STANFORD PEDIATRIC BIPOLAR DISORDERS PROGRAM

MEET THE TEAM

Kiki Chang, MD - Director
Dr. Chang is a Professor of Psychiatry and the Director of the Pediatric Bipolar Disorders Program.

Manpreet Singh, MD – Assistant Professor
Dr. Singh is a researcher and Co-Director of the Pediatric Mood Disorders Clinic

Amy Garrett, PhD – Senior Research Scientist
Dr. Garrett manages and assists in all aspects of neuroimaging data acquisition and analysis.

Victoria Cosgrove, PhD - Instructor
Dr. Cosgrove is an Instructor and clinical psychologist

Meghan Howe, LCSW - Clinical Research Manager
Ms. Howe is a research psychotherapist and manages clinical data acquisition and analysis.

Naama Barnea-Goraly, MD - Researcher
Dr. Barnea-Goraly is a researcher, specializing in neuroimaging.

Donna Roybal, MD – Postdoctoral Fellow, Chief Child Psychiatry Fellow
Dr. Roybal is a researcher, specializing in neuroimaging.

Ryan Kelley, BS - Neuroimaging Research Assistant
Mr. Kelley acquires and analyzes MRI and fMRI brain data.

Spencer Boucher, BA - Neuroimaging Research Assistant
Mr. Boucher acquires and analyzes MRI and fMRI brain data.

Sherrie Li, BA - Clinical Research Coordinator
Ms. Li coordinates all aspects of clinical and behavioral research.

Erica Marie Sanders, BA – Clinical Research Coordinator
Ms. Sanders coordinates all aspects of clinical and behavioral research.

Student Research Assistants
Paige Staudenmaier (Stanford)
Jennifer Kallini (Stanford)
Nicole Adams (UCSC)
Brittany Jaso (Cornell)
Chloe Rossin (Boston College)
Nicola Park (Rice)
Walter & Eleanor

Welcome!

Not pictured: Nicole Adams & Jennifer Kallini

Welcome to the eighth newsletter of the Pediatric Bipolar Disorders Program (PBDP) at the Stanford University School of Medicine! We publish this newsletter annually to keep you informed of our ongoing research studies, as well as breaking news in the field of ***pediatric bipolar disorders***. Many of you may already be familiar with our group from participation in our past research studies, or may be participating in our current studies, or a few of you may be waiting for the right study to join. This newsletter is for all individuals, families, and health professionals interested in our work on pediatric bipolar disorders. 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 page 2 for our contact information). We hope you find this newsletter is not only informative, but also provides a service not usually available to the general public. We especially hope those of you participating on our research feel part of the Stanford family as you join us in our mission to learn better ways of understanding, identifying, treating and preventing bipolar disorder (BD) in children and adolescents.

Our Mission

Pediatric BD is an understudied disorder that affects at least 1% of children and adolescents. The cause is unknown, though we do know that it is largely inherited. There are no genes or biological tests that can help to diagnose BD. There are very few conclusive studies regarding effective medications in pediatric BD.

We wish to use all our available resources to study pediatric bipolar disorder in the hopes of learning more about the causes and effective treatments. We are conducting various studies of children with BD as well as children of parents with BD, who are at generally higher risk of developing BD. We feel that certain bipolar offspring may be at even greater risk for developing BD – those who already have mood and/or behavioral problems. Most of our studies involve bipolar offspring, but some involve any child with a bipolar disorder. 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!

Clinical Trials

1. The Evaluation of Lamotrigine (Lamictal) for Bipolar I Disorder in Children and Adolescents

We are conducting a study for children ages 10-17 with bipolar I disorder who take at least one medication but are still experiencing mood symptoms. In the first phase of the study, all children who qualify will be given lamotrigine (Lamictal) in addition to their current medication(s). In the next phase, children will be randomized to either continue taking lamotigine or to receive placebo. There are no family history requirements for this study.

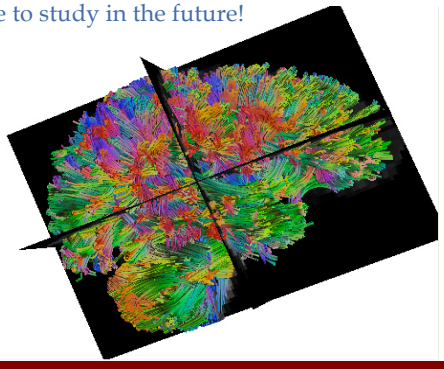
This study is funded by GlaxoSmithKline

2. The Evaluation of Asenapine (Saphris) for Bipolar I Disorder in Children and Adolescents:

We are conducting a study for children ages 10-17 with bipolar I disorder who are experiencing mood symptoms. In the first phase (3 weeks) of the study, all children who qualify will be randomized to either take Asenapine (Saphris) or to receive a placebo. In the next phase, all participants will be offered open treatment with Asenapine. There are no family history requirements for this study. All medications, visits with the psychiatrist, and other aspects of the study are free to participants during study participation.

This study is funded by Schering-Plough Research Institute

Below is a HARDI image (high angular resolution diffusion imaging) which is the latest technology for studying white matter tracts throughout the brain. White matter tracts are the physical connections through which brain regions communicate. This is something we hope to study in the future!



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. Participating families must have at least one parent with bipolar disorder and at least one child ages 9-17 who has significant mood problems. Family members receive thorough diagnostic evaluations, brain imaging, and are randomized to either 12 weeks family therapy treatment or a series of 3 family therapy sessions and 3 individual sessions.

This study is funded by the NIH

2. Effect of Group Cognitive Behavioral Therapy on Stress-Induced Inflammatory Response

We are studying response to stress and whether group cognitive behavioral therapy may impact this response in children ages 10-17 on the lives of children who have at least one parent with bipolar disorder, or who have bipolar disorder themselves, or who are healthy. This study involves interviews, questionnaires and blood draws as we are investigating both psychological and biological responses to stress. This study also offers group cognitive behavioral therapy.

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:

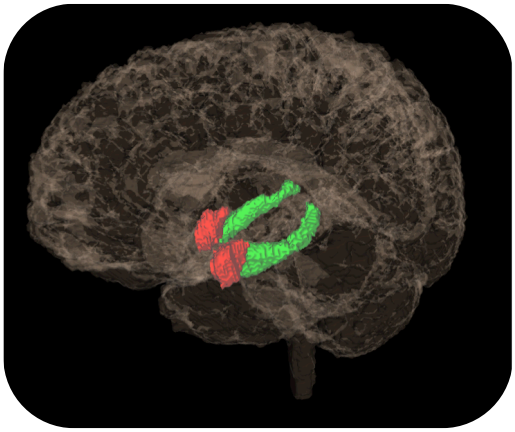
Phone: 650-725-6760
Fax: 650-723-5531
Email: PBDPStanford@gmail.com

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

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

Antidepressant Induced Mania

Meghan Howe, L.C.S.W.; A. Garrett, Ph.D.; E. M. Sanders, B.A.; R. Kelley, B.S.; J. Hallmayer, M.D.; Kiki Chang, M.D
Presented at the 2011 AACAP Annual Meeting, Toronto



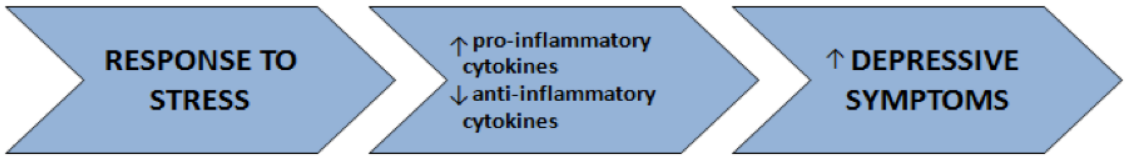
By studying youth with a family history of bipolar disorder (BD), the Pediatric Bipolar Disorders Program hopes to learn more about the development and prevention of BD in children and adolescents. Medication is often the first line of treatment for youth with mood disorders; however, it has been noted that antidepressants, including SSRI's, can initiate a period of mania, called anti-depressant induced mania (AIM), particularly in patients with a family history of bipolar disorder. Though some studies have investigated the relationship between patient characteristics and AIM, the best form of clinical treatment of these youth is still unclear. Thus, in our study we sought to determine what risk factors may make a child more likely to experience AIM when treated with an SSRI.

In our investigation, subjects with a biological parent with BD were examined using MRI scans and genetic analysis. We found 56% of our sample to have a history of AIM, indicating the common occurrence of this outcome in youth who have a parent with BD. We also found that those with AIM had significantly smaller amygdalar volume than those without AIM. Decreased amygdalar volume has consistently been found in youth with BD and thus it is possible that a reduced amygdalar volume could somehow be involved with increasing risk of AIM. However, it may also be that AIM may directly or indirectly lead to a smaller amygdala. Finally, an overwhelming number of subjects with AIM in our study had ADHD or anxiety, not always as the only diagnosis. Subjects who had only MDD, for example, had a much lower rate of AIM (17%), than those with MDD+ ADHD (70%). This suggests that the presence of ADHD or anxiety in youth with parents with BD should alert the clinician to increased risk for AIM. These findings are preliminary, but do suggest that certain characteristics may be associated with AIM in populations already at high-risk for mania. Clinicians may need to show additional caution when prescribing SSRIs for bipolar offspring with ADHD or anxiety.

Inflammation in Response to Stress as a Potential Risk Factor for Pediatric Bipolar Disorder

Victoria E. Cosgrove, Ph.D.; S. Li, B.A.; F. Dhabhar, Ph.D.; & K. D. Chang, M.D.

Figure 1. Development of biologically-mediated mood symptoms

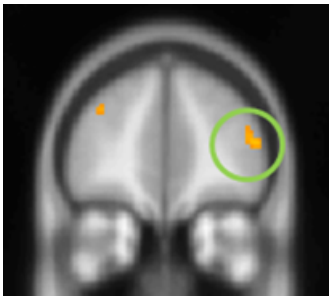


Youth with bipolar disorder (BD) may be uniquely sensitive to life stressors. Bipolar youth involved in high-conflict family interactions or with histories of early physical or sexual abuse report earlier onset of mood symptoms, more rapid cycling patterns, and increased suicidal ideation (Post, Leverich, Xing, & Weiss, 2001). Without treatment, both affected and at-risk youth with BD experiencing life stress may demonstrate compromised social, neurological, and emotional development. The purpose of this study is to gain insight into the relationship between the activation of cytokines (stress induced proteins found in the blood) and a response to stress by comparing at-risk youth to healthy controls. We believe that an elevated response to stress accelerates the development of BD in vulnerable individuals. Our preliminary results indicate that at-risk youth exhibit a unique biological response to stress. We hope that group CBT (Cognitive Behavioral Therapy) will help with reactivity to stress by providing individuals with coping skills and greater self-awareness.

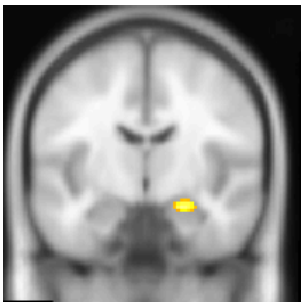
How does Family-Focused Therapy Influence the Brain?

Amy Garrett, Ph.D.; K. D. Chang, M.D.; M. Singh, M.D.; M. Howe, LCSW; A.L. Reiss, M.D.; D.M. Miklowitz Ph, D.
Presented at the 2011 AACAP Annual Meeting, Toronto

Family-focused therapy (FFT) is a type of therapy that includes not only the child, but the entire family in every treatment session. FFT teaches the family to recognize the symptoms of mood disorders and to identify 'stress triggers' that cause mood swings. FFT trains the whole family to communicate effectively with each other, and to solve problems in a non-stressful way. Previous studies have found that FFT reduces symptoms of depression in adolescent patients (Miklowitz et al., 2008). By understanding how the brain changes during successful treatment with FFT, we may better understand the process of symptom improvement, and this could lead to even better treatments in the future. Therefore, researchers in our lab obtained a grant that allowed us to collect functional magnetic resonance imaging scans from study participants before and after 4 months of FFT treatment. Twelve adolescents participated, and half of them received FFT and the other half received a comparison treatment, which was psychoeducation. The brain scans showed that 'getting better' is associated with consistent changes in the brain, no matter which therapy you receive, including (1) increased activation in the dorsolateral prefrontal cortex (an executive control region that helps to control mood as well as cognitive processes such as attention), and (2) decreased activation in the amygdala, (a brain region associated with emotional responses). These findings are very interesting because they show that brain function is becoming more similar to a healthy adolescent brain as symptoms improve. In fact, as symptoms of mania improve, prefrontal cortex activation increased. Finally, we found that patients who had more amygdala activation before treatment, benefitted the most from FFT. This result is exciting because it may help us in the future to determine the best type of treatment for a particular patient. Our current FFT brain imaging study is continuing this work.



Dorsolateral Prefrontal Cortex



Amygdala

Changes in Brain Function Overtime in Youth at High Risk for Bipolar Disorder

To be presented at the 2012 AACAP Annual Meeting, San Francisco

Children of parents with bipolar disorder (BD) are at high-risk for BD, especially those experiencing mood symptoms. Understanding how the brain changes over time in these patients may help us to predict and prevent symptoms from worsening. Twenty-five youth at high risk for BD, ages 9-17 years, were scanned at two timepoints, with an intrascan interval of 1.6 to 3.9 years. All had a parent with BD and current mood symptoms. Symptom severity (depression, mania, and total) was calculated from items on a clinical interview given at both timepoints. Functional MRI data were collected while subjects viewed fearful and neutral facial expressions. Some of the participants got better, but of those who got worse, we saw decreasing activation in executive function regions over time. We also saw increasing activation in the hippocampus over time, which may indicate increasing stress levels. Reducing stress in the environment may help patients to maintain or decrease symptoms.

We would like to thank all of the families who make this research possible by volunteering for our studies. We would also like to thank our donors, without whom this research would not be possible. In addition to our anonymous family donors, we would like to recognize the following institutions and donors who are currently funding or have funded our research: ***The Hahn Family, GlaxoSmithKline, the NIMH, the KTGF, NARSAD the Lucille Packard Children's Fund, the Sofaer Family, The John A. Pilafidis Memorial Fund, and the Prechter Fund.***