The MGH/MIT/HMS
Athinoula A. Martinos Center
for Biomedical Imaging

ANNUAL REPORT

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CONTENTS

CENTER FACILITIES UPDATE

Charlestown Navy Yard

The Athinoula A. Martinos Center's new space on the 2nd floor of Building 149 in the Charlestown Navy Yard was completed this past fall. The new area includes office space for the Center's faculty and students, wet labs, optical labs, and shared conference space. In addition to dedicated Martinos Center space, the renovation includes areas for the imaging programs of the Psychiatry and Neurology departments, as well as the MGH-MIT General Clinical Research Center's Imaging Core, making the Martinos Center the hub for a large multidisciplinary group of clinical and basic scientists with a common neuroimaging focus.

Plans are now being developed for a major first floor expansion of the Center's imaging equipment facilities. Renovations will include a new magnet bay for a third 3 Tesla MR system. Addition of this badly needed system for head and whole body imaging will alleviate the overcrowding on the present systems. Phase two of the expansion is the footprint for the Center's new PET Imaging Initiative. This area will include microPET, PET-CT, PET-MR, and high resolution head-only PET camera suites, a cyclotron facility and radiochemistry labs. After a complicated search process, an appropriate location for the PET Center (with proper vending, etc) has been identified on the first floor of Building 149. The project will now enter the detailed architectural planning phase.

With all this technological growth comes the need for additional office space to house the growing faculty of scientists and engineers to use and operate these facilities, and to relocate those whose work areas will be displaced by the new equipment bays and labs. We continue to pursue negotiations with the landlord of the adjacent Building 175 in the Navy Yard for a long-term lease of that building to provide space to accommodate this growth.

Neuro Intensive Care Unit Imaging

Our plans to place a 3.0 Tesla MRI device inside the MGH Neuro Intensive Care Unit (ICU), mentioned in last year's Annual Report, have met with some interesting twists. The good news is that the Neuro ICU itself will be increasing in size and scope. Our plans to add MR imaging capabilities right in the ICU were so well received that the hospital has decided to take the idea one step further and place a CT scanner there as well. This expansion represents an extraordinary opportunity to study the mechanisms and biology of many serious illnesses in patients who are not able to travel to the Martinos Center site in Charlestown. In addition, Dr. Greg Sorensen, who has bee heading up this effort, was awarded a National Center for Research Resources (NCRR) Shared Instrumentation Grant to partially fund the Neuro ICU MR system. The bad news, of course, is that the relocation of the Neuro ICU to its larger home that will accommodate MR and CT imaging and will increase the number of patient beds for the unit, will delay the project a bit -- a setback, but one that will undoubtedly prove to be worth the wait.

Martinos Magnet Facility on the MIT Campus

We are very excited that plans are taking shape for a long-awaited Martinos Center imaging facility on the MIT campus. This 3 Tesla human MRI system will be housed in MIT's new Neurosciences Center along with 400 square feet of dedicated Martinos Center office space. The facility will be operated in cooperation with the McGovern Center and the Brain & Cognitive Sciences (BCS) department. The magnet will be run by Professor John Gabrieli, who will be joining the MIT faculty with a joint HST–BCS appointment, with support and cooperation from the MR imaging and data processing experts at the Charlestown Martinos Center site. Principal users of the new facility will include, along with Dr. Gabrieli and the cognitive neuroscientists of BCS, Dr. Elfar Adelsteinsson, the first MIT-based Martinos Center faculty member and his lab. Please read more about Drs. Gabrieli and Adelsteinsson, and other new faculty members of the Athinoula A. Martinos Center for Biomedical Imaging, below.

NEW FACULTY

We are very happy to welcome two important new MIT faculty members, Dr Elfar Adelsteinsson and Dr. John Gabrieli to the Athinoula A. Martinos Center. Both Drs. Adelsteinsson and Gabrieli are joint hires, Dr. Adelsteinsson with Electrical Engineering & Computer Science (EECS), and Dr. Gabrieli with Brain & Cognitive Sciences (BCS), thus connecting HST and the Martinos Center to other vibrant programs at MIT. Four other new Martinos Center faculty members, Drs. Jean Augustinack, Thomas Deissboeck, Anna Moore and Anjali Rajadhyaksha are contributing to the Center's new cellular and molecular imaging initiatives.

Elfar Adelsteinsson, PhD

Dr. Elfar Adelsteinsson will be the first MIT-based Martinos Center faculty member. With joint appointments in HST and EECS he will connect the Martinos Center to the MIT campus and to the very strong engineering programs within EECS, and he will assist Dr. Gabrieli in operating the Center's new MRI facility on the MIT campus. Dr. Adelsteinsson was born and raised in Iceland, and is currently a senior Research Engineer at the Lucas Center for Magnetic Resonance Spectroscopy and Imaging in the Department of Radiology at Stanford University, where he has worked since receiving his doctoral degree in Electrical Engineering from that University in 1995. His work is focused on the development of advanced *in vivo* magnetic resonance imaging and spectroscopic imaging approaches for the study of health and disease in humans and animal models. His contributions include the methods required to optimally acquire MR data, image reconstruction and post processing. He is currently the principal investigator on a three-year grant from the National Institutes of Health (NIH) to develop and apply MR spectroscopic imaging in combination with conventional structural imaging to monitor disease progression and treatment response in Alzheimer's disease. He will conduct his imaging research at the Martinos Center in Charlestown, especially using our new 7T MRI system and will use and help build our new 3T MRI facility on the MIT campus. Dr.

Adelsteinsson is enthusiastic about teaching graduate-level classes that focus on *in vivo* medical imaging and developing classes on more specialized topics within MR, such as comprehensive presentation of data acquisition and reconstruction methods. It is our hope that he will bring many more high caliber MIT students to our Center and will be a conduit for bringing our technology to HST, EECS an all of MIT. Funds provided by the generosity of the Martinos family will allow him startup monies to support his students and to build his lab. As an engineer with deep concern for and extensive collaboration in clinical and basic neuroscience, Dr. Adelsteinsson will be an outstanding representative of the Martinos Center's mission.

John Gabrieli, PhD

Dr. John Gabrieli soon will be joining the MIT faculty, with joint appointments through HST and BCS. Dr. Gabrieli will actually be returning to MIT, where he received his PhD in Behavioral Neuroscience from BCS in 1987. He is currently Professor in the Department of Psychology and Neurosciences Program, and by courtesy, the Department of Radiology, and is Director of the Cognitive Neuroscience Laboratory at Stanford University. His research focuses on human cognitive neuroscience and neuropsychology, especially the neural basis of memory, perception, and cognition (including hemispheric specialization) as revealed in experimental analysis and brain imaging (functional MRI) of memory dysfunction in patients (amnesia, Alzheimer's disease, Parkinson's disease) and normal function in healthy people. Dr. Gabrieli will be primarily responsible for setting up the new Martinos Center 3T MRI facility on the MIT campus. He is challenged with the task of seamlessly connecting the imaging facilities across the two campuses – an undertaking in which he will be assisted by Dr. Adelsteinsson and members of the Charlestown faculty. Dr. Gabrieli will be a bridge between the Martinos Center's two locations, and between our imaging expertise and MIT's neuroscience students and community.

Jean Augustinack, PhD

Dr. Augustinack received her PhD from the University of Iowa where she was mentored by renowned neuroanatomist Dr. Gary Van Hoesen. It was here that she became interested in neuroanatomy and Alzheimer's disease (AD) neuropathology. She recently completed post-doctoral training with Dr. Brad Hyman in the Department of Neurology at Harvard Medical School and Massachusetts General Hospital. With Dr. Hyman, her research focused on the cellular mechanisms that occur in the formation of a neurofibrillary tangle, one of the two pathological markers required for a diagnosis of Alzheimer's disease. Her research described which sites on the tau protein (the main protein that makes up a neurofibrillary tangle) are affected in AD, tau's interaction with other proteins, and how the tau's conformation is changed. Dr. Augustinack's research at the Martinos Center will focus on the questions, why are particular neurons, especially in the medial temporal lobe, vulnerable to neurofibrillary tangle formation and others not, and what are the events that lead to the formation of a neurofibrillary tangle-detachment of tau from microtubules? She came to the Martino's Center because she was interested answering these questions by combining the neural systems approach that she acquired in graduate school and the cellular and molecular methodologies of her fellowship. Her current research correlates histology and neuropathology findings with magnetic resonance imaging scans in human brain samples. The Martinos Center's advanced magnetic resonance imaging capabilities and techniques provide an excellent environment to combine the two approaches and elucidate the differences between normal aging and Alzheimer's disease in our digital world.

Thomas S. Deisboeck, MD

Dr. Deisboeck received his MD from the Technical University in Munich, Germany. In 1997 he was recruited by the Neurosurgical Service at Massachusetts General Hospital based on an essay he wrote about "*Neuro-Oncology Research: Past, Present & Future*". During his postdoctoral fellowship at the MGH Dr. Deisboeck helped pioneer "interdisciplinary tumor complexity research", a field now considered to hold great promise for progress in both experiment and clinics, alike. Dr. Deisboeck is studying cancer as a complex dynamic, adaptive and self-organizing biosystem, which requires methods and techniques from oncology research, bioengineering, mathematical biology, computational and complex systems science. His related research interests include biomedical data visualization and innovative data-integration platforms as well as biosensor technology and assay development for which he also holds a US patent. Dr. Deisboeck's highly collaborative work spans academia, national laboratories and international corporations. The prospect of combining his efforts with cutting-edge biomedical imaging modalities was what brought him to the Athinoula A. Martinos Center for Biomedical Imaging. Upon arrival, he established the Complex Biosystems Modeling Laboratory (CBML) (http://biosystems.mit.edu/Index.htm) which is located in part in the HST-Biomedical Engineering Center at MIT. Research of his NIH-funded laboratory focuses on the development of a new class of multi-scaled tumor modeling algorithms. Dr. Deisboeck has organized several related workshops supported in part by the National Institutes of Health and the National Science Foundation. At the moment, he edits the first multi-authored textbook on "*Complex Systems Science in BioMedicine*" which is scheduled to appear in the fall of 2004 (Kluwer Plenum Academic Publishers). Dr. Deisboeck is currently Assistant Professor in Radiology at Harvard Medical School. He holds a Visiting Scientist appointment at MIT and is also a Faculty Member of MIT's Computational and Systems Biology Initiative (CSBi). In addition, he is an Associate at Harvard University's Division of Engineering and Applied Sciences (DEAS).

Anna Moore, PhD

Dr. Moore received her Ph.D. in Bioorganic Chemistry from the Russian Academy of Sciences and came to the MGH in 1991. Her research interests have been focused primarily on the uptake and processing of targeted contrast agents for molecular imaging, first at the Center for Molecular Imaging Research at MGH and now at the Athinoula A. Martinos Center for Biomedical Imaging. She has been particularly interested in creating target-specific contrast agents that will be able to detect tumor tissue with high specificity and with low binding to other tissues using multimodal imaging. As her work progressed, Dr. Moore became interested in the application of these powerful molecular imaging detection tools to other health care issues. She began work aimed at the development of noninvasive target-specific molecular imaging probes for the detection of the early stages of Type 1 diabetes and non-invasive assessment of beta-cell mass. She has published several papers on molecular imaging in both cancer and diabetes in leading peer-reviewed journals and obtained multiple grant awards from NIH and private funds (American Diabetes Association, RSNA, Juvenile Diabetes Foundation). Dr. Moore is an Assistant Professor of Radiology and a head of a group studying molecular imaging approaches to non-invasive detection of pathogenic conditions as well as a response to therapeutic intervention. In her new position at the Athinoula A. Martinos Center for Biomedical Imaging, she hopes to apply molecular approaches to imaging pathologic and normal processes in the brain.

Anjali Rajadhyaksha, PhD

Anjali Rajadhyaksha, PhD is a molecular neuroscientist interested in understanding the molecular mechanisms of learning and memory. She received her PhD in molecular biology from Purdue University, Indiana and in 1997 joined the Psychiatry Department at Massachusetts General Hospital as a postdoctoral fellow to apply her molecular biology background to study neurological and neuropsychiatric disorders. Dr. Rajadhyaksha recently joined the Martinos Center faculty with a Career Development Award from the National Institute of Drug Abuse to examine the molecular neurobiology of cocaine and amphetamine addiction. Addictive behavior is a learned process and shares similar mechanisms to learning and memory formation. However, how addictive drugs cause long-lasting changes that alter behavior remains elusive. Through her interaction with clinicians at MGH who deal with both juvenile and adult addicted patients, Dr. Rajadhyaksha has concluded that in order to reveal the mechanisms by which pleasurable, yet highly addictive drugs hijack the human brain, we must examine events at the molecular level to find the culprit molecules and genes that mediate this process.

Towards this goal of understanding such a complex problem, Dr. Rajadhyaksha is using a multi-modal approach in animal models of drug addiction that includes integration of information from behavioral, imaging (fMRI), cellular, molecular, and genetic techniques. Her innovative comprehensive approach spans science from the macroscopic level of the whole brain to a microscopic level of single molecules. In addition Dr. Rajadhyaksha is collaborating with several other Martinos Center faculty members to map brain activation after acupuncture in human subjects to individual genetic variability that would help us understand why people respond differently to acupuncture. Toward this end, she is using gene chip technology to correlate the fMRI signals to gene expression patterns in animal models of acupuncture. Dr. Rajadhyaksha continues to pursue her passion for teaching and has been involved in teaching second year medical students at the Harvard Medical School. However when it comes to exciting young minds about the fascinating world of science, her most captive audience is her 8 yr old daughter and her friends.

NEW RESEARCH INITIATIVES

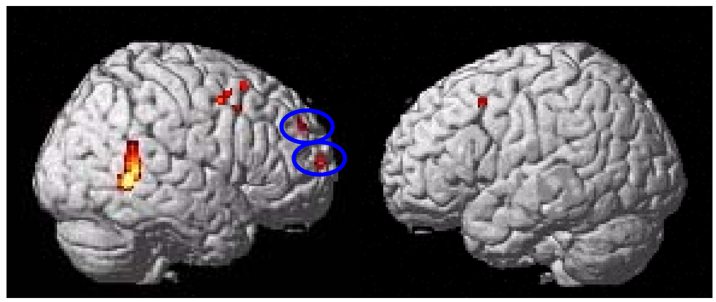
MIND Consortium

The Martinos Center has been asked by the Mental Illness and Neuroscience Discovery (MIND) Institute, a multi-institutional research foundation, to participate, and indeed take a lead in, their newly established Schizophrenia Consortium Study. The project, developed jointly by members of the MIND Consortium Group, including Nancy Andreasen, Robert McCarley, Dara Manoach, Randy Gollub, Vince Clark, John Lauriello, Lee Friedman, Kelvin Lim, Chuck Schultz, Dan O'Learly, and Vince Magnotta, aims to answer basic questions about the progression of schizophrenia in young adults, and the underlying changes in the brains of these patients. This project will involve four top notch sites from across our country (the Universities of New Mexico, the Minnesota, Iowa and our own Harvard University-coordinated via our Center) all studying a large group of patients at the disease’s earliest stages, as well as those with more advanced disease, with state of the art neuroimaging and behavioral techniques.

This Clinical Imaging Consortium Study will investigate two cohorts of patients and matched controls, recruited and studied at all four MIND Institute sites. The first clinical cohort will consist of first episode patients and demographically matched healthy controls, who will be evaluated comprehensively at intake, including collection of blood for genetic studies, and followed longitudinally with serial assessments of clinical, psychosocial, and neurocognitive measures, and functional and structural neuroimaging over five years. The basic elements of the behavioral neurogenetics protocol will include blood sample collection, processing, and selection of genetic variants for study, genotyping methods, and statistical analyses. This group of patients will be used to examine critical questions about the nature of course and outcome in schizophrenia, as well as questions about the nature of neural changes, as reflected by the quantitative structural and functional imaging data, over time. Once collected, this sample will give the investigative team an opportunity to track both the clinical course and changes in the brain, using state of the art technology and image analysis tools. Given the potentially large sample sizes, we will also be able to conduct comparisons in neuroleptic naïve vs. non-naïve patients, which will permit us to examine medication effects in these patients.

The second cohort will consist of chronic schizophrenic patients and demographically matched healthy controls. These patients will receive the same assessments that are used for the first episode patients, however; these patients will participate for a single assessment. They will not be followed longitudinally. Evaluation of this sample will require careful assessment of past treatment history, so that the effects of treatment on clinical status can be evaluated. This sample will be used for cross-sectional comparisons of first episode vs. chronic patients, which will permit investigation of initial indicators of the course and outcome of schizophrenia, as the longitudinal data is accumulating.

Over the long-term, The MIND Consortium will establish a federated database accessible from all participating sites. This, in turn, will permit the integration and cross-validation of clinical, cognitive, morphometric, and functional neuroimaging results gathered from unique samples of schizophrenia patients using a common investigational protocol across sites. By facilitating the integration of data obtained from multiple sites, the network will enable the exploration of relationships between variables that otherwise would obscure significant effects by adding to the variability and noise in the data. The proposed network will therefore support the primary clinical aims of this multi-site project: the identification of the neural substrates of the core cognitive deficits associated with schizophrenia, their link to the clinical features of the disorder and their alterations with disease progression and treatment.



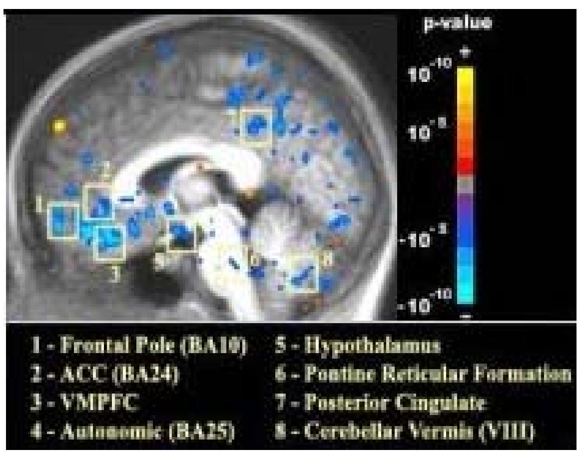
Reduced strategic processing during spatial working memory in schizophrenia: Brain regions, including areas of the prefrontal cortext that show a greater specialization for spatial working memory in healthy vs. schizophrenic subjects. (Manoach, et al, presented at the International Congress of Schizoprhenia Research, 2003.)

In addition, the MIND Institute continues to support the Athinoula A. Martinos Center-based neuroimaging work of several Boston area investigators in the field of schizophrenia research. This Boston Area Schizophrenia group includes psychiatrists, psychologists, radiologists, and anatomists from the MGH, Massachusetts Mental Helath Center, McLean Hospital and the Brockton VA Medical Center. Investigators Dara Manoach, Gina Kuperberg, Steve Stuffelbeam and Stephan Heckers at the MGH and McLean Hosptial are involved in investigations of prefrontal and temporofrontal function related to language and memory in schizophrenia. At the Brockton VA Hospital Bob McCarley's group continues their multimodal imaging and longitudinal work focused on temporal lobe neocortex, looking for relationships of functional and structural alterations to clinical symptomatology and for evidence of post-onset progression of brain abnormalities. Larry Seidman, Jill Goldstein and Ming Tsuang from the Massachusetts Mental Helath Center (MMHC) are pursuing studies of prefrontal and medial temporal lobe circuitry during working memory and verbal declarative memory, as risk indicators for schizophrenia during the adolescent period. All of this work has led to important contributions to the understanding of the cognitive and neurological pathology of schizophrenia (see the *Publications* section at the end of this report.)

Acupuncture Center of Excellence

Our on-going efforts to investigate the neural basis of acupuncture effects have been bolstered recently by the award of a “Center of Excellence for Research on Complementary and Alternative Medicine” grant from the National Center of Alternative and Complementary Medicine (NCCAM). Bruce Rosen is the Principal Investigator of this program project entitled *Neuroimaging Acupuncture Effects on Human Brain Activity*, the overall goal of which is to investigate in a rigorous and scientific way, the neurobiology of acupuncture. The project was initiated by Dr. Kathleen Hui, a Martinos Center investigator with a longtime clinical interest in acupuncture who feels that “for the healing art of acupuncture to be fully integrated into mainstream medicine, it needs to be examined within the evidence-based framework of the scientific method”.

To attain this goal, all three projects of this Center grant will investigate the possible brain pathways and circuitries involved in acupuncture. Project 1, headed by Dr. Hui, aims to define the central neural substrate of deqi, the acupuncture sensation that is related to clinical efficacy using high field fMRI and will compare the central effects of acupuncture for different treatment locations and different methods of stimulation. Project 2, under the direction of Iris Chen, PhD, will use animal models (rat and monkey) to investigate the fundamental neurochemical processes underlying the effects observed in the human neuroimaging studies, using invasive techniques of pharmacological MRI, PET and microdialysis. Project 3, is led by Randy Gollub, a psychiatrist, who will investigate whether and how acupuncture is different from placebo in a well-controlled mechanistic laboratory model. She will use quantitative brain imaging methods (fMRI and PET) to investigate the neurobiological mechanism of acupuncture analgesia, placebo analgesia, and their interrelationship. A final common theme across the three projects will be to investigate how the genotype of COMT (catechol-O-methyltransferase) an enzyme responsible for dopamine breakdown, may play a role in acupuncture action. We hope this grant will provide new information to advance the science of acupuncture by mapping it’s central effects, exploring the role of dopaminergic modulation its efficacy, and setting new standards for how this ancient form of medicine is understood.



PROJECT 1: Parasagittal section of Manual acupuncture at St 36 with deqi showing synchronized signal decreases at multiple brain areas.

Phenotype Genotype Project for Depression and Addictions

The Office of National Drug Control Policy's Counterdrug Technology Assessment Center (CTAC) oversees the counterdrug research and development programs of the USA's federal drug control agencies. CTAC's drug "demand reduction" program supports the National Drug Control Strategy by expanding the understanding of substance abuse and addiction in part through the funding of neuroimaging technology and research.

The ONDCP and CTAC have awarded $8 million dollars in funding to a large-scale proof-of-concept project proposed by Athinoula A. Martinos Center investigator, Hans Breiter, MD, to develop the experimental infrastructure to link alterations in specific brain circuits associated with addiction and related disorders such as depression, to the genes that confer susceptibilities to them. The goal of this research is to understand the genetic basis underlying brain circuitry alterations that confer susceptibility and resistance to cocaine (and nicotine) dependence and/or mood disorders in humans.

The study will employ neuroimaging profiles as *endophenotypes* for subsequent whole genome screens. Endophenotypes are heritable quantitative biological traits that provide a measure of an individual's risk of developing a disease but are not a hallmark of disease progression itself. The PGP for Addiction and Depression will link alterations in specific brain circuits associated with these neuropsychiatric diseases to the genes that confer susceptibilities to them. The project aims to characterize quantitative differences in brain reward/aversion circuitry structure and function (circuitry-based endophenotypes) that segregate in families with these illnesses and to identify the genetic basis of these susceptibilities.

The project will build on the use of functional imaging paradigms to target neural circuitry that has been implicated in addictions and depression in previous pioneering work at the Martinos Center and will incorporate several structural imaging techniques developed by different groups at the Center. Close to 900 subjects will participate in this ambitious, first-of-its-kind, three-year project including cocaine-dependent individuals, patients with recurrent major depressive disorder and unaffected family members of the probands.

NEW IMAGING EQUIPMENT ENABLES NEW IMAGING TECHNIQUES

We have acquired two important new imaging systems to spearhead the Center's molecular imaging initiative, a 14 Tesla vertical bore imager/spectrometer (which arrived at the Center just in time be pictured in last year's Annual Report), and a Concorde MicroPET small animal PET imaging system, also acquired late last year. With these two systems, Athinoula A. Martinos Center researchers are already conducting promising research using both PET- and MR–based molecular imaging techniques targeted at improving the understanding, diagnosis and treatment of diseases like stroke, cancer, Huntington's disease, Parkinson's disease and drug addiction.

14 Tesla MR System: Chemical Exchange Saturation Transfer (CEST) Molecular Imaging

Molecular imaging is a very powerful technique for studying molecular events such as cell signaling, gene delivery, protein expression, and cell growth *in vivo*. Traditional MRI molecular imaging techniques rely on an image contrast agent being delivered to a site in the body and specifically interacting with a particular molecule of interest at that destination. The poor sensitivity of these techniques makes detection of these contrast agents difficult, particularly in the brain, which has a natural barrier to exogenous chemicals.

A new technique known as Chemical Exchange Saturation Transfer (CEST), first described by Balaban and coworkers at the National Institutes of Health in 2000, and currently being developed at the Martinos Center for Biomedical Imaging, may provide a powerful new tool for MRI molecular imaging. In concept, CEST has three big advantages over traditional molecular imaging techniques: First, the endogenous molecules of interest, in some cases, can be directly detected, eliminating the need for contrast agent to be delivered to, and to specifically react with, the molecule of interest. Second, the image contrast is controlled with radio-frequency (RF) pulses and can be turned on and off at will. The location of specific molecules of interest can then be detected by comparing images with the contrast turned on to those where it is turned off. Finally, CEST is far more sensitive than traditional molecular imaging techniques and is able to detect even extremely small concentrations of particular molecules.

Dr. Christian Farrar is a chemist by training, who came to the Martinos Center two years ago with an interest in changing his research focus from studying biological events on the atomic scale (protein structure/function studies) to the cellular and organismal scale using MRI molecular imaging techniques. He is currently a postdoctoral fellow working with Dr. Bruce Rosen. Dr. Farrar and Dr. Young Kim, another postdoc in Dr. Rosen's lab, have begun *ex vivo* studies using CEST to detect the amino acid arginine.

Figure 1, below, shows images of a tube of this amino acid dissolved in water. In image (a), the contrast is "turned on" by saturating the amide proton resonance of arginine. Image (b) is a comparison image with the pulse sequence not set to detect arginine. Image (c) shows the difference of these two images and the location of the arginine concentrations. Dr. Farrar and Dr. Kim have also recently begun to investigate the use of CEST *in vivo,* to detect molecular changes in the brain following stroke in a mouse model. This work is funded in part by the MIND Institute.

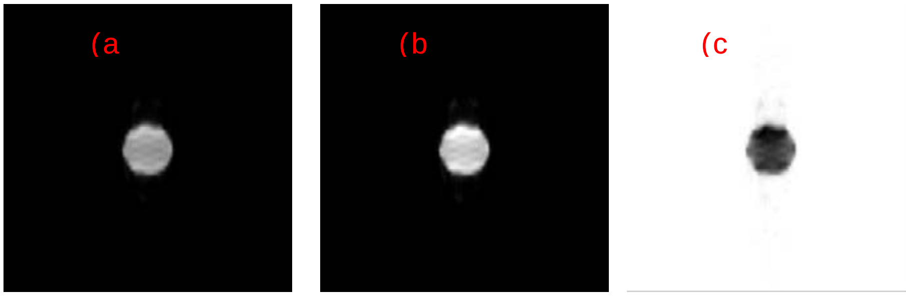


Figure 1: 14 Tesla FLASH MRI images of a 10 mm tube of arginine in water. (a) FLASH image acquired with a presaturation RF pulse applied with a frequency offset of +3 ppm from the water signal, corresponding to the amide proton resonance position; (b) FLASH image acquired with a presaturation RF pulse applied with a frequency offset of -3 ppm from the water signal, used as a control for the CEST effect; (c) Difference image (a-b) demonstrating the attenuation of the water signal due to the CEST effect.

Molecular and Cellular Imaging: MicroPET

This was an extremely productive year in the Experimental PET laboratory, headed by Dr. Anna-Liisa Brownell. With the arrival of the new MicroPET imager, several projects with collaborators from the MGH and McLean Hospital are off to a great start.

As part of a National Institute on Neurological Disease and Stroke (NINDS) Udall Parkinson's Disease Center of Excellence grant, Dr. Browell's team, in collaboration with Dr. Ole Isacson of McLean Hospital has been conducting studies to evaluate transplantation of embryonic stem cells for transplantation therapy for in rodent and primate models of neurodegenerative diseases like Parkinson's disease. This group was able to demonstrate differentiation of the transplanted embryonic stem cells to dopaminergic cells in a primate striatum, an area of the brain where dopamine depletion leads to many of the debilitating symptoms of this disease. The new MicroPET scanner, which allows simpler and more accurate co-registration with MRI data than previously possible, played a key role in the success of these studies.

Drs. Bruce Rosen, Barry Kosofsky and Bruce Jenkins as part of their National Institute on Drug Abuse supported Cocaine Program Project grant also used the new MicroPET system to investigate the brain mechanisms involved in the process of becoming addicted to cocaine. Their PET imaging studies showed that cocaine abuse resulted in decreased striatal dopamine transporter and D2 dopamine receptor function. While this research is just part of a growing body of evidence suggesting that D2 receptors play a major role in abuse of a number of drugs such as cocaine and methamphetamine, it is still not known whether the consequences of such a change are more important among the pre-synaptic D2 autoreceptors, which tend to antagonize dopamine action, or post-synaptic D2 receptors which enhance it. Obviously, the implications of this information are important for the understanding and treatment of substance abuse. Further exploration of this question is now underway at the Martinos Center and will be the focus of the resubmission of this important program project grant in October.

PET imaging has also allowed us, in collaboration with Dr. Kenneth Tanabe of MGH Oncolcogical Surgery Unit, to ask questions regarding cell functions that relate to cancer and to explore possibilities for new oncology therapies. Replication-competent viruses may be exploited for caner gene therapy because viral replication within cancer cells results in their destruction. These viruses selectively replicate in and destroy cancer cells rather than normal cells following intravascular administration. We have begun to explore this procedure, known as viral oncolysis, as a treatment for certain types of cancer. Drs. Taube and Brownell were able to image the replication of several mutations of these viruses in tumors by developing two new radioligands to evaluate proliferative potential in targeted cells. It is our hope that these imaging methods will speed the development of viral oncolysis techniques so that they may be used in clinical treatment evaluation within the next year or two.

EVENTS

BIOMAG 2004

The 14th biennial BIOMAG conference will be held in Boston this August and hosted by Athinoula A. Martinos Center for Biomedical Imaging investigators. This is *the* international conference for all scientists interested in biomagnetism - the study of magnetic fields produced by brains, hearts and other organs. The meeting will be held in the USA this year for the first time in almost a decade, after being held most recently in Germany, Finland and Japan.

The meeting will feature poster sessions, symposia and workshops addressing all aspects of biomagnetism and the use of magnetoencephalography (MEG) and other technologies that directly relate to biomagnetism such as some aspects of EEG, transcranial magnetic stimulation and MRI. Highlights will include sessions on fields evoked by sensory, motor, language and cognitive processes, forward and inverse methods, novel analysis techniques and instrumentation, applications to understanding and diagnosing neuropsychiatric and cardiac disease, and fetal measurements. The agenda includes poster presentations from contributed abstracts, educational symposia on several key topics featuring three to five invited speakers each, and interactive workshops and discussion groups. Attendance is expected to exceed 600 people, making this the best-attended BIOMAG event to date! The conference co-chairpersons are our own Drs. Jack Belliveau, David Cohen, Eric Halgren, Matti Hämäläinen.

Software Developers Summit

The Martinos Center and it's Regional Resource Grant, the Center for Functional Neuroimaging Technologies will present a Multimodal Imaging Software Developers

Summit this July at the historic Longfellow's Wayside Inn in Sudbury, MA. This will be the first official "meeting-of-the-minds" of the individuals at the Martinos Center involved in the development of software for functional MRI, MEG, EEG and Optical Imaging. The purpose of the summit is to compare and share information about existing software under parallel development, to examine commonalities and differences in the data processing needs of the various imaging modalities, and to explore possibilities for the integration of data and of analysis tools across imaging modalities. The agenda includes working sessions on a) the state of the art of current software tools for data collection and processing for the different imaging modalities, b) *Algorithmic Cross Fertilization and Common Platform Integration* involving considerations in the development of shared software across imaging modalities, and c) planning software for integration of multimodal imaging data collected simultaneously vs. in parallel. This summit will lead to priority setting and action planning for the Center's pioneering multimodal imaging challenges.

EDUCATIONAL INITIATIVES

Graduate Training in Psychology and Neuroimaging

Drs. Bruce Rosen and Moshe Bar of the Athinoula A. Martinos Center for Biomedical Imaging, and Dr. Stephen Kosslyn of the Harvard Psychology Department have developed a program to train graduate students of Psychology to use neuroimaging to investigate the workings of the brain and mind. This innovative new collaborative training program will prepare future cognitive neuroscientists to address key issues in psychology using behavioral methods in combination with cutting-edge neuroimaging techniques such as functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), electroencephalography (EEG), positron emission tomography (PET), and near-infrared spectrography (NIRS).

This demanding 5-year program was recently awarded funding by the National Institute of Mental Health, and will enroll its first students in September. Participating in the program will be 22 faculty members, half each from the Psychology Department at Harvard University and the Athinoula A. Martinos Center for Biomedical Imaging. Throughout their training, students will be co-advised by a pair of faculty members from each institution. Students will be admitted into a division in the Psychology Department and will be expected to fulfill the requirements of that specific division, including first-year, second-year and Ph.D. thesis research projects. In addition, every trainee will take two team-taught courses in their first two years: a course in Cognition, Brain and Behavior (taught by all the training faculty in psychology and faculty in cognitive psychology at the Martinos Center) and an intensive introduction to functional brain imaging (taught by training and other faculty from the Martinos Center). In subsequent years, trainees will enroll in a research seminar jointly taught by all faculty. Students will explore particular areas of cognitive and brain function in depth, develop skills for crafting experiments that dissect specific cognitive functions, present their research, and interact with other trainees in the program and at the Martinos Center. The goal of these requirements is to impart knowledge that is both broad and deep, about the human brain and about the cognitive functions that it performs. This program will bring exceptional new graduate students of psychology to the Martinos Center and we anticipate the development of many interesting intellectual collaborations between Martinos Center and Harvard Psychology faculty.

NEW RESEARCH FUNDING

Twenty-five new grants awarded to Martinos Center faculty were activated during this reporting period. Of these, twenty-two are federally funded, two are supported by private research foundations and one is industry sponsored (General Electric). Five of these grants are for training students and junior investigators, two are large Program or Center type grants, three are for capital equipment, and one is a small business innovative research (SBIR) program grant. Over the next five years, these grants together will bring close to $20 million in direct cost research dollars to the Martinos Center. Fifty-five new grant applications submitted this year are still pending. These numbers *do not* include grants awarded to our many collaborators and users of the Center's imaging equipment and technology based in other MGH departments and at other (non-MGH) institutions.

Below is a list of currently active grants awarded to core Martinos Center faculty. This represents much of the ongoing research at the Center.

Principal Investigator	**Grant Title**	**Sponsor**	**Agency**	**Mech.**
Aharon	Face Overgeneralization, Prejudice, and Stereotypes	NIH		R01
Aharon	Collaborative Research: Neuroscience of Self-Control	NSF	-	-
Aharon	Predicting Trait Impressions of Faces and Their Activations of Artificial Network for Human Brain Activities	NSF	-	-
Ahlfors	Optimization of combined source estimation methods for MEG/EEG and fMRI studies of brain activity in normal and clinical populations.	Whitaker Foundation	-	-
Bar	Revealing the perceptual and neural mechanisms of first impressions	MCDONNELL FOUNDATION	-	-
Bar	Top Down Cortical Facilitation	NIH	NINDS	R01
Belliveau	Spatiotemporal Brain Imaging Human Auditory Cognition	NIH	NICHHD	R01
Belliveau	Spatiotemporal Imaging of Human Visual System Processing	NIH	NINDS	R01
Boas	Advanced Technology for Ultra High Resolution Stuctural and Functional Imaging using Optical Coherence Tomography	Airforce/MIT	-	-
Boas	3D Optical Imaging and Digital X ray of Breast Lesions	NIH	NCI	R01

Boas	Breast Cancer Multi-Dimensional Diffuse Optical Imaging	NIH	NCI	U54
Boas	Imaging CMR02 with Combined DOT and MRI	NIH	NIBIB	R01
Boas	Engineering Research Subsurface Sensing & Imaging Systems (subcontract)	NSF	-	-
Bonmassar	Concurrent EEG and fMRI Studies of Human Brain Activity	NIH	NIBIB	R01
Bonmassar	EEG data Monitoring System used in Conjunction with fMRI	NIH	NIMH	SBIR
Bonmassar	Functional Imaging in Clinical Epilepsy	NIH	-	-
Brady	Nuclear Magnetic Resonance Research	NIH	NCI	T32
Breiter	Cocaine Addiction: Alternations in Reward Circuitry	NIH	NIDA	R01
Breiter	Cognitive, Pharmacological and fMRI studies of memory	NIH	NINDS	R01
Breiter	Validating High Field Functional and Structural MRI and Circuitry - Based Phenotyping to Drive Genotyping of Heritable Componets Leading to Cocaine Addiction and Mood Disorders	ONDCP	-	-
Brown	Statistical Analysis of Hippocampal Information encoding	NIH	NIMH	R01
Brown	Statistical Modeling of Neural Information Encoding	NIH	NIMH	R01
Brownell	Novel approaches to anti inflammatory Therapies	NIH	NINDS	R01
Dale	Spatiotemporal Brain Imaging: Microscopic and Systems Level	NIH	NIBID	R01
Dunn	Invivo Spatiotemporal Optical Imaging of Focal Ischemia	NIH	NINDS	K25
Fischl	Computeserver: Structural & Functional Image Analysis	NIH	NCRR	S10
Fischl	CRNS High Resolution Imaging and Modeling of Human Visual Cortex	NIH	NIBIB	R01
Fischl	Family Study of Psychosis Brain Genes & Prenatal Risk	NIH	NIMH	R01
Fischl	The VESTA Longitudinal MRI Twin Study of Aging	NIH	NIA	-
Fischl	Automated Analysis of Healthy and Diseased Brain Tissue	NIH	NCRR	R01
Franceschini	Optical monitoring of Cerebral Oxygenation in Infants	NIH	NICHD	R01
Giovanello	Age associated non-selective neural activation in episodic memory	NIH	NIA	F32
Goodman	Functional Brain Mapping of the Human Auditory Cortical Areas	NIH	NINDS	R01
Grant	Human Perinatal Brain Injury and Outcome:MRI Assessment	NIH	NINDS	K23

Gupta	Statistical Model of Face and Skull from CT Images	GENERAL ELECTRIC	-	-
Hadjikhani	Visual Social Cognition in Neurodevelopmental Disorders	NIH	NINDS	R01
Halgren	Neural Electromagnetic Hemodynamic Links in Humans 2	NIH	NINDS	R01
Halgren	Neural Generators of Endogenous Potentials in Humans	NIH	NINDS	R01
Halgren	Cognition and Action	NIH	NIMH	R01
Halgren	Neural Basis of Endogenous Potentials in Humans	NIH	NINDS	R01
Hochberg	Gene therapy for brain tumors	NIH	NCI	P01
Hui	Modulatory Effect of Acupuncture in Human Brain Activity	NIH	NCCAM	R21
Jenkins	Glutamate Metabolism And the Effects of Creatine Neuroprotection in FALS Mice	ALS Association	-	-
Jenkins	Imaging Dopamine - Mediated neurovascular coupling	NIH	NIDA	R01
Jenkins	Translational Imaging of Methylphenidate Exposure	NIH	NIDA	I-START
Mandeville	Iron fMRI: Improving Sensitivity and localization	NIH	NIBIB	R01
Mandeville	MRI Measurement of Relative CMR02: Validation using PET	NIH	NCRR	R01
Manoach	fMRI and TMS Studies of Working Mmory in Schizophrenia	NIH	NIMH	K01
Marenkovic	Alcohol and Multimodal Brain Imaging	NIH	NIAAA	K01
Moore	In Vivo MR Imaging of Insulitis in Autoimmune Diabetes	American Diabetes Foundation	-	-
Moore	High Resolution In vivo MR Imaging of Type 1 Diabetes Progression	Juvenile Diabetes Research Foundation	-	-
Moore	In Vivo Imaging of Autoimmune Attack in Type 1 Diabetes	NIH	NIDDK	R01
Moore	In Vivo Imaging of Disbetogenic Cytotoxic T-Lymphocytes	NIH	NIDDK	R01
Moore	Novel Multu-Modal Probes for In-Vivo Cance Imaging	NIH	NCI	R21
Moskowitz	Interdepartmental Stroke Program	NIH	NINDS	P50
Moskowitz	Migraine Pathophysiology and Treatment Mechanisms	NIH	NINDS	P01
Napadow	Exploring Neurocircuitry of Acupuncture Action with fMRI	NIH	NCCAM	K01
Poncelet	In Vivo Measurement of Myocardial Oxygen consumption	NIH	NHLBI	R01
Rajadhyaksha	Amphetamine Mediated CREB Phosphorylation & Gene Expression	NIH	NIDA	K01

Rauch	Basal Ganglia function in obsessive compulsive disorder	NIH	NIMH	R01
Rosen	Spatiotemporal Activation maps of Human Cortex by integrating MEG with MRI	MIND Institute	-	-
Rosen	Center for Functional Imaging Technologies	NIH	NCRR	P41
Rosen	Cholinergic Enhancement of Human Cortical Plasticity	NIH	NINDS	R21
Rosen	Cognitive Change in HIV: A FMRI Study	NIH	NINDS	R01
Rosen	Cyclotron & Radiochemistry Modules (SIG)	NIH	NCRR	S10
Rosen	Functional Brain Mapping of Cocaine Action	NIH	NIDA	P01
Rosen	MEMP Neuroimaging Training Program	NIH	NIBIB	T32
Rosen	Neuroimaging Acupuncture Effects on Human Brain Activity	NIH	NCCAM	P01
Rosen	Perfusion Imaging with Magnetic Resonance	NIH	NHLBI	R01
Salat	Diffusion Tensor Imaging of White Matter Change in AD	NIH	NIA	K01
Schaechter	fMRI and TMS of Motor Recovery after Hemiparetic Stroke	NIH	NINDS	K23
Sorensen	Diffusion Tensor and Functional Imaging of the Thalamus in Schizophrenia	Glaxo Smithkline	-	
Sorensen	MRI Diffusion/Perfusion Mismatch in Human Acute Stroke	NIH	NINDS	R01
Sorensen	A 3.0 Tesla MRI System in a Neuroscience ICU	NIH	NCRR	S10
Tootell	fMRI and neuronal Activity in awake behaving macaques	NIH	NIMH	R01
Tuch	Mapping the Cortical Connectivity of Macaque with MRI	NIH	NINDS	K25
van der Kouwe	Online MRI Positioning and Real-Time Motion Correction	NIH	NIBIB	R21
Vanduffel	Interactions Between Areas of the Visual Cortex	HFSP	-	-
Wagner	Brain Injury Memory Disorders Research Center	NIH	NINDS	P50
Wagner	Event Related Neuroimaging of Human Memory Formation	NIH	NIMH	R01
Wedeen	Diffusion MRI of Complex White Matter and Connectivity	NIH	NIMH	R01
West	Spatiotemporal Imaging of Semantic Processing	NIH	NIMH	K01

PUBLICATIONS

Below is a sampling of journal articles published by Athinoula A. Martinos Center for Biomedical Imaging investigators and collaborators since our last annual report.

Cancer

Mansury, Y. and T. S. Deisboeck (2003). "The impact of "search precision" in an agent-based tumor model." J Theor Biol 224(3): 325-37.

Moore, A., Z. Medarova, A. Potthast and G. Dai (2004). "In vivo targeting of underglycosylated MUC-1 tumor antigen using a multimodal imaging probe." Cancer Res 64(5): 1821-7.

Cardiovascular Imaging

Dou, J., W. Y. Tseng, T. G. Reese and V. J. Wedeen (2003). "Combined diffusion and strain MRI reveals structure and function of human myocardial laminar sheets in vivo." Magn Reson Med 50(1): 107-13.

Hinton, D. P., L. L. Wald, J. Pitts and F. Schmitt (2003). "Comparison of cardiac MRI on 1.5 and 3.0 Tesla clinical whole body systems." Invest Radiol 38(7): 436-42.

Cognitive, Emotional and Behavioral Neuroscience

Bar, M. (2003). "A cortical mechanism for triggering top-down facilitation in visual object recognition." J Cogn Neurosci 15(4): 600-9.

Clark, D. and A. D. Wagner (2003). "Assembling and encoding word representations: fMRI subsequent memory effects implicate a role for phonological control." Neuropsychologia 41(3): 304-17.

Cox, D. D. and R. L. Savoy (2003). "Functional magnetic resonance imaging (fMRI) "brain reading": detecting and classifying distributed patterns of fMRI activity in human visual cortex." Neuroimage 19(2 Pt 1): 261-70.

Dhond, R. P., K. Marinkovic, A. M. Dale, T. Witzel and E. Halgren (2003). "Spatiotemporal maps of past-tense verb inflection." Neuroimage 19(1): 91-100.

Dobbins, I. G., H. J. Rice, A. D. Wagner and D. L. Schacter (2003). "Memory orientation and success: separable neurocognitive components underlying episodic recognition." Neuropsychologia 41(3): 318-33.

Dobbins, I. G., D. M. Schnyer, M. Verfaellie and D. L. Schacter (2004). "Cortical activity reductions during repetition priming can result from rapid response learning." Nature 428(6980): 316-9.

Grill-Spector, K., N. Knouf and N. Kanwisher (2004). "The fusiform face area subserves face perception, not generic within-category identification." Nat Neurosci.

Hadjikhani, N. and B. de Gelder (2003). "Seeing fearful body expressions activates the fusiform cortex and amygdala." Curr Biol 13(24): 2201-5.

Jaaskelainen, I. P., J. Ahveninen, G. Bonmassar, A. M. Dale, R. J. Ilmoniemi, S. Levanen, F. H. Lin, P. May, J. Melcher, S. Stufflebeam, H. Tiitinen and J. W. Belliveau (2004). "Human posterior auditory cortex gates novel sounds to consciousness." Proc Natl Acad Sci U S A.

Jackson, O., 3rd and D. L. Schacter (2004). "Encoding activity in anterior medial temporal lobe supports subsequent associative recognition." Neuroimage 21(1): 456-62.

Jiang, Y. and N. Kanwisher (2003). "Common neural substrates for response selection across modalities and mapping paradigms." J Cogn Neurosci 15(8): 1080-94.

Jiang, Y. and N. Kanwisher (2003). "Common neural mechanisms for response selection and perceptual processing." J Cogn Neurosci 15(8): 1095-110.

Kensinger, E. A., S. Siri, S. F. Cappa and S. Corkin (2003). "Role of the anterior temporal lobe in repetition and semantic priming: evidence from a patient with a category-specific deficit." Neuropsychologia 41(1): 71-84.

Kensinger, E. A. and S. Corkin (2004). "Two routes to emotional memory: distinct neural processes for valence and arousal." Proc Natl Acad Sci U S A 101(9): 3310-5.

Kosslyn, S. M. and W. L. Thompson (2003). "When is early visual cortex activated during visual mental imagery?" Psychol Bull 129(5): 723-46.

Manoach, D. S., D. N. Greve, K. A. Lindgren and A. M. Dale (2003). "Identifying regional activity associated with temporally separated components of working memory using event-related functional MRI." Neuroimage 20(3): 1670-84.

Manoach, D. S., N. S. White, K. A. Lindgren, S. Heckers, M. J. Coleman, S. Dubal and P. S. Holzman (2004). "Hemispheric specialization of the lateral prefrontal cortex for strategic processing during spatial and shape working memory." Neuroimage 21(3): 894-903.

Marinkovic, K. (2004). "Spatiotemporal dynamics of word processing in the human cortex." Neuroscientist 10(2): 142-52.

Marinkovic, K., E. Halgren and I. Maltzman (2004). "Effects of alcohol on verbal processing: an event-related potential study." Alcohol Clin Exp Res 28(3): 415-23.

Marinkovic, K., R. P. Dhond, A. M. Dale, M. Glessner, V. Carr and E. Halgren (2003). "Spatiotemporal dynamics of modality-specific and supramodal word processing." Neuron 38(3): 487-97.

Saxe, R., S. Carey and N. Kanwisher (2004). "Understanding other minds: linking developmental psychology and functional neuroimaging." Annu Rev Psychol 55: 87-124.

Simons, J. S., W. Koutstaal, S. Prince, A. D. Wagner and D. L. Schacter (2003). "Neural mechanisms of visual object priming: evidence for perceptual and semantic distinctions in fusiform cortex." Neuroimage 19(3): 613-26.

Sperling, R., E. Chua, A. Cocchiarella, E. Rand-Giovannetti, R. Poldrack, D. L. Schacter and M. Albert (2003). "Putting names to faces: successful encoding of associative memories activates the anterior hippocampal formation." Neuroimage 20(2): 1400-10.

Tootell, R. B., D. Tsao and W. Vanduffel (2003). "Neuroimaging weighs in: humans meet macaques in "primate" visual cortex." J Neurosci 23(10): 3981-9.

Tsao, D. Y., W. A. Freiwald, T. A. Knutsen, J. B. Mandeville and R. B. Tootell (2003). "Faces and objects in macaque cerebral cortex." Nat Neurosci 6(9): 989-95.

Tsao, D. Y., W. Vanduffel, Y. Sasaki, D. Fize, T. A. Knutsen, J. B. Mandeville, L. L. Wald, A. M. Dale, B. R. Rosen, D. C. Van Essen, M. S. Livingstone, G. A. Orban and R. B. Tootell (2003). "Stereopsis activates V3A and caudal intraparietal areas in macaques and humans." Neuron 39(3): 555-68.

Wright, C. I., B. Martis, K. McMullin, L. M. Shin and S. L. Rauch (2003). "Amygdala and insular responses to emotionally valenced human faces in small animal specific phobia." Biol Psychiatry 54(10): 1067-76.

Computational Neuroanatomy

Fischl, B., A. van der Kouwe, C. Destrieux, E. Halgren, F. Segonne, D. H. Salat, E. Busa, L. J. Seidman, J. Goldstein, D. Kennedy, V. Caviness, N. Makris, B. Rosen and A. M. Dale (2004). "Automatically parcellating the human cerebral cortex." Cereb Cortex 14(1): 11-22.

Makris, N., S. M. Hodge, C. Haselgrove, D. N. Kennedy, A. Dale, B. Fischl, B. R. Rosen, G. Harris, V. S. Caviness, Jr. and J. D. Schmahmann (2003). "Human cerebellum: surface-assisted cortical parcellation and volumetry with magnetic resonance imaging." J Cogn Neurosci 15(4): 584-99.

Salat, D. H., R. L. Buckner, A. Z. Snyder, D. N. Greve, R. S. Desikan, E. Busa, J. C. Morris, A. M. Dale and B. Fischl (2004). "Thinning of the Cerebral Cortex in Aging." Cereb Cortex.

Wiegell, M. R., D. S. Tuch, H. B. Larsson and V. J. Wedeen (2003). "Automatic segmentation of thalamic nuclei from diffusion tensor magnetic resonance imaging." Neuroimage 19(2 Pt 1): 391-401.

Imaging Technique & Technology Development

Angelone, L. M., A. Potthast, F. Segonne, S. Iwaki, J. W. Belliveau and G. Bonmassar (2004). "Metallic electrodes and leads in simultaneous EEG-MRI: Specific absorption rate (SAR) simulation studies." Bioelectromagnetics 25(4): 285-95.

Bamett, A. H., J. P. Culver, A. G. Sorensen, A. Dale and D. A. Boas (2003). "Robust inference of baseline optical properties of the human head with three-dimensional segmentation from magnetic resonance imaging." Appl Opt 42(16): 3095-108.

Culver, J. P., A. M. Siegel, J. J. Stott and D. A. Boas (2003). "Volumetric diffuse optical tomography of brain activity." Opt Lett 28(21): 2061-3.

Franceschini, M. A. and D. A. Boas (2004). "Noninvasive measurement of neuronal activity with near-infrared optical imaging." Neuroimage 21(1): 372-86.

Franceschini, M. A., S. Fantini, J. H. Thompson, J. P. Culver and D. A. Boas (2003). "Hemodynamic evoked response of the sensorimotor cortex measured noninvasively with near-infrared optical imaging." Psychophysiology 40(4): 548-60.

Huisman, T. A. and A. G. Sorensen (2003). "Perfusion-weighted magnetic resonance imaging of the brain: techniques and application in children." Eur Radiol.

Kilmer, M. E., E. L. Miller, A. Barbaro and D. Boas (2003). "Three-dimensional shape-based imaging of absorption perturbation for diffuse optical tomography." Appl Opt 42(16): 3129-44.

Li, A., Q. Zhang, J. P. Culver, E. L. Miller and D. A. Boas (2004). "Reconstructing chromosphere concentration images directly by continuous-wave diffuse optical tomography." Opt Lett 29(3): 256-8.

Lin, C. P., V. J. Wedeen, J. H. Chen, C. Yao and W. Y. Tseng (2003). "Validation of diffusion spectrum magnetic resonance imaging with manganese-enhanced rat optic tracts and ex vivo phantoms." Neuroimage 19(3): 482-95.

Lin, F. H., Y. J. Chen, J. W. Belliveau and L. L. Wald (2003). "A wavelet-based approximation of surface coil sensitivity profiles for correction of image intensity inhomogeneity and parallel imaging reconstruction." Hum Brain Mapp 19(2): 96-111.

Lin, F. H., K. K. Kwong, I. J. Huang, J. W. Belliveau and L. L. Wald (2003). "Degenerate mode birdcage volume coil for sensitivity-encoded imaging." Magn Reson Med 50(5): 1107-11.

Lin, F. H., A. R. McIntosh, J. A. Agnew, G. F. Eden, T. A. Zeffiro and J. W. Belliveau (2003). "Multivariate analysis of neuronal interactions in the generalized partial least squares framework: simulations and empirical studies." Neuroimage 20(2): 625-42.

Siegel, A. M., J. P. Culver, J. B. Mandeville and D. A. Boas (2003). "Temporal comparison of functional brain imaging with diffuse optical tomography and fMRI during rat forepaw stimulation." Phys Med Biol 48(10): 1391-403.

Smith, J. J., A. G. Sorensen and J. H. Thrall (2003). "Biomarkers in imaging: realizing radiology's future." Radiology 227(3): 633-8.

Stott, J. J., J. P. Culver, S. R. Arridge and D. A. Boas (2003). "Optode positional calibration in diffuse optical tomography." Appl Opt 42(16): 3154-62.

Tuch, D. S., T. G. Reese, M. R. Wiegell and V. J. Wedeen (2003). "Diffusion MRI of complex neural architecture." Neuron 40(5): 885-95.

van der Kouwe, A. J. and R. C. Burgess (2003). "Neurointensive care unit system for continuous electrophysiological monitoring with remote web-based review." IEEE Trans Inf Technol Biomed 7(2): 130-40.

Wu, O., L. Ostergaard, W. J. Koroshetz, L. H. Schwamm, J. O'Donnell, P. W. Schaefer, B. R. Rosen, R. M. Weisskoff and A. G. Sorensen (2003). "Effects of tracer arrival time on flow estimates in MR perfusion-weighted imaging." Magn Reson Med 50(4): 856-64.

Wu, O., L. Ostergaard, R. M. Weisskoff, T. Benner, B. R. Rosen and A. G. Sorensen (2003). "Tracer arrival timing-insensitive technique for estimating flow in MR perfusion-weighted imaging using singular value decomposition with a block-circulant deconvolution matrix." Magn Reson Med 50(1): 164-74.

Neurologic and Psychiatric Disorders

Brownell, A. L., K. Canales, Y. I. Chen, B. G. Jenkins, C. Owen, E. Livni, M. Yu, F. Cicchetti, R. Sanchez-Pernaute and O. Isacson (2003). "Mapping of brain function after MPTP-induced neurotoxicity in a primate Parkinson's disease model." Neuroimage 20(2): 1064-75.

Hadjikhani, N., C. F. Chabris, R. M. Joseph, J. Clark, L. McGrath, I. Aharon, E. Feczko, H. Tager-Flusberg and G. J. Harris (2004). "Early visual cortex organization in autism: an fMRI study." Neuroreport 15(2): 267-70.

Heckers S, Weiss AP, Deckersbach T, Goff DC, Morecraft RJ, Bush G. Anterior cingulate cortex activation during cognitive interference in schizophrenia. Am J Psychiatry. 2004 Apr;161(4):707-15.

Kuperberg, G. R., M. R. Broome, P. K. McGuire, A. S. David, M. Eddy, F. Ozawa, D. Goff, W. C. West, S. C. Williams, A. J. van der Kouwe, D. H. Salat, A. M. Dale and B. Fischl (2003). "Regionally localized thinning of the cerebral cortex in schizophrenia." Arch Gen Psychiatry 60(9): 878-88.

Kuperberg GR, Sitnikova T, Caplan D, Holcomb PJ. Electrophysiological distinctions in processing conceptual relationships within simple sentences. Brain Res Cogn Brain Res. 2003 Jun;17(1):117-29.

Manoach DS, Greve DN, Lindgren KA, Dale AM. Identifying regional activity associated with temporally separated components of working memory using event-related functional MRI. Neuroimage. 2003 Nov;20(3):1670-84.

Manoach DS, White NS, Lindgren KA, Heckers S, Coleman MJ, Dubal S, Holzman PS. Hemispheric specialization of the lateral prefrontal cortex for strategic processing during spatial and shape working memory. Neuroimage. 2004 Mar;21(3):894-903.

Rosas, H. D., W. J. Koroshetz, Y. I. Chen, C. Skeuse, M. Vangel, M. E. Cudkowicz, K. Caplan, K. Marek, L. J. Seidman, N. Makris, B. G. Jenkins and J. M. Goldstein (2003). "Evidence for more widespread cerebral pathology in early HD: An MRI-based morphometric analysis." Neurology 60(10): 1615-20.

Rauch, S. L., L. M. Shin, E. Segal, R. K. Pitman, M. A. Carson, K. McMullin, P. J. Whalen and N. Makris (2003). "Selectively reduced regional cortical volumes in post-traumatic stress disorder." Neuroreport 14(7): 913-6.

Sailer, M., B. Fischl, D. Salat, C. Tempelmann, M. A. Schonfeld, E. Busa, N. Bodammer, H. J. Heinze and A. Dale (2003). "Focal thinning of the cerebral cortex in multiple sclerosis." Brain 126(Pt 8): 1734-44.

Schwartz, C. E., C. I. Wright, L. M. Shin, J. Kagan and S. L. Rauch (2003). "Inhibited and uninhibited infants "grown up": adult amygdalar response to novelty." Science 300(5627): 1952-3.

Schwartz, C. E., C. I. Wright, L. M. Shin, J. Kagan, P. J. Whalen, K. G. McMullin and S. L. Rauch (2003). "Differential amygdalar response to novel versus newly familiar neutral faces: a functional MRI probe developed for studying inhibited temperament." Biol Psychiatry 53(10): 854-62.

Seidman, L. J. and H. E. Wencel (2003). "Genetically mediated brain abnormalities in schizophrenia." Curr Psychiatry Rep 5(2): 135-44.

Seidman LJ, Valera EM, Bush G. Brain function and structure in adults with attention-deficit/hyperactivity disorder. Psychiatr Clin North Am. 2004 Jun;27(2):323-47.

Seidman LJ, Pantelis C, Keshavan MS, Faraone SV, Goldstein JM, Horton NJ, Makris N, Falkai P, Caviness VS, Tsuang MT. A review and new report of medial temporal lobe dysfunction as a vulnerability indicator for schizophrenia: a magnetic resonance imaging morphometric family study of the parahippocampal gyrus. Schizophr Bull. 2003;29(4):803-30.

Thermenos HW, Seidman LJ, Breiter H, Goldstein JM, Goodman JM, Poldrack R, Faraone SV, Tsuang MT. Functional magnetic resonance imaging during auditory verbal working memory in nonpsychotic relatives of persons with schizophrenia: a pilot study. Biol Psychiatry. 2004 Mar 1;55(5):490-500.

Neurovascular Disorders

Culver, J. P., T. Durduran, D. Furuya, C. Cheung, J. H. Greenberg and A. G. Yodh (2003). "Diffuse optical tomography of cerebral blood flow, oxygenation, and metabolism in rat during focal ischemia." J Cereb Blood Flow Metab 23(8): 911-24.

Orthopedic Imaging

Cho, G., Y. Wu and J. L. Ackerman (2003). "Detection of hydroxyl ions in bone mineral by solid-state NMR spectroscopy." Science 300(5622): 1123-7.

Wu, Y., J. L. Ackerman, E. S. Strawich, C. Rey, H. M. Kim and M. J. Glimcher (2003). "Phosphate ions in bone: identification of a calcium-organic phosphate complex by 31P solid-state NMR spectroscopy at early stages of mineralization." Calcif Tissue Int 72(5): 610-26.

Pain

Becerra, L., M. Iadarola and D. Borsook (2004). "CNS activation by noxious heat to the hand or foot: site-dependent delay in sensory but not emotion circuitry." J Neurophysiol 91(1): 533-41.

Borsook, D., A. F. DaSilva, A. Ploghaus and L. Becerra (2003). "Specific and somatotopic functional magnetic resonance imaging activation in the trigeminal ganglion by brush and noxious heat." J Neurosci 23(21): 7897-903.

Ploghaus, A., L. Becerra, C. Borras and D. Borsook (2003). "Neural circuitry underlying pain modulation: expectation, hypnosis, placebo." Trends Cogn Sci 7(5): 197-200.

Signal Physiology

Boas, D. A., G. Strangman, J. P. Culver, R. D. Hoge, G. Jasdzewski, R. A. Poldrack, B. R. Rosen and J. B. Mandeville (2003). "Can the cerebral metabolic rate of oxygen be estimated with near-infrared spectroscopy?" Phys Med Biol 48(15): 2405-18.

Devor, A., A. K. Dunn, M. L. Andermann, I. Ulbert, D. A. Boas and A. M. Dale (2003). "Coupling of total hemoglobin concentration, oxygenation, and neural activity in rat somatosensory cortex." Neuron 39(2): 353-9.

Harms, M. P. and J. R. Melcher (2003). "Detection and quantification of a wide range of fMRI temporal responses using a physiologically-motivated basis set." Hum Brain Mapp 20(3): 168-83.

Jasdzewski, G., G. Strangman, J. Wagner, K. K. Kwong, R. A. Poldrack and D. A. Boas (2003). "Differences in the hemodynamic response to event-related motor and visual paradigms as measured by near-infrared spectroscopy." Neuroimage 20(1): 479-88.

Substance Abuse

Elman, I., S. E. Lukas, K. H. Karlsgodt, G. P. Gasic and H. C. Breiter (2003). "Acute cortisol administration triggers craving in individuals with cocaine dependence." Psychopharmacol Bull 37(3): 84-9.