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PREDICTORS OF COURSE AND OUTCOMES IN YOUTHS AND YOUNG ADULTS WITH
BIPOLAR SPECTRUM DISORDERS

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Conclusions: While certainly preliminary based on sample size and the cross-sectional, nonspecific nature of the data on suicide risk, these data suggest that the use of data-driven models with coverage of self-report and physiological responses to stress may be useful in assigning levels of risk for suicide in children and adolescents. Implications for prospective studies will be discussed.

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8.2 BRAIN CONNECTIVITY IN ADOLESCENT GIRLS WITH AND WITHOUT A HISTORY OF NONSUICIDAL SELF-INJURY

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Objectives: Nonsuicidal self-injury (NSSI) is a serious clinical problem that is highly prevalent in adolescents and represents an important risk factor for future suicide attempts. This longitudinal study is examining how neural circuitry relates to NSSI and other risk factors across early adolescence to midadolescence.

Methods: We are recruiting 152 adolescent girls aged 12-16 years, with and without a history of NSSI, to participate in a 3-year longitudinal neuroimaging study. Clinical assessment includes the Self-injurious Thoughts and Behavior Interview (SITBI), the Beck Scale for Suicidal Ideation (BSSI), the Beck Depression Inventory (BDI), and the Childhood Trauma Questionnaire (CTQ).

Results: In this ongoing study, 100 adolescents have completed initial scanning, and data from 43 participants (mean age = 14.4 years; 31 adolescents with a history of NSSI, 12 adolescents without a history of NSSI) were available for preliminary analysis. Compared to girls with no history of NSSI, the NSSI group had higher average scores on the BDI (18.1 vs 3.5), BSSI (6.27 vs 0.09), and CTQ (40.34 vs 29.18), and the NSSI group had more suicide attempts (mean = 2, range 0-12, vs 0). Among those with a history of NSSI, mean lifetime NSSI episodes was 71.4 (range 1-400), with an average duration of 2.63 years (range 0-4 years). Resting-state functional connectivity between the left amygdala and left prefrontal cortex correlated inversely with BDI scores ($R = -0.35$; $p = 0.025$) and with NSSI severity (as measured by lifetime episodes; $r = -0.34$; $p = -0.038$).

Conclusions: Adolescent girls with NSSI report high rates of past traumatic experiences, current depression symptoms, and elevations in suicidal thoughts and behaviors. Our preliminary analyses suggest that impaired frontolimbic circuitry may relate to the depression and severity of NSSI behaviors in this sample. Future analyses will be conducted on the full sample of adolescent girls with and without NSSI.

ADOL, NEURODEV, SIB

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8.3 ABERRANT REWARD FUNCTION AND STRUCTURE IS ASSOCIATED WITH SUICIDAL IDEATION AND BEHAVIOR IN YOUTH WITH DEPRESSION AND OBESITY

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Objectives: Youth with depression and obesity report varying degrees of suicidal ideation (SI) and nonsuicidal self-injury (NSSI). Anticipatory reward dysfunction in the orbitofrontal cortex (OFC) is a key biobehavioral mechanism underlying the emergence of depression symptoms, but the association with the emergence of SI and NSSI is unknown. To better understand the neural mechanisms associated with SI and NSSI behaviors, we examined their relationship with reward structure and function in youth with depression and obesity.

Methods: A total of 76 depressed and overweight/obese youth (49 female; mean age: 14.97 ± 1.94 years; BMI: 30.5 ± 6.42) completed a structural and a function monetary incentive delay fMRI scan, from which we computed structural volumes in reward regions including the anterior cingulate,

thalamus, and striatum, and anticipatory reward function, respectively. To assess SI and NSSI we administered the Columbia Suicide Severity Rating Scale (C-SSRS). A total of 24 youth (32%) reported a history of NSSI. We conducted linear regression models to test the relations between C-SSRS on anticipatory reward function, reward network structure, and SI/NSSI as measured by the C-SSRS with age and sex as covariates.

Results: Across the entire sample, a higher SI severity score was associated with lower OFC activation during anticipation of rewards ($\beta = -0.354$; $t(45) = -2.53$; $p = 0.015$) and smaller right thalamic volume ($\beta = -0.434$; $t(41) = -3.134$; $p = 0.003$). Similarly, youth who reported a history of NSSI had reduced OFC activation during reward anticipation ($t(73) = -0.315$; $p = 0.004$) and smaller right thalamic volumes ($t(64) = 2.26$; $p = 0.03$) compared to youth who did not report a history of NSSI.

Conclusions: Decreased OFC activation and reduced thalamic volume may lead to aberrant reward function that contributes to suicide risk in youth with depression and obesity. Longitudinal research is needed to test whether altered trajectories in reduced OFC activation and right thalamic volume mediate links between reward dysfunction and suicidality in youth.

DDD, OBE, S

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8.4 ADVANCING WHAT IS KNOWN ABOUT BRAIN/BEHAVIOR MECHANISMS UNDERLYING NONSUICIDAL SELF-INJURY AND YOUTH SUICIDE

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Objectives: Despite our best clinical care, suicide has risen to become the second leading cause of death in 10- to 34-year-old individuals in the United States. Relatedly, nonsuicidal self-injury (NSSI)—defined as deliberate self-harm without intent to die—is also increasingly common, affecting upwards of 18% of children and adolescents. This presentation seeks to address both problems by discussing shared vs unique brain/behavior mechanisms in jargon-free language useful to child and adolescent psychiatrists.

Methods: We present data from 2 IRB-approved studies. The first study tested computerized emotional task performance in teenagers who: 1) made a suicide attempt but had not engaged in NSSI; 2) engaged in NSSI but had not made a suicide attempt; or 3) controls ($n > 40$ /group). The second study evaluated fMRI brain activity and symptom trajectories in 10- to 17-year-old children and adolescents engaged in NSSI vs those in the control group (total $N = 60$ and growing).

Results: Teenagers engaged in NSSI had unique alterations in response to peer acceptance/rejection and implicit attitudes toward suicide/death vs suicide attempters and controls. In the second ongoing study, youth in the NSSI group differed from controls in brain response to peer acceptance and rejection.

Conclusions: Together, these studies begin to suggest brain/behavior mechanisms for targeted novel diagnostic and treatment approaches that might address the national tragedy of youth suicide, NSSI, and self-harm behaviors.

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SYMPOSIUM 9

PREDICTORS OF COURSE AND OUTCOMES IN YOUTHS AND YOUNG ADULTS WITH BIPOLAR SPECTRUM DISORDERS

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Objectives: This Symposium will provide an overview of updated findings from the Course and Outcome of Bipolar Youth (COBY) and Predicting Adult Outcomes of Bipolar Youth (PROBY) studies, which have followed the same cohort longitudinally. Data will be presented regarding psychosocial functioning, energy, medication effects, and individualized risk prediction.

Methods: At intake, the COBY study enrolled 413 youth aged 7-17.11 years. Participants were interviewed with standard instruments on average every 7.4 months, for a median duration of 12.5 years, with an 88% rate of retention. Heather Hower, MSW, will present data on predictors of longitudinal psychosocial functioning. Jeffrey Hunt, MD, will review the course and outcomes of increased energy. Danella Hafeman, MD, PhD, will discuss the effects of lithium on clinical outcomes, as well as potential neural mechanisms. Boris Birmaher, MD, will describe the development of a personalized risk calculator for mood recurrence.

Results: Regarding psychosocial functioning, youth with remitted symptoms still exhibited current psychosocial functioning deficits. Regarding increased energy, youth who did vs did not endorse intake increased energy had no differences in energy at 5 years, and no differences on clinical/functioning outcomes at 12.5 years. In the study of medication effects, lithium (vs other mood stabilizers) was associated with decreased suicidality, less depression, and better psychosocial functioning. Using clinical risk factors for recurrence from the literature, a risk calculator for mood recurrence performed quite well, with an accuracy of 82% for 5-year risk. The most predictive risk factors were shorter recovery lengths, younger age at assessment, earlier mood onset, and more severe prior depression.

Conclusions: Follow-up data from the COBY and PROBY studies have been a valuable resource for better understanding the course of bipolar disorder in youth. These findings represent clinically applicable results regarding psychosocial functioning, diagnostic criteria, medication choices, and risk prediction.

BRD, LONG, DIAG

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9.1 PREDICTORS OF LONGITUDINAL PSYCHOSOCIAL FUNCTIONING IN YOUTH WITH BIPOLAR DISORDER TRANSITIONING TO ADULTS

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Objectives: In a sample of participants diagnosed with bipolar disorder (BD) in youth, we aim to: 1) examine longitudinal psychosocial functioning; 2) determine whether psychosocial impairment remains in those who remitted from mood disorders during later periods of follow-up; and 3) examine predictors of psychosocial impairment despite symptomatic remission.

Methods: A Course and Outcome of Bipolar Youth (COBY) subsample of 367 youth (>4 years follow-up data) were grouped into mood trajectories: 1) Class 1, predominantly euthymic; 2) Class 2, moderately euthymic; 3) Class 3, ill with improving course; and 4) Class 4, predominantly ill. Psychosocial functioning was assessed via the Children's Global Assessment Scale (CGAS) for those under 22 years of age, and via the Global Assessment of Functioning (GAF) scale for those older than 22 years of age. Current school, employment, and disability status were examined. Established predictors of symptomatic impairment were analyzed.

Results: The predominantly euthymic class had better psychosocial functioning, and they were more likely to be in school/employed. The predominantly ill class had worse psychosocial functioning and were more likely to receive disability. However, 44% of predominantly euthymic and 93% of ill with improving course participants continued to experience current psychosocial impairment. Early BD onset, low socioeconomic status (SES), and current comorbidity predicted poor psychosocial functioning. Low SES and current comorbidity predicted no school enrollment/unemployment.

Conclusions: In general, youth with persistent mood symptoms had worse psychosocial functioning; moreover, those with remitted symptoms still exhibited current psychosocial functioning deficits. High-risk individuals with predictors of impairment should be targeted for functioning interventions.

BRD, LONG, IMP

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9.2 CORRELATES, COURSE, AND OUTCOMES OF INCREASED ENERGY IN YOUTH WITH BIPOLAR DISORDER

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Objectives: The conceptualization of bipolar disorder (BD) has recently changed such that, in the DSM-5, diagnosing BD now requires the presence of increased energy as a gate A criterion for hypo/mania. This change has resulted in some conflicting reactions in the field. The current study assesses whether there are differences between youth with DSM-IV BD who endorsed increased energy, and those who did not, during their baseline worst lifetime mood episode. The longitudinal trajectories of increased energy as a symptom, mental health symptomatology, and clinical outcomes, are also analyzed.

Methods: A subsample of 430 participants from the Course and Outcome of Bipolar Youth (COBY) study were assessed utilizing the K-SADS, K-SADS Mania Rating Scale (K-MRS), and K-SADS Depression Rating Scale (K-DRS). Youth were grouped at baseline into those with increased energy (meeting DSM-5 Criteria A for mania) vs those without increased energy (meeting DSM-IV, but not DSM-5, Criteria A for mania) during their worst lifetime mood episode. The presence/absence of increased energy was also measured at each follow-up for 12.5 years. Longitudinal mental health symptomatology and clinical outcomes were evaluated utilizing the Adolescent Longitudinal Interval Follow-up Evaluation.

Results: Baseline analyses showed that, compared to the group without increased energy during their worst lifetime mood episode, those with increased energy (86% of participants) had significantly higher percentages of bipolar I disorder (BD-I) and BD NOS, higher K-MRS and K-DRS total scores, and poorer family/global functioning. However, frequency of increased energy between groups became comparable after 5 years, remaining consistent for the remainder of the follow-up. No significant group differences were found on clinical/functioning outcomes after 12.5 years.

Conclusions: Longitudinal examination of the trajectory of the increased energy criterion over 12.5 years shows that the initial distinction in energy level between groups was eliminated within 5 years. There were no significant group differences on clinical or functioning outcomes over 12.5 years of follow-up between the 2 groups identified at baseline.

BRD, LONG, DIAG

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9.3 LITHIUM VS OTHER MOOD STABILIZERS IN YOUTH WITH BIPOLAR DISORDER: CLINICAL FINDINGS AND POTENTIAL MECHANISMS

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Objectives: There is strong evidence in adults with bipolar disorder (BD) that lithium (LI) reduces mood recurrence, decreases suicide deaths, and reduces hospitalization rates; however, evidence in youth is limited. We use data from the Course and Outcome of Bipolar Youth (COBY) study to assess whether LI vs other mood-stabilizing medication (OMS) is associated with improved outcomes, including mood symptoms and suicidality. Here, we discuss these recently published clinical findings, as well as potential mechanisms for these effects.

Methods: COBY is a naturalistic, longitudinal study of 413 youth with BD, aged 7-17.11 years at intake, who have been followed for more than 10 years. A subset of these individuals (n = 78) contributed MRI data; healthy controls (HCs) were scanned for comparison. At each biannual visit, the Adolescent Longitudinal Interval Follow-Up Evaluation is used to assess medication exposure, mental health symptoms, and psychosocial function. For this analysis, we compared participants taking LI vs OMS (but not LI) to determine whether they differed regarding mood symptoms, suicidality, psychosocial function, hospitalization, aggression, and substance use. In participants with neuroimaging data, we assessed whether those with prolonged LI (n = 23) vs minimal/no LI (n = 49) exposure had associated structural brain differences, specifically a measure of gyrification in a region key to mood disorders and suicide (orbitofrontal cortex [OFC]).