Objective

- Signs and Symptoms of Mood Disorders
- Challenges Depressed Youth Face in Stress Regulation
- Assessment, Treatment and Prevention of Mood Disorders

Depression is a Serious Disorder

- Significant Impairment
- Associated with Morbidity²
  - 60-70% of suicides are associated with an existing mood disorder
  - 5-15% of those suffering from depression will die from suicide
- Leading cause of disability worldwide¹
  - 2000 4th ranking contributor to global burden of disease
  - 2020 projected to be the 2nd ranking contributor
    - The prevalence of depression has been increasing

¹,²,³

Disclaimer

- The contents of this handout are for informational purposes only and are not intended to be a substitute for professional advise, diagnosis or treatment. Materials in this handout may be copyrighted by the author or other third parties. Where appropriate, every effort has been made to give attribution to the source.

1. www.cdc.gov/nchs/data/databriefs/db07.htm
2. Brent & Kolko, 1990
**Depression: A Progressive Illness?**

- Recurrence: each episode increases the likelihood of a future episode\(^1\)
- Kindling hypothesis: episodes are more easily triggered over time\(^2\)
  - Lower threshold for impact of minor events vs increase in spontaneous dysregulation\(^3\)
  - Recurrence predicted by increasing number of episodes as opposed to stressful events\(^4\)
- Longer duration of untreated illness negatively influences the course of MDD\(^5\)


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**Relatively Recent Diagnosis for Children and Adolescents**

- Psychoanalysis
  - Classical psychoanalysts acknowledged the importance of early childhood experiences (e.g., loss) as a primary cause of adult depression
  - Spitz and Wolf's (1940's) seminal work in anaclitic (lean on) depression - suggested that depressive characteristics were found under some conditions early in life.
  - Bowlby (1960) argued that the upset an infant displays when confronted with separation from an attachment figure is comparable to adult mourning.

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**Relatively Recent Diagnosis for Children and Adolescents**

- The debate in the 50's to 70's
  - Do young children have the ego- and cognitive-developmental capabilities to experience complex emotions (guilt, mourning, despair) that were core to some etiological theories of depression?
  - Was depression manifested differently in children? Is it typically "masked" or manifest as "depressive equivalents" by the expression of somatic problems or behavioral disturbances?
  - Were children capable of or have a tolerance for sustained misery?

- By the 80s child and adult depression were widely considered isomorphic disorders.

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**Importance of Identifying and Treating Depression in Adolescence**

- Illness impedes achievement of developmental milestones
  - Social-emotional domain
  - Achievement domain
- Poor Prognosis for Early Onset
  - Greater severity of symptoms
  - Higher likelihood of episode recurrence
  - Increased suicidality
  - Higher comorbidity
  - Lower educational attainment and marriage rates

Reviewed in Cullen, Klimes-Dougan & Kumra, 2009; Cullen Klimes-Dougan, Kumra & Shultz, 2009
The neurobiological stress system is presumably still under development in adolescence.

**Plasticity**: extent to which the brain can respond to new experience or recover from injury
- Typically decreases with age (nervous system becomes specialized)

**Importance of Identifying and Treating Depression in Adolescence**

1. Scouras, 1999
2. Lenroot et al., 2007
4. Reviewed by Adam, Klimos-Dragan, & Gunnar, 2008

The hope is that the stress-regulatory systems are still malleable and amenable to intervention.
- Prevent initial episode?
- Limit the progression of the illness?
- Prevent reoccurrence?

**Mood Disorders**

**Description and Scope**

**Categorical Approaches**
- the medical model
  - Diagnostic Statistical Manual

**Dimensional Approaches**
- Degree of a problem
  - Internalizing Continuum
EMOTIONS ARE USEFUL / FUNCTIONAL

EMOTIONS provide a signal for us to organize our thoughts and actions
(I am feeling sad because my friends keep leaving me out of their plans)
They motivate us to act
(I am scared of failing a test so I better study hard)
They serve to communicate information to others
(She looks angry so I better give her some time to cool off)

Psycho evolutionary Perspective - Differential Emotions Theory

So if emotions are so functional, why do they cause so many problems?

- intensity, duration, frequency
  - Watson & Clark
- context (proximal, cultural)
  - Thompson
- flexibility and range
  - Malatesta-Magai / Cole

MAJOR DEPRESSIVE DISORDER

DIAGNOSIS OF MOOD DISORDERS
(Diagnostic and Statistical Manual - DSM-IV)

MAJOR DEPRESSIVE DISORDER
DYSTHYMIC DISORDER
BIPOLAR DISORDER

AFFECTIVE SYMPTOMS (FEELINGS)
- Depressed mood
- Irritable mood
- Anhedonia

VEGETATIVE SYMPTOMS (PHYSIOLOGY)
- Appetite/weight changes
- Sleep changes
- Psychomotor changes
- Fatigue/low energy

COGNITIVE SYMPTOMS (THOUGHTS)
- Diminished concentration
- Indecision
- Excessive guilt
- Poor self-concept
- Hopelessness
- Suicide ideation/behave
MORE PROTRACTED TYPE OF LOW-GRADE DEPRESSION

AFFECTIVE
- Depressed mood for most of the day, for more days than not for at least 1 year.

VEGETATIVE
- (e.g., poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue)

COGNITIVE
- (e.g., low self-esteem, poor concentration or difficulty making decisions, feelings of hopelessness)

MDD is a recurrent disorder. In adolescence it usually lasts about 5 to 6 months.
Most individuals recover, but 70% also have at least one additional episode within the next 5 years.
After recovery children tend to continue in a subclinical path with impairment in functioning (e.g., problems with interpersonal relationships, smoking, use of alcohol and other chemicals, early pregnancy, physical problems).
Poor prognosis for “Double Depression” (Dysthymia + Major Depressive Disorder)

Depression Rates

GENDER DIFFERENCES

- Many explanations have been offered:
  - Physical development -- changes more difficult for girls
  - Hormonal effects -- onset of puberty, perinatal period, and menopause
  - Stress perceptions -- greater in girls
  - Abuse/Trauma -- increased incidence of sexual abuse in girls
  - Attachment hypotheses -- Chaderow implicates symbiotic relationships of girls with mother
  - Emotion socialization -- girls socialized to express the vulnerable emotions
  - Self-medication -- boys/men may be self-medicating with alcohol, etc.
A distinct period of abnormally and persistently elevated, expansive, or irritable mood
- lasting at least 1 week
- requiring hospitalization

During the period of mood disturbance (additional symptoms)
- inflated self-esteem or grandiosity
- decreased need for sleep
- more talkative than usual or pressure to keep talking
- flight of ideas or subjective experience that thoughts are racing
- distractibility
- increased goal-directed activity or psychomotor agitation
- excessive involvement in pleasurable activities (high potential for painful consequences)

**ETIOLOGICAL MODELS**

**BIPOLAR I DISORDER**

**Bipolar I vs. Bipolar II vs. Bipolar NOS**

- **Bipolar I Disorder**
  - At least one Manic or Mixed Episode
  - +/- Depressive Episode

- **Bipolar II Disorder**
  - At least one Depressive Episode + hypomanic episode

- **Bipolar Disorder NOS**
  - Mood symptoms but not meeting criteria for I or II

**Depression as a Stress Regulatory Disease**

- **Internalizing Problems**
  - Mood Disorders
    - Major Depressive Disorder
    - Dysthymic Disorder
  - (Bipolar Disorder)
  - Anxiety Disorders
  - Somatoform Disorders
  - Eating Disorders


-Martins, Ressler, Binder, & Nemeroff, 2009
Psychopathology

Interaction of biology and environment

Diathesis (biological factors)
Stress (environmental factors)

Probability of disorder

Development → changes in biology and environment over time

Psychoanalytic Theories

- The focus has been on inadequate childhood experiences that adversely affect adulthood functioning. Some important themes have included real or imagined object or love loss as triggers of depression.

Cognitive-Behavioral Theories

- Seligman’s Learned Helplessness Model
  - Emphasizes attributional style (e.g., internal, stable, global attributions for negative events) and perceptions of hopelessness

- Beck’s Cognitive Theory of Depression
  - Emphasizes negative views of the self, the world, and the future

- Lewinsohn’s Interpersonal Theory
  - Emphasizes a restricted range of potentially reinforcing events and social skill deficits (e.g., social isolation) as a result—initially others unintentionally reinforce depressive symptoms and then eventually, become overwhelmed and withdrawn from the depressed individual

- Emotion Socialization Theory
  - During development, some affects may become monopolistic and dominate personality with mild distortions (personality style) or severe distortions (psychopathology)
  - Surfeit (too much) or deficient pathology may result according to what discrete emotion is facilitated or discouraged (e.g., too much sadness results in depression, too much happiness results in mania, Maletesta & Wilson, 1981)
First Degree Relative
- MDD Patient – relative 14.2% risk for MDD and 1.9% risk for BD
- BD Patient – relative 12.5% risk for MDD and 6% risk for BD

Twin Studies
- MDD heritability estimate is between 31% to 42%.
- BD heritability estimate is 59%.

Genetic Transmission
- Numerous Functional Polymorphisms (DNA sequence variations that alter the expression or the function of the gene product)
- Interaction between DNA and Environment

Plasticity: extent to which the brain can respond to new experience or recover from injury
- Typically decreases with age (nervous system becomes specialized)

Adolescent Development of the Frontal-Limbic Neurocircuitry
- Decreased Gray matter
- Increased White matter
- Fibers connecting limbic structures (amygdala) to prefrontal cortex mature through adolescence

Adolescent Development of HPA axis
- Increased basal
- Increased stress reactivity

Neurobiological Stress System: Under Development
- Seeman, 1999
- Lenroot et al., 2007
- Barts, 2003
- Reviewed by Adam, Klimza-Dougan, & Gunnar, 2008

Neural Circuitry of MDD
- Attention-cognition
- Vegetative / feeling

One of the most consistent findings in biological psychiatry is the disruption of the HPA axis in depressed adults. Approximately 50% to 80% of severely depressed patients will show hyperarousal of the HPA axis (non-suppression in response to dexamethasone (dex)). The precise mechanism by which cortisol exerts this influence on affect is just beginning to be understood.

A recent meta-analysis was conducted on MDD and NC adults. In response to a stressor, no differences in basal levels were noted. Differences noted for stress reactivity:

- Cortisol MDD = NC (both elevated)
- Differences noted for stress recovery:
  - Cortisol MDD > NC

Failure to suppress cortisol secretion after dex test associated with suicide.

- 6 times higher rate

References:
1. Gold et al, 2002
2. Burke, Davis, Otte, & Mohr, 2005
3. Coryell & Schlesser, 2001
4. Bostwick & Warzecha, in press
RODENT RESEARCH:
- In laboratory animal studies show that ELS leads to heightened stress reactivity and alterations in relevant neurocircuitry.
- Adults rats separated from dams for 180 min/day on postnatal days 2-14 exhibit three-fold increase in Cort responses to psychological stressors that control adults.

Ladd, et al., 2000; Plotsky & Meaney, 1993

ASSESSMENT

ASSESSMENT OF DEPRESSION

- **YIELDS DIAGNOSIS**
  - CLINICAL INTERVIEW
  - STRUCTURED OR SEMI-STRUCTURED INTERVIEWS
    - Schedule for Affective Disorders and Schizophrenia (K-SADS)
    - Diagnostic Interview Schedule for Children (DISC)
    - Structured Clinical Interview for DSM IV Axis I Disorders (SCID)

- **YIELDS SYMPTOMS OF DEPRESSION**
  - CHILDREN’S DEPRESSION INVENTORY (CDI)
  - BECK DEPRESSION INVENTORY (BDI)

- **YIELDS SYMPTOMS OF INTERNALIZING PROBLEMS**
  - CHILD BEHAVIOR CHECKLIST / YOUTH SELF-REPORT (CBCL / YSR)
  - BEHAVIORAL ASSESSMENT SCHEDULE FOR CHILDREN (BASC)

Child/Adolescent Assessment
- Multi-method
  - Interview
  - Rating Scales / Questionnaires
  - Observation
  - Projective Techniques
- Multi-informant
  - Child
  - Parents
  - Teachers
Children, more than parents or teachers, typically report higher levels of internalizing disorders, depressive symptoms, and suicidal thoughts and behaviors.

Depressed mothers report higher levels of problems in their offspring (e.g., child’s externalizing problems, mother’s blurred boundaries).

Sensitive behavior like suicidal ideation/behavior may be best assessed by self-reports or computer administered methods.

Suicide Content Recollection

Problems Associated with Inaccurate Recollection of Suicidal Content

Klima-Dougan, Safer, Romaville, Tinley, & Harris, 2006

Clinical Scenarios

- Self Injury
  - Without suicidal ideation
  - With suicidal ideation/intent/plan
- Suicidal ideation with or without intent/plan
- Suicide attempt
  - without current suicidal ideation/intent/plan
  - with ongoing suicidal ideation/intent/plan
Suicidal Ideation / Attempt

- Ideation
  - Thoughts life isn’t worth living, better off dead, etc.
  - If I didn’t wake up it’d be OK…
  - Thoughts of taking one’s life
- Attempt
  - Lethal or potentially lethal behavior
  - Must consider patient’s understanding of potential lethality
  - Assessment of Risk vs. Rescue

Suicidal Thoughts and Behavior

- Figure 1: Percentage of high school students reporting that they considered suicide, attempted suicide, or went to a hospital for an attempt during the previous year, Oregon, 1997.

Assessing Suicidal Ideation

- Difficult to accurately predict attempts
- Most adolescent suicides are impulsive
- Attempt:completion ratio = 50:1 to 100:1
- Consider various risk factors
- Determine level of intervention

Assessment of Suicidality

- Question the patient privately
  - “…ever thought about killing yourself or wished you were dead?”
  - “…ever done anything on purpose to hurt or kill yourself?”
  - “If you were to attempt, how would you kill yourself?”


Assessment of Suicidality

- Obtain collateral
  - Parents/guardians
  - Family
  - Boyfriend/girlfriend/friends
  - School reports
- Safety trumps confidentiality

Suicide Rates

Assessment of Suicide

- Hopelessness Scale for Children (Kazdin et al. 1986)
- Columbia Teen Screen (Shaffer et al. 1996)
- Suicidal Ideation questionnaire (Reynold 1987)
- Reasons for Living Inventory for Adolescents (Osman et al. 1998)
- Screening Instruments (clinician administered)
  - Child Suicide Potential Scale (Pfeffer 1979)
  - Suicide Potential Interview (Reynold 1991)

www.nccp.org/publications/pub_878.html

WHO

Distribution of suicide rates (per 100,000) by gender and age, 2000

- Males
- Females

*Note: based on 20 or fewer deaths may be unavailable.

National Center for Health Statistics, National Vital Statistics System

CDC Wonder

Age group

6-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75+

Rate

0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0

Males
Females
Suicidality Risk Factors

- **Fixed Risk Factors**
  - Family history of suicide/attempts
  - Previous suicide attempts (boys particularly)
  - Males
  - Parental mental health problems
  - History of physical or sexual abuse
  - Gay/bisexual orientation

- **Social/Environmental Risk Factors**
  - Firearms in the home
  - Impaired parent/child relationship
  - Living outside the home (homeless, corrections, etc.)
  - School problems; social isolation

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Suicidality Risk Factors

- **Personal Mental Health Risk Factors**
  - Mood disorder (e.g., depression, bipolar)
  - Anxiety disorder (e.g., PTSD, panic)
  - Substance abuse/dependence/intoxication
  - Psychotic disorder
  - Behavior disorder (e.g. conduct disorder, running away)
  - Aggression/impulsivity/severe anger/agitation

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Depression and Suicide

- Most depressed youth do not commit suicide.
- However, 7.7% of adolescents with severe depression diagnosed in childhood/adolescence died by suicide in a 15 year follow-up study.
- Those who die by suicide are likely to be suffering from depression.
  - More than 50% of youth that die by suicide suffer from a depressive illness
  - Some youth that are suicidal may not look depressed – may be oppositional, impulsive, and/or abusing substances

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Risk Factors Post Attempt

- Ongoing suicidal ideation; previous attempt
- Male / living alone
- Mental State
  - Ongoing depression/mood disorder
  - Substance abuse +/- mood disorder
  - Irritable/agitated/psychotic/violent
- Atypical means of attempt (e.g., not cutting/ingestion)

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Intervention – Levels of Care

- Outpatient with primary care provider
- Outpatient with mental health clinician
  - Non urgent referrals to Univ. of MN Depression Clinic
    (Dr. Kathryn Cullen; 612-273-8710)
- Day treatment or partial hospitalization
  - University of Minnesota Medical Center, Fairview
    (Intake Department; 612-672-2736)
- Inpatient psychiatric hospitalization
  - University of Minnesota Medical Center, Fairview
    (Intake Department; 612-672-6600)
What keeps people from suicide?

- The depressed patients who had not attempted suicide, compared to patients who had attempted suicide, expressed:
  - more feelings of responsibility toward family
  - more fear of social disapproval
  - moral objections to suicide
  - greater survival and coping skills
  - a greater fear of suicide than the depressed patients

Malone, Oquendo, Hsueh, et al., 2000

Available Treatments of Adolescents

Untreated Depression in Youth

Treatment Approaches

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PSYCHOSOCIAL INTERVENTIONS

Psycho-education

- Causes
- Symptoms
- Course
- Treatment options, risks and benefits
- Engage family as collaborators in decision making and treatment

Practice Parameter for treatment of child and adolescent depression

- Treatment phases:
  - Acute – until symptoms are in remission
  - Continuation – consolidate response and avoid relapse (all monthly for 6-12 months)
  - Maintenance – for some with severe, recurrent or chronic symptoms
- Roles Differ with Each Phase of Treatment:
  - Psycho-education
  - Supportive Management
  - Family and School Involvement


Psycho-education

- Important
  - for patient and family
  - education enhances treatment adherence
- Education re: MDD as an illness helps:
  - ↓ parental self-blame
  - ↓ blaming the patient
  - ↑ the parent's identification of their own symptoms
- Education of teachers can enhance identification of MDD in kids

Birmaher B, Brand E, et al. Practice Parameters for the Assessment and Treatment of Children and Adolescents with Depressive Disorders. JAACAP. 1998;37(10 Supplement):63S-83S.
### Supportive Management
- Active listening and reflection
- Restoration of hope
- Problem solving
- Coping skills
- Strategies for maintaining participation in treatment

### Family Involvement
- Essential for treatment of child or adolescent
- Motivation for treatment (often from parents)
- Observations of functioning or symptoms that the patient is not aware of or reluctant to share
- Monitoring patient progress and safety net

### Family Interventions
- Strengthen relationship between identified patient and caregivers
- Parenting guidance – conflict management
- Reduce family dysfunction
- Facilitate treatment referral for other family members with specific needs

### Cognitive Behavioral Therapy (CBT)
- **Lewinsohn and Clarke group: Adolescents Coping with Depression**
  - [Adolescents Coping with Depression](http://www.kpchr.org/public/acwd/acwd.html)
- **Brent group in Pittsburgh based on Beck’s work**
  - [Beck Institute site](http://www.beckinstitute.org/FolderID/200/SessionID/8413A020-950-B9E-837D04794B26/PageView/Library/InfoManage/Guide.htm)
- **Treatment of Adolescent Depression Study (TADS)**
  - [TADS Index](https://trialweb.dcri.duke.edu/tads/index.html)
Early evidence suggests that it is equally efficacious as CBT for adolescent depression.

**Focus on improvement of family interaction**
- Interpersonal Therapy site: [http://www.interpersonalpsychotherapy.org/](http://www.interpersonalpsychotherapy.org/)

**Behavioral Activation Therapy**
- BA attempts to help depressed people reengage in their lives through focused activation strategies.
- These strategies counter patterns of avoidance, withdrawal, and inactivity that may exacerbate depressive episodes by generating additional secondary problems in individuals' lives.
- BA is designed to help individuals approach and access sources of positive reinforcement in their lives, which can serve a natural antidepressant function.

**Dialectical Behavioral Therapy**
- A specific form of CBT based on the work of Marsha Linehan
- Has specific components based on dialectical theory and pragmatic considerations
- Receiving a lot of attention and research
- Particularly useful for high intensity cases including active suicidality, self harm, and/or borderline personality characteristics – emotional dysregulation
- Amazon site for Miller book on DBT with suicidal adolescents:

**Psychopharmacological Interventions**
Pharmacological Treatment of Pediatric MDD in the Acute Phase

- Studies: high placebo response
- If using a med...
  - SSRIs (in particular fluoxetine)
  - Possibly bupropion (particularly if comorbid ADHD)
  - SNRIs second line
  - TCAs not supported
- Assess @ 4 week intervals; titrate to remission
- If no improvement by week 8, consider alt agent

Antidepressants

- Method of Action:
  - Modify neurotransmitter levels
  - One mechanism: “reuptake inhibition”
  - Block action of cell structures that re-capture neurotransmitters after they are initially released
- Key Neurotransmitters:
  - Serotonin (5-HT)
  - Norepinephrine (NE)
  - Dopamine (D)

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Source: National Institute on Drug Abuse.
Over time, these increases in extracellular serotonin levels appear (due to SSRI blocking reabsorption) are found to help the symptoms of depression in many people.

- FDA Approved (MDD)
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)

- FDA Appproved (BP)
  - Olanzapine and Fluoxetine (Symbyax)

SSRIs: First Choice Medications for Depression

Treatment: Depression

- SSRIs
- SNRIs
  - Duloxetine (Cymbalta)
  - Venlafaxine (Effexor)

- NDRIs
  - Bupropion (Wellbutrin)

- Tricyclic antidepressants (TCAs)
  - e.g., Imipramine (Tofranil)

- Tetracyclic antidepressants
  - Mirtazapine (Remeron)

- MOA Inhibitors
- Lithium

NOT FDA APPROVED

- Compounds that target amino acids (e.g., glutamate)
  - LY354740, RU-38486

- St. John’s wort Hypericum perforatum L.
- Omega-3 fatty acids
- Light Therapy

Treatment: Refractive Adult Patients

- Electroconvulsive Therapy (ECT)
- Psycho-surgical Approaches
  - Vagal Nerve Stimulation (VNS)
  - Deep Brain Stimulation (DBS)

Antidepressants in Youth: Black Box Controversy

- Antidepressants (can) increase risk of suicidality
- Must balance risks and benefits in prescribing
- Monitoring
  - Physician
  - Family and patient
- Dispense smaller quantities
- Clarify off-label use of medication

Empirical Support

- March et al
  - TADS
- Goodyer et al
  - ADAPT
- Brent et al
  - TORDIA

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Three Types of Prevention
(as classified by the Institute of Medicine Report, 1994)

- **Universal** preventive interventions are administered to all members of a target population.
- **Selective** preventive interventions are given to members of a subgroup of a population whose risk is deemed to be above average.
- **Indicated** preventive interventions are given to individuals who manifest sub-clinical signs or symptoms of a given disorder.

Prevention

- **Stress Inoculation**
  - Stress exposures that are not overwhelming while still being significant enough to activate emotional and physiological coping processes, may inoculate or steel the individual against later stress exposures.\(^1,2\)
- **Cognitive Control**
  - "If you don't like something change it; if you can't change it, change the way you think about it." ~Mary Engelbreit
- **Healthful Living**
  - Ingest
  - Breathe / Exercise
  - Sleep

2. Rutter, 1995

Acknowledgements

**Children of Depressed Mother Study**
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- Pedro Martinez, M.D.

Current Lab Members:
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- Kristin Ballard
- Kristina Reigstad
- Megan Nelson
- Georges Han
- Dave Klingbeil
- Yoonhee Sung
- Undergraduate Research Assistants

**Adolescent Depression Study**
Primary Collaborators:
- Kathryn Cullen, M.D.
- Sanjiv Kumra, M.D.
- Kelvin Lim, M.D. and the CMRR/LNPI team

Current Lab Members:
- Alaa Houri
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- Dave Klingbeil
- Yoonhee Sung
- Undergraduate Research Assistants

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If you think you have depression or anxiety and are 12 to 18 years of age, you may be eligible to participate. The study includes a clinical interview, questionnaires, and physiological measurements. May include an MRI. Feedback & payment provided.

For more information, please call Ella at (612) 273-9924.