Summer 2013 Volume 9, Issue 1

STANFORD PEDIATRIC BIPOLAR DISORDERS PROGRAM

Meet the Team!

Kiki Chang, MD – Director

Dr. Chang is a Professor of Psychiatry at Stanford and the Director of the Pediatric Bipolar Disorders Program.

Manpreet Singh, MD, MS – Child Psychiatrist & Assistant Professor

Dr. Singh is an Assistant Professor at Stanford and is Director of The Stanford Pediatric Mood Disorders Clinic.

Amy Garrett, PhD – Researcher & Neuroimaging Manager

Dr. Garrett is an Instructor, conducts research and oversees neuroimaging data acquisition and analysis.

Meghan Howe, LCSW, MSW – Research Psychotherapist

Ms. Howe is a research therapist specializing in individual, family, and group therapy.

Victoria E. Cosgrove, PhD – Clinical Psychologist

Dr. Cosgrove is an Instructor, and conducts research and therapy.

Jade Garneau-Fournier, PhD – who is this?

Ryan Kelley, BS – Neuroimaging Research Assistant

Mr. Kelley acquires and anlyzes MRI and fMRI data.

Paige Staudenmaier, BA – Clinical Research Coordinator

Ms. Staudenmaier coordinates and aids in clinical research.

Jennifer Pearlstein, BS – Clinical Research Coordinator

Ms. Pearlstein coordinates and aids in clinical research.

Maisi Mayo – Neuroimaging Research Assistant

Ms. Mayo acquires and analyzes MRI and fMRI brain data.

Min-Hyeon Park – Visiting Scholar

Dr. Park is a child psychiatrist joining our lab from Korea.

Eunjoo Kim – Visiting Scholar

Dr. Kim is a child psychiatrist joining our lab from Korea.

Suzanna Chan – Administrative Assistant

Student Research Assistants:

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Shilpa Nataraj (Rice University)

Chloe Rossin (Boston College)

Welcome!

Welcome to the ninth newsletter of the Pediatric Bipolar Disorders Program (PBDP) at the Stanford University School of Medicine! This newsletter is released annually to provide you with information regarding current studies and breaking news in the field of ***pediatric bipolar disorders***. Many of you may already be familiar with the program through past or current studies, or you may be looking for the right study to join. This newsletter is for all individuals, families, and health professionals interested in the program and its work with pediatric bipolar disorders. Not only do we want this newsletter to be informative, but we also want it to provide a service not generally available to the public. We especially hope that those of you currently participating in our research studies feel part of the Stanford family. Please feel free to give us any feedback about this newsletter. If you wish to be added or removed from our mailing list, please contact us immediately (see second page for contact information). We welcome you to our newsletter and hope you will join our mission to learn better ways of understanding, identifying, treating, and ultimately preventing bipolar disorder (BD) in children and adolescents.

Our Mission

Pediatric BD affects approximately 1-2% of children and adolescents. The cause of the disorder is unknown, but we do know that it can be inherited. There are currently no genetic or biological tests to diagnose BD, and there are few studies regarding effective medications in pediatric BD.

Our mission is to study pediatric BD in hopes of learning more about the causes and effective treatments. We are currently conducting several studies involving children with BD and children at risk of developing BD. Certain children may be at an even higher risk of developing BD if they already have mood and/or behavioral problems. Most of our studies involve children with parents currently diagnosed with BD, but some studies involve any child with BD. Eventually, we hope to find ways of detecting children at very high risk for BD and ways to prevent them from developing BD.

Current Research

Now Recruiting!

Therapy Based Research

1. Early Intervention Using Family Focused Therapy for Youth at Risk for Bipolar Disorder:

We are studying the effects of Family Focused Therapy (FFT) in families who have a parent with bipolar disorder (BD). Children of a parent(s) with BD who experience mood symptoms are at risk of developing BD themselves. Pharmacological treatments for the prodrome of BD have not produced conclusive results (Miklowitz and Chang 2008). However, psychosocial interventions – particularly, those involving skill training with family members as well as high-risk youth – are well suited to children with or at risk for BD. The study will explore both psychosocial and neural activation variables that may be markers of vulnerability in high-risk youth that forecast disease onset and that may moderate the efficacy of treatment.

Families participating in this study have at least one parent diagnosed with bipolar disorder (BD) and at least one child aged 9-17 experiencing mood problems. The at-risk child receives diagnostic evaluations and brain imaging, and are randomized to either 12 weeks of family therapy treatment or a series of 3 family therapy sessions and 3 individual sessions. The proposed study will test whether or not a 4-month, 12-session family-focused treatment promotes symptom remission, prevents or delays illness onset, and enhances functioning among youth at high risk for BD over 2-4 years.

This study is funded by the NIMH.

2. Effects of Group Cognitive Behavioral Intervention on Stress-Induced Inflammatory Response in Youth at High Risk for Bipolar Disorder:

We are studying the effects of cognitive behavioral therapy (CBT) on youth with or at high risk for bipolar disorder (BD). Participants of the study are ages 12-17 and complete interviews, questionnaires, and blood draws as we attempt to investigate both the psychological and biological responses to stress.

This study is also examining stress-induced inflammatory response by doing a blood draw pre and post CBT intervention. During this blood draw, a stress test is conducted in order to evaluate pro-inflammatory and anti-inflammatory cytokine response. We are particularly interested in pro-inflammatory cytokines IL-6 and TNF-alpha and anti-inflammatory cytokine IL-10.

This study hopes to better understand the relation between stress and cytokine secretion in youth with or at risk for BD. We also hope to identify how psychosocial intervention interacts with immune-regulatory processes.

This study is funded by Spectrum Child Health, Stanford University School of Medicine and the Klingenstein Third Generation Foundation Fellowship.

3. Brain Connectivity and Mindfulness Training in Youth with Bipolar Disorder NOS:

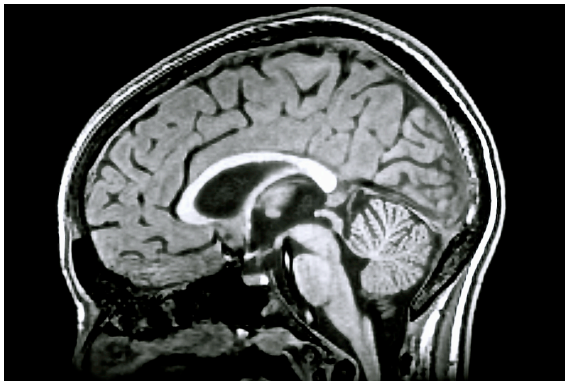
We are studying the behavioral and neural effects of Mindfulness Based Stressed Reduction for Teens (MBSR-T) therapy for individuals with bipolar disorder, not otherwise specified (NOS), an early form of BD. Mindfulness based-therapies (MBT) focus on being present in the moment, increasing awareness of the self, and attending to daily experience. MBSR-T was found to improve symptoms, functioning, and diagnostic outcome in 102 adolescents 14-18 years old with a variety of psychiatric conditions, including 52 with mood disorders (Biegel et al 2009). Participants of the study are aged 13-17 and have significant mood symptoms (Bipolar Disorder NOS) and a family history of bipolar disorder. Participants will complete interviews and MRI scans, and will participate in group therapy lasting 12 weeks.

This study is funded by the NIMH.

4. Therapy for Teens with Symptoms of Post-Traumatic Stress Disorder:

This research study looks at the effects of trauma-focused cognitive behavioral therapy (TF-CBT) on brain activity. Brain activity will be measured by conducting magnetic resonance imaging (MRI) scans before and after therapy. MRI is safe and does not involve any radiation or injections. Participants of the study are girls between the ages of 12 and 17 who have experienced abuse and may be having symptoms of PTSD and have no braces or non-removable piercings (for the scans). Participants not only receive free therapy but also compensation for their time and a picture of their brain from the scans. For more information, parents should call (650) 736-1874, and general information for participant's rights is available at 1-866-680-2906.

This study is funded by the NIMH.



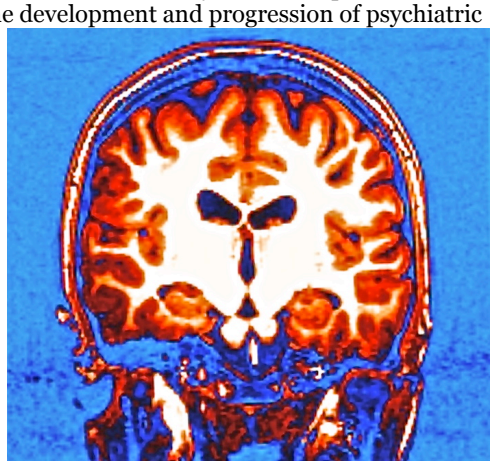
Any donations made to help fund our innovative research would be greatly appreciated. Please contact us if you would like to contribute!

Phone: (650) 725-6760 • Email: bipolarkids@stanford.edu • Website: pediatricbipolar.stanford.edu

Neuroimaging Studies

1. The Effects of Social Stress on Brain Activation and Inflammatory Cytokines in Youth with Bipolar Disorder:

We are conducting a study to understand the events that occur in the brain when youth are exposed to socially stressful situations and how these events may affect the development and progression of psychiatric conditions such as bipolar disorder. Participants of the study will undergo interviews, a blood draw, and magnetic resonance imaging to assess their response to social stress.



Past research has shown that laboratory controlled acute social stressors, that invoke social anxiety via social evaluation and the possibility of social rejection, activate the anterior insula and the dorsal anterior cingulate cortex (dACC) in healthy individuals (Eisenberger et al, 2007). However, to date, no published studies have examined the neural correlates of social stress in youth with BD nor examined these correlates with healthy controls (HC). The amygdala is also a structure widely known to be associated with anxiety, and fMRI studies show that it is hyperactivated within individuals suffering from certain anxiety disorders and BD (Rauch, Shin, and Wright 2003). Therefore, areas activated by social stress in HC have also been found abnormally overacted in youth with BD. This study is hoping to evaluate activity in the dACC, the anterior insula, and the amygdala in response to social stress in youth with BD compared with HC. We hypothesize that BD youth will have increased activation in these areas in comparison to HC.

This study is funded by AACAP and the Lilly Psychiatric Research Fellowship.

2. Neurobiologic and Immunologic Markers in Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS):

We are conducting a study to explore neurologic and immunologic markers of PANS in youth. The cause and treatment of PANS is not well understood, so this study hopes to better understand the markers associated with PANS in order to produce better treatment options in the future. Participants of the study include children or adolescents ages 4-18 years who have either: (a) experienced symptoms similar to PANS or (b) have no psychiatric diagnoses. Participants will undergo assessments, medical examinations, blood draws, and brain scans.

At LPCH, we recently opened a PANS clinic. As a collaboration between Psychiatry and Pediatrics/Rheumatology, we are a novel multidisciplinary clinic examining different angles of this disorder (rheumatologic, immunologic, infectious, neurologic, psychiatric). We also have pilot funds to conduct research to understand the cause of these disorders. Children with PANS can be extremely ill, with rage outbursts, extreme compulsive behaviors (licking shoes, barking), motor and vocal tics (whooping, wringing hands), school dysfunction (due to ADHD symptoms, cognitive regression) and psychiatric hospitalizations. This study is trying to provide a research basis for the clinical care of PANS.

This study is funded by Lucile Packard Foundation for Children's Health.

3. Resilience in Offspring of Parents with Mood Disorders:

Although both major depressive (MDD) and bipolar (BD) disorders in parents confer vulnerability for a broad range of difficulties for their children, we know far less about factors that boost resilience, specifically the capacity of youth to avoid unfavorable psychosocial and neural development that could then lead MDD or BD in themselves. This study hopes to better understand the biological correlates of resilience in offspring of parents with MDD or BD by assessing neural, neuroendocrine and cognitive factors that predict better functioning in high-risk youth. Through this study we can predict long-term outcomes for high-risk youth once we know which factors confer resilience versus risk and create better intervention through these resilient factors. The participants of the study are healthy offspring of parents with MDD or BD between the ages of 8-15 years. The participants of the study will complete interviews, assessments, and an MRI scan and will have their diurnal cortisol collected at baseline. Eighteen months later the participants will return for a follow up.

This study is funded by Spectrum Child Health, Stanford University School of Medicine.

Pediatric Bipolar Disorders Program Research Team Welcomes New Families!

We continue to look for paid research subjects. If any of these studies are of interest to you or someone you know, please contact us at:

Phone: 650-725-6760

Fax: 650-723-5531

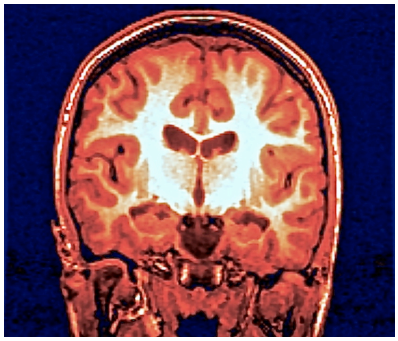
Email: bipolarkids@stanford.edu

We're now on Facebook! "Like" our page to receive updates on our lab!

Breaking Research Findings!

Amygdala Volumetric Correlates of Social Anxiety in Youth at High Risk for Bipolar Disorder

Min-Hyeon Park; A. Garrett, Ph.D.; S. G. Boucher; M. E. Howe, L.C.S.W; J. Pearlstein, B.S.; M. K. Singh, M.D.; K. Chang, M.D.

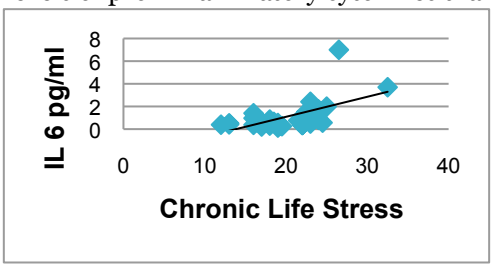


Offspring of parents with bipolar disorder (BD) are at a higher risk of developing an anxiety disorder compared to healthy controls. Bipolar offspring have an unusually high prevalence of both social anxiety disorder (9.1%) and generalized anxiety disorder (12.8%). Social anxiety disorder itself is profound in offspring of parents with BD because it increases their risk of developing mood disorders suicide in patients with BD. Previous fMRI studies have found some correlation between social anxiety disorder and abnormal brain activity in the amygdala (Milham et al., 2005), but no study has yet examined the correlation between amygdalar volume and degree of social anxiety symptoms. Thus, this study aims to compare social anxiety symptoms and amygdalar volumes between bipolar offspring with a high risk of developing mood disorders and healthy controls. The study found that bipolar offspring at high-risk for BD did have significantly higher levels of social anxiety compared to healthy controls. It was also found that there are significant negative correlations between amygdalar volumes and social anxiety symptoms in children who had elevated symptoms of social anxiety.

Environmental Stress and Inflammatory Cytokines in Adolescent Mood Disorders

Jennifer Pearlstein, B.S.; K. Chang, M.D.; PJ Staudenmaier, B.A.; S. Li, B.A.; F. Dhabhar, Ph.D.; V. Cosgrove, Ph.D.

Pyschopathology is a combination of genetic predisposition and life stress. Stress early in life relates to the onset and severity of symptoms present in bipolar disorder (BD) (Miklowitz & Chang, 2008), and environmental stress is correlated to inflammatory cytokine secretion. Kennery and Schedlowski found that psychological stress either suppresses or activates certain immune functions, leading to the persistence or termination of diseases (2007). The specific response to stress in the immune system involves the production of cytokines, which are proteins that either promote (pro-inflammatory) or inhibit (anti-inflammatory) inflammatory responses (Segerstrom & Miller 2004). This study hypothesizes that youth either at high risk (HR) or with BD have higher levels of pro-inflammatory cytokines than anti-inflammatory cytokines. The specific cytokines this study looks at include the pro-inflammatory cytokines IL-6 and TNF-alpha and the anti-inflammatory cytokine IL-10. The study found that diagnosis, symptom severity, and chronic life stress was significantly correlated with the pro-inflammatory cytokine IL-6, but not TNF-alpha or the anti-inflammatory cytokine IL-10. It was also found that HR and BD individuals reported more stress from close friendships, social life, family, romantic relationships, and academics than healthy controls (HC).



The Effects of Social Stress on Brain Activation in Youth with Bipolar Disorder

Donna Roybal, M.D.; V. Cosgrove, Ph.D.; A. Garrett, Ph.D.; S. G. Boucher; PJ Staudemaier, B.A.; J. Pearlstein, B.S.; J. Garneau-Fournier, B.A.; K. Chang, M.D.

Patients suffering from childhood-onset bipolar disorder (BD) also have a chance to suffer from anxiety disorder, a frequent comorbidity of BD. Youth suffering from BD usually have low social behavior and interpersonal functioning skills that can lead to social anxiety and rejection, followed by worse psychosocial function and triggering of mood episodes (Goldstein et al., 2006). A past study has shown that laboratory controlled acute social stressors that create social anxiety through social evaluation and the possibility of social rejection activate the anterior insula and the dorsal anterior cingulated cortex (dACC) in healthy individuals (Eisenberger et al., 2007). The amygdala has also been known to be associated with anxiety and is hyperactivated in fMRI studies concerning anxiety disorders and BD (Rauch et al., 2003). Based on these studies, it was hypothesized that the dACC, the anterior insula, and the amygdala would be significantly hyperactivated in response to social stress in youth with BD compared to healthy controls (HC). It was also hypothesized that the severity of social rejection would correlate with hyperactivation in these areas, leading to a higher risk for further mood episodes. This study found that there were no significant differences between BD and HC in the brain regions that were examined.