BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Manpreet Kaur Singh, MD MS

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

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

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

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

My training in child and adolescent psychiatry and neuroscience has allowed me to conduct studies integrating neurobiological and physiologic risk factors associated with the development of major mood disorders, including bipolar and major depressive disorder in youth. I also have extensive experience in the recruitment, assessment, and intervention of youth across this spectrum of major mood disorders. In my laboratory we have developed cutting-edge methods to integrate cognitive, behavioral, affective, and neural (functional, structural, and neurochemical) factors in children and adolescents with and at risk for mood disorders. I have published several manuscripts concerning the neurobiology of childhood-onset mood disorders and have received NIH, industry, and private foundation funding focused on neural and behavioral assessment of youth with and at risk for major mood disorders.

1. **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. doi:10.1001/jamapsychiatry.2014.1031. [Epub ahead of print] PMID: 25142103
2. Sun KL, Watson KT, Angal S, Bakkila BF, Gorelik AJ, Leslie SM, Rasgon N, **Singh MK**. (2018). Neural and Endocrine Correlates of Early Life Abuse in Youth with Depression and Obesity. In a special issue on "Brain-Metabolic Crossroads in Severe Mental Disorders - Focus on Metabolic Syndrome" *Frontiers in Psychiatry.* 9:721. doi: 10.3389/fpsyt.2018.00721. PMID: 30622489; PMCID: PMC6308296.
3. **Singh MK**, Leslie SM, Packer MM, Zaiko YV, Phillips OR, Weisman E, Wall D, Jo B, Rasgon NL, Brain and Behavioral Correlates of Insulin Resistance in Youth with Depression and Obesity. *Hormones and Behavior.*

4. Phillips O, Onopa A, Hallmayer JF, Mackey L, Taylor J, Gotlib IH, **Singh MK** (In Press), Beyond a Binary Classification of Sex: An Examination of Brain Morphism, Psychopathology, and Genotype. *J Am Acad Child and Adolesc Psychiatry*.
5. **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.

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
2009-2010 Acting Assistant Professor, Division of Child & Adolescent Psychiatry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine
2010-2018 Assistant Professor, Division of Child & Adolescent Psychiatry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine
2018- Associate 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
2017 Member, Society for Biological Psychiatry, Elected Junior Councilor, 2019-2021

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
2007-8 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 American Academy of Child and Adolescent Psychiatry (AACAP) KTGF Award for Research in Depression or Suicide
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 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 Outstanding Teaching Award from the Child and Adolescent Psychiatry Fellows at Stanford
2016 Brain and Behavior Research Foundation Independent Investigator Award
2018 Chairman's Award for Excellence in Research, Stanford University School of Medicine
2019 Blanche F. Ittleson Award for Research in Child and Adolescent Psychiatry, APA

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.
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.
c. **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
d. **Singh MK**, Leslie SM, Bhattacharjee K, Gross M, Weisman W, Staver A, Soudi L, Phillips O, Onopa A. Vulnerabilities in Sequencing and Task Switching in Healthy Youth Offspring of Parents with Mood Disorders, *Journal of Clinical and Experimental Neuropsychology*. 2017 Nov 23:1-13. PMID: 29168420

2. I have 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: 3381335.
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.

3. To expand on the current neural models of major mood disorders, I have examined brain regional and network-based abnormalities in youth and adults with mood disorders. 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. doi: 10.1111/bdi.12221. PMID: 24938878
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. doi:10.1001/jamapsychiatry.2014.1031. [Epub ahead of print] PMID: 25142103
d. **Singh MK**, Leslie SM, Packer MM, Weisman EF, Gotlib IH. Limbic Intrinsic Connectivity in Depressed and High-Risk Youth. *J Am Acad Child Adolescent Psychiatry*. 2018 Oct;57(10):775-785.e3. doi: 10.1016/j.jaac.2018.06.017. PMID: 30274652

5. I am leading and collaborating on studies aimed to investigate early preventing and intervention of mood disorders in youth. Specifically, I have investigated the benefits of family focused psychotherapy, mindfulness meditation, and medications in youth and adults with or at risk for mood disorders 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, 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
   b. 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
   c. Schneck CD, Chang KD, **Singh MK**, DelBello MP, Miklowitz DJ. (2017). A Pharmacological Algorithm for Youth Who Are At High Risk for Bipolar Disorder. *Journal of Child and Adolescent Psychopharmacology*, 27(9):796-805. PMID: 28731778
   d. Chang KD, DelBello MP, Garrett A, Kelley RG, Howe M, Adler CB, Rana M, Welge J, Strakowski S, Reiss AL, **Singh MK,*** Neurofunctional Correlates of Response to Quetiapine in Adolescents with Bipolar Depression. *J Child and Adolescent Psychopharmacology*. 2018 Jul/Aug;28(6):379-386. doi: 10.1089/cap.2017.0030.

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

D. Additional Information: Research Support and/or Scholastic Performance

Allergan 4/17/19-4/16/22
A Double-blind, Placebo- and Active-controlled Evaluation of the Safety and Efficacy of Levomilnacipran ER in Pediatric Patients 7-17 Years With Major Depressive Disorder $285,189
This is an industry-sponsored double-blind placebo controlled trial aimed to evaluate the efficacy, safety, and tolerability of levomilnacipran relative to placebo in pediatric outpatients (7-17 years) with major depressive disorder (MDD).

PCORI – Subcontract from Univ. of Cincinnati 4/1/19-6/30/20 Patient-Centered Outcomes Research Institute
Metformin for Overweight & Obese Children and Adolescents with Bipolar Spectrum Disorders Treated with Second-Generation Antipsychotics. This patient-oriented pragmatic clinical trial aims to determine if adding metformin to a healthy lifestyle program would help control medication-induced weight gain caused by atypical antipsychotics to treat mood disorders in children and teens ages 8-19 years.

Innovator Grant Program (PI Singh) 01/14/19-06/30/20 Stanford Department of Psychiatry
Evaluating the efficacy and tolerability of targeted transcranial magnetic stimulation in youth
The primary objective of this study is to evaluate the safety and efficacy of intermittent theta burst transcranial magnetic stimulation in a 6 week open study in adolescents with MDD who have not responded sufficiently to at least one antidepressant medication trial administered at a clinically adequate dose and duration.
Role: Principal Investigator

Janssen Research & Development (Site PI: Singh) 04/01/17-7/01/20 Johnson & Johnson

"An Observational Longitudinal Study in Offspring of Parents with Bipolar Disorder to Evaluate the Relationship of Impairment in Psychosocial Functioning with the Manifestation of Mood Symptoms over 24 months."
The primary objective of this study is to compare, over 24 months, the time spent with clinically significant mood symptoms (i.e. mania, depression), as measured by the Longitudinal Interval Follow-Up Evaluation (LIFE) and the Psychiatric Status Rating Scale (PSR), in offspring of bipolar parents with and without at least mild impairment in psychosocial functioning.
Role: Site Principal Investigator

Independent Investigator Award (Singh) 09/15/2016-09/14/2019 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

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. 120 overweight girls and boys (ages 9-17 years) seeking treatment for moderate to severe depressive symptoms, are assessed at baseline, 6 months, and 24 months with neural and behavioral markers of Approach Motivation, serum markers of insulin sensitivity, and clinical markers of depression.
Role: Principal Investigator

Maternal Child Health Research Institute (Singh) 09/01/13 – 08/31/19 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"
It is not known whether insulin resistance (IR) can predict cognitive decline in individuals younger than age 50 without overt mental illness. Using an innovative accelerated longitudinal design (ALD), this project aims to characterize trajectories of cognitive and neural biomarkers as moderated by non-modifiable risk factors for Alzheimer's disease (gender, and APOE4/family history).
Role: Co-investigator