

Annual Report of the Sackler Institute for Developmental Psychobiology
Weill Medical College of Cornell University

July 2005-July 2006

Under the continued direction of Dr. B.J. Casey, the Institute's international reputation in research and training on typical and atypical human brain development remains extremely high and the Institute is rapidly establishing a high profile in genomic research. Both the Institute's research and training programs emphasize genetic, imaging and behavioral methods. Select studies are highlighted in this report (see *Program of Research* and *Publications*). The faculty and fellows have received a number of grants and awards this year (See *Grants and Awards*) and the Institute continues to be home to several international and national faculty and fellows (See *Sackler National and International Fellows*) from England, Germany, Romania, The Netherlands and Finland. Training remains a priority at the Institute with an annual Summer Institute on the *Biology of Developmental Disabilities* and regularly organized meetings for fellows and junior faculty at the New York Academy of Sciences (see *Education, Training and Outreach*).

Academic Faculty and Staff

Sackler Faculty

Michael Posner, Ph.D., Director Emeritus

B.J. Casey, Ph.D., Director and Sackler Professor

James Swanson, Ph.D., Professor (Affiliation at Sackler and UC-Irvine)

Bruce D. McCandliss, Ph.D., Associate Professor of Psychology in Psychiatry

Dima Amso, Ph.D. Assistant Professor of Psychology in Psychiatry

John Fossella, Ph.D., Assistant Professor of Molecular Biology in Psychiatry

Nim Tottenham, Ph.D., Assistant Professor of Psychology in Psychiatry

Sackler Staff

Jason Buhle, Research Assistant

Alpana Choudhury, Research Assistant

Clayton Eccard, Institute Administrator

Jamie Ferri, Research Assistant

Alicia Galbraith, Research Assistant

Rebecca Gottlieb, Research Assistant

Eva Hulse, Research Assistant

Thomas McCarry, Research Assistant

Marcella Nurse, Research Assistant

Emmanuel Stein, IT Manager

Bruno Tagliaferri, Software Developer

National and International Fellows

Sackler Predoctoral Fellows

Adriana Galvin, Ph.D. student, Neuroscience

Todd Hare, Ph.D. student, Neuroscience

Conor Liston, M.D. Ph.D. student, Tri-Institutional Program

Sumit Niogi, Ph.D. student, Physiology
Yuliya Yoncheva, Ph.D. student, Neuroscience

Sackler Postdoctoral Fellows

Kevin Bath, PhD, Lasdon-Sackler Fellow
Barbara Ganzel, PhD, Cornell-Ithaca-Sackler Fellow
Minna Hannula, PhD, Sackler Fellow
Urs Maurer, PhD, Sackler Fellow
Jason Zevin, PhD, Sackler Fellow

International Sackler Scholars

Oana Benga, Babes-Bolyai University, Romania
Sarah Durston, University of Utrecht, The Netherlands
Annette Karmiloff-Smith, University College London, United Kingdom
Gaia Scerif, University of Nottingham, United Kingdom

Program of Research

This year, several empirical studies have been completed and published using the techniques of brain imaging, human genetics, electrophysiology, and behavioral methods, to study typical and atypical populations from childhood to adulthood (see Publications). Below, are highlights from a few of these studies representing three general domains of study: 1) studies of learning and development, 2) genomic investigations; and 3) clinical investigations.

Studies of Learning and Development

Behavioral and imaging studies of learning and development form the very foundation of the Institute's research program, laying the critical groundwork for genetic and clinical studies. The primary areas of research in this area encompass perceptual learning and development and motivational-based learning and development.

Object Learning in Infancy: Infants as young as 4 months show surprise when occluded moving objects fail to emerge from behind a static object. Extensive exposure with this task can move the age up for when the infant can perform this task. Dr. Dima Amso is using electrophysiological measures to constrain current developmental theory on how infants learn to recognize violations in expectations about objects that are occluded. Ultimately these measures may serve as early markers for learning disabilities. Preliminary findings are published in the *Proceedings of the National Academy of Sciences*.

Object Learning in Children: Faces are a special class of objects as humans have vast experiences with them over the life span. Dr. Nim Tottenham has found that children process faces faster than inanimate objects therefore suggesting that extensive experience with one class of objects can affect the speed of processing and explain developmental differences consistently found in the literature on face processing. Parallel imaging studies show that brain activity in the fusiform face area is enhanced in response to faces over other objects with age. Developmental disorders such as autism, in which faces appear to be processed differently, may be better

understood using information gained from this study. Preliminary findings from this work are published in *Developmental Science*.

Neural Basis of Statistical Learning: Dr. Dima Amso is examining the neural basis of statistical learning. This work is significant in the area of habituation and novelty preference studies in infants. The results show that the caudate nucleus appears to be involved in simple frequency-based learning (habituation) while the hippocampus appears to contribute to learning of associations between stimuli (novelty preferences). Dr. Amso is currently examining these abilities in infants and children using electrophysiological and magnetic resonance imaging methods. This work lays the groundwork for identification of learning disabilities early in life and forms the basis for a recent NIMH K01 submission. Preliminary findings are published in *Neuroimage*.

Development of Speech Perception in Children and Adults: Drs. Bruce McCandliss and Jason Zevin are examining the neural basis of language development, with a specific focus on the development of speech perception in American and Japanese native speakers. They are using functional neuroimaging to examine the neural basis for the finding that learning distinct sounds early in life depends on the degree of experience with these sounds. This work investigates the neural basis for the well-known changes in language learning that occur from childhood to adulthood, and seeks to develop broader neural theories for failures to learn language and was funded by an NRSA postdoctoral fellowship to Dr. Zevin and subsequently, by an NIH R01 award to Dr. McCandliss.

Rapid Visual Word Perception in Adults and Children: Dr. McCandliss and Dr. Urs Maurer, International Sackler Fellow from Switzerland, are actively pursuing the neural basis for specialization in recognizing visual words that support reading ability, through a series of electrophysiological studies contrasting responses to familiar words with other visual stimuli. Brain responses, as early as 200 milliseconds, show specialized responses over visual perception regions. They are now examining the development of this ability in typical and atypical development in children, which will inform research on reading development and dyslexia.

What Changes with Learning and Development: Dr. Casey, Conor Liston, a tri-institutional M.D., Ph.D. student, and Dr. Sarah Durston of the University of Utrecht are collaborating on cross-sectional and longitudinal brain imaging studies of cognitive control. Findings suggest that cortical function becomes fine-tuned with development. Brain regions associated with more basic functions such as sensory and motor processes mature first, followed by association areas involved in top-down control of behavior. This work is funded by an NIMH R01 to Dr. Casey and preliminary findings are published in *Developmental Science* and *Cerebral Cortex*.

Learning: Intermittent versus Continuous Reinforcement Schedules: Dr. Casey and Julie Spicer, a Ph.D. candidate at Columbia University, are studying the neural basis of intermittent versus continuous reinforcement-based learning. They have shown that the nucleus accumbens, a reward related brain structure, shows enhanced activity for intermittent reward relative to continuous reward. These findings provide a neural basis for the effects of different reward schedules on behavior and are relevant for understanding extinction of appetitive behaviors (e.g., addiction).

Reward learning and high risk behavior in adolescents: Dr. Casey and Adriana Galvan, a neuroscience PhD student, have examined the impact of varying the magnitude of reward on behavior and neural activity with fMRI. They have shown that adolescents have an exaggerated response in a subcortical appetitive brain system relative to children and adults that is correlated with the likelihood of engaging in risky behavior. These findings suggest that developmental changes in appetitive circuitry may explain the propensity for adolescents to make suboptimal social decisions (e.g., substance use and unprotected sex) leading to poor outcomes. This work is supported by grants from the National Institute of Drug Addiction (NIDA). Preliminary findings are published in the *Journal of Neuroscience*.

Individual and Developmental Differences in the Delay of Gratification: Drs. Casey and Fossella have been working with Dr. Walter Mischel of Columbia University to relate preschoolers' ability to delay gratification with their cognitive control abilities in adolescence. Preliminary results suggest those individuals most able to wait for a reward, as a toddler, were better able to resolve conflict on cognitive control tasks as adolescents. An addition to this project is the imaging and genotyping of these subjects that is now in progress. These added data will help to explain the biological basis for the observed individual differences in this ability. A collaborative National Science Foundation grant involving Columbia University, University of Washington and University of Michigan has been submitted to support this program of research. Preliminary findings are published in *Psychological Science*.

Development of Emotion Regulation: Dr. Casey and Todd Hare, a Neuroscience PhD student, are examining the interaction of limbic and prefrontal circuitry in regulation of emotions in children. Preliminary results show tension between subcortical appetitive and limbic regions in approaching and avoiding positive and negative information (e.g., happy and fearful facial expressions, Hare & Casey, 2005). Todd Hare was awarded an NIH predoctoral fellowship to support this work and is examining the development of structural and functional connectivity within and between these circuits. This project forms the foundation for parallel studies of children with problems in emotional and behavioral regulation (e.g., PTSD, anxiety, depression and, previously institutionalized).

Genomic Investigations

The Sackler Institute is rapidly establishing a high profile in genomic research that represents an elegant mapping of human and animal projects, that examine gene-environment interactions in developing humans and transgenic mouse models.

Genetics of Normal Attentional Development (Alerting, Orienting and Executive Attention): Dr. Fossella continues his investigations into genetic influences on attention that were initiated under the direction of Dr. Posner. These studies are aimed at exploring how various neurotransmitter genes influence the specific processes of alerting and executive attention. Dr. Fossella was recently awarded an NIMH K Award to investigate the development of these systems using genetic imaging under the mentorship of Dr. Casey. Preliminary work in this area is published in the *Proceedings of the National Academy of Sciences*.

Imaging Genetics of ADHD: Drs. Fossella and Casey, in collaboration with Dr. Durston of University Medical Center Utrecht, have begun to link different genotypes to brain morphometry and function in attention deficit hyperactivity disorder (ADHD). Some of the most consistently implicated genes in ADHD have been those involved in dopaminergic neurotransmission including the gene coding for the dopamine-4 receptor (DRD4), the dopamine transporter (DAT). The DRD4 receptor is preferentially expressed in prefrontal cortex, whereas the dopamine transporter is preferentially expressed in the striatum. They have shown a dissociation between the effects of the DAT and DRD4 genotypes, with those heterozygous for the DAT polymorphism impacting caudate volumes, but not prefrontal gray matter volumes; and those with the DRD4 variant genotype impacting prefrontal gray matter volume, but not caudate volume. More recent findings show differential activation of these regions as a function of genotype. These results are published in *Molecular Psychiatry*, *American Journal of Psychiatry* and *Biological Psychiatry*.

Genetics and Treatment of ADHD: Dr. Fossella and Professor Stephanie Hammarman, Rutgers University Medical School, completed and published findings in the *Journal of Child & Adolescent Psychopharmacology* on the role of the DRD4 gene in ADHD. This study found a significant association between DRD4 genotype and response to methylphenidate. Dr. Fossella is a collaborator on an NIMH funded study of the genetics of ADHD, under the direction of Professor Jeff Halperin, Queens College, CUNY. This project will link genetic variation in several serotonergic genes with measures of response to serotonergic medications. This project is still in the early stages of data collection.

Genomics Initiative in Psychiatry: Dr. Fossella has begun to explore how genetic technology will be applied in the clinical setting. In two articles, “Aligning the stakeholders” published in *Pharmacogenomics* and “On the valuation of genetic tests” published in *Personalized Medicine*, Dr. Fossella has examined progress in the field of genomic medicine and discussed the role of population genetic structure in the development of new genetically optimized therapies.

Genes, Brain, and Behavior: Drs. Casey and Fossella have co-edited a special issue of the journal *Cognitive, Affective, and Behavioral Neuroscience* that includes studies of cognitive genetics, imaging genetics and transgenic mouse models of variability in human behavior. This special issue outlines the current state of the field and provides future directions for the field.

Gene-Environment Interactions across Development: In a unique marshaling of the talents of a distinguished group of scientists with expertise in pediatric imaging, molecular biology, mouse models, and endocrinology, Dr. Casey (PI) in collaboration with Dr. Francis Lee of Psychiatry, Dr. Bruce McEwen of The Rockefeller University and Dr. Megan Gunnar of the University of Minnesota, have submitted an NIMH P50 Interdisciplinary Developmental Research Center application to examine the impact of brain-derived neurotrophic factor (BDNF) and experiential events (e.g., stress, trauma, enrichment) on learning and development, and on vulnerability and resistance to psychopathology. The Center proposal is comprised of 4 highly interdependent projects using both human imaging and transgenic mouse models to track the developmental trajectory of brain systems involved in associative and cued learning as a function of the BDNF genotype; to characterize the impact of early adversity (stress) on these brain systems during

development as a function of BDNF genotype; and to test the extent to which the BDNF phenotype can be rescued genetically and environmentally. This proposal builds on pilot data supported by the generous gift of the Mortimer D. Sackler family and based on collaborations among faculty and fellows of Lasdon Laboratories and the Sackler Institute within the Department of Psychiatry.

Clinical Investigations

The overarching mission of the Sackler Institute is to delineate the biological mechanisms underlying developmental disabilities to direct treatments and interventions and hopefully ameliorate these disorders in the future. The majority of studies currently underway focus on treatments and interventions for the disorders of dyslexia, ADHD and autism. Other areas of research in this area include examination of the long-term effects of physiological (e.g., brain trauma) and psychological stressors (e.g., institutionalization). These latter studies are moving the field toward individualized treatment and intervention approaches to stress related diseases, based on identified genetic and environmental risk factors.

Enhancing Literacy through Tutors and Computers: Dr. McCandliss, together with collaborators at the University of Pittsburgh, continues to provide empirical support for a child-friendly computer program designed to guide a minimally trained tutor and a child with reading disability through 20 sessions of intervention. Results from this computer-based tutorial program show improvements in reading, and decoding scores are equivalent to the gains in standardized scores produced by the laboratory study upon which the intervention was based. In a remarkable and wonderful development, an active intervention control study is currently underway in the New York Public Schools.

Learning-based changes in academic skills in children: Dr. McCandliss has been funded by the McDonnell Foundation to explore novel learning paradigms that engage adults in learning a new alphabetic writing system with novel fMRI activation tasks to measure the impact of learning. A follow-up National Science Foundation funded project, in collaboration with Stanford, uses learning-based changes in fMRI responses by children to contrast different computer-based intervention programs designed for basic reading and numerical skills. A central theoretical focus involves comparisons of the neural impact of interventions that target a specific cognitive operation (i.e., parsing phonemes or comparing magnitudes) vs. interventions that attempt to integrate two sets of codes (i.e., grapheme-phoneme correspondence and number symbol-magnitude correspondences).

Attention and the learning of literacy and numeracy: Drs. McCandliss and Posner are exploring methods of enhancing attention abilities in children that will no doubt prove beneficial to children with attention deficits. They have shown, together with Dr. Jin Fan of Mt. Sinai Medical Center, that both linguistic and nonlinguistic forms of conflict activate similar regions of the anterior cingulate cortex. Manipulations to reduce conflict with training appear to reduce activity in this region. This work is funded in part by the National Science Foundation and is now being conducted in the New York City public elementary schools.

Double Blind Cross-Over Placebo-Ritalin Challenge: In an NIMH collaboration with Duke, Columbia, Stanford and University of California at Berkeley, Dr. Casey is examining the imaging profiles of children with ADHD and their parents. Behavioral assays she has developed at the Institute are studied to assess for changes with medication. Preliminary findings on this clinical population were published in *Biological Psychiatry* and an editorial on the impact of such studies and the future of individualized medicine in psychiatry has been published in the *American Journal of Psychiatry* by Dr. Casey.

Studies of Autism: A number of recent studies of autism have suggested a deficit in eye gaze that may underlie problems in joint attention in this disorder. Autistic patients appear to attend more to the mouth than the eyes of faces, unlike typically developing populations. Dr. Nim Tottenham, in collaboration with Margaret Hertzog of the Department of Psychiatry, is examining this ability in individuals with autism. Dr. Tottenham has developed a paradigm that cues patients to the eyes of face stimuli and is examining changes in orientation and neural systems with extended training on this paradigm. This work has served the basis for a recent grant application to National Alliance for Autism Research.

Traumatic Brain Injury and Predictors of Outcome: Dr. McCandliss, as co-Principal Investigator, has joined forces with Dr. Ghjar, President of the Brain Trauma Foundation, on a 3-year multimillion dollar grant from the J. S. McDonnell Foundation entitled "Cognitive and Neurobiological Research Consortium in Traumatic Brain Injury." The central hypothesis of this project is that deficits in mild Traumatic Brain Injury (TBI) in both adults and children can be systematically linked to specific patterns of diffuse white matter tract damage, as measured by Diffusion Tensor Imaging based fiber tract tracings. Sumit Niogi, a Physiology PhD student, has been instrumental in developing methods for this project that have recently been published in *Neuropsychologia*.

Brain Development following Institutionalization: The long-term outcomes of children reared in orphanages abroad has become a primary health concern given the rising number of adoptions of these children to the United States. The effects of prior institutionalization on the structural and functional development of limbic circuitry using magnetic resonance imaging (MRI), are being explored by Drs. Casey and Tottenham. They are examining the association of hippocampal and amygdala volume with length of institutionalization, age of institutionalization, and length of time with an adopted family. The preliminary findings are consistent with the animal and human imaging work on chronic stress leading to structural and functional changes in the hippocampus and amygdala that are inversely related and somewhat transient. These preliminary data have resulted in a NIMH funded R01 grant to Dr. Casey and served, in part, as preliminary data for a NIMH Center grant application by Casey.

Long-term Effects of Psychological Stress: Dr. Casey and Conor Liston, a tri-institutional M.D., Ph.D. student and recipient of the Soros and Perry Awards, are examining in humans and animals the impact of moderate stress in collaboration with Dr. Bruce McEwen of The Rockefeller University. Both populations show changes in attention shifts, but not behavioral set shifting, following stress that normalizes once the stressor is removed. Human imaging and animal

histological studies show changes in prefrontal cortical regions that support attention shifting. This project illustrates a vertically integrated program of research across animal models through complex human imaging.

Preliminary imaging data from this study have recently been published in *Neuron* and formed the basis for a NIMH Center for Excellence in Research in Complementary and Alternative Medicine grant submission by Dr. Mary Charlson, Chief of General Internal Medicine, to elucidate the biological and neural mechanisms through which meditation acts to ameliorate the psychological and functional consequences of stress and improve quality of life among patients with early stage breast cancer.

Education, Training and Outreach

A significant objective of the Institute is in training, education and outreach. The Institute's network has broadened this past year with new international collaborations now established in Romania, London, Cambridge and Glasgow, in addition to existing national ones at Berkeley, Boston College, Brookhaven Laboratories, Brown University, Cornell-Ithaca, Columbia, Duke, Mt. Sinai, NIMH, NYU, University of Oregon, Pennsylvania, Princeton, Rockefeller, Stanford, UC-Irvine, University of Pittsburgh and Yale and with research fellows from Finland, Germany and The Netherlands. Highlights of the Institute's training and outreach program are provided below.

Summer Institute on the Biology of Developmental Disabilities. Casey has received funding for a sixth year to direct a week-long course on the *Biology of Developmental Disabilities* from the John Merck Fund. This year's course is co-directed by Bruce McCandliss of the Sackler Institute and Brad Schlaggar of Washington University, all three directors are previous John Merck Faculty Scholars. The course trains psychologists and neurobiologists in methods used in developmental science (imaging, genetics, and behavior) in the context of the central themes of learning and development (see: <http://www.sacklerinstitute.org/cornell/summerinstitute/>).

Developing Researchers in Neuropsychiatric Imaging. The Institute actively participates in summer workshops with the Functional Neuroimaging Laboratory directed by Drs. David Silbersweig and Emily Stern as part of a NIMH R25 Grant to train researchers in neuropsychiatric imaging.

Weill Graduate School of Medical Science. Dr. Casey has rotated from Director of the Neuroscience Program at Weill Graduate School of Medical Science to the executive committee that advises the program. The program includes over 80 faculty and graduate students. The Institute has taken a significant role in both teaching and sponsoring student rotations and PhD candidates from that program and from the Tri-institutional MD PhD program.

Ithaca-Weill Joint Graduate Program in Development and Learning. Dr. Casey in collaboration with Dr. Barbara Finlay of Cornell University-Ithaca hosted two joint campus meetings of psychology and neuroscience faculty and fellows on October 20-21, 2005 (Ithaca) and April 20-21, 2006 (Manhattan at NYAS) that led to a recent NIH T32 joint institutional interdisciplinary training grant submission for predoctoral fellows in development and learning.

NYAS Imaging Discussion Group. Dr. Casey, together with Drs. Truman Browne of Columbia University and Joe Helpern of NYU, continue to serve on the steering committee of the Imaging Discussion Group that is organized through the New York Academy of Sciences. This group facilitates interactions and collaborations among neuroimagers in the New York Metropolitan area, especially among predoctoral and postdoctoral fellows, as part of their training initiative.

NYAS Symposium. The advent of neuroscience has opened a new avenue for understanding choices that people make. On October 26, 2005, the Imaging Discussion Group of the New York Academy of Sciences sponsored a special symposium that explored unexplained aspects of human decision making and the brain processes that may underlie them. The event was organized by BJ Casey of the Sackler Institute. The speakers included Dan Ariely and Drazen Prelec of the Massachusetts Institute of Technology and the Institute for Advanced Study, Elizabeth Phelps of New York University and Jonathan Cohen of Princeton University

NYAS Symposium. No longer is it sufficient to consider genetics or environment alone when explaining human behavior. Gene-environment interactions are essential in understanding variation in behavior. On June 8th, 2006, the Imaging Discussion Group of the New York Academy of Sciences will sponsor a special symposium on *Genes, Brain and Behavior on Stress* organized by BJ Casey that will showcase faculty and fellows affiliated with the Sackler Institute. The speakers will include Drs. Nim Tottenham, Barbara Ganzel and Conor Liston of the Sackler Institute and Drs. Francis Lee and Kevin Bath of Lasdon Laboratories in the Department of Psychiatry.

Grants and Awards

Dr. Mortimer D. Sackler and family provided a gift of \$500,000 to help build a program in genomics at the Institute. This gift will support genetic imaging and the development of transgenic mice relevant to learning and development and facilitate scientific genomic links between the Cornell Ithaca and Cornell Medical campuses and within the Department of Psychiatry including Lasdon Laboratories and the Division of Child Psychiatry.

Drs. McCandliss and Zevin were awarded an NIMH R01 that was scored in the first percentile to examine the development of speech perception and the neural basis of the critical period effect in language learning.

Dr. McCandliss, Dr. Zevin and Bruno Tagliaferri were awarded a NIH-STTR grant to help develop and distribute software that addresses challenges faced by cognitive neuroscience research laboratories that attempt to combine eye-tracking, electrophysiology, and fMRI data collection techniques, thereby furthering the Sackler Institute's role as both a site of innovation and a source of useful techniques for the rest of the field.

Dr. Fossella received an NIMH K01 award to train in pediatric neuroimaging under the mentorship of Dr. Casey to combine genetics and imaging to further characterize development of attentional processes and individual variability in these processes.

Todd Hare received an NIMH NRSA predoctoral grant award sponsored by Dr. Casey on the development and neurobiology of affective regulation using fMRI.

Conor Liston, a Tri-Institutional M.D., Ph.D. candidate won the Perry Award from the Department of Psychiatry this year. This prestigious award will support his program of research on the effects of stress on the brain in rats and in humans under the co-direction of Drs. Casey and Dr. Bruce McEwen of the Rockefeller University.

Pending Grants and Awards

Dr. Amso has a pending NIMH K01 award application to examine statistical learning in infants and children using electrophysiological and magnetic resonance imaging methods under the mentorship of Dr. Casey. This work will form the basis for later studies on identification of learning disabilities early in life.

Dr. Casey (PI) together with Dr. Francis Lee of the Department of Psychiatry, Bruce McEwen of The Rockefeller University and Megan Gunnar of the University of Minnesota have submitted a NIMH P50 Center for Interdisciplinary Developmental Research grant to examine the interaction of genes and environment across development. The application focuses on the impact of stress and polymorphisms in the brain derived neurotrophin factor (BDNF) gene on learning and development.

Dr. Casey and Conor Liston, in collaboration with Dr. Mary Charlson (PI), Chief of General Internal Medicine, submitted a NIMH Center for Excellence in Research in Complementary and Alternative Medicine grant to elucidate the biological and neural mechanisms through which meditation acts to ameliorate the psychological and functional consequences of stress and improve quality of life among patients with early stage breast cancer.

Dr. Casey has a pending competitive NIMH RO1 renewal to investigate what changes with learning and development. The proposed program of research examines the effects of a controlled amount of training on cognitive control tasks at different ages to determine windows of development that may be more sensitive to future interventions to help regulate behavior.

Dr. Casey in collaboration with Dr. Barbara Finlay of Cornell University-Ithaca submitted an NIH T32 cross campus interdisciplinary training grant for predoctoral fellows in development and learning. This application bridges imaging, genetic and clinical approaches from the Medical College together with computational, behavioral and theoretical approaches from the Ithaca campus in psychology and neuroscience.

Drs. Casey and Fossella, together with Dr. Walter Mischel of Columbia University, Dr. Yuichi Shoda (PI) of the University of Washington and Dr. John Jonides of the University of Michigan have submitted a collaborative NSF grant application that will use imaging, genetics and behavioral methodologies to explain individual differences in self regulation across development.

Dr. Nim Tottenham, in collaboration with Margaret Hertzog of the Department of Psychiatry, has submitted a recent grant application to National Alliance for Autism Research to examine eye gaze in individuals with autism. Dr. Tottenham has developed a paradigm that cues patients to the eyes of face stimuli and she will be examining changes in perceptual and neural systems with extended training on this paradigm that has direct implications for treatment and intervention.

The Institute directly, and in collaboration with others, has grants and awards from NSF, NIMH, NIDA, NICHD, the McDonnell Foundation, and the John Merck Fund. This funding supplements the generous gifts by the Mortimer D. Sackler family.

Publications

- Abdullaev, Y. & Posner, M.I. (2005) How the brain recovers following damage. *Nature Neuroscience* 8,1424-1425.
- Amso, D., & Casey, B.J. (2006). Beyond *what* develops *when*: Neuroimaging may inform *how* cognition changes with development. *Current Directions in Psych Science*, 15(1), 24-29.
- Amso, D., & Casey, B.J. (in press). The Development of Cognitive Control. In *The New Encyclopedia of Neuroscience*. Larry Squire (Ed.). Elsevier.
- Amso, D., Davidson, M. C., Johnson, S. P., Glover, G., Casey, B. J. (2005). The contributions of the hippocampus and the striatum to simple association and frequency-based learning. *NeuroImage*, 27, 291-198.
- Amso, D. & Johnson, S. P. (2005). Selection and inhibition in infancy: Evidence from the spatial negative priming paradigm. *Cognition*, 95(2), B27-B36.
- Amso, D., & Johnson, S.P. (2006). Visual Selection and Object Perception. In *Proceedings of The Fifth International Conference on Development & Learning*.
- Amso, D., & Johnson, S.P. (in press). Learning by Selection: Visual Search and Object Perception in Young Infants. *Developmental Psychology*.
- Beutel, M.E., Klockenbrink, P., Witink, J., Dietrich, S., Tiede, R., Fan, J., & Posner, M.I., Attention and executive functions in patients with severe obesity: A controlled study using the Attention Network Test (2005) *Der Nervenarzt*.
- Bishop, SJ, Cohen, JD, Fossella, JA, Casey, B.J. & Farah, M.J. COMT genotype influences prefrontal response to emotional distraction. *Cognitive, Affective and Behavioral Neurosciences* (in press).
- Brem, S., Lang-Dullenkopf, A., Maurer, U., Halder, P., Bucher, K., & Brandeis, D. (2005). Neurophysiological signs of rapidly emerging visual expertise for symbol strings. *Neuroreport*, 16(1), 45-48.
- Casey, B.J., Galvan, A. & Hare, T. (2005). Changes in Cerebral Functional Organization during Cognitive Development. *Current Opinions in Neurobiology* (available on-line).
- Casey, B.J., Tottenham, N., Liston, C., Durston, S. (2005). Imaging the developing brain: What have we learned? *Trends in Cognitive Sciences*, 9, 104-110.
- Casey, B. J., Amso, D., & Davidson, M. C. (2006). Learning about learning and development with modern imaging technology. *Processes of Change in Brain and Cognitive Development, Attention & Performance XXI*. In Yuko Munakata & Mark H. Johnson (Eds.). Oxford University Press.
- Casey, B.J. (2006) Frontostriatal and Frontocerebellar Circuitry underlying Cognitive Control in U Mayr, E. Owh & SW Keele (Eds) *Developing Individuality in the Human Brain*. American Psychological Association: Washington, DC.
- Casey, B.J., Amso, D. & Davidson, M.C (in press). Learning about learning and Development with Neuroimaging. In M. Johnsons & Y. Munakata (Eds). *Attention and Performance XXI: Processes of Change in Brain and Cognitive Development*. Cambridge, MA: MIT.
- Casey, BJ, Durston, S., Tottenham, N., Spicer, J, Eigsti, I.-M., Galvan, A., Davidson, M.C. & Fossella, J. (in press). Disruption of Frontostriatal Circuitry, Dopamine and Cognitive Control

- in ADHD. In D.Barch (Ed.) *Cognitive and Affective Neuroscience of Psychopathology* Oxford Press.
- Casey, B.J. and Fossella, J.A. (in press). Invited Special Issue on Genes, Brain and Behavior, *Cognitive, Affective and Behavioral Neuroscience*.
- Cicchetti, D. & Posner, M.I. (2005) [editorial] Cognitive and affective neuroscience and developmental psychopathology. *Development and Psychopathology* 17, 569-575.
- Clarkin JF & Posner M (2005) Defining the mechanisms of borderline personality disorder *Psychopathology* 38, 56-63.
- Davidson, M., Amso, D., Cruess, L., & Diamond, A. (2006). Development of cognitive control and executive functions from 4-13 Years: Evidence from manipulations of memory, inhibition, and task switching. *Neuropsychologia*.
- Durston S & Casey BJ: What have we learned about cognitive development from neuroimaging? *Neuropsychologia*, in press Durston, S., Davidson, M.C., Tottenham, N., Galvan, A., Spicer, J., Fossella, J.A., Casey, B.J. (2006). A shift from diffuse to focal cortical activity with development. *Developmental Science*, 9(1):1-8.
- Durston, S., Fossella, J.A., Casey, B.J., Hulshoff Pol, H.E., Galvan, A., Schnack, H.G., Steenhuis, M.P., Minderaa RB, Buitelaar JK, Kahn RS, van Engeland H. (2005). Differential effects of DRD4 and DAT1 genotype on fronto-striatal gray matter volumes in a sample of subjects with attention deficit hyperactivity disorder, their unaffected siblings, and controls. *Mol Psychiatry*, 10(7):678-85.
- Durston S, Casey BJ: A shift from diffuse to focal cortical activity with development: The authors' reply. *Dev Science* 2006;9(1):18-20
- Durston, S & Casey, B.J. Imaging Studies of ADHD. In (Ed.) *Progress in Attention-Deficit/Hyperactivity Disorder Research (in press)*.
- Durston S, Davidson MC, Tottenham NT, Galvan A, Spicer J, Fossella JA, Casey BJ: A shift from diffuse to focal cortical activity with development. *Dev Science* 2006;9(1):1-8
- Durston S: Integrating neurodevelopmental imaging and genetic designs. *Psychiatry* 2005;4(12):35-37
- Durston S, Mulder M, Casey BJ, Ziermans T, van Engeland H: Activation in ventral prefrontal cortex is sensitive to genetic vulnerability for Attention Deficit Hyperactivity Disorder. *Biol Psychiatry*, in press
- Durston S, Fossella JA, Casey BJ, Hulshoff Pol HE, Galvan, A, Schnack HG, Steenhuis MP, Minderaa RB, Buitelaar JK, Kahn RS, Van Engeland H: Differential effects of DRD4 and DAT1 genotype on fronto-striatal gray matter volumes in a sample of subjects with Attention Deficit Hyperactivity Disorder, their unaffected siblings and controls. *Molecular Psychiatry* 2005;10(7):678-685
- Eigsti, I-M, Zaya, V, Mischel, W, Shoda, Y, Ayduk, O, Dadlani, MB, Davidson, MC, Aber, JL & Casey, B.J. Attentional Control in preschool predicts cognitive control at age eighteen. *Psychological Science*. (in press).
- Fan, J., McCandliss, B.D., Fossella, J., Flombaum, J.I., & Posner, M.I. (2005). The activation of attentional networks. *Neuroimage*, 26(2):471-9.
- Fossella, JA & Casey, B.J. Genes, Brain and Behavior: Bridging Disciplines. *Cognitive, Affective and Behavioral Neuroscience* (in press).
- Galvan, A, Hare, T, Spicer, J, Davidson, M, Glover, G & Casey, B.J. The role of basal ganglia thalamocortical circuitry in reward magnitude-based learning. *Journal of Neuroscience* 2005, 25(38):8650-8656

- Gardner, T.W., Dishon, T.J. & Posner, M.I. (2005) Attention and adolescent tobacco use: a potential self regulatory dynamic underlying nicotine addiction. *Addictive Behavior*.
- Greenwood, P.M., Fossella, J.A., & Parasuraman, R (2005). Specificity of the effect of a nicotinic receptor polymorphism on individual differences in visuospatial attention. *Journal of Cognitive Neuroscience*, 7(10):1611-20.
- Hare, TA & Casey, B.J. The neurobiology and development of cognitive and affective control. *Cognition, Brain, Behavior* 2005, 9: 273-285.
- Hare, TA, Tottenham, N, Davidson, MC, Glover, GH & Casey, B.J. Contributions of Amygdala and Striatal Activity in Emotion Regulation, *Biological Psychiatry*, 2005; 57:624–632
- Ivry RB, Mayr U, Corcos DM, Posner MI (2006) Psychological processes and neural mechanisms for action: The legacy of Steven W. Keele J. *Motor Behavior* 38, 3-6.
- Johnson, S. P., Hannon, E., Amso, D. (2005). Perceptual Development. In *The Cambridge Encyclopedia of Child Development*, Brian Hopkins (Ed.). Cambridge: Cambridge University Press.
- Kotsoni, E, Byrd, D & Casey, B.J. Special Considerations for fMRI of Pediatric Populations. *Journal of Magnetic Resonance Imaging (in press)*.
- Ladouceur, CD, Dahl, RE, Williamson, DE, Birmaher , B, Ryan, ND, & Casey, B.J. Altered Emotional Processing in Pediatric Anxiety, Depression, and Comorbid Anxiety-Depression. *Journal of Abnormal Child Psychology* 2005 33(2):165-77.
- Liston, C., Matalon, S., Hare, T., Davidson, M.C., Casey, B.J. (2006). Anterior cingulate and posterior parietal cortices are sensitive to dissociable forms of conflict in a task switching paradigm. *Neuron* (in press).
- Liston, C., Watts, R., Tottenham, N., Davidson, M., Niogi, S., Uluğ, A.M., Casey, B.J. (2006). Frontostriatal microstructure predicts individual differences in cognitive control, *Cerebral Cortex*, 16, 553 - 560.
- Maurer U., Brandeis D., & McCandliss, B. D. (2005). Fast, visual specialization for reading in English revealed by the topography of the N170 ERP response. *Behavioral and Brain Functions*, 1:13.
- Maurer U., & McCandliss, B. D. (in press). The development of visual expertise for words: the contribution of electrophysiology In E. L. Grigorenko & A. Naples (Eds.). *Single-Word Reading: Cognitive, behavioral and biological perspectives*. Mahwah, NJ: Lawrence Erlbaum Associates.
- Myachykov, A. & Posner, M.I. Attention in language In Itti, L, Rees, G., & Tsotsos, J.K. (2005) *Neurobiology of attention*. San Diego: Elsevier 324-329.
- Myachykov, A., Tomlin, R.S. & Posner, M.I. (2005) Attentional and empirical studies of grammar *Linguistic Review* 22, 347-364.
- Nigg, J & Casey, B.J. An Integrated Model of ADHD as a Disorder of Prediction and Reward related Cognitive and Neural Mechanisms. *Dev and Psychopath*, (in press).
- Niogi, S.N., & McCandliss, B. D. (in press). Left lateralized white matter microstructure accounts for individual differences in reading ability and disability. *Neuropsychologia*.
- Noble, K. G., Farah, M. & McCandliss, B. D. (in press). Socioeconomic background modulates cognition-achievement relationships in reading. *Cognitive Development*.
- Noble, K. G. & McCandliss, B. D. (2005). Reading Development and Impairment: behavioral, social, and neurobiological factors. *Journal of Developmental and Behavioral Pediatrics*, 26 (5):370-8.
- Noble, K, Tottenham, N & Casey, B.J. Neuroscience Perspectives on Disparities in School

- Readiness and Cognitive Achievement. *Future of Children*. 2005; 15:1-19.
- Palmen SJMC, Durston S, Nederveen H, van Engeland H: No evidence for preferential involvement of medial temporal lobe structures in high-functioning autism. *Psychol Med*, in press
- Palmen SJMC, Hulshoff Pol HE, Kemner C, Schnack HG, Durston S, Lahuis BE, Kahn RS, M van Engeland H: Increased gray matter volume in medication naive high-functioning children with autism spectrum disorder. *Psychol Med* 2005;35(4):561-570
- Parasuraman, R., Greenwood, P.M., Kumar, R., Fossella, J. (2005). Beyond heritability: neurotransmitter genes differentially modulate visuospatial attention and working memory. *Psychol Science*, 16(3):200-7.
- Parasuraman, R, Greenwood, P, Kumar, R, & Fossella JA- Neurotransmitter Genes Differentially Modulate Visuospatial Attention and Working Memory. *Psychological Science*, 2005 – 16(3) : 200-207.
- Posner, M.I. (2005) Timing the brain: mental chronometry as a tool in neuroscience. *Pub L. of Sci Biology* 3, 204-206.
- Posner, M.I. (2005) How I got here in S.W. Keele & E. Awh & U.Mayr (eds) *Developing individuality in the human brain*. Washington DC: APA Books.
- Posner, M.I. (2005) Genes and experience shape brain networks of conscious control In S. Laureys ed. *Progress in Brain Research* Vol. 150 Ch. 12, pp 173-183.
- Posner, M.I. (2005) Commentary on Becoming Aware of Feelings. *Neuro- Psychoanalysis* 7, 55-57.
- Posner, M.I. & Rothbart, M.K. (2005) Influencing brain networks: implications for education. *Trends in Cognitive Science* 9, 99-103.
- Posner, M.I. & Rothbart, M.K. (in press) Research on attentional networks as a model for the integration *Annual Review of Psychology*.
- Posner, M.I. & Rothbart, M.K. (in press) *Educating the human brain*. Washington D.C.: APA Books.
- Posner, M.I., Rueda, M.R. & Kanske, P. (in press) Probing the Mechanisms of Attention in Cacciopo (ed) *Handbook of Psychophysiology*.
- Radley, J.J., Rocher, A.B., Miller, M., Janssen, W.G.M., Liston, C., Hof. P.R., McEwen, B.S., Morrison, J.H. (2006). Repeated stress induces dendritic spine loss in the rat medial prefrontal cortex. *Cerebral Cortex*, 16, 313-320.
- Raz, A. Lieber, B., Soliman, F., Buhle, J., Posner, J., Peterson, B.S. & Posner, M.I. (2005) Ecological nuances in functional magnetic resonance imaging (fMRI): psychological stressors, posture and hydrostatics *Neuroimage*, 25, 1-7.
- Raz, A, Fan, J. & Posner, M.I. (2005) Hypnotic suggestion reduces conflict in the human brain. *Proc. Nat Acad. Of Sci. USA* 102, 9978-9983.
- Rothbart, M.K. & Posner, M.I. (2005) Genes and experience in the development of executive attention and effortful control. In L.A. Jensen & R.W. Larson (eds) *New horizons in developmental theory and research*. San Francisco: Jossey-Bass p.101-108.
- Rothbart, M.K. & Posner, M.I. (2006). Temperament, attention, and developmental psychopathology. in D. Cicchetti & D. J. Cohen (eds.), *Handbook of Developmental Psychopathology Vol. 2* Revised. New York: Wiley Press. 465-501.
- Rothbart, M.K., Posner, M.I. & Kieras, J. (2006) Temperament attention and self regulation. In K. McCartney & D. Phillips (eds.) *Handbook of early childhood development*. Ch. 17 pp. 338-357.
- Rueda, M.R., Rothbart, R.K., McCandliss, B. D., Saccomanno, L., & Posner, M.I. (2005). Training, maturation, and genetic influences on the development of executive attention. *Proceedings of*

- the National Academy of Sciences*, 102(41):14931-14935.
- Rueda, M.R., Rothbart, M.K., & Saccamanno, L. & Posner, M.I. (2005) Training, maturation and genetic influences on the development of executive attention. *Proc. U.S Nat'l Acad of Sciences* 102 14931-36.
- Rueda, M.R., Rothbart, M.K., Saccomanno, L., & Posner, M.I. (in press) Modifying Brain Networks Underlying Self Regulation In Romer, D ed.
- Ruz M., Worden M. S., Tudela P., McCandliss, B. D. (2005). Inattentive amnesia to words in a high attentional load task. *Journal of Cognitive Neuroscience*, 17(5): 768-776.
- Ruz, M., Wolmetz, M.E., Tudela, P., & McCandliss, B. D. (2005). Two brain pathways for attended and ignored words. *Neuroimage*, 27 (4):852-61.
- Scerif, G, Kotsoni, E & Casey, BJ Functional neuroimaging of development. To appear in Roberto Cabeza and Alan Kingstone, (Eds.) *Handbook on Functional Neuroimaging of Cognition: Second Edition, MIT Press. (in press)*.
- Scerif, G, Worden, MI, Yu, J, Casey, B.J. Context modulates early stimulus-processing when resolving stimulus-response conflict. *J of Cognitive Neuroscience*. (in press).
- Seidenberg, M. S. & Zevin, J. D. (in press). Computational models in cognitive development: The case of critical periods in language learning. In Johnson, M. & Munakata, Y. *Attention and Performance XXI :Processes of Change in Brain and Cognitive Development*. Oxford, UK: Oxford University Press.
- Stevenson, J., Asherson, P., Hay, D., Levy, F., Swanson, J., Thapar, A., Willcutt, E. (2005). Characterizing the ADHD phenotype for genetic studies. *Dev Sci* 8(2): 115-121.
- Suh M., Kolster R., Sarkar R.,McCandliss, B. D., J. Ghajar, & CNRC TBI (in press). Deficits in predictive smooth pursuit after mild traumatic brain injury. *Neuroscience Letters*.
- Tamm, L., McCandliss, B. D., Liang, B. A., Wigal, T. L., Posner, M. I., & Swanson, J. M. (in press). Can attention itself be trained? Attention training for children at-risk for ADHD. In K. McBurnett (Ed.), *Attention Deficit/Hyperactivity Disorder: A 21st Century Perspective*. New York: Marcel Dekker.
- Tottenham, N., Leon, A., & Casey, B.J. (2006). The Face Behind the Mask: A Developmental Study. *Developmental Science*, 9(3), 288-294.
- Treiman, B., Kessler, B., Zevin, J.D., Bick, S. & Davis, M. (2006). Influence of Consonantal Context on the Pronunciation of Vowels: Evidence From Children. *Journal of Experimental Child Psychology*, 93, 1-24.
- Tricoli, E., Delgado, M. R.,McCandliss, B. D., McClelland, J. L., & Fiez, J. A. (in press). Performance feedback drives caudate activation in a perceptual learning task. *Journal of Neuroscience*.
- Voss, H.U., Ulug, A.M., Dyke, J.P., Watts, R., Kobylarz, E.J., McCandliss, B., Heier, L.A., Beattie, B.J., Hamacher, K.A., Vallabhajosula, S., Goldsmith, S., Ballon, D., Giacino, J.T., Schiff, N.D. (in press). Axonal re-growth in late recovery from the minimally conscious state? *Journal of Clinical Investigation*.
- Voss, H U., Zevin, J. D. & McCandliss, B. D. (in press) Functional MR imaging at 1.5 and 3.0 T: A practical review. *Neuroimaging Clinics of North America*.
- Wang, K. J., Fan,J., Dong Y. Wang C., Lee TMC & Posner M.I (2005) Selective impairment of attentional networks of orienting and executive control in schizophrenia *Schiz. Research* 78, 231-241.
- Zhang, L., Thomas, KM, Davidson, MC, Casey, B.J., Heier, LA Ulug, AM. MR Quantitation of Volume and Diffusion Changes in the Developing Brain, *Amer J Neuroradiol*, 2005; 26: 45-49.

- Zeegers M, van der Grond J, Durston S, Nieuvestein RJ, Witkamp Th, van Daalen E, Buitelaar J, van Engeland H: Radiological findings in autistic and developmentally delayed children. *Brain & Development*, in press.
- Zevin, J.D., & McCandliss, B.D. (2005). Dishabituation of the BOLD response to speech sounds. *Behavioral and Brain Functions*.1:4.
- Zevin, J.D. & Seidenberg, M. S. (2006). Simulating Consistency Effects and Individual Differences in Nonword Naming: A Comparison of Current Models. *Journal of Memory and Language*, 54, 145-160.