Development of Alcohol and Drug Use in Youth With Manic Symptoms

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Objective: This analysis examined alcohol and drug use over a 6-year follow-up of children in the Longitudinal Assessment of Manic Symptoms (LAMS) study.

Method: LAMS screened 6- to 12.9-year-old children visiting 9 child outpatient mental health (MH) clinics, using the Parent General Behavior Inventory 10-item mania scale. All children with scores ≥12 and a matched group with scores ≤12 were invited to enroll. Children were assessed every 6 months. Assessments included demographics, family, MH history, child diagnoses, child stress, and alcohol and drug use. Univariate, bivariate, and interval censored survival analyses were conducted.

Results: Of those >9 years at baseline, 34.9% used alcohol at least once, with 11.9% regular users; 30.1% used drugs at least once, with 16.2% regular users. Predictors of any alcohol use were parental marital status, older age at study entry, a primary diagnosis of disruptive behavior disorders at baseline, and number of impactful child life events. Predictors of regular alcohol use included parental marital status, age, and sustained high mania symptoms over the first 24 months of follow-up. Predictors of any drug use were single parent, parental substance use, and stressful child life events. Predictors of regular drug use were parental marital status, stressful child life events, and a baseline disruptive behavior disorder diagnosis. Baseline medications decreased the risk of regular drug use.

Conclusion: Longitudinal data on youth with elevated manic symptoms suggest that comorbid disruptive behavior disorder, manic symptom burden, family environment, and stress are predictors of initiation and regular use of substances.

Key words: manic symptoms, substance use, bipolar disorders

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Substance use during adolescence is related to a host of serious health risks throughout the lifespan.[1] Although recent data suggest that cigarette smoking and alcohol use have declined, many US adolescents use substances, and one group of adolescents, the 13% to 20% of those with mental health (MH) problems, are at greatly increased risk for co-occurring substance use and abuse.[1-3]

Longitudinal data suggest that the risk for developing substance use disorders (SUD) is greatly elevated for adults with baseline MH disorders, particularly bipolar spectrum disorders (BPSD).[4] Considerable data suggest that youth with BPSD are also at risk for SUD,[5] and that those youth with comorbid SUD are more likely to be less adherent to medications[6] and to have poor functional outcomes.[7] However, little is known about whether youth with symptoms characteristic of BPSD, namely mania, are at comparable risk for developing SUD. Very few studies have examined the prevalence and risk factors for SUD in youth with manic symptoms who did not meet criteria for BPSD, although severity and persistence of attention-deficit/hyperactivity disorder (ADHD) symptoms have been shown to be related to substance use.[8] Examining children with symptoms of mania longitudinally is important, because it appears that the BPSD begins with nonspecific, nonmood pathology in children and evolves to mood pathology. Given that manic symptoms may be an important risk factor for SUD, the risk for development of SUD is likely to increase with the clinical evolution of mood disorder.[9-11]

That BPSD and mania are related to SUD is not surprising, given what is known about the neurobiology of addiction. It is estimated that 40% to 60% of the vulnerability to addiction is genetic, due both to variability in drug metabolism and to the reinforcing effects of a drug, specifically the increase in dopamine in the limbic brain regions.[12] However, development of SUD is multifactorial, and one pathway is a deviation in somatic and neurological maturation.[13] When such a deviation is combined with adverse environments, such as those characterized by poor parenting, abuse, and stress,[14] it produces affective and behavioral dysregulation.[15] Sloboda et al.[15] argue that dysregulation begins as teratogenic injury or difficult temperament in infancy, moves to poor impulse control/self-regulation in childhood, to substance use by early adolescence, and then to severe SUD by early adulthood. Tarter et al.[16] describe youth at high risk for SUD as impulsive, exhibiting reactive aggression, sensation seeking, and excessive risk taking. These authors postulate that these characteristics emanate from disinhibition produced by dysfunction of the prefrontal cortex, although the precise role of temperament[17] and pathology, as well as factors that modify the relationship, need to be further explored.[18]

Children with BPSD have more difficult temperaments (e.g., irritability, affective lability)[19] prior to diagnosis, considerable behavioral disinhibition, and high rates of ADHD.[20] Data suggesting that impulsiveness and high

behavioral approach system sensitivity mediate the relationship between BPSD and SUD[21] argue strongly for examining the development of substance use in youth whose symptoms suggest increased risk for the development of BPSD. Therefore, this study aimed to determine rates of use and regular use of alcohol and drugs over a 6-year follow-up of a cohort of children, most of whom had elevated symptoms of mania when enrolled; and to examine predictors of use/regular use of alcohol and drugs. Based on the findings of Wilens *et al.*,[22] we expected that there would be different predictors of drug and alcohol use/regular use, so they were examined separately.

METHOD

Data for these analyses came from the Longitudinal Assessment of Manic Symptoms (LAMS) study. LAMS screened 6- to 12.9-year-old children at an initial visit to 9 child outpatient clinics. Participating adults of eligible children completed the Parent General Behavior Inventory–10 Item Mania Scale (PGBI-10M)[23,24] and answered 4 demographic questions. All children with a PGBI-10M score ≥12 (elevated symptoms of mania [ESM]) were invited to enroll in the longitudinal phase of the study, and a smaller matched group (on age, sex, race/ethnicity, insurance) of children with scores <12 were randomly selected with replacement and invited.[25,26] A total of 707 children (n = 621 with ESM; n = 86 without ESM) agreed to enroll in the longitudinal cohort, and 685 were eligible after the baseline assessment.

Measures

Demographics. Age, sex, race/ethnicity, health insurance status, family structure, and a brief medical history for the child were collected.

Family History. The Modified Family History Screen (FHS)[27] collected information on 15 psychiatric disorders, including substance abuse in biological parents.

Child Diagnoses. Children and their guardians were administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Episode (K-SADS-PL),[28] with additional depression and manic symptom items derived from the Washington University in St. Louis Kiddie Schedule for Affective Disorders (Wash-U K-SADS).[29,30] The K-SADS also captures alcohol and drug dependence. Unmodified *DSM-IV* diagnostic criteria were used, and the criteria for BP–not otherwise specified (NOS) followed the criteria used in the Course and Outcome of Bipolar Youth Study (COBY).[31] All diagnoses were reviewed and confirmed by a licensed child psychiatrist or psychologist.

24-Month Manic Trajectories. Using growth mixture modeling of mania symptoms over the first 24 months of follow-up data, Findling *et al.*[32] found that 15% of the cohort belonged to 2 classes (high and rising, and unstable mania symptoms). These 2 classes of mania symptoms were characterized by high rates of diagnostic conversion to BPSD.

Child Stress. The Stressful Life Events Schedule (SLES)[33] asked parents to report whether 80 events occurred in their child's life during the past 12 months and the impact of each event. Events that parents rated as having a lot or somewhat of an impact on their child (versus a little or none at all) were coded as impactful. The SLES has good test–retest reliability.[33]

Child and Adolescent Symptom Inventory. The Child and Adolescent Symptom Inventory (CAASI-4) is a 163-item behavioral rating scale for emotional and behavioral disorders that was completed by parents of children 8 to 17 years of age at each visit.[34] The CAASI-4

has high internal consistency (0.74−0.94) and significant test−retest reliability (*p* < .001).

Youth's Inventory. The Youth's Inventory (YI-4), a 128-item self-report measure that assesses the presence and severity of behavioral, cognitive, and affective symptoms described in the *DSM-IV*, was completed by participants aged 13 to 17 years.[34,35] The YI-4 has good internal consistency (0.66−0.87) and test−retest reliability (r = 0.54−0.92).[34]

Adult Self-Report Inventory. Participants aged 18 years completed the Adult Self-Report Inventory (ASRI-4), a 166-item self-report measure on the presence and severity of behavioral, cognitive, and affective symptoms described in *DSM-IV*.[36]

Outcomes: Substance Use/Regular Use. Three self-report measures developed by the Centers for Disease Control and Prevention (CDC) were used to assess whether participants had ever used alcohol or drugs, and how often they had used alcohol and drugs during the past 30 days.

Students aged 10 to 12 years completed the middle school Youth Risk Behavior Survey (YRBS-MS); those aged 13 to 18 years completed the high school YRBS (YRBS-HS)[37]; and participants who finished high school and were 18 to 22 years of age completed the Youth Adult Risk Questionnaire (YARQ).[38,39] The YRBS has good reliability (κ ≥0.60),[40,41] and three measures were used to assess the frequency of alcohol, marijuana, and other drug use during the past 6 months using a 4-point ordinal scale (never, sometimes, often, very often).

Any alcohol use was defined as having more than a few sips of alcohol on at least one occasion (ASRI-4, CAASI-4, K-SADS, YARQ, YI-4, YRBS). Regular alcohol use was defined as drinking ≥3 days during the past 30 days (YRBS), drinking ≥5 drinks in a row on ≥2 days during the past 30 days (YRBS and YARQ), or having ≥1 drink on ≥3 days in the past 30 days (YARQ). Any drug use was defined as any use of marijuana, cocaine/crack/freebase, inhalants (glue, aerosols, paints), methamphetamines, heroin, ecstasy, or hallucinogens (ASRI-4, CAASI-4, K-SADS, YARQ, YI-4, YRBS). With the exception of the K-SADS, which assesses drug dependence, regular drug use was not measured in children before high school. For individuals high school age and beyond, regular drug use was defined as using drugs ≥3 times in the past 30 days (YRBS and YARQ). For each outcome, if the criteria were met on any of the relevant instruments, that outcome was coded as positive. SUD diagnoses were infrequent and therefore were not examined.

Data Analysis

Categorical data were summarized using counts and percentages. Normally and nonnormally distributed measures were described using means ± standard deviations and medians (25th and 75th percentiles), respectively. Bivariate associations of baseline characteristics and the 24-month manic trajectories[32] with the outcomes were assessed via the χ^2 test, two-sample *t* test, and the Wilcoxon rank-sum test as appropriate. As the time interval during which the substance use occurred is known but the exact time it occurred is unknown, interval-censored survival analysis was used to examine adjusted associations with each outcome. Interval-censored proportional hazards models were fitted with a two-knot spline baseline hazard. The results are summarized using adjusted hazard ratios (HR) and their 95% CIs. Analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC).

Participants who reported no alcohol use at baseline (n = 662, 96.6%) and no drug use at baseline (n = 669, 97.7%) but had some data on alcohol and drug use over the 6-year follow-up were included in the analyses of any use. The analysis of regular alcohol use included the 579 (84.5%) participants who reported their alcohol use during the past 30 days at each assessment over the 6-year follow-up. In addition, the analyses of regular drug use included