

The Sackler Institute for Developmental Psychobiology
Weill Cornell Medical College
Annual Report for May 2008-April 2009

The Institute maintains a strong reputation for expertise in typical and atypical learning and the genetic and environmental factors that influence these processes across development. Faculty and fellows have received a number of awards this year (See *Grants and Awards*) and training remains a priority with the continuation of the annual *Summer Institute on the Biology of Developmental Disabilities* and increased involvement in medical and graduate student training and elementary and high school (see *Education, Training and Outreach*). We have published nearly 60 manuscripts this past year and highlight a few of these studies in this report (see *Program of Research and Publications*).

Academic Faculty, Fellows and Staff

Sackler Faculty

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

B.J. Casey, Ph.D., Director and Sackler Professor of Developmental Psychobiology

Liat Levita, Ph.D., Instructor of Psychology in Psychiatry

Michael Posner, Ph.D., Professor of Psychology in Psychiatry, Emeritus

James Swanson, Ph.D., Part-time Professor of Psychology in Psychiatry

Jason Zevin, Ph.D., Assistant Professor of Psychology in Psychiatry

Sackler Staff

Deanne Lamb, Institute Administrator and Emmanuel Stein, IT Manager

Sackler Research Assistants

Juliet Davidow, Eva Hulse, Brian Kramer, Vicki Libby, Erika Ruberry and Theresa Teslovich

Sackler Predoctoral and Postdoctoral Fellows

Thomas Farmer, Cornell-Weill Sackler psychology Ph.D. student

Yang Jianfeng, Ph.D., Postdoctoral Fellow

Rebecca Jones, Neuroscience Ph.D. student

Conor Liston, M.D.-Ph.D., Weill Cornell Psychiatry Resident

Jeremy Skipper, Ph.D., Postdoctoral Fellow

Fatima Soliman, Tri-Institutional M.D.-Ph.D. student

Leah Somerville, Ph.D. Postdoctoral Fellow

Yuliya Yoncheva, Neuroscience Ph.D. student

Kevin Bath, Ph.D., Lasdon-Sackler Postdoctoral Fellow

Distinguished Sackler Scholars

Oana Benga, Babes-Bolyai University, Romania

Sarah Durston, University of Utrecht, The Netherlands

Annette Karmiloff-Smith, University College London, United Kingdom

Urs Maurer, Swiss National Science Foundation, Switzerland

Bruce D. McCandliss, Ph.D., Vanderbilt University, Tennessee

Gaia Scerif, University of Oxford, United Kingdom

Nim Tottenham, Ph.D., UCLA, California

Program of Research

This year, several empirical studies have been completed and published using the techniques of brain imaging, human genetics, electrophysiology, eye tracking and behavioral methods, to study typical and atypical populations from childhood to adulthood (see Publications). In addition to the award of a NIMH P50 Center, affiliated Sackler faculty and fellows have submitted and received several grants (see Grants). Below, are highlights from a few of studies representing three general domains of study: 1) learning and development, 2) imaging and behavioral genetics; and 3) neurobiology and risk factors for developmental disorders.

Studies of Learning and Development

Behavioral and imaging studies of learning and development form the very foundation of the Institute's research program and lay the critical groundwork for our genetic and clinical studies. Therefore we highlight several of these studies below across the domains of perceptual, emotional and cognitive learning.

Neural Basis of Statistical (Unsupervised) Learning. Dr. Dima Amso is examining the neural basis of unsupervised learning in habituation and novelty preference studies. She is currently examining these abilities in infants and children using eye tracking and magnetic resonance imaging methods. This work lays the groundwork for identification of learning disabilities early in life and forms the basis of Dr. Amso's recent NIMH K-award and a recently awarded NIMH Center grant to The Institute.

Attention and Perceptual Learning in Infancy. Saccades early in infancy are largely reflexive, with voluntary attention-directed eye movements emerging at approximately three to four months of age. In a series of studies, Dr. Amso is investigating the mechanisms of the development of visual selection and how they play a role in efficient attenuation of distractor information during learning. Her work suggests that where infants look determines what they perceive and is dependent on their ability to control their eye movements.

Object Learning in Infancy. Infants as young as 4 months fail to show surprise when occluded moving objects fail to emerge from behind a static object, indicating that they do not form a visual memory of the object and its trajectory while it was occluded. By 6 months, infants indicate understanding of this continuity and can use this information to guide crawling and reaching. When infants are exposed to the relevant information about an object's trajectory they can perform this task at an earlier age. Dr. Amso is using electrophysiological measures to constrain current developmental theory on how infants can use repetition to learn to organize their environment.

Social Learning in Infancy. The ability to discriminate emotional expressions in others' faces is a key component of normal social interaction. A first step in this process is the ability to discern *perceptual* differences between faces and to generalize the encoded emotion across individuals. Drs. Amso and Tottenham together with Sackler fellows Megan Fitzgerald, Juliet Davidow, and Tara Gilhooly, are examining how individual differences in information gathering, via shifts of eye gaze, support the ability to discriminate between emotional expressions in infants. This work provides a developmental framework for examining face processing deficits in autism and has been submitted for publication.

Peers as Secondary Reinforcers. Rebecca Jones, a Neuroscience PhD candidate, is examining the effects of peer interaction on behavior and underlying neural circuitry. Under the mentorship of Casey, she is parametrically manipulating the frequency of interaction with peers from 33, 66 and 100% building on nonhuman primate and recent imaging studies of reward at The Institute to determine whether these interactions activate the same systems and alter behavior in the same way as primary (juice) and other secondary reinforcers (money).

Fear Conditioning and Extinction. A core problem in many children with anxiety and depression is difficulty learning what cues and settings signal safety or danger and unlearning such associations when they no longer exist. M.D.-Ph.D. student Fatima Soliman and Dr. Liat Levita, an instructor at The Institute, under the mentorship of Casey and Lee, have developed paradigms for examining this type of learning with fMRI and galvanic skin responses. Parallel studies are being performed in the rodent in collaborative studies with Drs. Lee and Bath and two PhD students, Siobhan Pattwell and Rebecca Jones.

Development of Speech Perception: Dr. Jason Zevin, in continued collaboration with Dr. Bruce McCandliss, now at Vanderbilt, is examining the neural basis of language development, with a specific focus on the development of speech perception in American and Japanese native speakers. They have completed a series of fMRI studies designed to establish the core paradigm of the proposal and its sensitivity to differences in native language, and have begun collecting data from a new cohort that will form the central data set of the project. This work is supported by an NIDCD R01 to Drs. McCandliss and Zevin. A related project, undertaken in collaboration with Arturo Hernandez (U Houston) and Christof Karmonik (Methodist Hospital) examines speech perception in native Spanish speaking children and young adults and is funded by an internal IBIS pilot award.

Distributed Phonetic Representations in the Brain. Dr. Jason Zevin is adapting novel neuroimaging analysis techniques (multivariate pattern analysis) to the study of speech perception. The goal is to identify patterns of activity that reflect the extraction of categorical information from continuous and infinite variability in the physical properties of speech. Speech sound categorization is associated with many communication disorders, and the techniques developed here are also applicable to other disorders of which perceptual categorization (e.g., of facial expressions in autism) is a central feature. This work is supported by an R21 from NIDCD that began in January 2009.

Importance of Context in Spoken Communication. Spoken communication is accompanied by a wealth of contextual information and knowledge or expectations of the listener. Most neurobiological research on speech perception discards context in favor of studying isolated speech sounds or words. Dr. Jeremy Skipper, under the mentorship of Dr. Jason Zevin, is examining the neural mechanisms of language comprehension in real-world settings, where the brain can make use of context to aid in communication. This work serves as the basis of a recently submitted NIH K99 grant application (PI: Skipper).

Reading in multiple languages. Yang Jianfeng is a postdoctoral fellow working with Dr. Zevin on computational modeling of the development of reading in multiple languages. The focus of this work is to study the differential contribution of basic perceptual and cognitive processes to reading in different writing systems, which will help explain why reading disorders present in culturally-specific ways, despite significant overlap in the neural substrates for reading across languages. An NSF proposal to support this work was submitted in January.

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.

Gene-Environment Interactions Across Development: The Institute received a NIMH P50 Interdisciplinary Developmental Research Center grant 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. This work 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 and forms the foundation for parallel studies of children with problems in emotional and behavioral regulation (e.g., PTSD, anxiety, depression, and previously institutionalized),

Genetic Influences on Emotional Regulation in Adolescents. Taking a vertical integration approach, Charles Glatt (PI) in collaboration with BJ Casey is examining the molecular, neural and behavioral phenotype of a newly discovered polymorphism in the serotonin transporter gene across development, specifically focusing on adolescence when there is an increase in incidence of depression-related suicide and prevalence of affective disorders. This work is supported by a Hartwell grant and a NIMH R01 application that is currently under review.

Individual Differences in Fear Conditioning and Extinction. Fatima Soliman, under the mentorship of Drs. Casey and Francis Lee, has developed paradigms for examining the effects of BDNF Val66Met on fear conditioning, reversal learning and extinction in humans and mice. In humans she is using fMRI, response latency to cues of threat, and galvanic skin responses to cues of threat, and freezing behavior in mice. Parallel collaborative studies are being performed in the rodent with Drs. Francis Lee and Kevin Bath and two Ph.D. students, Siobhan Pattwell and Rebecca Jones.

Individual Differences in Transient and Sustained Emotional Processes. Leah Somerville, a post doctoral fellow working in collaboration with BJ Casey, is examining transient and sustained emotional processes across development. This program of research uses resting state fMRI and DTI together with fMRI to identify developmental and individual differences in neural circuitry underlying emotional processes that may put some individuals at risk for anxiety, depression and mood disorders.

Clinical Investigations: Risk Factors and Interventions

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 risk factors for mental illness, treatments and interventions related to developmental disabilities, anxiety and depression, addiction, and the long-term effects of psychological stressors (e.g., institutionalization and everyday stress). 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 discussed in editorials and reviews in the *American Journal of Psychiatry* and *Current Opinions in Neurology*.

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 are being explored by Drs. Casey and Tottenham, now at UCLA, using magnetic resonance imaging (MRI). The 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 (see Tottenham et al. in press). Current investigations focus on the functional significance of these anatomical changes and on the genetic contributions to these phenotypes following stress. These data have resulted in a NIMH funded R01 grant to Dr. Casey and served, in part, as preliminary data for a NIMH Center grant, which we have been awarded.

Effects of Psychological Stress on Prefrontal Cortex: BJ Casey and Conor Liston, MD, PhD, now a psychiatry resident at Weill Cornell Medical College and prior recipient of the Soros and Perry Awards, have examined in humans and animals the impact of moderate stress in collaboration with Dr. Bruce McEwen of The Rockefeller University. Both species 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 (see Liston, McEwen & Casey, 2009 PNAS).

Studies Relevant to Addiction. Casey, together with Drs. Elke Weber and Bernd Figner of Columbia University, is examining the development of risky behaviors linked to addiction in adolescents using both fMRI and a gambling card task. Behavioral data show teens to be more risky than children or adults. These results are consistent with earlier work at the Institute and are supported by a recent NSF grant (PI: Weber). They form the basis for a developmental framework for examining risk for substance abuse in teens.

Casey has been working with Dr. Walter Mischel of Columbia University to relate preschoolers' ability to delay gratification with their cognitive control abilities in adolescence. Toddler measures of delay of gratification are associated with substance abuse in adulthood. Preliminary results suggest those individuals most able to wait for a reward as toddlers are better able to resolve conflict on cognitive control tasks as adolescents. A collaborative National Science Foundation grant (PI: Shoda) involving University of Washington, Columbia University, Berkeley, and University of Michigan has been awarded to support this program of research. Preliminary findings are published in *Psychological Science* and are currently being submitted to a special issue of *SCAN*.

Obesity-Related Genetic Imaging Study. Casey is collaborating with investigators on a genetics imaging study of obesity in children focusing on the effect of the FTO gene and neural circuitry underlying sensitivity to food cues in children. This work has been submitted as part of a special RFA initiated RO1 to the NIH and uses behavioral paradigms developed at the Institute.

Education, Training and Outreach

A significant objective of the Institute is in training, education and outreach. The Institute's network has international collaborations established with Romania, London, Switzerland and The Netherlands in addition national ones with Berkeley, Cornell, Columbia, Duke, Mt. Sinai, NIMH, NYU, University of Oregon, Pennsylvania, Princeton, Rockefeller, Stanford, UC-Irvine, and Yale. 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 ninth 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 Drs. Leah Somerville and BJ Casey of the Sackler Institute and Barbara Finlay of Cornell University and will focus on training psychologists and neurobiologists in methods used in developmental neuroscience (imaging, genetics, and behavior) in the context of the central themes of learning and development (see: http://www.sacklerinstitute.org/cornell/summer_institute/2009/).

Developing Researchers in Neuropsychiatric Imaging. The Institute actively participates in summer workshops as part of a NIMH R25 Grant (PI: Casey) to train researchers in neuropsychiatric imaging.

Weill Graduate School of Medical Science. Dr. Casey is the Director of the Neuroscience Program at Weill Graduate School of Medical Science. The program includes over 60 faculty and graduate students. The Institute has taken a significant role in recruitment, teaching and sponsoring student rotations and Ph.D. candidates from the graduate program and from the Tri-institutional M.D.-Ph.D. program.

Residency Education. Drs. Amso, Casey, and Levita all played significant roles this year in teaching both adult and child psychiatry residents at Weill Cornell Medical College as part of the Residency program curriculum.

Brain to Mind. Drs. Amso, Casey, Levita and Zevin all played significant roles this year in teaching medical students at Weill Cornell and Weill Quatar about developmental systems neuroscience. Each faculty member provided lectures and labs for the students that have resulted in participation of the medical students in rotations and Sackler seminars.

Neuron to Brain. Drs. Amso, Casey, Levita and Zevin all played significant roles this year in teaching Weill Biomedical Graduate Program in Neuroscience related courses that link brain and behavior. Some of the best teaching evaluations were given to this group, with highest praise to Dr. Amso, for her lectures on attention and developmental neuroscience.

Ithaca-Weill Joint Graduate Program in Development and Learning. Dr. Casey in collaboration with Dr. Barbara Finlay of Cornell University-Ithaca has hosted joint campus meetings of psychology and neuroscience faculty for the past three years and has submitted a NIH T32 joint institutional interdisciplinary training grant submission for predoctoral fellows in development and learning (see <http://neuroscience.cornell.edu/imagine.html>). The grant received a 119 priority score.

Columbia-Cornell Sackler Institute Meeting. A Cornell-supported symposium, both organized and chaired by Dr. Jason Zevin, was held at the annual Winter Meeting on Developmental Psychobiology, co-directed by Bill Fifer of the Sackler Institute at Columbia and Gordon Barr. These meetings have resulted in joint mentorship of fellows and collaborative research studies between the two institutes.

Grants and Awards

Grants and Awards (2008-2009)

Dr. Casey received a NIMH P50 center grant to study the impact of gene by environment interactions across development on learning May 1, 2008. This center involves both the Ithaca and Manhattan Cornell campuses and several faculty within the psychiatry department including Francis Lee, Dima Amso, and Charles Gatt were instrumental in the success of this grant application as were the generous gifts of the Dr. Mortimer D. Sackler family.

Dr. Casey received a grant from the John Merck Fund to support the 9th annual Summer Institute on the Biology of Developmental Disabilities that she has been directing for the past eight years. This course exposes students to animal, imaging, genetic, epidemiologic, and computational modeling approaches to understanding learning within typical and atypical development.

Dr. Casey in collaboration with Dr. Barbara Finlay of Cornell University-Ithaca received a 119 priority score on 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.

Dr. Jeremy Skipper received a priority score of 110 for his K99/R00 to investigate neural mechanisms of language comprehension in real-world settings, where the brain can make use of context to aid in communication. His work has shown that spoken communication is accompanied by a wealth of contextual information, yet most neurobiological research on speech perception discards context in favor of studying isolated speech sounds or words.

Fatima Soliman, M.D.,Ph.D. candidate, received a UNCF scholarship for her thesis research on the effects of BDNF on learning and extinction in mice and humans.

Dr. Zevin was awarded an NIH R21 grant to study phonetic representation in temporal cortex using novel applications of multivariate analysis techniques. He will use machine learning models to identify patterns of brain activity that correspond to particular speech sound categories. The proposed combination of data collection and analysis techniques has great

potential for use in basic, translational and clinical research on the development and plasticity of speech perception as well as communication disorders including dyslexia and language impairment related to deficits in speech sound categorization.

Dr. Zevin received an IBIS seed grant to conduct an fMRI study of native Spanish speakers learning English as a second language in collaboration with Arturo Hernandez (U Houston) and Christof Karmonik (Methodist Hospital). The project will apply methods developed in Dr. Zevin's research on the sensitive period to a population that includes some speakers who eventually become "English-dominant," so that they are more comfortable and fluent in their second language than their first.

Pending Grants and Awards

Dr. Amso has submitted an administrative supplement request as part of the NIH stimulus package specific to her K01 award activities.

Dr. Casey has submitted a Howard Hughes Medical Information in Graduate training grant application that combines a suite of innovative training activities to provide graduate training at the forefront of disease-related neurobiological research. Via participation of basic and clinical research scientists, the program will include interactive exposure to patients, state-of-the-art and in-development methodologies for diagnosis, treatment, and prevention of disease, and training in the ethics of clinical research.

Dr. Casey is collaborating with investigators on a genetics imaging study of obesity in children focusing on the effect of the FTO gene and neural circuitry underlying sensitivity to food cues in children. This work has been submitted as part of a special RFA initiated RO1 to the NIH and uses behavioral paradigms developed at the Institute.

Dr. Leah Somerville submitted a NIH K99/R00 application to examine transient and sustained emotional regulation processes across development. This grant uses resting state fMRI and DTI together with fMRI to identify developmental and individual differences in neural circuitry underlying emotional processes that may put some individuals at risk for anxiety, depression and mood disorders.

Dr. Charles Glatt submitted a NIH R01 to investigate the effects a new serotonin transporter polymorphism on emotion regulation using a vertically integrated approach from mouse to human. Dr. Glatt is focusing on adolescence, a time when affect-related disorders are diagnosed at peak levels.

Dr. Zevin has submitted an NSF proposal to support his computational modeling work on reading across different writing systems. The goal of this research is to understand how different patterns of reading disorder can emerge as a result of the interaction between core deficits (in perceptual or semantic processing) that are common to all readers and the computational demands specific to each reading system.

Dr. Zevin has submitted an administrative supplement in support of his R21 grant. The supplement will be used to employ a full-time computer programmer.

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

Publications

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