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Introduction

This report covers the eleventh year of operation of the Sackler Institute, established at Columbia April 27th 2001 with a gift from the Sackler Foundation made in December 2000 and was the product of the vision of Mortimer D. Sackler, MD who saw the need to better understand the developmental processes leading to health and disease. The Institute is an organization within the College of Physicians and Surgeons and the Department of Psychiatry that brings together federally funded scientists actively investigating developmental questions at all levels of inquiry. To this mission, our faculty has brought more than 15 million dollars of federal and other outside support in the last year. The generous endowments of the Institute provide income to support new directions in faculty research, salary support for two young investigators (Sackler Awardees), ISDP travel awards to graduate students and postdoctoral fellows engaged in developmental research and funds the biannual Sackler Prize for distinguished contributors to our understanding of developmental processes of mind, brain, and behavior. Lastly, the endowments support the Director and the administrative efforts to oversee ongoing efforts while continually expanding the activities of the Institute in support of its mission.

The administrative structure and faculty on June 30, 2012 are as follows:

Director, Dr. Jay Gingrich (appointed 3/1/2011)
Assistant Director, Dr. William P. Fifer
Administrators, Heidi Fitterling and Jennifer Knowles

Director, Basic Developmental Science Division – Dr. Jay Gingrich
Sackler Scientists - Drs. Mark Ansorge, Christoph Kellendonk, Frances Champagne

Directors, Clinical Developmental Neuroscience Division - Drs. Michael Myers and William Fifer
Sackler Scientists – Dr. Catherine Monk

Director, Translational Epidemiology Division - Dr. Myrna Weissman
Sackler Scientist - Dr. Alan Brown

Director, Developmental Neuroimaging Division - Dr. Bradley Peterson
Sackler Scientist – Dr. Andrew Gerber

Directors, Sackler Parent Infant Project – Drs. Catherine Monk and Andrew Gerber
Sackler Scientists – Drs. Archana Basu, Nina Burtchen and Elizabeth Werner

Department of Pediatrics (Neonatology) – Drs. Raymond Stark and Marianne Garland

Sackler Awardee: Dr. Andrew Gerber
Part I – Highlights

Sponsored Meeting and Symposia: The Mortimer D. Sackler M.D. Winter Conference in Developmental Psychobiology was held January 4th-7th 2012 in O'ahu, Hawaii. The growing reputation of this invited-only conference has enabled developmental researchers from disparate fields to share data, ideas and techniques and form long lasting and often unique collaborations. The organizing committee (William Fifer, Gordon Barr, Mark Ansorge, BJ Casey, Harlene Hayne, and Regina Sullivan) brought together another outstanding group of the world experts on topics ranging from mirror neurons to memory and sleep (see attached).

In November 2011, we also sponsored a symposium at the 44th Annual International Society for Developmental Psychobiology Annual Conference held in Washington, DC entitled: “Sackler Symposium: Infant Learning and Memory: Age, Experience and Individual Differences”. Our sponsorship allowed this to be a truly international symposium with Jane Herbert, University of Sheffield; Mikael Heimann from University of Gothenburg, Sweden; Petra Hauf from St. Francis Xavier University, Antigonish, NS, Canada; Olivier Pascalis from Université Pierre Mendes France; and Harlene Hayne from University of Otago, New Zealand.

Student Travel Awards
This year 21 Travel Awards were given to support students from 7 countries (Mexico, New Zealand, UK, Australia, France, Canada, and the US) to attend the ISDP meeting allowing them to present their work to peers and get feedback from more experienced investigators. The support of the Sackler Institute to these students often makes the difference between them attending or not attending such an international meeting. Moreover, many were able to extend their stay and attend the Society for Neurosciences meeting that begins immediately following ISDP.

Sackler Awardees 2011
Dr. Andrew Gerber received a second year of funding for his research in “An fMRI Investigation of Social Cognitive Deficits in Adults with High Functioning Autism Spectrum Disorder”

The final progress report from the 2011-2012 Sackler Awardee is provided in the “Sackler Awardee” portion (section vi) of this report.

Faculty Awarded Research Grants
Our Sackler faculty continues their tradition of securing federal and competitive funding from foundations. Our faculty also continued their tradition of collaboration amongst Sackler Faculty across divisions. Specifically, William Fifer and Michael Myers received $3.68 million over five years from the National Institute of Child Health and Human Development for “Prenatal Alcohol in Sudden Infant Death Syndrome (SIDS) and Stillbirth (PASS) Network.” In addition, Catherine Monk and Bradley S. Peterson received $3.1 million over five years from the National Institute of Mental Health for “The Effects of Prenatal Stress & Poor Nutrition on Brain and Cognition.” Catherine Monk and Frances Champagne received a grant from NIMH to study: “Prenatal stress: The epigenetic basis of maternal and perinatal effects”. The Sackler Faculty was also instrumental in organizing a very successful site visit by NIMH of our Silvio O. Conte Center for
Translational Developmental Neuroscience. The site visitors concluded by saying that our Conte Center was the “crown jewel” in their portfolio, and an sterling example “of how Conte Centers should be organized”.

**NEW INITIATIVES:**

**The Sackler Parent-Infant Program (SPIP)**
Founded and supported through a generous gift of Ilene Sackler-Lefcourt, the Sackler Parent–Infant Program (SPIP) was established 14 months ago to bring a new scientific focus to the study of the parent-infant dyad as a regulator of development. Consistent with its scientific mission, the SPIP was officially designated as a new division of the Institute. Andrew Gerber, MD, PhD and Catherine Monk, PhD were appointed co-directors and were charged with the goal of making Columbia a leader in parent–infant intervention research. New endowments will support a clinical fellow and provide travel funds to allow the trainee to integrate into the broader developmental research community through dissemination of their work. As a reporting entity of the Institute, SPIP trainees and researchers will draw on the research expertise of Sackler colleagues to create state–of–the–art clinical programs that provide evidence–based services and advance our scientific understanding of the parent-infant relationship. Going forward, we expect close collaboration between the SPIP and our Divisions of Clinical Developmental Neuroscience and Developmental Neuroimaging.

**The Sackler Parent-Infant Symposium**
In acknowledgement of the founding of the Sackler Parent-Infant Program it was decided to host a research conference that would bring together the leading lights of infant developmental research. This Symposium will take place October 4-5th 2013 at Uris Auditorium and the Italian Academy. In light of the loss of Daniel Stern, MD in the last year, we plan to acknowledge his tremendous contributions to our understanding of the mother-infant relationship during the public portion of the Symposium and at the inaugural reception and dinner the evening of October 4th.
Part II – Research Programs

DIVISION OF BASIC DEVELOPMENTAL NEUROSCIENCE  
(FORMERLY BASIC SCIENCE)

Division Director: Jay A. Gingrich, MD, PhD  
Division Members: Mark Ansorge, PhD  
Christoph Kellendonk, PhD  
Frances Champagne, PhD

Overview of Basic Developmental Neuroscience.

Our division continues to enjoy a close relationship amongst the different laboratories. We meet weekly to have trainees share data with all the labs in attendance (except for the Champagne lab which is downtown). Dr. Kellendonk was named a Schaefer Research Scholar Award in this last year, Dr. Ansorge was selected as a Travel Awardee for the American College of Neuropsychopharmacology, and Dr. Champagne was awarded a new RO1 grant to study maternal stress and fetal outcomes with Dr. Monk (co-Director, Parent-Infant Program).

Architectural and space plans were completed for the East wing of Pardes 4 which will eventually house the laboratories of Sackler Basic Science faculty in the Division of Developmental Neuroscience. Construction is expected to begin in late 2013.

Jay A. Gingrich, MD, PhD, Director – Developmental pathways to health and disease

Publications

Grants

5P50MH090966-02 (Gingrich) 07/01/10 to 06/30/15
NIH / NIMH
Silvio O. Conte Centers for Basic and Translational Mental Health Research
Serotonergic Modulation of Brain Development: Genetic and Pharmacologic Influences on Structure, Function, and Behavior
This study aims to determine whether low-expressing 5httlpr variants of the serotonin transporter (SERT) and pharmacologic inhibition of SERT function produce similar effects on brain maturation and ultimately behavior and increase the risk for clinical diagnoses such as affective and anxiety-related disorders.
Role on Project: Center PI and Co-PI of Project 4

NIMH (1R01MH080116-01A1) (Gingrich) 02/01/08 to 11/30/12
Serotonin and the Modulation of Brain Development
Study of the mechanisms underlying the impact of early SSRI exposure on adult emotional function in mice.
Role: Principal Investigator

Simons Foundation Autism Research Initiative (Gingrich) 10/1/07 to 11/30/2012
Three year project to identify specific loci that are most prone to aberrant methylation with advancing Age, and are transmitted frequently to affected offspring.
Role: Principal Investigator

NIDA (P01 DA12923) (Weinstein) 08/01/07 to 06/30/12
Hallucinogens on 5-HT2A Receptors: Mechanisms and Effects. Five year project to examine the role of 5-HT2A receptors in the mechanism of hallucinogens such as LSD. Proposes to generate several knock-in mutations of 5-HT2A receptors that selectively perturb different aspects of receptor function (ligand binding, G-protein coupling, desensitization.
Role on Project: PI of Project 3.

NIMH (5 R01-MH076026) (Gingrich) 07/01/06 to 02/29/2012
Gene - Environment Interactions and Vulnerability to Neuropsychiatric Disorders
This study examines the environmental factors that contribute to the worsening or amelioration of the depressive phenotype that have been described in the 5HTT knockout mice.
Role: Principal Investigator

Mark Ansorge, PhD, Sackler Scientist – Role of serotonin signaling in limbic system development

Serotonin (5HT) functions both as a neurotransmitter and as a growth factor during the maturation of the central nervous system (CNS) and has been implicated in the etiology and treatment of numerous neuropsychiatric disorders such as depression, anxiety, autism, obsessive-compulsive disorder, and anorexia nervosa.
Our efforts investigate the effects of altered serotonin signaling during development on brain maturation and adult behavior in mice.

**Publications**


**Grants**

NIMH (4R00MH083044-03) (Ansorge) 04/01/08 to 03/31/13
Developmental Origins of Affective Disorders.
This study examines the effects of early-life 5-HTT blockade on the development of raphe function.
Role on Project: Principal Investigator

NIMH (1 P50 MH90966-01) (Gingrich) 07/01/10 to 06/30/15
Serotonergic Modulation of Brain Development: Genetic and Pharmacologic Influences on Structure, Function, and Behavior.
Projects 1–3 of this Conte center study the consequences of developmentally perturbed serotonin signaling on human brain development and behavior. Project 4 investigates serotonin-mediated genetic and pharmacologic influences on the development of brain structure and behavior of rodents and primates.
Role on Project: Co-Investigator, Co-PI Project 4

NIMH (1 R01 MH080116-01) (Gingrich) 12/01/07 to 11/30/12
Serotonin and the Modulation of Brain Development.
This project investigates critical developmental periods during which serotonin transporter inhibition alters adult emotional behavior.
Role on Project: Co-Investigator

Frances Champagne, PhD, Sackler Scientist - Environment influences on epigenetic mechanisms underlying brain development.

**Publications**

2. Wan M, Bolger N, Champagne FA (in press) Human perception of fear in dogs varies according to experience with dogs. PLoS ONE
Grants

Current Funding

**NIH 2P01ES009600-11** Champagne (Co-Project Leader) 2009-2014
*Molecular/disease consequences of prenatal BPA, PAH exposure across generations*
Co-Investigator with Dr. Rachel Miller (CUMC)
This project explores the transgenerational consequences of prenatal exposure to bisphenol A and polycyclic aromatic hydrocarbons for neurodevelopmental, metabolic, and immune outcomes.

**NIH – R01** (Co-Investigator with Monk C & Tycko B) 2011-2016
*Prenatal stress: The epigenetic basis of maternal and perinatal effects*
This project combines research in humans and in a rodent model exploring the link between prenatal stress, epigenetic dysregulation, and offspring development.

**NIH 1P20HG005535-01** Champagne (Co-PI; Steering Committee) 2010-2015
*Center for ELSI Research on Psychiatric, Neurologic, and Behavioral Genetics (P20)*
This project is aimed at establishing a training/research forum for studies on the ethical, social, legal, and health consequences of genetic risk of neurological, psychiatric, and behavioral disorders.

**NIH 1DP2OD001674-01** Champagne (PI) 2007-2012
*Epigenetic Mechanisms Mediating the Inheritance of Reproductive Behavior*
This project explores the reproductive consequences of mother-infant interactions in rodents and the role of DNA methylation in mediating these effects.

**NIH 5R01MH057987-13** Young (PI) 2010-2012
*Central vasopressin receptors and affiliation*
This project explores the effects of variation in the vasopressin receptor (V1a) gene promoter for receptor levels/distribution and behavior.

**Christoph Kellendonk, PhD, Sackler Scientist** - *Role of subcortical dopamine signaling in brain development*

In the classical model of basal ganglia, striatal output projections are organized into two distinct pathways; the direct pathway – which directly projects to the substantia nigra (SNr) – and the indirect pathway – which projects to the external globus pallidus (GPe) and then relays through intermediate neurons to the SNr. These two pathways are thought to exert opposing effects on motor activity. However, single-cell tracing studies have challenged the strict dichotomy between these pathways revealing that the vast majority of “direct” neurons possess collaterals to the GP. In the last year, we have shown that these collaterals, which bridge between the direct and indirect pathway, are highly plastic in the adult animal and are bi-directionally regulated by striatal dopamine D2 receptors (D2R).
Overexpression of D2R in the striatum selectively increases the extent of GPe collaterals of the direct pathway by altering excitability of the indirect pathway. In contrast, genetic downregulation of D2Rs as well as chronic administration of the D2R antagonist haloperidol, a widely-used antipsychotic medication selectively decrease the density of striatonigral GPe collaterals. Using optogenetic tools in vivo, we further revealed the behavioural significance of the bridging collaterals for the control of motor behaviour. Our findings give mechanistic insights into how the balance of the basal ganglia circuitry is regulated in the adult animal and how chronic treatment with antipsychotic medication alters the neuronal connectivity of basal ganglia circuitry.

The function of the medio-dorsal thalamus in cognition:

Cognitive deficits are central to schizophrenia, but the underlying mechanisms still remain unclear. Imaging studies performed in patients point to decreased activity in the medio-dorsal thalamus (MD) and reduced functional connectivity between the MD and prefrontal cortex (PFC) as candidate mechanisms. However, a causal link is still missing. We used a pharmacogenetic approach in mice to diminish MD neuron activity and examined the behavioral and physiological consequences. We found that a subtle decrease in MD activity is sufficient to trigger selective impairments in prefrontal-dependent cognitive tasks. In vivo recordings in behaving animals further revealed that MD-PFC beta-range synchrony is enhanced during acquisition and performance of a working memory task. Decreasing MD activity interfered with this task-dependeant modulation of MD-PFC synchrony, which correlated with impaired working memory. These findings suggest that altered MD activity is sufficient to disrupt prefrontal-dependent cognitive behaviors, and could contribute to the cognitive symptoms observed in patients with schizophrenia.

Publications


Grants

NIMH Silvio O. Conte Center, 1P50MH086404-01A1 (Abi-Dargham, PI) 07/01/2010-06/30/2015 "Dopamine Dysfunction in Schizophrenia": Project 4: "The Role of Striatal Postsynaptic Dopamine Receptor Activity in the Cognitive Symptoms of Schizophrenia" Role: Co-Investigator on Project 4

NIMH RO1 MH093672-01 (Kellendonk, PI) 05/20/2011-06/30/2016 "Medium spiny Neuron Excitability and Motivation"

2011 Schaefer Research Scholar Award (Kellendonk, PI) 07/01/2011-06/30/2012 “Consequences of maternal immune response for the maturation and integration of cortical interneurons"

DIVISION OF CLINICAL DEVELOPMENTAL NEUROSCIENCE (FORMERLY BEHAVIORAL NEUROSCIENCE)

Division Director: Bill Fifer, PhD
Division Members: Michael Myers, PhD
Catherine Monk, PhD

Dr. William Fifer, Associate Director, Sackler Institute - Human Fetal and Infant Behavior and Intrauterine Influences on Vulnerability to Psychiatric Illness

Our general research program focuses on the effects of the early environment on fetal and infant brain/behavior development. Our funding from National Child Health and Human Development and the National Institute on Deafness and Communicative Disorders supports our investigations into the effects of prenatal risk factors including maternal stress, depression, nicotine, alcohol and poor nutrition on brain/behavior development. With Dr. Kimberley Noble in Pediatrics and the Sergievsky Center we published on the long-term effects on infants born “near term” (37-38 weeks) on reading and math test scores in the 2nd grade. This paper published in Pediatrics generated an enormous amount of media coverage, since from a public health perspective this finding may have important consequences, particularly in the realm of identifying children who may be at risk for poorer school achievement and in light of the increasing trend for performing elective early deliveries for nonmedical reasons. Researchers, clinicians, and parents are now urged to consider this graded relationship between weeks of gestation and school performance. With Dr. Nina Burtchen in the Division of Developmental Neuroscience we continue to investigate the roots of this adverse outcomes by focusing on alterations in newborn patterns of EEG and learning are in “late preterm” infants and prediction of neurobehavioral outcome at 15 and 21 months of age. With Dr. Ismee Williams, a
fetal cardiologist, we are looking at the same markers in children born with congenital heart disease. With Dr. Myers we continue our NIH study on risk for neurodevelopmental disorders in high-risk populations in South Africa and the Dakotas. Following up on our discovery that newborn infants can demonstrate learning during sleep, we are investigating, with Dr. Joel Yang in the Division of Developmental Neuroscience, if this learning can extend to the ability to learn about olfactory stimuli and whether this ability may be predictive of later neurodevelopmental disorders within a cohort of high-risk low birth weight infants.

Sackler Serotonin Project: Drs. Peterson, Monk, Myers and Fifer are continuing work on the clinical research arm of this project as part of the Conte Grant. We are investigating the effects of SSRI antidepressant exposure during pregnancy on fetal and infant neurobehavioral development as part of this project and with the Glasgow Sackler Center in a group of pregnant women diagnosed with depression and who are also treated with SSRI's. We are using a combination of Sackler and NIH funding to carry out a pilot study which will follow these infants into later infancy and early childhood.

Publications


Grants

U01 HD55155 (Fifer) 09/01/2006 – 07/31/2016
Nichd
Prenatal Alcohol in Sudden Infant Death Syndrome and Stillbirth (PASS) Network
Co-operative Agreement for directing the Physiological Assessment Center for the fetal alcohol network.

R37 HD32774 (Fifer) 04/01/2006 - 03/30/2016
Nichd
Perinatal Assessment of At-Risk Populations
This is an investigation of underlying mechanisms and early assessment of risk for Sudden Infant Death.

P50 (MH090966) (Gingrich and Weissman) 07/01/10 – 06/30/15
NIMH
Serotonergic Modulation of Brain Development: Genetic and Pharmacologic Influences
Principal Investigators: Gingrich, J and Weissman, M.
To investigate the role of serotonin (5HT) signaling in human and mouse brain development by examining the effects of 5HT transporter gene variants as well as the effects of in utero exposure to serotonin reuptake inhibitors.

R13 (MH HD58769) (Fifer and Shair) 10/01/00 – 09/30/15
NICHD
International Society for Developmental Psychobiology Student Travel Grant

**Michael Myers, Division Chief, Division of Developmental Neuroscience - Early Experience and Brain Development**

Work in this laboratory continues to focus on the effects of normal and abnormal variation in the environment during pregnancy and in the early postnatal period on brain development. An evergrowing body of evidence supports the idea that vulnerability for physical and mental illnesses can be shaped by events occurring during these sensitive periods of development. Characterizing such long-term effects of early experiences remains a central focus of researchers in the field of Developmental Psychobiology and rapid advances in developmental neuroscience, genetics and molecular epigenetics now make it possible to study the developmental processes that account for enduring changes in risk and resilience to disease. There are four major efforts related to this theme.

Within the Conte Center, which was based on initial funding from the Sackler Institute, I work with Drs. Peterson, Monk, and Fifer on a project that focuses on the effects of SSRI antidepressant exposure during pregnancy and how naturally occurring genetic variation in regulation of synaptic reuptake of serotonin affects the development of brain structure and function of human infants.

Another major effort involving Drs. Myers and Fifer is a project supported by NICHD and NIAAA. This large network study is addressing the impact of Prenatal Alcohol exposure on Stillbirth and SIDS (PASS). When completed the 12,000 women and children enrolled will provide the most comprehensive data base regarding early adverse exposure on risk for the most catastrophic outcomes related to abnormal brain function during early life.

A third area relates to our findings showing discontinuities in developmental patterns of cortical activity from 34 to 44 weeks post-conceptional age (PCA). This work, which was published this year, proposes that the early increase and decrease in EEG activity reflects the transition in effects of the neurotransmitter GABA from a depolarizing, neurotrophic agent, to a hyperpolarizing inhibitory neurotransmitter In addition, it now appears that specific patterns of
activity that account for these findings may reflect activity within thalamocortical circuits that are formed during the late fetal period but which then regresses as the mature cortex is formed. These findings have stimulated a new focus on early transient cortical circuits as targets for the effects of early experience.

The fourth area of focus is on translational studies testing the hypothesis that adverse developmental outcomes that are commonly seen in babies born prematurely can be ameliorated by interventions during the infants’ stay in the NICU. This randomized controlled trial completed enrollment (150 infants) this year and a series of papers are expected to results from this study.

Publications


Grants

T32 MH018264 (Myers, M.M., PI) 07/01/08-06/30/13
NIMH
“Research Training in the Psychobiological Sciences”
Postdoctoral research training grant for MDs and PhDs in Psychobiology.

2U01HD055155 (Fifer, W.P. & Myers, M.M Co-PIs) 08/01/2011-07/31/2016
NICHD
“Prenatal Alcohol in Sudden Infant Death Syndrome and Stillbirth (PASS) Network”
Co-operative Agreement for Physiological Assessment Center.

RO1HD32774 (Fifer, W.P., PI; Myers, M.M. Co-Inv) 04/01/11-03/30/16
NICHHD
“Perinatal Assessment of At-Risk Populations”
Investigations of underlying mechanisms and early assessment of risk for Sudden Infant Death.

MH090966 (Gingrich PI, Myers, Co-Inv) 09/01/2010-08/31/15
NIMH
“Serotonin Signaling During Early Development”
MRI and EEG correlates of genetic polymorphisms in the serotonin transporter and prenatal exposure to SSRIs.

**Catherine Monk, Sackler Scientist** - M.O.O.D.S. Laboratory: Mother-Offspring Outcomes and Developmental Studies

**Publications**


**Grants**

R21: MH092665-01 (Monk) 01/1/11–12/30/13
NIMH
Behavioral Change in the Mother-Infant Dyad: Preventing Postpartum Depression
The goal of this project is to prevent postpartum depression in vulnerable women using a newly developed coaching intervention.
Prenatal Stress: the Epigenetic Basis of Maternal and Perinatal Effects
NIMH
The goal of this project is to characterize epigenetic processes contributing to biobehavioral effects of antenatal stress on pregnant women and the developing child.

1 R01MH093677-01A1 (Monk, C.) 9/23/11 – 06/30/16
The Effects of Prenatal Stress & Poor Nutrition on Brain & Cognition
NIMH
The goal of this project is to identify brain and behavior effects of prenatal maternal distress and poor nutrition while also considering the influence of the social–environmental context postnatally.

3R01 MH093677-02S1 9/23/11 – 06/30/16
The Effects of Prenatal Stress & Poor Nutrition on Brain and Cognition
NIMH
Supplement

1P50MH090966-01(Gingrich, J., Peterson, Monk) 07/01/10 - 06/30/15
NIMH
Serotonergic Modulation of Brain Development: Genetic & Pharmacologic Influences on Structure, Function and Behavior
The goal of our project on this P50 is to identify variation in newborn neurobiological development associated with maternal prenatal SSRI use and/or untreated depression and also to consider the contribution of different serotonin genotypes to the outcomes.

2 R01 ES013543-05A1 (Whyatt, R) 12/01/04 – 03/31/15
NIEHS
Early-life Phthalate Exposure, Thyroid Function and Child Cognitive Development
The goals of this study are to examine prenatal exposure to these toxicants and maternal thyroid function in relation to child development.

R21: MH092665-01 (Monk) 01/11–12/30/13
NIMH
Physical Activity & Inflammation in Pregnancy: Relevance for Perinatal Outcomes
The goals of this application are to determine the feasibility of an exercise intervention with pregnant women and to monitor immune activation throughout gestation
Translational Epidemiologic & Clinical Studies of Genetic Risk and Biological Markers in the Development of Mood and Anxiety Disorders

The aim of the Division is to translate human, clinical and epidemiologic observational findings into understanding of mechanisms using modern tools of imaging, genetics and animal models.

A focus of our research continues to be a longitudinal three-generation study of offspring at high and low-risk for major depression (MDD) which includes MRI, EEG, and DNA collection. Funds from the Sackler Serotonin Transporter Project were important in enhancing our collaborations with Drs. Gingrich, Brown, Bruder, Peterson, Bansal, and Gerber.

We are actively engaged in data collection of the 6th wave of the three generation study. We have completed 107 structural and functional MRI scans, 133 EEG’s, collected 411 DNA samples, and have re-interviewed 415 subjects. The Sackler funds allowed us to collect DNA and clinical data on the full, rather than partial sample. Since human experience and behavior can have an effect on brain function, we followed up on an interesting clinical finding that subjects who said that belief in the importance of religion/spirituality was highly important to them, and who were at high risk for major depression (MDD) had a 90% decreased risk of developing MDD over ten years (Miller et al., 2012). We also showed that family members at high risk for MDD showed 30% more cortical thinning whether or not they developed MDD (Peterson et al., 2010). In the new analysis, we found that those who had a strong belief in religion/spirituality and were at high risk had significantly thicker cortices (Miller/Bansal et al., submitted 2012). These effects were not accounted for by religious attendance or denomination. We also detected differences in the posterior alpha brain waves using EEG measure in individuals who considered religion/spirituality highly important to them, especially if they had a history of MDD (Tenke et al., submitted). These studies add to others showing a possible cognitive neural foundation of religious belief, and ground religion within an adaptive cognitive function.

We continued analysis of positive outcomes termed resilience in high risk subjects. Using functional magnetic resonance imaging (fMRI), we examined a possible brain basis of resilience. Identifying risk and resilience endophenotypes for MDD and distinguishing them from the marker of lifetime illness requires that they be sought in multi-generational families at either high or low risk for illness. We used fMRI to measure brain function during performance of a self-regulatory task in 143 individuals at high or low familial risk for depression. A risk endophenotype comprised increased activation of the cortical attentional circuits. A resilience endophenotype included increased activation of the dorsal anterior cingulated cortex. Markers for lifetime illness were common in both risk groups and comprised greater deactivation of default-mode circuits. These findings help identify the neural systems that increase risk for depression, those that likely protect from the illness, and those that endure following illness onset, and they suggest circuits to target for developing novel preventive and therapeutic interventions (Peterson et al., submitted 2012).

We began preliminary gene/MRI analysis. We first identified common polymorphic variants that are associated with risk status (high/low risk), diagnosis, and variation in cortical volumes/thickness (i.e. summary measure of structural MRI data) in persons at increased familial
risk for major depression. We observed a significant distortion in the transmission of the T allele of SNPs rs9870680 and rs9815274 of the gene GRM7. These findings suggest that this distortion could be potentially related to the transmission of susceptibility to MDD from affected parents to at-risk offspring who had not yet progressed to full development of the clinical symptomology. In the second and third generation, the T alleles are significantly less transmitted than expected by chance. We have identified a potential association between the T allele of SNP rs9815274 and a neuroimaging endophenotype of MDD in an at-risk population. These findings suggest that GRM7 might modulate grey matter volume in the rPHG, a cortical brain region known to be involved in memory encoding and retrieval. While far from definitive, this study may serve as an illustration of the power to efficiently integrate genetic and brain-imaging data in the context of family-based multi-generation design to elucidate the biological underpinnings of susceptibility to MDD in genetically at-risk populations.

Dr. Talati, using a follow-up of the 3-generation cohort, studied the relationship between prenatal exposure to maternal smoking and long-term offspring outcomes, and investigated how variation in genes, brain structure, and circuitry may contribute to these outcomes. Clinical interviews, assessments of smoking, and behavioral questionnaires on 170 (out of the originally stated goal of 240) subjects have been completed thus far. Funding from the Sackler Institute has enhanced collection of DNA samples and genotype of 35 single nucleotide polymorphisms. Prenatal nicotine exposure was associated with long term substance abuse problems in the offspring as well as conduct disorder, particularly in boys, earlier in adolescence. These associations were independent of maternal psychopathology or substance use. In preliminary genetic analyses based on the sub-sample collected to date, genetic variation in BDNF (both in val66met and four other flanking morphisms) was found to moderate the association between prenatal exposure and offspring externalizing problems. Dr. Talati is currently analyzing the genetic and structural MRI data in this sample and was awarded a new NARSAD Young Investigators Award to analyze functional MRI data.

A new direction has been involvement in the Sackler Parent/Infant Program (SIPI). Working with Drs. Gerber, Monk, and Gingrich, we reviewed their initial protocols and interviewed candidates for the new position. We will assist in finding methods for linking their clinical findings to ongoing work in other studies using imaging or genetics.

The Sackler Fund helped provide some support for a new group of talented young investigators - post doctoral fellows Zagaa Odgerel, PhD, a molecular geneticist and Guia Guffanti, PhD, a junior faculty in neuroscience with experience in analyzing MRI and genetics data. A junior faculty Ardesheer Talati, PhD also has a K Award studying the effect of in utero nicotine exposure on brain development and psychopathology.

With the help of Sackler funds, we were also able to centralize and enter into a computer tracking system over 8,000 DNA samples from studies of depression and anxiety disorder which had been in scattered sites at Columbia and from UCSF. The centralizing of the sample provides more easy access for studies related to the Center. We undertook the genotyping and analyses of the serotonin genes in a comparative sample of Europeans (EA) and African Americans (AA). A number of independent studies have now reported African American (AA) populations having lower rates if major depressive disorder (MDD) as well as many anxiety disorders than
their Caucasian counterparts. We genotyped the two polymorphisms 5-HTTLPR and rs25531 in the 954 AA and 2622 EA subjects and conducted an association study. Our study shows that subjects of AA, as compared to EA ancestry, have significantly lower rates of both the s allele and it's homogenous genotype at 5-HTTLPR. These rates were generally consistent with earlier studies. A rare, extra long xL variant occurs more often in African Americans. Overall, the allelic distributions of the two polymorphisms have significantly different rates in AA than EA. These results are being prepared for publication and will be useful for understanding population stratification in genetic studies.

Professional Honors & Activities

- Brown was elected a fellow of the American College of Neuropsychopharmacology.
- Talati received a NARSAD Young Investigator award to analyze fMRI data in offspring exposed to nicotine in utero and who are now adults.
- M. Weissman was elected to the Scientific Council of the Society of Biological Psychiatry.

Publications


Grants

1 R01 MH036197 (Weissman) 07/01/10 – 06/30/15
(NIMH)

Children at High and Low Risk for Depression. In this 6th wave we will gain a deeper understanding of the right hemisphere abnormalities in familial MDD in the 216 individuals imaged thus far. This represents the largest MRI study published for MDD to date, and it is the
only sample studying 3 generations of individuals at high or low risk for MDD. We will collect additional MRI and EEG measures, as well as clinical and cognitive neuroscience data, that will inform us about the neural bases of the right hemisphere thinning and their consequences for brain function and emotional processing. We will also determine whether additional cortical thinning in the left cerebral hemisphere predicts new or recurrent MDD in those people who were imaged in Wave 5.

1 R01 MH082255 (Weissman) 07/01/07 – 06/30/13
Parental Remission from Depression. This is a study of 100 depressed parents undergoing treatment and 200 of their children to replicate and refine previous findings that successful treatment of a depressed parent leads to improvement in their children. These findings, if replicated in this study, will provide new strategies for helping symptomatic children of depressed parents.

1 RC2 MH089916 (Levinson) 09/30/09 – 08/31/12
Stanford U Subcontract (Weissman Sub PI)
Depression Susceptibility Genes and Networks: Expression, eQTL and GWAS Analysis. Work on this subcontract is collection of clinical data through standardized diagnostic assessments from some 650 referred and consented subjects and transmission of collected clinical data to the central site at Stanford University.

Templeton Foundation (Weissman) 01/01/10-11/15/2012
Understanding the Role of Belief in the Resilience of Families at Risk for Depression: Religion, Brain Structure, and Genetics. A study linking 3 areas of research: beliefs, brain structure and function, and genetic endowment. The overarching goals of the proposal are (1) to extend original observations about the protective effects of belief and determine the stability of the findings, and (2) to integrate the clinical and religious variables with brain structure and function, and genetic data in order to answer comprehensive questions about vulnerability and resilience to depression.

1 P50 MH090966-01 (Gingrich) 07/01/10 – 06/30/15
(NIH/NIMH)
Silvio O. Conte Centers for Basic and Translational Mental Health Research: Serotonergic Modulation Influence on Structure, Function, and Behavior
Weissman (co-principal investigator)
Several lines of evidence indicate that in species from rodents to humans, serotonin acts as a neural growth factor during early phases of brain maturation to influence brain structure, neurophysiology, and ultimately, behavior. Serotonin signaling can be affected by either genetic (5httlpr) or pharmacologic (SSRI, MAOI) variables during early life. We hypothesize that low-expressing 5httlpr variants of the serotonin transporter (SERT) and pharmacologic inhibition of SERT function produce similar effects on brain maturation and ultimately behavior and increase the risk for clinical diagnoses such as affective and anxiety-related disorders.
**Biosignatures of Treatment Remission in Major Depression.** This study will examine multiple, carefully selected clinical and biological markers, using both existing state-of-the-art technologies as well as pioneering, innovative approaches. Evaluation of the usefulness of these markers in a carefully conducted clinical trial comparing an antidepressant to placebo will assist in developing a depression treatment response index (DTRI) to help clinicians match treatments to patients with MDD, resulting in timely selection of treatments best suited for individual patients and thus approaching personalized treatment.

**Grants - Brown**

1 R01ES019004 (Brown) 09/28/09 – 07/31/11
(NIH-NIMH)
**Prenatal Factors and Risk of Autism in a Finnish National Birth Cohort,** The major goal of this project is to examine if environmental factors during pregnancy are related to the likelihood that the offspring will be diagnosed with autism in a large birth cohort in Finland.

1 R01 MH073080 (Brown) 02/16/05 – 01/31/12
(NIH-NIMH)
**Prenatal factors and risk of bipolar disorder,** The major goals of this project are to investigate the relationship between early developmental insults and risk of adult bipolar affective disorder.

2 K02 MH065422 (Brown) 07/01/08 – 06/30/13
(NIH-NIMH)
**Epidemiology of prenatal factors in adult psychopathology,** This is a renewal of a previous K02 award. The major goal of this project is to extend ongoing research by investigating prenatal nutritional and genetic factors involved in the etiology of schizophrenia, and the examination of the specificity of prenatal factors previously associated with schizophrenia by investigating their relationship to bipolar disorder.

1 R01MH082052 (Brown) 07/01/08 – 06/30/13
(NIH-NIMH)
**Prenatal Factors and Risk of Schizophrenia in a Finnish National Birth Cohort,** The major goal of this project is to examine the relation of early life exposures to the risk of schizophrenia and other schizophrenia spectrum disorders, using serologic methods to document the exposure of interest in a large birth cohort in Finland.

1P50MH090966 (Gingrich) 07/01/10 – 06/30/15
(NIH/NIMH)
**Silvio O. Conte Centers for Basic and Translational Mental Health Research: Serotonergic Modulation Influence on Structure, Function, and Behavior**
Brown (co-principal investigator)
Sourander (co-principal investigator)
Several lines of evidence indicate that in species from rodents to humans, serotonin acts as a neural growth factor during early phases of brain maturation to influence brain structure, neurophysiology, and ultimately, behavior. Serotonin signaling can be affected by either genetic (5httlpr) or pharmacologic (SSRI, MAOI) variables during early life. We hypothesize that low-expressing 5httlpr variants of the serotonin transporter (SERT) and pharmacologic inhibition of SERT function produce similar effects on brain maturation and ultimately behavior and increase the risk for clinical diagnoses such as affective and anxiety-related disorders.

Grants - Talati

1K01DA029598 (Talati) 08/01/10-07/31/15
NIH/NIDA
Prenatal Smoke Exposure and Offspring Substance Use: An Imaging-Genetics Approach
The overall goal of this Mentored Research Scientist Development Award (K01) is to enable Dr. Talati to develop expertise in applying translational methods to study the etiology of substance use, by identifying specific genetic and neurobiological pathways that mediate individual risk to substance use and its related behavioral disorders. Exposure to prenatal smoking provides an excellent model with which to obtain these skills, while simultaneously tackling a serious public health problem.

Young Investigator Award 02/01/2013-01/30/2015
NARSAD
Effects of Prenatal Smoke Exposure on Offspring Brain and Behavior
The overall goal is to study brain function by measuring the subject’s response to performing the Simon Task. Doing the task correctly require attention and control, and activates regions in the brain’s frontal lobe. These regions may be disrupted or less efficient among people with behavioral disorders. In this study, the goal is to examine whether nicotine exposed offspring have different brain responses while performing the Simon Task, and if these differences can further explain why they have more behavioral problems.

Grants - Murphy

(Murphy) 09/01/11 – 08/31/16
(NIH)
Influences on the Familiality of Major Depression Among African-Americans. This Career Transition Grant in Health Disparities (K22) includes a 2-year intramural phase of research training in health disparities at the National Institutes of Health followed, by a 3-year extramural phase of additional mentoring and training and execution of the research plan described in this proposal. The goal of this award is to develop the candidate’s expertise in gene-environment research methodology for psychiatric disorders, and to facilitate transition of the candidate into an independent research career in health disparities. During the extramural phase of this award, the candidate will execute a research plan, the specific aims of which are to (1) successfully recruit from the New York City area, a sample of 120 black probands with Major Depressive Disorder (MDD) and 120 non-MDD “controls” matched by age and sex, with up to 2
first degree relatives per proband. Murphy is currently at the NIMH intramural program in Bethesda and will return in 2014.

Division of Developmental Neuroimaging

Division Director: Bradley Peterson, MD, PhD
Division Members: Andrew Gerber, MD, PhD

Normal Brain Development and the Neural Basis of Psychiatric Disorders

Our lab has reported several important discoveries in the past year, including:
(1) Anatomical MRI scans were shown to be able to diagnose accurately a variety of psychiatric illnesses (Tourette syndrome, ADHD, bipolar disorder, familial depression, and schizophrenia), using only those scans and no human input.
(2) The anatomical endophenotype for familial depression, which we previously showed involved thinning of the cortical mantle in the right cerebral hemisphere, was also shown to involve the underlying white matter tracts that are anatomically connected to the cortex of the right hemisphere, and in direct proportion to the degree of cortical thinning.
(3) In collaboration with investigators at the Mailman School of Public Health at Columbia University, we were able to show that exposure to a common pesticide (chlorpyrifos) during fetal life was associated with abnormalities in brain structure at 7 years of age. The abnormalities in brain structure include enlargement of white matter tissue in the temporal lobes of the brain, likely representing the scarring effects (called “gliosis”) of earlier damage from the pesticide. These abnormalities in brain tissue seemed to account for lower measures on standardized tests of intelligence in these children.

Publications


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**Grants**

2006  Simons Foundation Simons Simplex Family Resource (B. Peterson, PI)
The aim of the resource is to rapidly collect 1000 standard set of phenotypic data from proband with Autism or Autism Spectrum Disorder (ASD) and at least one full sibling without evidence of Autism or ASD, and two biological parents who are unaffected. 11/1/06 – 4/31/12

2008  **NIEHS** RO1 ES015579 Impact of Chlorpyrifos on Brain Function (V. Rauh, PI) The goal of this study is to evaluate the effects of chlorpyrifos on brain function and neurobehavior at age 9 years following prenatal exposure.
12/01/08-11/30/13

2010  **NIMH** 2T32 MH16434-31 (B. Peterson, PI) Translational Research Training in Child Psychiatry The program trains postdoctoral psychiatrists, psychologists, and developmental neuroscientists to become investigators in translational neuroscience research of child and adolescent psychiatric disorders. The grant supports ten M.D. and/or Ph.D. trainees for up to three years.
7/01/10 - 06/30/15

2010  **NIMH** 1P50MH090966-01 Silvio O. Conte Centers for Basic and Translational Mental Health Research Serotonergic Modulation of Brain Development: Genetic and Pharmacologic Influences on Structure, Function, and Behavior (J Gingrich, PI) Several lines of evidence indicate that in species from rodents to humans, serotonin acts as a neural growth factor during early phases of brain maturation to influence brain structure, neurophysiology, and ultimately behavior. Serotonin signaling can be affected by either genetic (5htlpr) or pharmacologic (SSRI, MAOI) variables during early life. We hypothesize that low-expressing 5htlpr variants of the serotonin transporter (SERT) and pharmacologic inhibition of SERT function produce similar effects on brain maturation and ultimately behavior and increase the risk for clinical diagnoses such as affective and anxiety-related disorders.
07/01/10-06/30/11

2010  NIMH MH36197 Children at High and Low Risk for Depression (M. Weissman. & B. Peterson, Co-PI's)
To identify the brain-based correlates of children and adults at high or low risk for depressive illness using anatomical and functional MRI.
7/1/10-6/30/15

2010  NIDA R01DA027100 Impact of Prenatal and Early Childhood Environmental Tobacco Smoke Exposure on Brain Development (V Rauh & B Peterson, Co-PIs) The purpose of this study is to assess the effects of prenatal and early childhood exposure to environmental tobacco smoke (ETS) on brain structure and function in a cohort of 250 inner-city children who are 9-10 years of age. We will use MRI to study detailed brain anatomy, fiber tracts, and metabolites in these children, and we will assess cognitive and attentional functioning using an array of neuropsychological tasks.
7/1/10-6/30/15

2011  NIMH 1R01MH093677 The Effects of Prenatal Stress & Poor Nutrition on Brain and Cognition (K. Monk & B. Peterson, Co-PI's)
The goal of this project is to assess the influence of maternal prenatal self, reported stress and endocrine activity, as well as poor nutrition, on neonatal brain structure and function, and to relate the imaging measures to cognitive outcomes in early childhood.
09/23/11-06/30/16

SACKLER PARENT INFANT PROJECT

Division Directors: Catherine Monk, PhD
Andrew Gerber, MD, PhD

Division Members: Archana Basu, PhD
Nina Burtchen, MD, PhD
Elizabeth Werner, PhD

The Sackler Parent–Infant Program (SPIP) was established 14 months ago as a component of the Sackler Institute at Columbia University. Broadly speaking, it aims to establish Columbia as a leader in parent–infant intervention science, drawing on developmental neuroscience research from Sackler colleagues to generate state-of-the-art clinical programs that provide for individual well-being and evidence-based services for families.

The earliest childhood experiences — even those that occur before birth — are an essential foundation from which later emotional well-being emerges. Compromised beginnings lead to compromised futures. In the last decade, neuroscientists and developmental psychologists, many of them at Columbia, have made dramatic strides in specifying key aspects of the child’s early social world that affect early brain and behavioral development, and even the biological pathways by which these influences occur. Remarkably, across U.S. academic institutions, an equally rigorous science aimed at formulating and testing early parent–infant interventions to
improve children’s futures, is virtually non-existent. Most of the clinical work with parents and infants occurs independent of scientifically established methods and close interaction with experts in developmental neuroscience. Findings from neurodevelopment research are not fully leveraged and applied to situations outside of the laboratory, and an opportunity to build a portfolio of evidenced-based early prevention programs — ones that might diminish the risk of mental illness before it alters a child’s life — is forfeited. The explosive growth in brain development in utero and during the first few years of life — and in the recent scientific knowledge showing the impact of parent–infant interactions on this brain–behavior functioning — demands that we develop an equally rigorous intervention science aimed at optimizing the child’s earliest experiences. To that end, SPIP was founded, and we are very grateful for the support it has received.

SPIP had a productive first year that included: recruiting two postdoctoral fellows (Drs. Archana Basu and Nina Burtchen) whose work and interests will benefit SPIP as their interaction with the entire Sackler Institute promotes their academic development, initiating on–site training in an evidenced based parent infant psychotherapy program (Child Parent Psychotherapy, CPP), and solidifying collaborations to include other early intervention program under the SPIP umbrella. (Please see the attached diagram illustrating key aspects of SPIP). In what follows, we detail these developments.

CPP STUDY

The goal of this study is to conduct a randomized controlled trial of Child Parent Psychotherapy (CPP), an evidenced based treatment for young children and their caregivers, developed by Drs. Alicia Lieberman and Patricia van Horn (University of California, San Francisco). We aim to assess the feasibility and acceptability of providing CPP as a dyadic preventive intervention for children (ages 3 to 5) who are displaying signs of emotional and behavioral difficulties in the context of maternal depression. Specifically, this study proposes to compare the effectiveness of CPP to that of usual care (usual care defined as: referral to therapists in the community and within Columbia University Medical Center) in improving maternal depressive symptoms and child emotional and behavioral disturbances as reported by parents and teachers, and observed in laboratory protocols. In addition to assessing mental health outcomes, we also will compare pre– versus post–treatment neurobiological indicators of emotion regulation, including mother and child stress hormone levels during free play, and ultimately other hormones related to stress regulation and the quality of attachment (e.g., immune markers and oxytocin), as well as the characterizations of brain development via EEG assessment as well as potentially brain MRI. Dr. Archana Basu, who earned her doctorate at Michigan State where she focused on maternal functioning and child development in the context of trauma, is a postdoctoral fellow taking a leading role in the initiation of the CPP study.

Progress to Date:

- Hired part–time Research Assistant (RA), Rachael Esman, a recent Columbia College graduate who studied at the Toddler Center at Barnard
- Submission of IRB materials, expected study start up in February, 2013
- Successful initiation of CPP training at CUMC/NYSPI
Sackler Institute for Developmental Psychobiology

- Lecture (35 attendees) in foundational trauma theory and training in CPP (18 attendees), which was offered to outside clinicians to offset cost of CPP training for CUMC/NYSPI (copy of program flyers attached)
- Six attendees from CUMC/NYSPI for CPP training, each of whom will begin a training case and serve as a clinician in the CPP study
  - Submitted a grant to Policy Relevant Mental Health Services Research RFP, to Office of Mental Health (not funded)
  - Plan to submit for NIH funding through a R21 or R34 mechanism in June, 2013

PRACTICAL RESOURCES FOR EFFECTIVE POSTPARTUM PARENTING (PREPP)

This is an initial, exploratory study funded by the NIMH (through December, 30, 2013) that aims to reduce the risk for postpartum depression (PPD) in vulnerable pregnant women. Building on developmental data showing the profound bi-directionality of emotional and behavioral influences between mother and infant, we are collecting feasibility and pilot data on a novel intervention protocol. Practical Resources for Effective Postpartum Parenting, PREPP), that challenges the standard, individually-focused treatment paradigm. Our intervention is based on the conceptualization of PPD as a potential disorder of the dyad, and one that can be approached through behavioral change in and effective engagement between mother and child. Specifically, in this proposed intervention, we aim to treat at–risk women by promoting maternally-mediated behavioral changes in their infants. Specifically, this study entails ‘teaching’ parenting skills to increase infant nocturnal sleep and reduce fuss/cry behavior during three perinatal sessions, then evaluating infant behavior at 6 and 14 weeks, and maternal mood at 6,10 and 14 weeks postpartum. We also are investigating basic brain–behavior processes by using state–of–the–art fetal and EEG monitoring to characterize early biomarkers associated with infant behavior and behavior change.

Progress to Date:

- Hired full–time RA
- Hired part–time psychologist as study clinician
- Enrolled n=35 women, half in PREPP, half in treatment as usual
- Preliminary results on n=18 (too few to run statistical analyses) seems to suggest better postpartum mood in women who underwent PREPP compared to those assigned to treatment as usual
- Application submitted to the Robin Hood Foundation to apply PREPP to vulnerable pregnant women based on their psychosocial circumstances (e.g., living below the poverty level, high levels of daily stress). A Robin Hood Program Officer came to our laboratory for a site visit; we anticipate hearing about a funding decision in late spring.

FUSSY BABIES: ASSESSMENT & TREATMENT

This initiative, under the direction of Dr. Nina Burtchen, aims to establish a “Fussy Baby Clinic” at CUMC where parents can find help that draws on multiple disciplines. At the moment, services for “fussy babies” are still largely compartmentalized. Studies have shown that specialists
interpret the chief complaint of “my baby cries too much” in relation to their training background: Pediatricians are likely to prescribe medications, e.g. anti-reflux medication, occupational therapists tend to suggest the baby might have “sensory integration disorder”, and psychologists diagnose an emotional problem in the child and/or the parents. At the proposed clinic, the approach will be integrative. It will transcend the current practice of categorizing “fussy infants” as having either a medical or an emotional problem. To receive comprehensive psycho-social care, this clinic will not require babies to be medically cleared by a pediatrician. Instead, there will be a thorough evaluation process assessing both medical and psychosocial factors in both the infant and the parents. Parent-Infant Psychotherapy will not be offered as an adjunct to medical therapy. Rather, an individual therapy program will be tailored to the needs of each family. Children will receive anti-reflux medicine where indicated, but at the same time parents might be referred for psychiatric services if there are signs of parental depression. Dr. Burtchen’s unique training and research background — spanning pediatric surgery, newborn medicine, developmental neuroscience and psychoanalysis — has enabled her to develop this initiative and makes her exceptionally well-suited to direct it and build a strong research program aligned with its clinical goals.

DOMESTIC VIOLENCE INITIATIVE

In response to a donor’s initiative, faculty at Columbia, specifically Dr. Elizabeth Fitelson from the Women’s Program, and Dr. Monk, are developing a proposal to bring clinical services and research projects to a Family Justice Center in New York City. While still in the early stages, this project has the potential for valuable collaborations with SPIP, in particular with respect to offering CPP services to women and children at the Family Justice Center and thereby allowing for an additional site for CPP intervention and research.
An fMRI Investigation of Social Cognition Deficits in Adults with High Functioning Autism Spectrum Disorder

In the second year of the project, we completed data collection in a sample of 10 adults with high functioning autism spectrum disorder (HFASD) and 15 controls matched on age, gender, and IQ without psychiatric diagnoses. In behavioral analysis of these data we found that our prediction of schema-based memory was supported in both the control sample (as was shown in the previous year of the project in a sample of 40 young adults without psychiatric diagnosis) and in the HFASD sample. Though we were surprised to find that HFASD controls also displayed the schema behavioral effect.

Upon further analysis of the data we were interested to learn that though both groups displayed the schema behavioral effect (i.e., giving higher average memory recognition scores for non-taught discreptors taken from significant-other-resembling targets than for yoked-control-resembling targets), the reaction times in the HFASD sample were significantly longer. This ties into a recent meta-analytic finding in the literature (Gerber and Leibovitz, in preparation) that across all tasks of global vs. local preference in visuospatial cognition (e.g., the Navon task), individuals with HFASD are as accurate as a control group when given an unlimited amount of time, but take longer in the task and are less accurate when time is severely limited. This has led us to refine our original hypothesis. On the basis of our findings, rather than think of individuals with HFASD as being unable to use schemas, we believe that the use of such schemas requires more to-down (i.e., frontal-temporal) control, which is a slower cognitive system, than originating within the temporal...
cortex as it does in non-HFASD individuals (as suggested by our imaging work in healthy controls).

We have begun to test this newer hypothesis by analyzing the neuroimaging data from our study, comparing functional brain activity in individuals with and without HFASD. We found that as with our previous study of normal controls exposure to schema-relevant stimuli is associated with increasing activity in the bilateral fusiform/inferior temporal cortex and decreasing activity in anterior portions of the brain, including the anterior cingulate (Fig 1). Meanwhile, in individuals with HFASD, the same contrast shows decreasing activity in the fusiform cortex and superior frontal cortex. This supports our hypothesis that front-temporal connectivity is related to schema usage and to differences between individuals with and without HFASD.

Over the past year, I have presented these results in several academic psychiatric settings (University College London, Yale Child Study Center Grand Rounds, Tufts University Grand Rounds) and to the audiences of families and mental health practitioners (National Alliance for Mentally Ill). I am preparing a publication with these results and beginning to design a next series of studies that use a modified version of our schema paradigm with faces (instead of words) that is suited for children and lower functioning ASD adults. I am awaiting decision on an NIH/Irving Center sponsored K award and plan to submit other applications for funding in the coming months.
### Part III - Financial Report

Columbia University  
Sackler Institute for Developmental Psychobiology  
Department of Psychiatry  
Revenue and Expenses  
July 2011 through June 2012

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<th>Revenue and Support</th>
<th>FY '12</th>
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<td>Prior Year Balance (as of June '11)</td>
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<td>Other Support*</td>
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<td><strong>Total Available Funds</strong></td>
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*Other Support includes departmental subsidies, state salary support

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<th>Expenses</th>
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| Net Surplus/(Deficit)                | $447,699.00 |
## Endowment Valuations as of June 30, 2012

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