

The Sackler Institute for Developmental Psychobiology
Weill Cornell Medical College
2011-2012

The Sackler Institute has established a high profile in genomic research translating transgenic mouse models to human behavior and disease and maintains a distinguished international reputation under the ten-year leadership of Director and Sackler Professor, BJ Casey. The faculty and fellows have received additional awards (see *Grants and Awards*) and published over 50 scientific papers (see *Publications*). Training remains a priority with numerous local and international sponsored events (see *Training and Education*). Outreach activities involving the public range from those related to developmental neuroscience to public policy and the law (see *Outreach Activities*). This report highlights several of the accomplishments of this past year.

Academic Faculty and Staff

Sackler Faculty

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

Barbara Finlay, Ph.D., Adjunct Professor of Psychology in Psychiatry, Cornell

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

James Swanson, Ph.D., Adjunct Professor of Psychology in Psychiatry, UCI

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

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

Sackler Affiliated Faculty

Francis S. Lee, M.D., Ph.D., Associate Professor

Charles E. Glatt, M.D., PhD., Assistant Professor

Sackler Staff

Deanne Lamb, Institute Administrator

Jae Woo, M.D., IT Manager

Sackler Research Assistants

Patrick Harvey, Research Assistant

Eva Hulse, Research Coordinator

Natasha Mehta, Research Assistant

Alisa Powers, Research Assistant

Sackler Predoctoral and Postdoctoral Fellows

Kris Caudle, Ph.D., Postdoctoral Fellow

Hia Datta, Ph.D., Postdoctoral Fellow

Suzanne Dikker, Ph.D., Postdoctoral Fellow

Stephanie Duhoux, Ph.D., Postdoctoral Fellow

Cate Hartley, Ph.D., Postdoctoral Fellow

Chelsea Helion, Joint Cornell-Weill Ph.D. Candidate

Rebecca Jones, Neuroscience Ph.D. student
Matthew Malter-Cohen, Neuroscience Ph.D. student
Siobhan Pattwell., Ph.D., Postdoctoral Fellow
Leah Somerville, Ph.D., Postdoctoral Fellow
Theresa Teslovich, Neuroscience Ph.D. student

Distinguished Sackler Network Scholars

Oana Benga, Ph.D., Babes-Bolyai University, Romania
Sarah Durston, Ph.D., University of Utrecht, The Netherlands
Annette Karmiloff-Smith, Ph.D., University College London, United Kingdom
Urs Maurer, Ph.D., Swiss National Science Foundation, Switzerland
Bruce D. McCandliss, Ph.D., Vanderbilt University, Tennessee, United States
Gaia Scerif, Ph.D., University of Oxford, United Kingdom

Program of Research

The overarching objective of the Institute is to delineate the biological mechanisms underlying mental health and illness and their development and to determine the efficacy of innovative therapies and preventive strategies for disorders as a function of developmental status and potential genetic effects inferred from mice and humans. This year, several empirical studies have been completed and published in high profile journals (*PNAS*, *Journal of Neuroscience*, *The Neuroscientist*, *Developmental Science*) using the techniques of brain imaging, human and mouse genetics, psychophysiology, and behavioral methods, to study typical and atypical populations from childhood to adulthood (see *Publications*). Below are highlights from a few studies on mental health and illness relevant to: 1) communication disorders; 2) substance abuse and addiction; 3) anxiety disorders; and 4) eating disorders.

Computational modeling and Imaging Studies relevant to Communication Disorders

The institute is involved in a number of basic studies of speech and language led by Dr. Jason Zevin that lay the critical groundwork for the identification, treatment and prevention of communication disorders.

Speech Perception and Development. Understanding how non-native speakers compensate for atypical speech sound processing may provide the basis for novel remediation strategies for communication disorders. Dr. Jason Zevin is examining the neural basis of language development, with a specific focus on the development of speech perception in American and Japanese native speakers. Several papers comparing neural responses to native and non-native speech contrasts have been published from this work.

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. 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 is the basis of a funded NIH K99 grant application (PI: Skipper), and forms the basis of a new proposal to

incorporate the role of context into investigations of second language speech perception (PI:Zevin). Dr. Skipper has transferred this award to his new position at Hamilton College, where he continues to collaborate on research with Dr. Zevin's lab.

Typical and atypical development of the reading circuit across languages. In collaboration with colleagues at Beijing Normal University and Haskins Laboratories, Dr. Zevin is pursuing a program of research that combines computational modeling and functional neuroimaging to study how the reading system develops in response to the demands of different writing systems. This work has resulted in multiple high-profile publications, one of which (Yang et al., 2011, *Brain and Language*) was covered in *EurekaAlert!*, a publication of the AAAS. Dr. Zevin will be pursuing this work as a visiting professor at Beijing Normal University next year and will teach graduate courses and supervise research studies as part of our collaborative network of Sackler initiatives.

The role of memory in literacy. Dr. Zevin is examining the role of episodic memory and consolidation in predicting success in literacy acquisition, in collaboration with Kenneth Pugh and colleagues at Haskins Laboratories. They are examining a previously under-studied relationship between individual differences in basic memory processes and literacy skill.

Behavioral and Imaging Studies relevant to Substance Abuse and Risk Taking

The Influence of Peers on Behavior. Rebecca Jones, a former Neuroscience Ph.D. student, together with Drs. Somerville and Casey have recently published their work on how peers act as reinforcers to bias behavior using a task that parallels nonhuman primate studies of reinforcement learning (Jones et al 2011 *J Neuroscience*). They show that individuals are faster to respond to a peer who has interacted with them more relative to one who has not interacted with them as much. These behavioral changes are paralleled by changes in reward-related circuitry implicated in primary reinforcement and addiction. In a follow-up study, Dr. Jones shows that adolescents relative to adults and children are more easily influenced by peers even without conscious awareness.

The influence of Incentives on Adolescent Decision Making. Adolescents have been shown to be differentially sensitive to rewards relative to children and adults often resulting in more impulsive decision-making (Somerville et al. 2011 *J Neuroscience*). PhD student Theresa Teslovich is examining how rewards can be used to optimize adolescent decision making. She is showing that adolescents appear to work harder by actually slowing down when rewards are at stake, prior to making a decision. This change in behavior is associated with enhanced recruitment of reward related circuitry. These findings have recently been submitted for publication.

Neural Correlates of Delay of Gratification. Dr. Casey together with Dr. Walter Mischel of Columbia University and colleagues from University of Washington, Stanford, Berkeley, Cornell University and Michigan have published their study examining behavioral and neural correlates of preschoolers' ability to delay gratification 40 years later (Casey et al 2011 PNAS). The findings suggest that our ability to resist temptation varies, not only by how well we can control our impulses, but also by how sensitive we are to alluring cues or contexts in the environment and is supported by reward related circuitry implicated in addiction and substance abuse. This work was funded by a collaborative NSF grant (PI: Shoda) and has been highlighted by the *NY Times*, *USA Today*, *Time Magazine*, *Wall Street*

Journal, EurekAlert and other media. As a follow-up, Dr. Casey with Drs. Mischel and Kevin Ochsner (PI) of Columbia University are using the delay of gratification, appetitive go/nogo and emotion regulation tasks that they have each developed to understand the development of neural mechanisms that enable us to regulate the appetitive pull of potentially unhealthy substances (e.g., fattening foods or drugs) and the aversive push of unpleasant emotions that might motivate one to seek these substances in the first place. This work is funded by a collaborative grant by NICHD (PI: Ochsner).

Genetic and Imaging Studies relevant to Anxiety Disorders

SERT (rs3813034) and Fear Extinction Retention. Drs. Glatt and Casey in collaboration with Drs. Cate Hartley and Liz Phelps of NYU have published a recent study examining how two polymorphisms (Hartley et al 2012 *PNAS*) tied to variation in 5-HTT expression are associated with differences in extinction retention. The 5-HTT KO mouse shows impaired extinction retention. Using a two-day fear conditioning paradigm of acquisition and the initial extinction phase, followed by day two of a second extinction phase, they show that the polyadenylation polymorphism in the serotonin transporter (rs3813034) is associated with individual variation in extinction retention, as well as trait anxiety and depressive symptoms, while the serotonin transporter-linked promoter region (5HTTLPR) was not associated with these measures. These results suggest that genetically-mediated differences in extinction retention may be associated with risk for anxiety.

Development of Extinction. Siobhan Pattwell, a neuroscience student in Dr. Francis Lee's lab, and Dr. Stephanie Duhoux, a post doctoral fellow with Dr. Casey, and Ipe Ninan of NYU have submitted a study examining the development of extinction related behavior in pre-, peri- and post adolescent mice and humans. They show less extinction learning and less infralimbic activity in adolescents. These findings have significant implications for when exposure therapy may be most beneficial for treatment of anxiety disorders given that exposure therapy relies on principles of extinction. An NIMH collaborative PI R01 application has been submitted by Drs. Casey and Lee to follow-up these findings.

Biobehavioral Markers for Anxiety Disorders. Childhood anxiety disorders are a prevalent public health issue affecting as many as one in ten children and increasing risk for psychiatric disorders throughout the lifespan. Dr. Leah Somerville, a postdoctoral fellow working with Dr. Casey, who is moving to Harvard next year for a faculty position has developed a paradigm to delineate brain systems critical to symptoms of anxiety across development and provide preliminary evidence for their role in anxiety disorders and their predictive merit for risk in familial cases. Ultimately this work should provide biologically valid behavioral markers of risk for anxiety disorders that will facilitate early identification and prevention as well as new outcome measures for clinical trials optimizing personalized treatment. This work is funded by an NIMH K99/R00.

Genetic and Imaging Studies of Eating Disorders

Effects of Diet Restriction on Anxiety. MD PhD candidate, Megan Riddle under the mentorship of Dr. Charles Glatt is examining the anxiolytic effects of diet restriction in mice. Preliminary findings suggest that the decrease in anxiety like behavior is related to enhanced fear extinction learning with caloric restriction that is largely dependent on associated

changes in the expression of the serotonin transporter. These findings have significant implications for anorexia nervosa.

Genetic Studies of Obesity. Dr. Casey is collaborating with investigators at NYSPI on a genetic 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.

Delay of Gratification and Anorexia Nervosa. Drs. Casey and Kris Caudle are involved in a collaborative study recently funded by the Klarman Foundation to examine neural correlates of delay of gratification, discounting and impulse control in anorexia nervosa with Drs. Tim Walsh and Joanna Steinglass (PI).

Sensitivity to Reward and Emotional Cues in Bulimia. Dr. Casey is collaborating with investigators at Columbia (Allegra Broft and Tim Walsh) on an imaging study of Bulimia Nervosa to identify neural circuitry underlying sensitivity to emotional, reward and food cues in this patient population. This work has been submitted as a RO1 application to the NIH and uses behavioral paradigms developed at the Institute.

Education and Training

A significant objective of the Institute is in training, education and outreach. The Institute's network has international collaborations established with the United Kingdom, Switzerland and The Netherlands in addition to national ones with Cornell, Columbia, Connecticut, NIMH, NYU, UCLA, Vanderbilt, University of Oregon, University of Pennsylvania, Princeton, Rockefeller, Stanford, UC Irvine, UCSD, Scripps, University of Hawaii, MGH and Yale. Highlights of the Institute's training activities are provided below.

Residency Education. Drs. Zevin, Casey, and Somerville 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 and Mind. Drs. Casey, Somerville 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. Casey, Somerville and Zevin all played significant roles this year in teaching Weill Cornell Biomedical Graduate Program in Neuroscience related courses that link brain and behavior.

Fundamentals of Cognitive Neuropsychology. Dr. Jason Zevin teaches an honors seminar at Barnard College as an adjunct faculty member. A number of students from this course have gone on to pursue graduate studies in related areas, including Gina Marrone, a current doctoral candidate in the Neuroscience Program.

Mortimer D. Sackler, MD Summer Institute. This year will mark the first summer institute since it was renamed, the Mortimer D. Sackler, M.D. Summer Institute and supported by a generous gift by the Mortimer D. Sackler, M.D. Sackler family. This year's course will be co-

directed by Drs. Casey and Bill Fifer of the Sackler Institute at Columbia University and held in New York City and will focus on learning and plasticity.

Weill Graduate School of Medical Science. Dr. Casey has served as the Director of the Neuroscience Program at Weill Graduate School of Medical Science for five years and will resign this year. The program includes over 80 faculty and graduate students. The Institute has taken and will maintain 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.

Biology of Neural Disease Course: Molecule to Bedside. Drs. Casey, Betsy Ross and Giovanni Manfredi are co-directing a course on biology of neural diseases focusing on three categories of disorders: neuropsychiatric (anxiety), neurodevelopmental (autism), and neurodegenerative (Parkinson's disease). The course is geared toward providing Ph.D. students with exposure to specific patient populations.

Neuroscience and Journalism. Dr. Casey developed and directed a course on interacting with the media in neuroscience. The course included tips on dealing with newspaper, television and radio media and included presentations from science writers and journalists for *Scientific American*, *HBO*, *the Today Show*, *Wall Street Journal* and the *New York Times*.

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 5 years and has received an NICHD T32 joint institutional interdisciplinary training grant submission for predoctoral fellows in development and learning (see <http://neuroscience.cornell.edu/imagine.html>).

Recruitment of Underrepresented minorities. Dr. Casey participates in the Gateway and Access programs that provide summer mentorship for underrepresented minorities who may be potential MD, PhD and PhD applicants to Weill Cornell.

Outreach Activities

This year has been a significant one for outreach related activities in local, national and international settings. We provide a few examples of these efforts below.

Neuroscience and the Law. Dr. Casey was recently interviewed by Alan Alda as part of a PBS Special on "Brains on Trial". In addition, Dr. Casey is currently involved in a report sponsored by the IOM on Juvenile Justice Reform.

Board on Children Youth and Families. Dr. Casey sits on the Board of Children, Youth and Families as an expert in developmental neuroscience. She is focusing on cognitive impairment in children following chronic disease and on concussions in school athletes.

Foundation for Behavioral and Brain. Dr. Casey was a keynote speaker at an OAH meeting on teen pregnancy intervention, during which she presented the science of risk taking behavior in teens.

Media Publicity. Dr. Casey's PNAS 2011 paper on delay of gratification revisited after forty years was covered by *The NY Times*, *EurekaAlert*, *Science News*, *NY Daily News*, *USA Today*, *Times of India*, *Health Day*, *Cornell Daily Sun*, *Time* magazine, and the *LA Times* in addition to her work being covered in University publications and websites.

Special Issue of Biological Psychiatry. Dr. Amy Arnsten of Yale and Dr. Casey co-edited a special issue of *Biological Psychiatry* to emphasize the role of systems neuroscience in psychiatric research and medicine that was published this year.

Special Issue of Current Directions in Psychological Science. . Dr. Casey co-edited a special issue of *Current Directions in Psychological Science* on the adolescent brain with the editor, Dr. Randy Engle.

Grants and Awards

Grants and Awards (2011-2012)

Dr. Casey received the 2012 Excellence in Teaching Award from the Medical College. This award acknowledges her teaching and service to the college over the past 10 years.

Dr. Casey received a multi-site grant from the MacArthur Neuroscience and the Law Network related to juvenile justice policy. She and her colleagues will examine behavioral and brain development specifically relevant to socioemotional contexts most common to criminal behavior in cohorts of youth in the LA and NY area.

Pending Grants and Awards

Drs. Casey, Glatt and Lee have submitted an R01 application to examine the development of basic forms of emotional learning and memory in mice and humans that are at the very core of different anxiety disorders and behavioral therapeutics. The objective is to determine the efficacy of innovative therapies and preventive strategies for psychiatric disorders as a function of developmental status.

Dr. Casey is collaborating with investigators at Columbia (Laurel Mayer and Michael Rosenbaum) 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. Casey is collaborating with investigators at Columbia (Allegra Broft and Tim Walsh) on a imaging study of Bulimia to identify neural circuitry underlying sensitivity to emotional, reward and food cues in this patient population. This work has been submitted as an RO1 application to the NIH and uses behavioral paradigms developed at the Institute.

PhD student, David Johnson has submitted an NIH NRSA predoctoral grant application to examine the development of reconsolidation update of fear memories using psychophysiological measures under the mentorship of Casey.

PhD student, Theresa Teslovich has submitted a NIH NRSA predoctoral grant application to examine the development of delay of gratification using impulse control tasks including adapted go/nogo and temporal discounting tasks.

Dr. Zevin was included as Co-Investigator on a P01 application submitted to NICHD by Robin Morris (co-PI, GA Tech), Maureen Lovett (co-PI, Hospital for Sick Children) and Kenneth Pugh (co-PI, Haskins Labs). The project will use a well-respected intervention program for reading disability to identify "non-responders" and examine their profiles on a set of general measures of language and memory processing abilities.

Dr. Zevin was included as Co-Investigator on a P01 application submitted to NICHD by

Kenneth Pugh (PI, Haskins Laboratories) to study the relationship between spoken and written communication across five languages (English, Spanish, Chinese, Hebrew and Japanese) with an international team of collaborators, bringing together behavioral and fMRI studies and computational modeling.

Dr. Zevin, collaborating with Bruno Tagliaferri (co-PI, Perception Research Systems), is preparing to submit an NIMH R43 application to develop software that will enable researchers to easily design experiments and collect data using tablet devices (such as the iPad, which has obvious advantages for developmental research).

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

Publications

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