Links Between Physical and Mental Health among Youth with Bipolar Spectrum Disorders

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Learning Objectives

1. Recognize the increased and premature cardiovascular risk of bipolar disorder

2. Appreciate how conventional and novel vascular measures can yield insights regarding the burden of bipolar disorder

3. Consider the implications of the heart-bipolar link for treatment and stigma-reduction

**Bottom line: major problem, major opportunity**

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**Premature Heart Disease in Adults with Bipolar Disorder in the General Population**

- BD-I
- BD-II
- MDD
- Controls

17 years

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“Not at all infrequently and in comparative youth arteriosclerosis is present”

—Emil Kraepelin, 1921
Step 1: Risk Stratification by Disease Process

**Tier I: High Risk**
- Diabetes mellitus, type 1 and type 2
- Chronic kidney disease/end-stage renal disease/post kidney transplant
- Post heart transplant
- Kawasaki disease with current coronary artery aneurysms

**Tier II: Moderate Risk**
- Kawasaki disease with regressed coronary aneurysms
- Chronic inflammatory disease
- HIV
- Nephrotic syndrome
- Major depressive disorder or bipolar disorder (NEW)

≈0.5%
≈10%

Step 2: Assess Cardiovascular Risk Factors

- Family history of early CVD in expanded 1st degree pedigree (♂ ≤ 55y; ♀ ≤ 65y)
- Fasting lipid profile*
- Smoking history*
- Blood pressure (BP), 3 separate occasions, interpreted for age/sex/height percentile
- Height, weight, body mass index (BMI)*
- Fasting glucose (FG)
- Diet, physical activity/exercise history*

*Increased prevalence among adolescents with bipolar disorder

If ≥2 Risk Factors, move to Tier I
Reasons for Excessive and Premature Cardiovascular Disease among People with Bipolar Disorder

**Biology**
- Inflammation
- Oxidative stress
- Autonomic dysfunction
- Endothelial dysfunction

**Behavior and Environment**
- Early adversity/abuse
- Sleep disturbance
- Sedentary lifestyle
- Suboptimal nutrition
- Tobacco, alcohol, and substance use

**Medication**
- Antidepressants: weight gain (mild)
- Second generation antipsychotics: weight gain (significant), glucose/lipid changes

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**Psychiatric Correlates of Cardiovascular Risk Factors in Bipolar Disorder**

- More manic and depressive episodes
- More time spent with depression*
- More psychiatric hospitalization*
- Worse global symptom severity
- Worse global functional impairment*
- More substance use disorders*
- More suicide attempts*
- *Would improving heart health improve mental health?*

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*Findings from COBY study*
**Obesity is Associated with Reduced Brain Volume and Thickness in Bipolar Disorder**

[A] CW P-value=0.027
Size (mm²) = 1544.41
Cluster peak: Medial OFC
Encompasses: Caudal and Rostral ACC, Superior Frontal

[B] CW P-value=0.0001
Size (mm²) = 3197.35
Cluster peak: Caudal ACC
Encompasses: Posterior cingulate, superior frontal, rostral ACC, medial & lateral OFC

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**Higher Cholesterol is Associated with Lower Hippocampal Volume in Bipolar Disorder**

- \( \beta = 0.26 \) \( p = 0.03 \)
- \( \beta = -0.27 \) \( p = 0.007 \)
- Interaction \( p = 0.001 \)

'SControlling for age, sex, BMI, and intracranial volume

Kennedy et al, *under review*
Higher Triglycerides Associated with Reduced Cognitive Flexibility in Bipolar Disorder

HC: $r=0.057, p=0.74$

BD: $r=-0.396, p=0.02$


Mental Health and Physical Activity

Preliminary evidence of disparities in physical activity among adolescents with bipolar disorder

Laura Jewell 5, Robert Abtan 5, Antonette Scavone 4, Vanessa Timmins 4, Brenda Swampili 4, Benjamin L Goldstein 4, 4, *5

*p=0.005
Cardiorespiratory Fitness (CRF)

“potentially a stronger predictor of mortality than established risk factors such as smoking, hypertension, high cholesterol, and type II diabetes mellitus”

--American Heart Association

In adults with bipolar disorder:

• Lower CRF vs. matched controls
• Lower CRF = more severe current/future depression
• Higher CRF = better physical and mental quality of life

American Heart Association 2016; Vancampfort et al, J Affect Disord, 2016; Psychiatry Res, 2017

Reduced Cardiorespiratory Fitness among Youth with Bipolar Disorder

F = 4.66, p = 0.03, η² = 0.04

0.91 ± 0.32

1.01 ± 0.30

Bipolar disorder n=53

Healthy control n=54

Popel et al, Bipolar Disorders 2020
Lower Cardiorespiratory Fitness Associated with Depression in Youth with Bipolar Disorder

![Graph showing correlation between current depression score and cardiorespiratory fitness.](image)

\[ r = -0.31 \ p = 0.02 \]

Exercise-related Changes in Cerebral Blood Flow among Youth with Bipolar Disorder

MacIntosh et al, J Affect Disord 2017
**Next Steps: Aerobic Exercise for Bipolar Disorder**

Low rates of aerobic exercise among youth with bipolar disorder

Multiple potential benefits on brain, mind, heart

Benefits are within reach for vast majority, regardless of weight loss

Greatest benefits come to those who are most aerobically unfit

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**Toward Exercise as Medicine for Adolescents with Bipolar Disorder (TEAM-BD)**

- Weekly phone calls
- Motivation enhancement sessions
- Psychoeducation
- Aerobic fitness testing
- Measures of physical activity
- Exercise coaching
- Family-focused counseling
- Peer support

**Exercise Intervention**

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“To us, the heart not only represents dedication and care, but it is a symbol that bipolar disorder is linked to cardiovascular risk and affects mind, brain, and body”

--Centre for Youth Bipolar Disorder
Conclusions

• Youth with bipolar disorder have increased cardiovascular risk from a convergence of factors

• Cardiovascular risk factors are associated with psychiatric symptoms, brain structure and brain function among youth with bipolar disorder

• The heart-bipolar link may offer clues toward understanding the causes of bipolar disorder, developing novel treatment approaches, and reducing stigma.

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