Adolescent Development and Suicide Research: Brain and Sleep
A Neuroimaging View

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Range of Symptoms in Mood Disorders and Risk for Suicide

1st Mania

DEPRESSION

Emotions

Mood

Thoughts

ATTENTION

Self Esteem

Activity

Behavior

NANNA

Increased activity, pleasure

Reduced function, depression

Difficulty concentrating

Withdrawn

Decreased

Inability to sustain attention

Increased

Decreased

Feeling slowed, pained

Reduced

Sleep

Energy

Emotions

MANIA

Increased activity, pleasure

Reduced function, depression

Difficulty concentrating

Withdrawn

Decreased

Inability to sustain attention

Increased

Sleep

Energy

Emotions

Frontal System in STBs

- Increased activity, pleasure
- Reduced function, depression
- Difficulty concentrating
- Withdrawn
- Decreased
- Inability to sustain attention
- Increased

Developmental Sequence of Region Differences

VOLUME

- Amygdala and PFC differences in development
- Hypothalamus and PFC differences in development
- Amygdala and PFC differences in development

Multi-modality MRI Scanning Methods

High Resolution Structural MRI:
- Morphology
- Functional MRI (fMRI):
  - Regional Responses
  - Functional Connectivity
- Diffusion Weighted Imaging:
  - White Matter Microstructure
  - Structural Connectivity

Early Amygdala and Progressive PFC and Connectivity Differences in Adolescents with BD

Adolescent & Young Adult Mood Disorders & Suicide

- Great progress, although a great deal to do
  - Convergent brain circuitry findings in study of suicide thoughts and behaviors (STBs) to target
    - Many ways to target the brain circuitry to prevent suicide
      - Pharmacological
      - Non-pharmacological
        - Regulating sleep and other daily rhythms
        - Robust
        - Potential for broad international dissemination
      - Energy
      - Self-empowerment

Progress and a Hopeful Future

- Critical Period of adolescence/young adulthood
- Mood disorders and suicide behavior emerge
- Frontal systems regulating emotion and impulses end of cognitive flexibility and decision-making maturing
- Major preventable causes of early mortality
  - Stabilized neurodevelopment and maladaptive trajectories
  - Prevent progression and suicide - need more research in youths

Adolescent & Young Adult Mood Disorders & Suicide Attempters

- Main diagnoses in persons who die by suicide
- Critical Period of adolescence/young adulthood
- Mood disorders and suicide behavior emerge
- Frontal systems regulating emotion and impulses end of cognitive flexibility and decision-making maturing
- Major preventable causes of early mortality
  - Stabilized neurodevelopment and maladaptive trajectories
  - Prevent progression and suicide - need more research in youths

Hopelessness key risk factor

Differences may continue to progress
- Magnitude may be predictive of future attempts
- Some similarities in attempters with BD & major depressive disorder
- Increased
- Amygdala
- Decreased
- PFC
- Prefrontal cortex & its inputs mature in adolescents/young adults
- Cognitive flexibility to consider options and decision-making
- Control of impulses/responses to internal states and pain
- Emotional processing, regulation, reactivity
- Decreased
- PFC functioning and regulation
- Weaker PFC functioning and regulation
- Increased negative (dysphoria, anxiety), decreased positive (anhedonia)

Weathers et al., JCAAP, 2018

Najt et al., Bipolar Disord, 2009

Kalmar et al., JINS, 2009

Lippard et al., Am J Psychiatry, 2009

Schmaal et al., Bipolar Disord, 2019

Gray et al., JAMA Psychiatry, 2018

Kalmar et al., JAMA Psychiatry, 2019

Lippard et al., Am J Psychiatry, 2019

Bipolar Disord

Mood disorders and suicide behavior emerge

Molecular Psychiatry, 2020

Potential for broad international dissemination

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Are changes in the hypothalamus even earlier?

Are changes in the hypothalamus even earlier?
HOPES International Consortium: Help Overcome and Prevent the Emergence of Suicide

1. Longitudinal study of BD & NDD, n=62 females
2. Future (3y) (85.9%) and 5y (10.5/9)
3. Frontal cortical thickness and white matter differences
4. Additional white matter differences in SAs

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Suicide Attempters with BD

- Intrinsic Connectivity Distribution (ICD)
- Identifies hubs of dysconnectivity as potential prevention targets

Venotromeda PPC Anterior Insula

van Harmelen et al., Translational Psychiatry, 2015

BE-SMART: Brain Emotion Circuitry-Targeted Self-Monitoring And Regulation Therapy-DR

- Modification of Social Rhythm Therapy (SRT) component of P3PS in collaboration with Dr. Holly Swartz
- Incorporate smartphone ecological momentary assessment (EMA) with Drs. Kathleen Jonas & Poeng Park
- Reduced hopelessness

Subjective compared to objective

- Depression
- Anxiety
- Anger
- Fatigue
- Heightened awareness

Mood circumplex

Concise Health Risk Tracking Scale, Suicide Propensity subscale (CHRT)

NHM-funded study of adolescents and young adults with BD I, II, OS

Reduction in both elevated and depressed mood symptoms

Young Mania Rating Scale (YMRS)

- Reduction of excessive amygdala responses
- Increased PFC engagement
- Correlation with changes in symptoms and behaviors

- Actigraphy continuous & Smartphone ecological momentary assessment
- Smartphone for increased temporal resolution and proximal risk

Increased PFC engagement

- Actigraphy complementary objective information
- Increased PFC engagement
- Correlated with changes in proximal suicide risk

Mood disorders focus and mMARCH collaboration

Temporal variability

Proximal suicide risk factors

- Decreased depression
- Increased hopelessness

Improvement in suicidal thoughts and behaviors

- Changes in rest
- Changes in suicidal thoughts and behaviors

- Increased PFC engagement
- Correlation with changes in symptoms and behaviors

- Reduced suicidality

Improved emotion regulation

- Improved regularity of sleep and other daily rhythms, including social rhythms

- Identification of suicidal thoughts and behaviors

- Symptom of Bipolar Disorder or Major Depressive Disorder

Future (2y) SI (35.9%) and MDD, n=92 females

Genetic & Environmental Mechanisms and Brain Circuitry Targets

- Hypothesized improvement in frontal executive function regulatory circuitry
- Identification of suicide attempters
- Increased PFC engagement
Study STR-1-002-20

- Ages 16 - 29y
- Symptoms of Bipolar Disorder or Major Depressive Disorder
- History of suicide thoughts or behaviors

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