

**The Sackler Institute for Developmental Psychobiology**  
**Weill Cornell Medical College**  
**2013-2014**

“We are at a moment in time when we have enormous opportunity and obligation to move psychiatric research more quickly from bench to bedside. This task will require basic and clinical scientists to come together to move this agenda forward, as no single discipline, profession, or method can do this alone (Casey, Oliveri & Insel, 2014).” The Sackler Institute is directly responding to this charge with their interdisciplinary research program, translating transgenic mouse models to human behavior, disease and treatment under the leadership of Director and Sackler Professor, Dr. BJ Casey. She has partnered with Dr. Francis Lee, Vice Chair of Research on the developmental neurobiology and Dr. John Walkup, Division Head of Child and Adolescent Psychiatry, on the clinical translation, both within the Department of Psychiatry under the leadership of Dr. Jack Barchas.

This is an exciting time for The Institute with the greatest synergy to date between basic and clinical investigators and the addition of two new faculty: Dr. Cate Hartley, an Assistant Professor of Psychology in Psychiatry and Dr. Conor Liston, an Assistant Professor recently recruited to the Brain and Mind Research Institute at Weill Cornell Medical College. Both faculty members bring new technology and expertise to the interdisciplinary research program of the Sackler Institute. The faculty and fellows have received several awards (see *Grants and Awards*) and published nearly 60 empirical and policy papers in high profile journals including *The Proceedings of the National Academy of Sciences*, *Nature Reviews*, and *Nature Communications*.

Mentoring and training the next generation of basic and clinical scientists remains a high priority for The Institute under Dr. Casey’s leadership. This year she will direct the annual Mortimer D. Sackler M.D. Summer Institute with Dr. Bill Fifer, the Sackler Institute Associate Director at Columbia University and Dr. Declan Murphy, the Sackler Institute Director at Kings College London in addition to numerous other teaching and mentoring activities (see *Training and Education*). Public lectures are an essential part of The Institute’s Outreach and Policy activities. Translation of the latest neuroscientific discoveries for the media and the public is at an all time high with coverage by *NPR*, *PBS*, *Discovery News*, *Simple Magazine* and *New York Magazine* (see *Outreach Activities*). This report highlights just a few of the many accomplishments of this past year and new directions.

**Academic Faculty and Staff**

***Sackler Affiliated Faculty***

B.J. Casey, Ph.D., Director and Sackler Professor of Developmental Psychobiology, WCMC  
and Adjunct Professor, The Rockefeller University

Charles E. Glatt, M.D., Ph.D., Associate Professor of Psychiatry, WCMC

Cate Hartley, Ph.D., Assistant Professor of Psychology in Psychiatry

Francis S. Lee, M.D., Ph.D., Sackler Professor of Psychiatry and Vice Chair of Research,  
Department of Psychiatry, WCMC

Conor Liston, M.D., Ph.D., Assistant Professor, Brain and Mind Research Institute, WCMC

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

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

Fred Morrison, PhD. Professor, University of Michigan, Visiting Scholar, WCMC

Jason Zevin, Ph.D., Associate Professor, University of Southern California

### ***Sackler Staff***

Gloria Pedersen Research Coordinator

Danielle Dellarco, Research Coordinator

Jae Woo, M.D., IT Manager

### ***Sackler Predoctoral and Postdoctoral Fellows***

Ali Cohen, 2<sup>nd</sup> year Neuroscience Ph.D. student

Hugo Decker, M.D. Ph.D. tri-institutional student

Michael Dreyfus, M.D. Ph.D. tri-institutional student

Andrew Drysdale, M.D. Ph.D. tri-institutional student

Jennie Grammer, Ph.D. Sackler Visiting Scholar, WCMC, Albert Einstein College of Medicine

Aaron Heller, Ph.D., Postdoctoral Clinical Fellow

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

David Johnson, 4<sup>th</sup> year Neuroscience Ph.D. student

Frederico Lourenco, 4<sup>th</sup> year Neuroscience Ph.D. student

Theresa Teslovich, 5<sup>th</sup> year Neuroscience Ph.D. student

### **Program of Research**

The overarching objective of the Institute is to: 1) delineate the biological mechanisms underlying learning and development and how they go awry in neurodevelopmental and neuropsychiatric disorders; and 2) 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. Below are highlights from work specific to anxiety and stress disorders; eating disorders; and cognitive and behavioral disorders.

#### ***Anxiety and Stress Disorders***

The Institute is involved in a rich set of basic and clinical studies of affective and cognitive processes impacted by stress and anxiety. This work merges mouse, computational and human and clinical research by Drs. Francis Lee, Charles Glatt, Cate Hartley, Conor Liston, John Walkup and Casey. These studies lay the critical groundwork for the identification, treatment and ultimate prevention of these disorders.

*Role of the Endocannabinoid System in Anxiety.* In collaborative cross-species research involving Drs. Lee, Glatt, Hartley, Liston and Casey and MD PhD student Andrew Drysdale are examining whether the propensity to respond actively or passively to fear is modulated by the endocannabinoid system. Parallel imaging work in genetically altered mice and in humans is shedding light on how genetic variants within this system lead to circuit changes that result in behavioral phenotypes relevant to anxiety disorders and addiction. This work is the basis of an upcoming R01 submission and may shed light upon the neuromodulatory systems that may predispose individuals toward

internalizing or externalizing disorders.

*Preclinical to Clinical Trials.* MD, PhD student Andrew Drysdale in collaboration with Drs. Walkup, Casey, Lee, and Hartley published a translational perspective paper in *Biological Psychiatry*. This paper provides proof of principle for when to treat children with anxiety disorders based on preclinical developmental human and mouse preclinical studies showing diminished extinction learning on which CBT exposure therapy is based.

*Persistently attenuating fear memories in Adolescence.* Another exciting study is underway to examine alternative ways to persistently attenuate fear memories in adolescents who show diminished extinction learning. This project is led by Casey and 4<sup>th</sup> year PhD student, David Johnson. They are using reconsolidation update to alter fear memories by retrieving and updating them prior to extinction, bypassing the need for prefrontally mediated extinction processes, that are immature in the adolescent.

*Predictors of CBT response in Anxiety Disorders.* In collaboration with Dr. Shannon Bennett, we examine how fear extinction learning predicts treatment response to CBT therapy. Ultimately she will test the effectiveness of basic CBT exposure therapy versus CBT that builds on the reconsolidation work in adolescents by Casey and Johnson to test novel CBT methods for those who do not respond to traditional CBT exposure.

*Understanding PTSD in Veterans with TBI.* In collaboration with Judith Cukor we will examine extinction learning in veterans with brain trauma and PTSD to understand mechanisms by which individuals with traumatic brain injury may be more vulnerable to PTSD. This work is in collaboration with Drs. Joann Difede and Casey and neuroscience student, Dave Johnson.

*Predicting Fear Recovery following Extinction.* Dr. Hartley, in collaboration with Dr. Sam Gershman at MIT, are using computational approaches to examine how differences in memory formation during extinction learning predict the subsequent recovery of fear. This work has implications for understanding cognitive mechanisms that might confer vulnerability to anxiety disorders. This work has been submitted for publication.

*Smart Phone Technology and affective functioning.* Dr. Aaron Heller, a postdoctoral fellow at the Sackler Institute with Casey is using brain imaging together with real world field measures assessed with smart phone technology in collaborative efforts with Dr. Debra Estrin of Cornell Tech. This work will target the most vulnerable and accessible populations of young people who have the highest rates of psychopathology and are the highest users of smart phone technology to explore alterations in positive emotions related to anhedonia. This work will bridge the medical college campus and the new Cornell Tech campus of New York City currently housed at Google's headquarters has been submitted as a NIMH K99R00 Pathway to Independence application.

*Transcranial magnetic stimulation (TMS) and Depression.* Repetitive TMS of the dorsolateral prefrontal cortex is an established treatment for depression, but its underlying mechanism of action remains unknown. Abnormalities in two large-scale neuronal networks—the frontoparietal central executive network and the medial prefrontal-medial parietal default mode network are consistent findings in depression and potential therapeutic targets for TMS. Liston in collaboration with MarDubin and Andrew Drysdale are examining the impact of TMS on activity in these networks and their relation to treatment response. Preliminary findings have been published in *Biological Psychiatry* this year.

### ***Eating Behavior and Disorders***

The Institute is involved in a number of collaborative NIH studies with Columbia University on eating behavior led by Drs. Casey that lay the critical groundwork for the identification, treatment and prevention of eating disorders.

*Neural Correlates of Delay of Gratification.* Dr. Casey with Drs. Mischel and Kevin Ochsner (PI) of Columbia University is examining 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) and involves PhD students Chelsea Helion and Theresa Teslovich.

*Genetic Studies of Obesity.* Dr. Casey, together with Rosenbaum and Mayer (PIs) from Columbia New York State Psychiatric Institute, received a five year R01 grant entitled *Functional imaging and eating behavior among FTO genotypes in pre-obese children*. This joint institution collaboration involves 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 using behavioral paradigms developed at the Institute.

*Temporal Discounting and Anorexia Nervosa.* Drs. Casey and MD PhD student Hugo Decker are involved in a collaborative study funded by the Klarman Foundation to examine neural correlates of temporal discounting (delaying self gratification) in Anorexia Nervosa with Drs. Tim Walsh and Joanna Steinglass (PI), Bernd Figner and Elke Weber of Columbia University.

*Role of Negative Affect on Impulsivity in Bulimia.* Dr. Casey and MD PhD student Michael Dreyfus are collaborating with investigators at Columbia (PI: Dr. Allegra Broft and Dr. Tim Walsh) on an NIMH funded study of Bulimia Nervosa to examine the aversive push of unpleasant emotions toward eating related behaviors.

### **3) Delinquency, Behavioral and Personality Disorders**

The Institute is involved in a number of studies on cognitive and behavioral disorders relevant to disorders of ADHD and delinquent behavior. These studies are led by Drs. Casey Hartley and Liston and lay the critical groundwork for understanding the emergence of cognitive and behavioral problems during development.

*Capacities relevant to delinquency.* Dr. Casey is the PI of a multisite (WCMC, UCLA, Temple, Penn, Columbia, NYU and OSHU) MacArthur Foundation funded study to examine capacities relevant to criminal responsibility under circumstances in which individuals often commit antisocial acts (e.g., emotional arousal, peer presence, etc.) that involves PhD candidates Ali Cohen, Frederico Lourenco and Chelsea Helion and postdoctoral clinical fellow Aaron Heller. Evidence from this study may bear on important legal questions regarding culpability and punishment of adolescents. This work has received significant attention from the media by NPR and PBS and is also part of The Institute's program on outreach and policy. Ali Cohen and Casey recently published an article highlighting this work "Rewiring juvenile justice: the intersection of developmental neuroscience and legal policy" in *Trends in Cognitive Science*.

*Instructed versus experiential learning across development.* In recent work with MD PhD student Hugo Decker and fellow Frederico Lourenco, Dr. Hartley is examining developmental changes in the efficacy of learning about rewards and punishments through instructions versus experience. This work has potential implications for public health informational campaigns that rely upon instruction to deter adolescents from risky behavior.

*Goal-directed and habitual action selection across development.* Recent work conducted by Dr.

Hartley and MD PhD student Hugo Decker has examined how the balance between goal-directed versus habit-driven action changes across development. Habitual action has been implicated as a mechanism in the etiology of substance abuse, as well as in other disorders that involve habit-like compulsive thoughts and actions related to stress. This work forms the basis of a recently submitted NIDA R03 Imaging Science Track Award for Research Transition (I/START) grant (PI: Hartley).

*ADHD studies.* Imaging studies led by Drs. Casey and Liston suggest that deficits in prefrontal connectivity in ADHD might arise from a common etiologic mechanism. This mechanism is thought to involve altered modulation of synaptic potentiation (plasticity) and pruning by dopamine and other factors during development that might persist into adulthood. Using state of the art optogenetic and microendoscopic imaging tools- never before used to examine the development of prefrontal connectivity and function, Liston will test this hypothesis.

*Borderline Personality Disorder.* Drs. Casey and Hartley together with Psych Intern Rachel Higier are collaborating with Drs. Otto Kernberg and John Clarkin to examine neural correlates and predictors of treatment responses in individuals with Borderline Personality Disorder. The studies focus on negative affect and impulsivity in addition to basic learning mechanisms implicated in expectations of others that are targeted by psychotherapy.

*SES Effects on Academic Performance.* Drs. Casey and Glatt together with Dr. Fred Morrison, a visiting scholar from the University of Michigan will examine the effects of socioeconomic status, self-regulation and the brain during the school transition. They have submitted a NIH P01 that will measure behavioral, neuroendocrine, DNA methylation, brain imaging and environmental measures to identify how socioeconomic status and the home and school environments impact school achievement and the underlying neural circuitry. The study will occur in the context of the natural December school off for kindergarten, comparing cohorts of similar age but a year of formal schooling versus none.

### **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 Netherlands and Calgary in addition to national ones with Cornell, Columbia, NYU, UCLA, OHSU, Penn, Temple University, University of Pennsylvania, Rockefeller and Vanderbilt. Highlights of the Institute's training activities are provided below.

*Mortimer D. Sackler, MD Summer Institute.* Last year marked the first summer institute since it was renamed, the Mortimer D. Sackler, M.D. Summer Institute and supported by a generous gift from the Sackler family. The course was co-directed by Drs. Casey and Bill Fifer of the Sackler Institute at Columbia University and held in New York City and focused on learning and plasticity. Twenty of nearly 100 applicants are being selected from around the world. This year's course will be co-directed by Drs. Casey, Fifer and Declan Murphy, the new director of the Sackler Institute at Kings College London and has an all-star line-up of leaders in the field of developmental and cognitive neuroscience.

*Residency Education.* Dr. Casey plays a significant role in teaching both adult and child psychiatry residents at Weill Cornell Medical College as part of the Residency program curriculum. Lecture

*Medical Students.* Drs. Casey and Hartley played significant roles this year in teaching medical students at Weill Cornell and Weill Qatar about developmental and cognitive neuroscience by providing lectures and labs for the students that have resulted in participation of the medical students in Sackler seminars.

*Neuroscience Students.* Drs. Casey and Hartley played significant roles this year lecturing to neuroscience graduate students of the Weill Cornell Biomedical Graduate Program on brain and behavior.

*Tri-institutional MD PhD Students.* Dr. Casey helps teach the MD PhD 2<sup>nd</sup> Year Scientific Frontiers course, exposing them to neuroscientific discoveries and currently mentors three MD PhD students.

*Clinical Psychology Interns.* The Sackler Institute provides opportunities for Psych Interns to carry out research while completing their clinical psychology requirements in the training program directed by Dr. Susan Evans. Last year intern, Aaron Heller, joined the group and then began postdoctoral fellowship at The Institute with Dr. Casey on the emergence of anhedonia in adolescents, a core symptom of depression. This year, Rachel Higier has begun working with members of The Institute on studies of Borderline Personality Disorder.

*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.

*Summer Volunteers and Interns.* Each year numerous volunteers from local high schools and colleges take part in research opportunities at The Institute. These opportunities provide them with additional credentials for applying to subsequent undergraduate, graduate and medical programs.

### **Policy and 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.

*Media Publicity.* Research by Dr. Casey and others at the Sackler Institute has been covered by NPR: “Drawn to Danger: Why teens react rather than withdraw from threat”, PBS: “Brains on Trial”, New York magazine: “Why You Truly Never Leave High School”, Science News for Kids: “The teenage brain”, Discovery News: “The Teen Brain on Rage: How it's Different”, See [http://www.sacklerinstitute.org/cornell/sackler\\_in\\_the\\_news/](http://www.sacklerinstitute.org/cornell/sackler_in_the_news/) for specific links to news and feature articles.

*Special Issue of Current Directions in Psychological Science on The Teen Brain.* Dr. Casey edited a special issue of this journal that highlights what we have learned about the teen brain from imaging and nonhuman animal studies to policy. Four of the articles of this issue are in the top ten most downloading papers of 2013. She is completing a second special issue for the journal Developmental Neuroscience with colleagues Pradeep Bhide and Barry Kosofsky which has already received attention from NPR.

*Mental Health Research and Policy.* Casey has coauthored a commentary with NIMH Director Tom Insel and Molly Oliveri on the importance of neurodevelopmental research for understanding mental health and illness. Francis Lee and Casey published a commentary in Nature Reviews with other leaders in the field of mental health research on how the new DSM V and new NIMH Research Domain Criteria (RoDC) complement one another.

*Neuroscience and the Law.* Casey was part of a PBS Special that aired this year on “Brains on Trial” narrated by Alan Alda. In addition, Dr. Casey was a committee member and co-wrote the IOM report on Juvenile Justice Reform: A Developmental Approach. She has given numerous lectures to state and federal judges and is a member of the MacArthur Foundation Research Network on Law and Neuroscience.

*IOM and NAS National Council for Research (NCR).* Dr. Casey served on the special committee on *Sport Concussions in Youth* that came out this year and has received world wide attention.

*School Education.* Dr. Casey sits on the Board of two New Vision Schools based on JFK high school campus providing guidance on effective learning, the adolescent brain and mental health.

*Parent Education.* Dr. Casey spoke at the Parents & Science Program at The Rockefeller University on the “The Challenges of Adolescence: Balancing Risk, Novelty, and Self-Control” in April.

## **Grants and Awards**

### ***Grants and Awards (2012-2013)***

Dr. Casey received an honorary doctorate from Utrecht University.

Dr. Casey serves as a member of the NIMH Council.

Dr. Casey, in collaboration with investigators at Columbia (Laurel Mayer and Michael Rosenbaum), received a R01 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.

Drs. Casey and Liston have recently received a generous gift from the Rosen family to examine neurobiology underlying attention problems and new insights for treatments.

Ali Cohen received a NSF predoctoral award to examine the effects under the mentorship of Casey.

Dr. Cathy Lord, Director of the Center for Autism and Brain Development and former Sackler fellow Dr. Rebecca Jones received DOD grant AR130106 - “Implicit Learning Abilities Predict Treatment Response in Autism Spectrum Disorders”. Dr. Casey will help oversee the imaging studies.

Dr. Hartley received the 2013 Samuel W. Perry III, M.D. Distinguished Award in Psychiatric Medicine.

### **Pending Grants**

Dr. Casey submitted a P01 with Dr. Fred Morrison (PD) of the University of Michigan. This P01 will use a longitudinal design and behavioral, neuroendocrine, DNA methylation, imaging and environmental measures to identify how SES, the home and school environments impact variation in school achievement. Casey will serve as PI of Project 3 and the Data Acquisition Core.

Dr Hartley has submitted an R03 I/START application to NIDA to examine the neurocognitive mechanisms underlying the development of habitual versus goal-directed action selection.

Dr. Aaron Heller, a postdoctoral fellow at the Sackler Institute has submitted a NIMH K99R00 Pathway to Independence award application to use brain imaging together with real world field measures assessed with smart phone technology. This work will bridge the medical college campus and the new Cornell Tech campus of New York City currently housed at Google’s headquarters.

The Institute directly, and in collaboration with others, has grants and awards from diverse sources including the NIMH, NIDK, NICHD, the Dewitt Wallace Readers Digest, and the MacArthur Foundation. This funding supplements the generous gifts by the Mortimer D. Sackler, M.D. family and the continued support by the Department of Psychiatry (see Financial Statements).

## Publications

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Bhide, P., Kosofsky B & Casey BJ (in press). *Teen Brain: Thinks Differently*. Developmental Neuroscience (Special Issue Invited Editors).

Casey, B.J. (2013). The teenage brain: An Overview. (Special Issue Invited Editor) *Curr Dir Psychol Sci*.

Casey, B.J. (in press). Beyond Simple Models of Self Control to Circuit-based Accounts of Adolescent Behavior. *Ann Rev of Psychology*.

Casey, B.J., Oliveri, M.E., & Insel, T. (In press). A neurodevelopmental perspective on RDoC. *Biol Psychiatry*.

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Dreyfuss, M.D., Caudle, K., Drysdale, A.T., Johnston, N.E., Cohen, A.O., Somerville, L.H., Galván, A., Tottenham, N., Hare, Y.A., & Casey, B.J. (In press). Teens impulsively react rather than retreat from threat. *Dev. Neurosci.*

Drysdale, A.T., Hartley, C.A., Pattwell, S.S., Ruberry, E.J., Somerville, L.H., Compton, S.N., Lee, F.S., Case, B.J., & Walkup, J.T. (2013). Fear and anxiety from principle to practice: Implications for when to treat youth with anxiety disorders. *Biol Psychiatry*.

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