions, memory and attention -- are affected, as are reaction times. Parkinson's disease also can affect psychology, causing depression and anxiety, and can alter sleep rhythms and vision."

Uc also noted that the medications designed to alleviate tremors and stiffness caused by the disease can actually worsen other functions by making the patient sleepy or decreasing attention span.


Selected Publications:


Yuriy M. Usachev, Ph. D.
Yuriy-usachev@uiowa.edu

-Associate Professor of Pharmacology

Research in my laboratory is focused on the Ca2+-dependent regulation of neuronal function in the context of pain signaling, synaptic plasticity and neuronal survival. Ca2+ is a ubiquitous second messenger that controls numerous neuronal functions. Combining the properties of a signaling molecule and an ion that rapidly moves across the plasma membrane during excitation, Ca2+ enables coupling between electrical activity and intracellular signaling events. Multiple Ca2+ targets within neurons differ in their Ca2+ affinity, subcellular distribution and sensitivity to the duration of [Ca2+]i elevation. Accordingly, distinct Ca2+-mediated neuronal responses are encoded and determined by the amplitude, subcellular localization and the length of Ca2+ signal. We are using molecular and genetic approaches combined with patch-clamp recordings and fluorescent microscopy to better understand how Ca2+ signals are generated in the neuronal somata, presynaptic boutons and postsynaptic dendritic spines, and how specific patterns of Ca2+ transients regulate synaptic plasticity, gene expression, excitability of pain-conducting neurons and neuronal survival. We also use behavioral animal models to further explore in vivo the functional significance of the described processes. Research in my laboratory is supported by three NIH R01 grants: NS054614 (PI: Usachev), NS035563 (PI: Hell; Co-PI: Usachev) and NS056244 (PI: Strack; Co-PI: Usachev).

Selected Publications:


Shaun Vecera, Ph.D.
shaun-vecera@uiowa.edu

Professor of Psychology

Professor Vecera is a specialist in visual cognition, with specific interests in visual attention and perception and the neural bases of these visual processes. He is an associate professor in the cognition and perception area in the Department of Psychology at the University of Iowa. His research program chiefly relies on experimental investigations with neurologically normal college-aged participants. However, Professor Vecera also relies on neurologic populations to constrain his theoretical views of visual processing. For example, two recent projects from his lab investigated attentional orienting in clinical populations—patients with unilateral parietal damage and patients with frontal-lobe damage. The results from these studies are highly translational in nature, informing theories of both normal attentional processing and attentional impairments following brain injury. Professor Vecera's expertise with various visual cognition paradigms would allow these paradigms to be adapted for use with special populations (e.g., neurologic or psychiatric populations), and the use of such paradigms with special populations would give trainees a unique experience of integrating theoretically-motivated tasks into clinical research.

Selected Publications:


Edward Wasserman, Ph.D.
ed-wasserman@uiowa.edu

- Professor of Psychology

My research concerns the experimental investigation of cognitive processes in animal behavior, with particular interests in comparing cognition and perception in human and nonhuman animals. Specific research topics include: conceptual behavior, visual pattern recognition, short-term memory, and causal perception.

http://www.psychology.uiowa.edu/faculty/wasserman/

Selected Publications:


A defining attribute of the vertebrate nervous system is the remarkable specificity with which different neuronal subtypes interact during development. Specific cell-cell interactions are critical for setting up the correct patterns of histogenesis, neuronal survival, axon outgrowth, and synapse formation. Research in our laboratory is focused on understanding the roles that adhesion molecules, which protrude from the cell membrane to link adjacent cells together, play in these processes.

**PROTOCADHERINS**

Three large clusters of cadherin-related genes (Protocadherin-α, -β, and -γ) lie in a tandem array on a single chromosome in mammals. The γ cluster, on which we focus, consists of 22 "variable" exons, each of which encodes the extracellular, transmembrane, and partial cytoplasmic domains of a single protocadherin isoform. Each variable exon is spliced to a set of three "constant" exons which encode a shared C-terminal domain. Thus, a variety of adhesive specificities may link into a common signaling pathway.

Our work has shown that γ-protocadherins are expressed exclusively in the nervous system during development, and are concentrated at synapses. Mice in which the entire γ-protocadherin locus is deleted lack voluntary movements and reflexes and die at birth due to massive apoptosis of spinal interneurons and loss of synapses. We have recently genetically dissociated these two phenotypes to show that control of synapse development is a primary function of γ-protocadherins.

We are currently addressing several questions using multiple lines of mutant and transgenic mice: 1) What is the relationship between the observed synaptic defects and apoptosis?; 2) How are γ-protocadherins localized to synapses and what signaling pathways do they require?; 3) Why are only certain interneurons affected, since most neurons express γ-protocadherins? We hope to use insights gained from studying the phenotype of protocadherin mutant mice to elucidate general mechanisms of neuronal survival and synaptic specificity.

**ALCAM**

The immunoglobulin superfamily molecule ALCAM is expressed by subsets of neurons and has been implicated in the control of numerous developmental and pathological processes. To test hypotheses about ALCAM function, we have disrupted its gene via homologous recombination. In mice lacking ALCAM, both motor neuron and retinal ganglion cell axons fasciculate poorly and are occasionally misdirected. In addition, ALCAM mutant retinae exhibit dysplasias with photoreceptor ectopias that resemble the retinal folds observed in some human retinopathies. This appears to be due to loss of ALCAM in the choroid, a pigmented vascular tissue that lies behind the neural retina. Because ALCAM has been associated with melanoma metastasis, we hypothesize that defects in choroidal melanocyte adhesion and/or motility underlie the mutant phenotypes. We now are determining the specific cellular defect and examining its relationship to ocular development and disease processes.

**Selected Publications:**


*co-first author


Michael Welsh, M.D.
michael-welsh@uiowa.edu

-Professor of Internal Medicine; Molecular Physiology & Biophysics
-Carver Trust-Roy J. Carver Biomedical Chair in Internal Medicine
-Howard Hughes Medical Institute Investigator
-Co-Director, Medical Scientist Training Program, Carver College of Medicine

The major neuroscience effort of the laboratory focuses on the biology of DEG/ENaC channels. These are a novel class of non-voltage gated cation channels, including ASIC1, -2, and -3 in mammals and the Pickpocket genes in Drosophila. The laboratory is interested in the function of these channels in the peripheral nervous system where they may serve as sensory receptors, including sensors for touch, temperature, salt taste, moisture, and pain. We are examining the function, cell biology, physiology and behavioral role of these channels in vitro and in genetically altered flies and mice. We also study the function of these channels in the central nervous system where they play an important role in synaptic plasticity, learning and memory. They may also make an important contribution to fear, including panic disorders. The lab offers the opportunity to take a variety of approaches to this field, and it provides the opportunity to work with investigators with diverse expertise. This research should lead to a better understanding of neuronal sensory systems and novel targets for therapeutic intervention. The other major focus of the lab is to understand the biology of cystic fibrosis, a common lethal genetic disease. We are investigating the function of the CFTR chloride channel, the pathogenesis of the disease, and the development of gene therapy.

Selected Publications:


My lab uses genetic manipulation in mice to study the effects of Acid Sensing Ion Channels (ASICs) on behavior.

Because one of these channels, ASIC1, is abundant in the amygdala complex, we tested whether it plays a role in Pavlovian fear conditioning. We found that ASIC1a knockout mice have reduced fear conditioning, whereas transgenic mice overexpressing ASIC1a have increased fear conditioning. These data suggest that ASICs may play an important role in fear, and raise the possibility that they might contribute to anxiety disorders in humans and might provide a pharmacological target for treating anxiety. Ongoing studies in my lab are exploring these possibilities.

Selected Publications:


The primary goal of our laboratory is to identify genetic and epigenetic risk factors for suicidal behavior. Family, twin, and adoption studies make clear that suicidal behavior has a substantial heritable component. While there is evidence that this heritability is accounted for in part by a liability to mood disorder, other evidence suggests an independent heritable facet that may cut across multiple psychiatric disorders. In an effort to better understand the biological basis of this behavior, we have conducted a genome-wide association study (GWAS) using attempted suicide as the phenotype, an effort that identified a promising association signal on 2p25 as well as candidate genes implicating the Wnt signaling pathway and excitatory neurotransmission. These findings have prompted us to launch a large-scale whole exome sequencing project, with the goal of identifying functional variants associated with suicidal behavior on 2p25 and throughout the genome. Environmental stressors, such as child abuse and early parental loss, are also known to play important roles in triggering suicidal behavior, likely through interaction with genetic vulnerability factors. With this in mind, we have begun an epigenetics project that involves assessing genome-wide methylation patterns in post-mortem brains of suicide completers and controls, with the goal of identifying differentially methylated candidate genes and regions associated with suicidal behavior.

Selected Publications:

Association study of serotonin pathway genes in attempted suicide.

A genome-wide association study of attempted suicide.

Monoamine oxidase A regulates antisocial personality in whites with no history of physical abuse.

Genome-wide association study of suicide attempts in mood disorder patients.

Case-control association study of TGOLN2 in attempted suicide.
Research interest concerns the cellular mechanisms regulating functional and developmental plasticity in the nervous system. Synaptic terminals and growth cones in Drosophila mutants deficient in learning ability are analyzed by a combination of electrophysiological, anatomical, and genetic techniques. These learning mutants are defective in specific steps of second messenger systems and cause abnormal synaptic function, and growth cone motility, and neurite growth. Another class of mutations that affect ion channels are used to study the influence of neuronal activity on behavioral and developmental plasticity. Double-mutant combinations allow us to determine how channel activity and second messenger systems interact to regulate neuronal growth and synaptic function required in learning and memory processes. Genetic mosaics mosaicism and targeted expression of transgenes can be constructed used to analyze the behavioral and physiological consequences of introducing mutant neurons to alter different parts of the neural circuits involved in specific behavioral tasks.

Selected Publications:


Our lab is studying neural control of feeding behavior and etiology of eating-associated disorders, such as obesity and anorexia nervosa, in genetic mouse models. Feeding behavior is tightly regulated at several levels in the central nervous system. Peripheral hormonal and nutritional signals impinge onto several hypothalamic and brainstem nuclei to regulate appetite and energy metabolism in a largely subconscious manner. Meanwhile, higher cognitive centers also modulate food intake. A challenging question is how neural circuits that underlie the basic drive to feed interact with those representing conscious wish to mediate feeding-related activities. Hypothalamic AgRP neurons are critical for regulation of feeding and body weight, as acute ablation of these cells in adult mice leads to anorexia and profound weight loss. We demonstrated that such anorexic phenotype is fully reversible with the aid of a GABA-A receptor agonist and that GABA release from AgRP neurons onto neurons in the lateral parabrachial nucleus (PBN) is essential for maintenance of appetite and body weight. Therefore, we proposed that a novel hindbrain circuit and associated signaling pathways underlie neural adaptive control of anorexia and obesity through bi-directional modulation.

Current projects:

(1) Characterize functional connectivity of metabolic-sensing PBN neurons and their roles in control of feeding and energy homeostasis. We would expect to reveal the anatomical and functional organization of the PBN and how it interacts with other brain regions to promote compensatory adaptation after ablation of AgRP neurons. Moreover, we would expect to establish precise physiological roles and pivotal signaling mechanisms of distinct subpopulations of the PBN neurons in control of appetite and body weight.

(2) Identify a hindbrain neural circuit and associated signaling pathways that mediate feeding and addictive response to food in transgenic mouse models. Our preliminary results indicated that a hindbrain neural circuit might be functionally organized by several critical signaling pathways that integrate metabolic inputs from the hypothalamus along with gustatory and vagal stimuli to promote long-term adaptation to different homeostatic level. The potential outcome will illuminate a more complete feeding circuitry in the mammalian brain and novel adaptive mechanisms at synapse level that might contribute to developing therapeutic approaches against obesity and eating disorders.

Selected Publications:


My research efforts are directed towards understanding molecular mechanisms involved in the regulation of signal transduction pathways relevant to inflammatory diseases of the CNS including Multiple Sclerosis/EAE, Alzheimer’s disease, and Parkinson’s disease. The recent focus of my laboratory is to investigate Glia maturation factor (GMF) signaling mechanisms involved in potentiation of CNS inflammation using cellular, and molecular techniques in primary brain cells and in GMF-knockout/ transgenic mouse models. GMF is a novel brain protein, discovered, sequenced and cloned in our laboratory at the Dept. of Neurology, University of Iowa. We have a VA Merit Review Award funded program on the role of Glia Maturation Factor in dementia, an NIH RO1-funded program on GMF in CNS inflammation, and an NIH RO1-funded program on GMF-dependent neuroinflammation and neurodegeneration. Our work embraces neurochemistry, molecular neurobiology, and neuroimmunology.

Selected Publications:


The University of Iowa
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1178 Med Labs
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