BIOGRAPHICAL SKETCH

NAME: Manpreet Kaur Singh, MD MS

eRA COMMONS USER NAME (credential, e.g., agency login): SINGH.MANPREET

POSITION TITLE: Assistant Professor of Psychiatry and Behavioral Sciences, Member, Bio-X, Stanford University School of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Michigan, Ann Arbor, MI	B.S.	1994-1997	Biology and Philosophy
Michigan State University, College of Human Medicine, East Lansing, MI	M.D.	1998-2002	Medicine
University of Michigan, Ann Arbor, MI	M.S.	2005-2007	Clinical Research Design and Statistical Analysis
Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine, Cincinnati, OH	Residency	2002-2007	Pediatrics, Psychiatry, and Child & Adolescent Psychiatry
Center for Interdisciplinary Brain Sciences Research, Stanford University School of Medicine	Post-doctoral Scholar	2007-2009	Multimodal Neuroimaging in Pediatric Bipolar Disorder

A. Personal Statement

Mood disorders are common precursors and denominators for all ten of the most common causes of death in the United States (tobacco, overweight/obesity, poor diet, physical inactivity, alcohol misuse, exposure to toxic agents, motor vehicle accidents, injury and violence, risky sexual behavior, and substance abuse). My training in child and adolescent psychiatry and neuroscience has allowed me to conduct studies integrating neurobiological and physiologic mechanisms and risk factors associated with the development and prevention of mood disorders, with the ultimate goal of reducing these common causes of death. Given the increasing burden of illness and disability associated with major mood disorders worldwide, this research critically aims to discover novel treatment targets that can be engaged to prevent the development and progression of lifelong mood problems and associated disability. In my Pediatric Emotion And Resilience Laboratory (PEARL), we have developed innovative methods to investigate and integrate early cognitive, behavioral, clinical, genetic, and neural (functional, structural, and neurochemical) factors that contribute to an early onset of mood disorders. I have been a clinician and researcher in the neurobiology and treatment of emotional dysfunction in youth for the past ten years. I have extensive experience in the recruitment, assessment, and treatment of youth with a family history of major depressive and bipolar disorders, and integrating investigations of behavioral, neural (functional, structural, and neurochemical), environmental, and genetic factors associated with risk for emotional dysfunction. I have published extensively on risk and resilience factors associated with the development of emotional dysfunction in youth and completed a K23 Career Development Award focused on neural and behavioral characteristics of emotion regulation in healthy offspring of parents with bipolar disorder. My current research has the following prevention-oriented foci: 1) prospective neural and behavioral assessment of youth with depression and obesity to understand factors that predict the development of insulin insensitivity, 2) an investigation on the mechanisms underlying antidepressant-related adverse events in high risk youth to prevent the development of future mood disorders, and 3) understanding the neurobiological basis of sex differences in pediatric psychopathology to personalize treatment. Thus, with the specific expertise in these key research areas and combined with clinical knowledge on behavior change, I am well poised to develop primary, secondary, and tertiary prevention strategies for common causes of mortality in the U.S.

1. **Singh MK**, Kelley RG, Chang KD, Gotlib IH. Intrinsic amygdala functional connectivity in youth with bipolar I disorder. *J Am Acad Child Adolesc Psychiatry*. 2015;54(9):763-770. PMCID: PMC4548854.
2. **Singh MK**, Garrett AS, Chang KD. Using neuroimaging to evaluate and guide pharmacological and psychotherapeutic treatments for mood disorders in children. *CNS Spectr*. 2015; 20(4):359-368. PMID: 25659836.
3. **Singh MK**, Kelley RG, Howe M, Reiss AL, Gotlib IH, Chang KD. Reward Processing in Healthy Offspring of Parents with Bipolar Disorder. *JAMA Psychiatry* 2014 Oct 1;71(10):1148-56. PMID: 25142103.
4. **Singh MK**, Chang KD, Kelley RG, Saggar M, Reiss AL, Gotlib IH. Early signs of anomalous neural functional connectivity in helathy offspring of parents with bipolar disorder. *Bipolar Disord* 2014;26(7):678-689. PMCID: PMC4213354.

B. Positions and Honors

2002- 2007 Resident in Pediatrics, Psychiatry, and Child & Adolecent Psychiatry, Cincinnati Children's Hospital Medical Center (CCHMC) and University of Cincinnati College of Medicine
2007-2009 Instructor, Division of Child & Adolescent Psychiatry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine
2007-2009 National Institute of Mental Health T32 Post-doctoral Fellow, Center for Interdisciplinary Brain Sciences Research, Stanford University School of Medicine
2009- Assistant Professor, Division of Child & Adolescent Psychiatry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine

Professional Memberships:

2004-2007 Resident/Fellow Member, American Academy of Pediatrics
2005-2006 Resident Member, American Psychiatric Association
2006- Member, American Academy of Child and Adolescent Psychiatry
2008-2010 Trainee Member, Organization for Human Brain Mapping
2015- Associate Member, American College of Neuropsychopharmacology

Selected Honors:

2005 Resident Research Award, University of Cincinnati Department of Psychiatry
2006 Chief Resident, Triple Board Program, Cincinnati Children's Hospital
2007 American Psychiatric Association (APA) Resident Research Award for Best Paper
2007 Adolescent Medicine Award, Division of Adolescent Medicine, Cincinnati Children's Hospital
2007 Dean's Fellowship for Post-doctoral Scholars, Stanford University School of Medicine
2007-2014 National Institutes of Health, Pediatric Loan Repayment Program
2008 Career Development Institute for Bipolar Disorders, University of Pittsburgh
2008 Travel Grant Award Winner, Society of Biological Psychiatry
2008 Research Colloquium for Junior Investigators, American Psychiatric Association
2008 Dean's Fellowship Award for Post-doctoral Scholars, Stanford University School of Medicine
2008 American Academy of Child and Adolescent Psychiatry (AACAP) KTGF Award for Research in Depression or Suicide
2009 AACAP Program Committee Travel Scholarship to 2009 Annual AACAP Meeting
2009 Travel Grant Award Winner, American College of Neuropsychopharmacology (ACNP)
2010 Distinguished Young Alumni Award, Michigan State University
2011 American Society of Clinical Psychopharmacology New Investigator Award
2012 Honorable Mention for the Gerald R. Klerman Award for outstanding clinical research achievement by a Brain & Behavior Research Foundation Young Investigator
2013 Child Health Research Institute Akiko Yamazaki and Jerry Yang Faculty Scholar Award in Pediatric Translational Medicine
2014 Samuel Gershon Award for Junior Investigators, International Society for Bipolar Disorders
2015 Appointed to the Bass Society of Pediatric Scholars, Lucile Packard Children's Hospital
2015 Outstanding Teaching Award from the Child and Adolescent Psychiatry Fellows at Stanford
2016 Brain and Behavior Research Foundation Independent Investigator Award

C. Contribution to Science

1. My early publications investigated whether family history of bipolar disorder predisposes children and

adolescents to factors that can lead to lifelong psychopathology. These publications found that child offspring of parents with bipolar disorder have distinct prenatal risk factors, temperaments, psychopathologies, and neurocognitive profiles compared to youth without any family history of any psychiatric disorders. By providing evidence of these key characteristics, this body of work has challenged current clinical standards to examine and consider early risk factors for developing bipolar disorder well before adulthood. I served as primary (PI) or co-investigator in all of these studies.

a. **Singh MK**, DelBello MP, Stanford KE, Soutullo C, McDonough-Ryan P, McElroy SL, Strakowski SM. Psychopathology in Children of Bipolar Parents. *J Affect Disord*. 2007;102(1-3):131-136. PMID: 17275096.
b. **Singh MK**, DelBello MP, Soutullo C, Stanford KE, McDonough-Ryan P, Strakowski SM. Obstetrical Complications in Children at High Risk for Bipolar Disorder. *J Psychiatr Res*. 2007;41(8):680-685. PMID: 16698037.
c. **Singh MK**, DelBello MP, Fleck DE, Shear PK, Strakowski SM. Inhibition and Attention in Adolescents with Nonmanic Mood Disorders and a High Risk for Developing Mania. *J Clin Exp Neuropsychol.* 2009;31(1):1-7. PMCID: PMC3382063.
d. **Singh MK**, DelBello MP, Strakowski SM. Temperament in Child Offspring of Parents with Bipolar Disorder. *J Child Adolesc Psychopharmacol.* 2008;18(6):589-593. PMCID: PMC3048461.

2. I have also directly documented that there are key vulnerabilities in the brain that present in youth offspring of bipolar parents who have already developed some emotion dysregulation symptoms including anhedonia. These studies found that brain structural and chemical abnormalities previously reported in youth with bipolar disorder may not present in high risk youth until the disorder has fully developed, and that there may be early neuroprotective mechanisms in play to prevent the development of mood disorders in high risk youth. I served as the PI or co-investigator in all of these studies.

a. **Singh MK**, Delbello MP, Adler CM, Stanford KE, Strakowski SM. Neuroanatomical Characterization of Child Offspring of Bipolar Parents. *J Am Acad Child Adolesc Psychiatry.* 2008;47(5):526-531. PMCID: PMC3381335.
b. **Singh MK**, Spielman D, Adleman N, Alegria D, Howe M, Reiss A, Chang KD. Brain Glutamatergic Characteristics of Pediatric Offspring of Parents with Bipolar Disorder. *Psychiatry Res.* 2010;182(2):165-171. PMCID: PMC2866778.
c. **Singh MK**, Spielman D, Libby A, Adams E, Acquaye T, Howe M, Kelley R, Reiss A, Chang KD. Neurochemical Deficits in the Cerebellar Vermis in Child Offspring of Parents with Bipolar Disorder. *Bipolar Disord.* 2011;13(2):189-197. PMCID: PMC3066452.
d. **Singh MK**, Jo B, Adleman NE, Howe, M, Bararpour L, Kelley RG, Spielman D, Chang KD. Prospective Neurochemical Characterization of Child Offspring of Parents with Bipolar Disorder. *Psychiatry Research: Neuroimaging*, 2013; 214(2):153-160. PMCID: PMC3796054.

3. To expand on the current neural models of major mood disorders, I have examined brain regional and network-based abnormalities in youth with bipolar disorder and adults with major depressive disorder. I found that youth close to their onset of mania excessively activate key prefrontal and subcortical regions during response inhibition and reward processing, which may relate to their symptoms of impulsivity and novelty seeking. I have also found that in adults with depression, there is dysynchrony between regions that form critical networks for emotion regulation. I served as the PI or co-investigator in these studies.

a. **Singh MK**, Chang KD, Mazaika P, Garrett A, Adleman N, Kelley R, Howe M, Reiss A. Neural Correlates of Response Inhibition in Pediatric Bipolar Disorder. *J Child Adolesc Psychopharmacol.* 2010;20(1):15-24. PMCID: PMC2835388.
b. **Singh MK**, Chang KD, Chen M, Bararpour L, Reiss A, Gotlib I. Volumetric Reductions in the Subgenual Anterior Cingulate Cortex in Adolescents with First Episode Mania. *Bipolar Disord.* 2012;14(6):585-96. PMCID: PMC3433284.
c. **Singh MK**, Chang KD, Kelley R, Cui X, Sherdell L, Howe ME, Chang KD, Gotlib IH, Reiss AL. Reward Processing in Adolescents with Bipolar I Disorder. *J am Acad Child Adolesc Psychiatry.* 2013;52(1):68-83. PMCID: PMC3530159.
d. **Singh MK**, Kesler S, Husseini H, Kelley R, Amatya D, Hamilton J, Chen M, Gotlib I. Anomalous Gray Matter Structural Networks in Major Depressive Disorder. *Biological Psychiatry*. 2013;74(10):777-85. PMCID:PMC3805751.

4. Most studies in risk for bipolar disorder have been conducted in already symptomatic youth. This has limited our ability to disentangle true disease-related neural characteristics from common illness-related confounds such as comorbidities and treatment effects. Witha team of interdisciplinary investigators interested in endophenotypes for major mood disorders, I have published among the first studies to demonstrate that youth offspring of parents with depression or bipolar disorder have key trait-like abnormalities that precede the onset of frank mood symptoms, and that these abnormalities may be related to certain temperaments or genotypes. I served as the PI or co-investigator in all of these studies.
    a. Gotlib IH, Hamilton JP, Cooney RE, **Singh MK***, Henry ML, Joormann J. Neural Processing of Reward and Loss in Girls at Risk for Major Depression. *Archives of General Psychiatry.* 2010;67(4):380-387. PMCID: PMC2852176.
    b. **Singh MK**, Chang KD, Kelley RG, Saggar M, Reiss AL, Gotlib IH. Early Signs of Anomalous Neural Functional Connectivity in Healthy Offspring of Parents with Bipolar Disorder. *Bipolar Disorders*. 2014 Nov;16(7):678-89. PMCID: PMC4213354.
    c. **Singh MK**, Kelley RG, Howe M, Reiss AL, Gotlib IH, Chang KD. Reward Processing in Healthy Offspring of Parents with Bipolar Disorder. *JAMA Psychiatry* 2014 Oct 1;71(10):1148-56. PMID: 25142103.
    d. Park MH, Chang KD, Howe ME, Kim E, Hong SC, **Singh MK***. Anxiety symptoms in bipolar offspring with the brain-derived neurotrophic factor (BDNF) Val66Met genotype. *Journal of Psychiatric Research* 2014 Nov 27. PMID: 25498133.

5. I am involved in collaborations aimed to investigate methods of treating problems associated with and leading up to mood disorders in youth. Specifically, I have examined the benefits of family focused psychotherapy, mindfulness meditation, and medications in youth offspring of parents with bipolar disorder to reduce mood symptoms and family stress. I have also reviewed the neural effects of medication and psychotherapy in youth. These areas of research hold considerable promise to impact our understanding of the core mechanisms and early interventions for pediatric onset mood disorders.
    a. Miklowitz DJ, Chang KD, Taylor DO, George EL, **Singh MK***, Schneck CD, Dickinson LM, Howe ME, Garber J. Early Psychosocial Intervention for Youth at Risk for Bipolar I or II Disorder: A One-Year Treatment Development Trial. *Bipolar Disord.* 2011;13(1):67-75. PMCID: PMC3077951.
    b. Miklowitz DJ, Schneck CD, **Singh MK*,** Taylor DO, George EL, Cosgrove VE, Howe M, Dickenson LM, Garber J, Chang KD. Early Intervention for Symptomatic Youth At Risk for Bipolar Disorder: A Randomized Trial of Family-Focused Therapy. *J Am Acad Child Adolesc Psychiatry*. 2013;52(2):121-31. PMCID: PMC3558946.
    c. Goldsmith M, **Singh MK***, Chang KD. Antidepressants and Psychostimulants in Pediatric Populations Is There an Association with Mania? *Pediatric Drugs.* 2011;13(4):225-243. PMCID: PMC3394932.
    d. **Singh MK**, Garrett A, Chang KD. Using neuroimaging to evaluate and guide pharmacological and psychotherapeutic treatments for mood disorders in children. *CNS Spectrums* (In Press). PMID: 25659836.

List of my published work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40595600/?sort=date&direction=ascending

D. Research Support

Independent Investigator Award (Singh) 09/15/2016-09/14/2018 Brain and Behavior Foundation
Neurobehavioral Response During Antidepressant-Related Dysfunctional Arousal in High-Risk Youth.
This is a multi-site project with the University of Cincinnati that aims to examine the neurobehavioral mechanisms of antidepressant-related dysfunctional arousal in youth at high risk for bipolar disorder.
Role: Principal Investigator

1R01MH105469-01A1 (Singh) 09/23/2015-7/31/2020 NIMH
2/2-Mechanism of Antidepressant-Related Dysfunctional Arousal in High-Risk Youth
This is a multi-site project with the University of Cincinnati that aims to examine the neurobehavioral mechanisms of antidepressant-related dysfunctional arousal in youth at high risk for bipolar disorder.
Role: Principal Investigator

1R01MH105469-01A1 (Singh) 03/28/2016-7/31/2020 NIMH
2/2-Mechanism of Antidepressant-Related Dysfunctional Arousal in High-Risk Youth
This supplement supports medical monitor oversight of a multi-site project with the University of Cincinnati that aims to examine the neurobehavioral mechanisms of antidepressant-related dysfunctional arousal in youth at high risk for bipolar disorder.

1R01MH106581-01A1 (Singh) 09/16/2015-6/30/2020 NIMH
Neurobehavioral trajectories of Pediatric Depression and Insulin Sensitivity
This project utilizes an RDoC approach to dysfunctional Approach Motivation to investigate the mechanisms and risk factors for worsening depressive symptoms in youth with comorbid depression and insulin sensitivity. To accomplish these aims, 120 overweight girls and boys (ages 9-15 years) seeking treatment for moderate to severe depressive symptoms, will be assessed at baseline, 6 months, and 24 months with cognitive and behavioral markers of Approach Motivation, serum markers of insulin sensitivity, and clinical markers of depression. Youth will be scanned with multimodal MRI at baseline and at 6 months. We aim to determine whether worsening depressive symptoms in youth with depression and impaired insulin sensitivity is mediated by changes in neural reward circuitry, and to identify clinical, demographic, and familial risk factors for developing worsening depression in these youth.
Role: Principal Investigator

1R56MH107243-01 (Singh) 08/04/15-07/31/17 NIMH
Neurodevelopmental Features of Sexual Dimorphism in Pediatric Psychopathology: This is a secondary data analysis of the Philadelphia Neurodevelopmental Cohort database, specifically aimed to examine sexual dimorphism in the development of psychopathology in youth using neuroimaging, genetic, and behavioral data.
Role: Principal Investigator

Child Health Research Institute (Singh) 09/01/13 – 08/31/18 Stanford University
Risk and Resilience in Youth at Familial Risk for Mood Disorders: This project aims to chart the evolution of mood disorders in youth at risk starting from health in order to understand ideal times and methods for intervention to prevent the onset of serious mood problems and their progression into adulthood.
Role: Principal Investigator

1R01AG050345-01A1 (Rasgon) 09/1/16-5/31/21 NIA
“Insulin Resistance and Accelerated Cognitive Aging”
This proposal aims to advance our understanding of the mechanisms of insulin action in the living human brain, before overt neurodegeneration has begun, thus identifying the earliest signs of Alzheimer’s disease. It’s not known whether insulin resistance (IR) can predict cognitive decline in individuals younger than age 50 without overt mental illness. We propose to use an innovative accelerated longitudinal design (ALD) to characterize trajectories of cognitive and neural biomarkers and to: 1) describe baseline cognitive and neural biomarkers of brain function across the spectrum of IR in persons ages 25-50; 2) assess how the baseline IR and change in IR at a younger age affects the pattern of decline in cognitive and neural biomarkers and 3) explore the effects of baseline IR on changes in cognitive and neural variables of interest as moderated by non-modifiable risk factors for Alzheimer’s disease (gender, and APOE4/family history).

1R01MH101495-01 (Gotlib) 07/01/13 - 06/30/17 NIMH
The Effects of Early Life Stress on Neurodevelopment in Children and Adolescents: This study aims to examine the influence of early life stress on the maturation of neural circuits and neuroendocrine and cognitive processes that are critical to psychological health in children.
Role: Co-Investigator