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Course of Longitudinal Psychosocial Functioning in Bipolar Youth Transitioning to Adults

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Abstract

Objectives: Few studies have examined domain-specific psychosocial functioning in Bipolar Disorder (BD) youths. This prospective study examines 1) Interpersonal Relationships with Family; 2) Interpersonal Relationships with Friends; 3) School/Work; 4) Recreation; 5) Life Satisfaction, in BD youths.

Method: A Course and Outcome of Bipolar Youth subsample (n=367; mean intake age = 12.6 years, SD = 3.3; 46.6% female) was previously grouped into 4 Classes based on their illness trajectories and percentage of time euthymic using Latent Class Growth Analysis: Class 1 *Predominantly Euthymic*; Class 2 *Moderately Euthymic*; Class 3 *Ill with Improving Course*; Class 4 *Predominantly Ill.* Psychosocial functioning within the domains were examined for greater than 10 years using the Adolescent Longitudinal Interval Follow-Up Evaluation.

Results: Class 1 demonstrated better functioning across all domains; Class 4 demonstrated worse functioning across all domains. Class 2 showed worsening relationships and recreation, and improvement in work/schoolwork. Class 3 showed variable domain declines and improvements. Despite symptomatic remission, 13%−20% of Class 1 and 20−47% of Classes 1/3 still had impairments across different domains. Early age of BD onset impacted impairment across most domains, and low SES significantly predicted impairment in family relationships.

Limitations: The study does not have a healthy control group to compare functioning findings.

Conclusions: Participants with more symptomatic mood trajectories had greater impairment across domains. Moreover, even with symptomatic remission, participants still exhibited impairment. Each Class and domain had different trajectories for impairment. Results suggest the importance of examining specific (vs. global) domains for targeted treatment, even when symptomatically remitted.

1. Introduction

The Diagnostic and Statistical Manual of Mental Disorders-IV and 5 (DSM-IV/5) criteria for depression and hypo/mania episodes necessitate that related symptoms cause a change in, or marked impairment of, psychosocial functioning (Association, 2004, 2013). However, there is comparatively little knowledge of how this functioning may change prospectively in those with youth-onset Bipolar Disorder (BD) as they transition into young adulthood. Prior studies are constrained by retrospective reports of functioning by adults, as well as cross-sectional study designs which cannot capture longitudinal developmental trajectories (Ernst and Goldberg, 2004; Leverich et al., 2007; Suominen et al., 2007; Tasha, 2003). They additionally solely examine global psychosocial impairment, using scales such as the Children's Global Assessment Scale (C-GAS) (Shaffer et al., 1983) for those under age 22 years old, or the Global Assessment of Functioning (GAF) (Jones et al., 1995) for those over age 22 years old, rather than specific functional domains (e.g., interpersonal relationships,

school/work, recreation, life satisfaction), which may be meaningfully different. Furthermore, C-GAS/GAF scores do not differentiate the specific functional domains that contribute to global functional impairment.

The Course and Outcome of Bipolar Youth (COBY) study is a multisite naturalistic longitudinal study assessing the mood and psychosocial functioning trajectories of BD youth through young adulthood (Axelson et al., 2006; Birmaher et al., 2006). Findings from COBY intake noted significant impairment in interpersonal, work, recreation, and life satisfaction functioning domains, as well as global psychosocial functioning (Goldstein et al., 2009). Moreover, even during predominant euthymia, this impairment persists (Axelson et al., 2006). Subsequent longitudinal analyses 5.1 years after intake found that participants with greater mood severity also had worse interpersonal relationships (Siegel et al., 2015). A recent COBY study showed that youth with persistent mood symptoms had worse global psychosocial functioning, and that those with remitted symptoms still exhibited current psychosocial functioning deficits (Hower et al., 2019). However, longitudinal domain-specific (interpersonal relationships, school/work, recreation, life satisfaction) functional impairment has not yet been examined in this sample of BD.

Utilizing assessments comparable to COBY, including the Longitudinal Interval Follow-Up Evaluation-Range of Impaired Functioning Tool (LIFE-RIFT) (Leon, 2000; Leon et al., 1999), the Collaborative Depression Study (CDS), at a mean of 17.4 years after intake, reported the development of psychosocial impairment in the third decade of life in those with BD onset prior to 20 years old. This impairment was evident in the domains of school, work, household duties, relationships, recreation, and subjective life satisfaction (Coryell et al., 2013; Judd et al., 2008; Solomon et al., 2004). CDS also found that functional impairment persisted after symptom remission (Judd et al., 2008; Solomon et al., 2004), which suggests that mood symptomatology and psychosocial functioning trajectories do not necessarily correspond. Results indicate that the developmental challenges of transition-age young adults (e.g., increased responsibilities, decreased structure and social opportunities), including those with BD (e.g., (Coryell et al., 2013)), may have differential impacts on various domains of psychosocial functioning, thus warranting a closer examination of specific functional domains.

Research on other severe psychiatric disorders has revealed prospective domain-specific psychosocial impairment that persist after symptomatic remission. Studies on schizophrenia have reported psychosocial impairment, including the ability to maintain social relationships, sustain employment, and to live independently, which remains constant after "positive" symptoms have remitted (Harvey, 2013, 2014; Harvey et al., 2012; Strassnig et al., 2018). Personality Disorder studies have reported significant impairments across domains of social functioning, vocational pursuits, and leisure activities, that remain significantly impaired after behavioral improvement (Gunderson et al., 2011; Skodol et al., 2005a; Skodol et al., 2005b; Zanarini et al., 2007). However, to the best of our knowledge, the course of specific domains of psychosocial functioning have not yet been examined in youth-onset BD.

Thus, based upon these findings, we sought to examine longitudinal psychosocial functioning in specific domains (interpersonal relationships with family, interpersonal relationships with friends , school/work, recreation, life satisfaction) in an exploratory descriptive study to further hypothesis generation. We focused on the differences in trajectories across domains, due to the multifaceted changes that occur during the transition to adulthood. We also examined whether functioning outcomes correspond to mood trajectory outcomes ascertained in a prior COBY study (Birmaher et al., 2014).

2. Method

2.1 Participants

The COBY methods have been presented in detail previously (Axelson et al., 2006; Birmaher et al., 2006). Briefly, the intake sample was enrolled from October 2000 to July 2006, and was composed of 446 youth, ages 7–17.11 years, with DSM-IV diagnoses of BD-I, BD-II, or COBY operationally defined BD not otherwise specified (BD-NOS); please refer to prior COBY studies for operationalized BD-NOS criteria (Axelson et al., 2006; Birmaher et al., 2006).

The current study included 367 participants with youth-onset BD (BD-I, n=218; BD-II, n=26; BD-NOS, n=123) with 4 years of cumulative follow-up time (median = 11.5 years). 47% were female, and 42% lived with both biological parents. They had an average socioeconomic status (SES) score of 3.4 +/− 1.2, indicating Hollingshead Class III (Middle Class) at intake, calculated by the participants' parents' highest reported levels of education and occupation (Hollingshead, 1982) (Table 1). A prior COBY study (Birmaher et al., 2014) had grouped participants based on Latent Class Growth Analyses (LCGA) using their mood symptoms as reported on the Adolescent version of the Longitudinal Follow-Up Evaluation (A-LIFE) (Keller et al., 1987)[1]. Four classes were derived: Class 1 *Predominantly Euthymic* (n=88; 24.0%) was euthymic on average 84.4% of the cumulative follow-up time, and had 44.2 maximum consecutive months of euthymia. Class 2 *Moderately Euthymic* (n=127; 35.0%) was euthymic on average 47.3% of the cumulative follow-up time, and had 12.6 maximum consecutive months of euthymia. Class 3 *Ill with Improving Course* (n=70; 19.1%) was euthymic on average 42.8% of the cumulative follow-up time, and had 20.1 maximum consecutive months of euthymia. Class 4 *Predominately Ill* (n=82; 22.3%) was euthymic on average 11.5% of the cumulative follow-up time, and had 5.5 maximum consecutive months of euthymia (Birmaher et al., 2014) (Supplemental Figure 1).

2.2 Procedure

Each participating study site's Institutional Review Board reviewed/approved the study protocol before enrollment of any participant. Informed consent/assent was obtained before initiation of the assessments from the participating youth/their parents. Adolescents and parents were interviewed separately about the participant's functioning, while younger children (<12) were interviewed with the parent. When participants turned 18 years old, they

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[1]Mood symptoms operationalized along a Psychiatric Status Ratings (PSR) system, a six-point scale of increasing levels of symptom severity and impairment (Supplemental Table 2).

could elect whether to include reports from parents or secondary informants (e.g., spouses). The COBY research staff presented the participants' symptomatology/psychosocial functioning reports to study investigators, who were ultimately responsible for the clinical ratings. The current analyses are based upon the consensus scores of the participants, parents, and secondary informants.

2.2.1 Measures

2.2.1.1 Functional Assessments: The A-LIFE Psychosocial Functioning Schedule (PSF) (Keller et al., 1987) was used to assess longitudinal psychosocial functioning (Supplemental Table 1). The A-LIFE is an interview with excellent reliability/validity (Axelson et al., 2011). Changes in longitudinal psychosocial functioning in each domain were tracked monthly via a procedure similar to the Timeline Follow-Back (TLFB) method. At each interview, there was a retrospective recall of psychosocial functioning during the most impaired week of each month, from the previous interview to the current interview (M = 8.7 months, SD = 5.2 months), utilizing a calendar and several memory aids (Sobell, 2008). The A-LIFE PSF has shown sound psychometric properties in COBY (ICCs=0.92–0.98), and other populations (Leon, 2000; Leon et al., 1999; Miklowitz, 2006; Phillips et al., 2006).

We selected the specific domains of psychosocial functioning most relevant to our sample: 1) Interpersonal Relationships with Family; 2) Interpersonal Relationships with Friends; 3) School/Work; 4) Recreation; and 5) Life Satisfaction. We combined School and Work, as participants usually transitioned from the former to the latter in young adulthood. Monthly ratings reflecting the most impaired week within each month were assigned for each domain.

Consistent with previous COBY studies (Hower et al., 2013; Siegel et al., 2015), we recoded the PSF Interpersonal Relationships functioning scales prior to data aggregation. PSF scores were re-coded on a 1–5 scale: (1) "very good;" (2) "good, with at least one relationship in the category = good/very good;" (3) "fair;" (4) "poor, with no relationships in the category = good;" and (5) "very poor/not able to function due to psychopathology." Thus, lower scores corresponded to better psychosocial functioning. For some analyses, PSF scores were further dichotomized at a cut-off score indicating "good" (scores 1 and 2) vs. "fair/poor" functioning (scores 3–5).

2.2.1.2 Mood Trajectory Assessments: The weekly symptom ratings were ascertained using the PSR scales of the A-LIFE linked to DSM-IV criteria, where PSR 1 = no symptoms, PSR 2 = minimal symptoms, PSR 3 = subthreshold symptoms, mild impairment, PSR 4 = subthreshold symptoms, moderate impairment, PSR 5 = threshold symptoms, significant impairment, and PSR 6 = threshold symptoms, severe impairment (Keller et al., 1987) (Supplemental Table 2). The reliability of the COBY PSR is good/very good, as reported in a prior study (Axelson et al., 2011). The Intraclass Correlation (ICC) of percentage of time meeting full DSM-IV criteria for a syndromal mood episode was 0.85; subthreshold mood symptoms was 0.82. Throughout the COBY cumulative follow-up time, there was an average Kendall's W of 0.8 (Axelson et al., 2011).

2.2.1.3 Demographic and Clinical Assessments: Intake demographic variables analyzed as predictors include (Table 1): age at intake, race, sex, BD diagnosis, living with both biological parents, and disability status, all assessed at intake by the Youth Self-Report (YSR) for Ages 11–18 (Achenbach, 1991), and SES (Hollingshead scale assessed at intake/ most recent follow-up) (Hollingshead, 1982). Intake clinical variables analyzed as predictors include (Table 1): age of BD onset, BD subtype (BD-I, BD-II, BD-NOS), family psychopathology, history of physical/sexual abuse, and history of psychiatric treatment, all assessed at intake by the Schedule for Affective Disorder and Schizophrenia for School-Age Children Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997)). Intelligence Quotient (IQ) was evaluated at intake by the Wechsler Abbreviated Scale of Intelligence (WASI) Vocabulary and Matrix Reasoning subtests (Wechsler, 1999).

2.2.2 Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences SPSS® Version 22.0 (IBM Corporation, Armonk NY, USA) and R Version 3.3.1.

We conducted Analyses of Variance (ANOVA) (Fisher, 1921) models to determine whether cumulative follow-up time with "good" (PSF scores 1–2) psychosocial functioning for each specific domain differed by Class. We identified intake sociodemographic variables, listed in the Demographic and Clinical Assessments section above, that had been utilized previously in COBY (e.g., Birmaher et al., 2014) and other studies (e.g., Judd et al., 2005; Wilens et al., 2014) as predictors of psychosocial functioning outcome, and then tested them in a series of univariate analyses. The variables found to be significant (**p < .05**; early age of BD onset, race, IQ, family history of SUD) were subsequently included into each Multiple Analyses of Variance (MANOVA) as covariates (Table 2) using a family-wise Bonferroni correction of p<.01.

We also analyzed longitudinal psychosocial functioning in each of the specific domains by Class, to examine whether different trajectories were observed. Line graphs were created to illustrate trends. To better discern the psychosocial functioning/time relationship, we used Linear Mixed Effects (LME) Modeling (Laird, 1982) with maximum likelihood estimation, in which we examined psychosocial functioning score fluctuations across time, accounting for the fixed effects of time, Class, and their interaction. Each model also included a random intercept, accounting for differences attributable to participants, to enhance model fit. We controlled for significant differences using family-wise Bonferroni correction of p<.00625. (Table 3; Supplemental Figures 2–6). Any time points with missing psychosocial functioning scores were omitted.

To assess psychosocial impairments in those with current symptomatic remission we focused our analyses on participants in Class 1 *Predominantly Euthymic* and Class 3 *Ill with Improving Course* (Supplemental Figure 1). Of note, we did not include those in Class 2 *Moderately Euthymic*, as this Class had significantly less maximum consecutive months in euthymia (12.6 months) compared to those in Class 3 (20.1 months), and they were not in symptomatic remission at the most recent follow-up (Birmaher et al., 2014) (Supplemental Figure 1). Class 3 began stable remission at the 84-month follow-up interval, showing significant differences with Class 2, but no significant differences with Class 1 (Table 1).

Poor functioning was operationalized by the PSF score cutoff of "fair-poor-very poor" (PSF scores 3–5). In addition, we analyzed these same frequencies in Class 1 *Predominantly Euthymic* alone, to examine functional impairments across specific domains for participants who were symptomatically euthymic for most of the cumulative follow-up time. As symptomatic remission for Class 3 *Ill with Improving Course* participants did not develop until the 84-month follow-up, we selected the most recent follow-up for analyses, as this served as a proxy for current functioning status, when these two Classes were in remission. Finally, we employed logistic regression analyses to evaluate potential predictors of domain-specific impairment in both of these remitted Classes (Table 5).

3. Results

3.1 Demographic/Clinical Characteristics of the Four LCGA Mood Trajectory Classes

The current study results are based on the longitudinal assessment of 367 participants with 4 years of cumulative follow-up time (median = 11.5 years), interviewed a mean of 10.0 times (SD = 3.2), on average every 8.7 months (SD = 5.2). For more details, please see a prior COBY study (Birmaher et al., 2014). At the most recent follow-up, when all participants were > 18 years old, 74 participants were enrolled in College or Trade/Technical school, while a total of 274 participants were engaged in Full-Time (n = 150) or Part-Time (n = 124) employment.

For differences in intake demographic variables, *Predominantly Euthymic* participants were significantly older than *Ill with Improving Course* participants and *Predominantly Ill* participants. They also had higher SES compared to the other Classes, and were more frequently living with both biological parents than *Predominantly Ill* participants (p <0.03). There were no other significant demographic differences among the four Classes. For differences in intake clinical variables, *Predominantly Euthymic* participants and *Moderately Euthymic* participants had a significantly older age of BD onset compared to *Predominantly Ill* participants. *Predominantly Euthymic* participants were less likely to have experienced childhood sexual abuse (in comparison to *Moderately Euthymic* and *Persistently Ill* participants), and had higher IQs (p<.05). There were no other clinical differences among the four Classes, including BD subtypes. Attrition analyses revealed that there were no significant differences at intake in demographic, clinical, or functioning variables between participants who continued with the cumulative follow-up assessments, and those who withdrew.

3.2. "Good" vs. "Fair/Poor" functioning of the Four LCGA Mood Trajectory Classes

Results from the MANOVA models revealed significant differences between Classes in each specific domain of functioning over the cumulative follow-up time (Table 2). Precisely, *Predominantly Euthymic* participants spent significantly less time with "fair/poor" functioning (PSF 3–5 in each domain), over the cumulative follow-up time compared to all other Classes across all domains. *Predominantly Ill* participants spent significantly more time with "fair/poor" psychosocial functioning over the cumulative follow-up time compared to all other Classes, with the exception of Interpersonal Relationships with Friends, in which there was no difference between *Predominantly Ill* and *Ill with Improving*

Course participants. These results were consistent with those of models that accounted for other significant predictors of "fair/poor" psychosocial functioning in the univariate model (i.e., early age of BD onset, race, IQ, family history of SUD).

3.3 Longitudinal Specific Domain Functioning of the Four LCGA Mood Trajectory Classes

We employed LME models to describe psychosocial functioning change and the dependence of change on Class over the cumulative follow-up time (Table 3; Supplemental Table 3; Supplemental Figures 2–6). Our models used the *Predominantly Euthymic Class* as the reference group, given that this group distinctly had the highest levels of specific domain psychosocial functioning over the cumulative follow-up time. We calculated one series of Cohen's d for each Class to show how much the outcome is expected to change over 72 months in pooled intake standard deviation (SD) units, and another series to show how much more the outcome is expected to change over 72 months relative to the *Predominantly Euthymic* reference Class in pooled intake SD units, with related effect sizes. We found significant Class x Time interactions for nearly all psychosocial functioning outcomes, except for Life Satisfaction.

For the Interpersonal Relationships with Family outcome at intake, relative to the *Predominantly Euthymic* reference Class, all other Classes had greater functional impairment. The *Predominantly Euthymic* reference Class demonstrated a significant improvement in Interpersonal Relationships with Family over the cumulative follow-up time. In comparison, the *Moderately Euthymic* and *Predominantly Ill* Classes showed a trivial to small effect of worsening Interpersonal Relationships with Family outcomes over cumulative follow-up time (d=0.14; p<.001), (d=0.36; p<.001), respectively (Table 3; Supplemental Table 3; Supplemental Figure 2).

For the Interpersonal Relationships with Friends outcome at intake, relative to the *Predominantly Euthymic* reference Class, all other Classes had greater functional impairment. The *Predominantly Euthymic* reference Class demonstrated improvement in Interpersonal Relationships with Friends over the cumulative follow-up time. In comparison to the *Predominantly Euthymic* reference Class, the other Classes had net positive (worsening) slopes; the *Moderately Euthymic* Class (d=0.32; p<.001), *Ill with Improving Course* Class (d=0.36; p<.001), and the *Predominantly Ill* Class (d=0.54; p<.001), demonstrated small to moderate effects of worsening over the cumulative follow-up time (Table 3, Supplemental Table 3, Supplemental Figure 3).

For the School/Work outcome at intake, the *Predominantly Euthymic* Class demonstrated improved School/Work functioning over all other Classes, and improved functioning over cumulative follow-up time. In comparison to the *Predominantly Euthymic* reference Class, the *Moderately Euthymic* Class (d=0.24; p<.001), and the *Ill with Improving Course* Class (d=0.12; p<.001) demonstrated slightly less improvement. In the *Predominantly Ill* Class, compared to the *Predominantly Euthymic* reference Class, School/Work worsened over cumulative follow-up time (d=0.47, p<.001) (Table 3, Supplemental Table 3, Supplemental Figure 4).

For the Recreation outcome at intake, there were no strong between-group differences relative to the *Predominantly Euthymic* Class. The *Predominantly Euthymic* reference Class demonstrated improvement in Recreation over cumulative follow-up time, as did the *Moderately Euthymic* Class. However, in comparison to the *Predominantly Euthymic* reference Class, the *Ill with Improving Course* Class and *Predominantly Ill* Class showed significant impairment in the Recreation outcomes (d=1.36, p<.001; d=1.29, p< .001, respectively) (Table 3, Supplemental Table 3, Supplemental Figure 5).

For the Life Satisfaction outcome at intake, there were no significant between-group differences relative to the *Predominantly Euthymic* Class. The *Predominantly Euthymic* reference Class demonstrated minimal improvement in Life Satisfaction over cumulative follow-up time, but this trend was not significantly different from any of the other Classes; all groups had relatively stable impairment in Life Satisfaction over cumulative follow-up time (Table 3, Supplemental Table 3, Supplemental Figure 6).

3.4 Most Recent Functioning of the Two Current Remission LCGA Mood Trajectory Classes

We examined the frequency of "fair/poor" psychosocial functioning (PSF 3–5) in symptomatically remitted participants from Class 1 (*Predominantly Euthymic*) alone, and combined with Class 3 (*Ill with Improving Course*), across all domains at the most recent follow-up assessment, as this was a proxy for the current functioning status, when both Classes were in remission (Table 4). Across the functioning domains, 13–20% of Class 1 only, and 23–47% of the combined Classes 1 and 3, were found to exhibit "fair/poor" functioning at the most recent follow-up assessment.

3.5 Poor Functioning Predictors of the Two Current Remission LCGA Mood Trajectory Classes

We examined predictors of "fair/poor" psychosocial functioning (PSF 3–5) in symptomatically remitted participants in Class 1 (*Predominantly Euthymic*) and Class 3 (*Ill with Improving Course*) across all specific functioning domains at the most recent follow-up assessment, as this was a proxy for the current functioning status, when both Classes were in remission (Table 5). Early age of BD onset predicted "fair/poor" psychosocial functioning across all specific domains except Recreation, but with family-wise Bonferroni correction, the only statistically significant effects were in Interpersonal Relationships with Family. Disability status predicted "fair/poor" psychosocial functioning across all specific domains, except Interpersonal Relationships with Friends, but with Bonferroni correction, the only statistically significant effects were in the work domain. Low SES predicted "fair/poor" psychosocial functioning in Interpersonal Relationships with Family, but not with Bonferroni correction. BD subtype, family psychiatric history, lifetime history of physical/sexual abuse, and IQ were not significant predictors of "fair/poor" psychosocial functioning in any specific domains.

3. Discussion

There were four major findings from this study. First, participants with more symptomatic mood trajectories had significantly greater psychosocial impairment across all domains of functioning. These results extend beyond previous COBY studies, indicating global psychosocial impairment for these same participants (Birmaher et al., 2014; Hower et al., 2019).

Second, as expected, we noted that some specific psychosocial functioning domains had different trajectories. We hypothesize that this could be due to the unique developmental challenges of transition age young adults, including those with BD (e.g., Coryell et al., 2013), such as increased responsibilities, and decreased structure and social opportunities.

We found that Interpersonal Relationships with Family worsens over all follow-up years in the *Moderately Euthymic* Class and *Predominantly Ill Class,* but does improve in the *Predominantly Euthymic* Class and *Ill with Improving Course* Class. It is possible that symptomatic improvements of those in the *Predominantly Euthymic* Class and *Ill with Improving Course* Class translated into improved family relationships, or vice versa. In addition, the BD symptom burden, regardless of mood trajectory, could have left a "functional scar" on family relationships. These results build upon a previous COBY study, noting greater mood severity was associated with worse interpersonal relationships (Siegel et al., 2015). The findings of increased family interpersonal impairment observed in the *Moderately Euthymic* and *Predominantly Ill* Classes are consistent with COBY and other studies on BD youth and adults (e.g., Geller et al., 2000; Goldstein et al., 2009; Wilens et al., 2003).

We observed a different effect with Interpersonal Relationships with Friends, in which all Classes, except *Predominantly Euthymic,* experienced worsening of interpersonal functioning over time. These results correspond with COBY and other studies on BD youth, finding worse peer interpersonal relationships among BD youth (Geller et al., 2000; Goldstein et al., 2009; Siegel et al., 2015). Developmental literature on the normative change of friendships in the transition to young adulthood is mixed, with studies concluding that emotional intimacy is largely derived from friendships or romantic relationships as opposed to family, though the evolution of the quality of these relationships over time is unclear (Chow, 2012). The findings of significantly worsening impairment in all but the *Predominantly Euthymic* Class may be consistent with effects from both social skill impairment from BD symptoms, and the transition to having less access to peers as participants age out of school.

School/Work improved in all Classes, except the *Predominantly Ill* Class. It is possible that the improved functioning reflects that participants at this adult age have chosen the routine of their post-secondary school education and employment, and therefore are more engaged in individualized pursuits, compared to the relatively uniform, mandatory process of K-12 education. However, those in the *Predominantly Ill* Class are much more likely to receive disability compensation, and not participate in the workforce (full or part-time).

Recreation appeared to generally worsen across Classes, except the *Predominantly Euthymic* Class. These results are consistent with a normative developmental decline due to decreased time for leisure activities as young adults enter the workforce (Kirk and Rhodes, 2012), and undertake additional household responsibilities. It is also possible that they do not have the same social structure (e.g., team sports) or access to peers (Allender et al., 2006), as they transition out of school. Another consideration is the increase in the use of social media, which may correspond with a decrease in other recreational activities (Coyne et al., 2013). The *Predominantly Euthymic* Class may exhibit improvement in this domain due to having a longer time spent in euthymia, allowing space to integrate more leisure activities into their schedules.

One striking finding is that, despite clear differences between Classes on multiple other domains of specific functioning, there were no significant differences between Classes on Life Satisfaction. This may indicate all participants' acceptance of the chronicity of BD illness, and its associated impairments. An additional explanation is that Life Satisfaction tends to remain moderately stable over time across development. Demographic characteristics and life circumstances have been found to not affect subjective well-being measures, and this seems to remain stable, in spite of BD symptoms (Lucas and Donnellan, 2007).

Third, as predicted, we found that 13–20% of *Predominantly Euthymic only participants, and 20-47%* of the combined *Predominantly Euthymic* and *Ill with Improving Course* participants, despite current remission of symptoms, experienced continued, but varying, levels of impairment across all domains. These results expand upon previous findings which indicate that, despite being predominantly euthymic, psychosocial impairment may continue in a meaningful minority of participants (Axelson et al., 2006; Judd et al., 2008; Solomon et al., 2004). Our study is unique in that, to the best of our knowledge, it is the first to prospectively examine different domains of psychosocial functioning over time in BD youths, who in general belong to specific mood trajectories. Psychosocial impairment may persist after symptomatic remission for several reasons. One possibility is that, after experiencing many consecutive years of full threshold depression and hypo/mania episodes, functional "scars" may develop that are not readily amenable to improvement.

Fourth, similarly to previous studies (e.g., (Birmaher et al., 2014; Coryell et al., 2013)), we observed that early age of BD onset, disability, and low SES at intake predicted psychosocial impairment across all domains in participants with current symptomatic remission. In particular, early age of BD onset had the strongest correlation to impairment in family relationships, indicating a need for consistent interventions, such as family and interpersonal therapy, throughout periods of symptomatic remission.

IQ, BD subtype, 1st and 2nd degree family history, and history of physical/sexual abuse did not seem to affect most recent psychosocial functioning. Potentially, the effects of the more distal variables weaken over time. It is also conceivable that these variables were addressed in psychosocial interventions, thus mitigating the extent of deleterious impact.

Improving our knowledge about the specific domains of psychosocial impairments that are experienced by those with BD has important clinical implications. Our results emphasize the value of early (secondary) intervention in the course of BD if possible, not only to target mood symptoms, but also to decrease, or ideally prevent, chronic psychosocial impairment. Thus, it is important to have systematic ongoing assessments of specific domains of psychosocial functioning, and management of factors associated with poor psychosocial functioning (e.g., comorbid disorders), that could target specific interventional goals. Pilot studies on the efficacy of Acceptance and Commitment Therapy (ACT) for BD in adults suggest that ACT as a modality could aid adjustment to illness in those with BD, and give a framework for psychoeducation to their support system (Heffner et al., 2019; Pankowski et al., 2017; Sazvar, 2017). Other possible psychotherapeutic interventions that target the interpersonal impairments, such as family or interpersonal therapy, may also be efficacious in addressing relationship concerns (McMahon et al., 2016). Further work with larger sample sizes would better delineate possible benefits to consistent psychotherapeutic intervention in those with BD. Our results also underscore the importance of future research about the bidirectional influence of symptoms and specific domains of functioning.

4.1 Limitations

The findings of the current study should be noted in the context of the below limitations. First, while every effort was made to collect accurate information, the data assessed through the A-LIFE (utilizing a method similar to TLFB, as noted above) are vulnerable to a retrospective recall bias. Nonetheless, TLFB has been widely employed in research (clinical and nonclinical) for over 30 years (Sobell, 2008). Second, the majority of study participants from the three study sites were self-reported White, and were recruited primarily from clinical settings, which may in turn limit the generalizability of the findings. However, course and morbidity in non-clinically referred BD youth have been reported to be similar to those youth in referred populations (Lewinsohn et al., 2000). Third, as a longitudinal naturalistic phenomenology study focused on BD youth, COBY did not recruit a cohort of control youth, so we cannot draw conclusions about specific domains of psychosocial functioning compared to healthy controls. Fourth, there was a significant amount of missing data for the WASI at intake (36.2%). Although we did control for IQ, this was based on a subset of the original study sample. Fifth, as more complex functional forms for time were difficult to distinguish among the Classes, we opted to use linear models to describe broad trends over time. We recognize that our models are a crude summary of the complex nature of changing psychological symptoms over time. Sixth, the analyses of treatment effects were beyond the scope of this study, especially given COBY is a naturalistic study, in which treatment was confounded by indication and highly variable, and interdependent with both symptomatic and psychosocial functioning courses. Finally, the time-varying interactions between symptoms and functioning domains are outside of the purview of the present study, but will be explored in future studies. Nonetheless, our findings suggest significant psychosocial functional impairment across a number of specific domains, even among BD youth with improved symptomatology.

4. Conclusions

In summary, participants with more symptomatic mood trajectories had greater impairment across domains. Moreover, even with symptomatic remission, participants still exhibited impairment. Domains had different trajectories; impairment was not generalized across domains. Clinical implications from these findings include determining specific psychosocial functioning treatment targets for BD individuals over the course of their lives, not just during the most acute portions of their illness. For example, specific assessment of family relationships, peer support, and recreation opportunities among transition-age adults may be warranted, particularly for those who remain symptomatic. Our results suggest the importance of early, continuing, and nuanced assessment of specific (vs. global) domains for targeted treatment. Therapeutic modalities such as ACT, family, and interpersonal therapies may address the various domains of functional impairments that persist, even beyond symptomatic remission.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Highlights

- Youth with predominant euthymia had better psychosocial domain functioning

- Youth with persistent mood symptoms had worse psychosocial domain functioning

- Youth with remitted symptoms still showed psychosocial domain functioning deficits

- Limitations include lack of a healthy control group to compare functioning findings

Table 1

Demographic and Clinical Characteristics of Youths with Bipolar Disorder of the Four Latent Class Growth Analyses (LCGA) Mood Trajectory Classes.

	Class 1 Predominantly Euthymic (n=88)	Class 2 Moderately Euthymic (n=127)	Class 3 Ill with Improving Course (n=70)	Class 4 Predominantly Ill (n=82)	Statistic	p-Value
Demographics						
Age at Intake	13.6 ± 3.4[3,4]	12.8 ± 3.1	12.3 ± 3.3[1]	11.7 ± 3.3[1]	F=5.39	0.001
Age at Most Recent Follow-up	25.3 ± 4.0[3,4]	24.7 ± 3.8	23.5 ± U[1]	23.6 ± 4.2[1]	F=3.83	0.01
Sex (% Female)	48.9	43.3	47.1	48.8	χ^2=0.90	0.8
SES	3.9 ± 1.2[2,3,4]	3.4 ± 1.1[1]	3.3 ± 1.1[1]	3.0 ± 1.3[1]	F=8.36	<.001
Race (% Self-Reported White)	83.0	84.3	82.9	79.3	χ^2=0.88	0.8
Living with Both Biological Parents (%)	52.3[4]	43.3	38.6	31.7[1]	χ^2=7.81	0.05
Length of Follow-up Time (weeks) *	610.7 ± 116.1	624.1 ± 87.2	594.9 ± 110.3	599.9 ± 121.5	F=1.415	0.24
Clinical Factors						
BD (%)					χ^2=7.42	0.3
BD-I	63.6	59.8	55.7	57.3		
BD-II	9.1	7.9	1.4	8.5		
BD-NOS	27.3	32.3	42.9	34.2		
Age Onset of Mood Symptoms	10.4 ± 4.3[2,3,4]	8.3 ± 4.0[1,4]	7.7 ± 3.9[1]	6.9 ± 3.2[1,2]	F=13.1	<.001
Age Onset First Manic	12.1 ± 4.0[4]	10.4 ± 4.2	11.4 ± 4.1	9.1 ± 3.8[1]	F=3.64	0.01
Age Onset First MDE	12.4 ± 3.4[2,3,4]	10.3 ± 3.8[1]	10.3 ± 3.7[1]	9.3 ± 3.8[1]	F=4.85	0.003
Physical/Sexual Abuse	6.8[2,4]	24.4[1]	20.0	24.4[1]	χ^2=12.3	0.006
Physical Abuse	6.8	12.6	15.7	18.3	χ^2=5.45	0.1
Sexual Abuse	1.1[2,4]	16.5[1]	8.6	14.6[1]	χ^2=14.4	0.003
% of time well at 6-Month follow-up *	57.1 ± 35.3[2,3,4]	39.8 ± 33.9[1,3,4]	28.3 ± 37.4[1,2]	16.7 ± 28.1[1,2]	F=16.2	<.001
% of time well at or most recently following 84-Month follow-up *	85.0 ± 28.1[2,4]	47.0 ± 37.6[1,3,4]	77.7 ± 28.4[2,4]	25.0 ± 37.1[1,2,4]	F=53.39	<.001
C-GAS at Intake	54.0 ± 14.8	56.0 ± 11.4	54.7 ± 11.7	54.4 ± 10.7	F=0.54	0.7
C-GAS Most Severe Past	39.1 ± 9.0	36.9 ± 11.6	38.9 ± 10.1	36.5 ± 11.2	F=1.37	0.3
WASI IQ[+]	112.0 ± 16.7	105.2 ± 13.8	105.6 ± 15.8	103.1 ± 14.4	F=36.67	<.001
Outpatient Treatment before Intake (%)	88.6[4]	96.1	98.6	98.8[1]	χ^2=13.0	0.009
Psychiatric Hospitalization be'ore Intake (%)	45.5	53.5	50.7	57.3	χ^2=2.67	0.5

	Class 1 Predominantly Euthymic (n=88)	Class 2 Moderately Euthymic (n=127)	Class 3 Ill with Improving Course (n=70)	Class 4 Predominantly Ill (n=82)	Statistic	p-Value
Exposure to Any Psychotropic Medication by Intake (%)	93.2	96.1	94.3	96.3	χ^2=1.32	0.7

[*] Denotes variables that were assessed at follow-up

[1] Significant (p 0.05 after Bonferroni correction) between class differences with Class 1

[2] Significant (p 0.05 after Bonferroni correction) between class differences with Class 2

[3] Significant (p 0.05 after Bonferroni correction) between class differences with Class 3

[4] Significant (p 0.05 after Bonferroni correction) between class differences with Class 4

[+] WASI data is based upon a subset of the study sample.

These analyses were conducted in a prior Course and Outcome of Bipolar Youth study (Birmaher et al, 2014).

SES: Socio-Economic Status

BD: Bipolar Disorder; BD-NOS: Bipolar Disorder Not Otherwise Specified

MDE: Major Depressive Episode

C-GAS: Children's Global Assessment Scale

WASI: Wechsler Abbreviated Scale of Intelligence (including Vocabulary and Matrix Reasoning Subtests)

IQ: Intelligence Quotient

Table 2

Proportion Over Cumulative Follow-up Time with "Fair/Poor" Psychosocial Functioning by Latent Class Growth Analyses (LCGA) Mood Trajectory Class.

	Class 1 (n = 88) M (SD)	Class 2 (n = 127) M (SD)	Class 3 (n = 70) M (SD)	Class 4 (n = 82) M (SD)	F	P	Partial η²
Interpersonal Relations, Family	.34 (.34) [a]	.55 (.30) [b]	.61 (.26) [b]	.73 (.24) [c]	26.58	<.001	.18
Interpersonal Relations, Friends	.23 (.23) [a]	.41 (.29) [b]	.48 (.33) [b,c]	.56 (.30) [c]	20.95	<.001	.15
School/Work	.27 (.26) [a]	.44 (.23) [b]	.51 (.2,) [b]	.60 (.25) [c]	26.93	<.001	.18
Recreation	.12 (.15) [a]	.27 (.23) [b]	.23 (.22) [b]	.39 (.28) [c]	20.25	<.001	.14
Satisfaction	.20 (.22) [a]	.41 (.26) [b]	.46 (.25) [b]	.61 (.28) [c]	39.88	<.001	.25

Note: Superscripts that are different indicate significant pairwise contrasts.

Means represent proportion of cumulative follow-up time with "fair to poor" psychosocial functioning.

"Fair to Poor" psychosocial functioning: Adolescent Longitudinal Interval Follow-Up Evaluation (A-LIFE) Psychosocial Functioning Schedule (PSF) scores 3–5.

Class 1: *Predominantly Euthymic*; Class 2: *Moderately Euthymic*; Class 3: *Ill with Improving Course*; Class 4: *Predominantly Ill*

Table 3

Fixed Effects Estimates in Linear Mixed Effects (LME) Models in Specific Psychosocial Functioning Domains Over Cumulative Follow-Up Time.

	Estimate	SE	*t*	*P*
Interpersonal Relations, Family				
(Intercept)	2.3	0.1	31.2	**<0.001**
Psychosocial Functioning Month (Time)	−0.0005	0.0002	−2.516	0.012
Class 2	0.4060	0.0969	4.188	**<0.001**
Class 3	0.7651	0.1120	6.833	**<0.001**
Class 4	0.7070	0.1073	6.590	**<0.001**
Time x Class 2	0.0020	0.0003	7.843	**<0.001**
Time x Class 3	−0.0007	0.0003	−2.360	0.018
Time x Class 4	0.0053	0.0003	18.358	**<0.001**
Interpersonal Relations, Friends				
(Intercept)	2.1287	0.0813	26.181	**<0.001**
Psychosocial Functioning Month (Time)	−0.0042	0.0002	−18.123	**<0.001**
Class 2	0.2057	0.1058	1.944	0.052
Class 3	0.3438	0.1222	2.814	**0.005**
Class 4	0.4136	0.1171	3.533	**<0.001**
Time x Class 2	0.0052	0.0003	17.864	**<0.001**
Time x Class 3	0.0058	0.0003	16.591	**<0.001**
Time x Class 4	0.0089	0.0003	27.026	**<0.001**
School/Work				
(Intercept)	2.4426	0.0720	33.940	**<0.001**
Psychosocial Functioning Month (Time)	−0.0067	0.0003	−24.991	**<0.001**
Class 2	0.2756	0.0937	2.941	**0.003**
Class 3	0.5769	0.1087	5.306	**<0.001**
Class 4	0.4931	0.1038	4.748	**<0.001**
Time x Class 2	0.0040	0.0004	11.312	**<0.001**
Time x Class 3	0.0020	0.0004	4.600	**<0.001**
Time x Class 4	0.0077	0.0004	18.500	**<0.001**
Recreation				
(Intercept)	3.0126	0.4482	6.722	**<0.001**
Psychosocial Functioning Month (Time)	−0.0138	0.0020	−6.930	**<0.001**
Class 2	−0.5544	0.5829	−0.951	0.342
Class 3	0.9849	0.6736	1.462	0.144
Class 4	−0.3917	0.6453	−0.607	0.544
Time x Class 2	0.0123	01)26	4.797	**<0.001**
Time x Class 3	0.0188	0.0030	6.217	**<0.001**
Time x Class 4	0.0179	0.0029	6.216	**<0.001**
Satisfaction				
(Intercept)	3.5743	0.6759	5.288	**<0.001**

	Estimate	SE	*t*	*P*
Psychosocial Functioning Month (Time)	−0.0064	0.0031	−2.065	0.039
Class 2	1.6258	0.8791	1.849	0.064
Class 3	1.4582	1.0159	1.435	0.151
Class 4	1.5854	0.9732	1.629	0.103
Time x Class 2	−0.0072	0.0039	−1.835	0.067
Time x Class 3	0.0026	0.0047	0.557	0.578
Time x Class 4	0.0043	0.0044	0.975	0.330

Class 2: *Moderately Euthymic,* Latent Class Growth Analysis Class 2

Class 3: *Ill with Improving Course,* Latent Class Growth Analysis Class 3

Class 4: *Predominantly Ill,* Latent Class Growth Analysis Class 4

BOLD indicates significance with family-wise Bonferroni correction of $p < 0.00625$

Adolescent Longitudinal Interval Follow-Up Evaluation (A-LIFE) Psychosocial Functioning Schedule (PSF) scores: lower scores correspond to "good" psychosocial functioning (PSF scores 1–2), while higher scores denote "fair to poor" psychosocial functioning (PSF scores 3–5).

Table 4

Frequency of Poor Psychosocial Functioning in Symptomatically Euthymic Participants at Most Recent Follow-up

Interpersonal Relationships with Family	0.35	0.47
Interpersonal Relationships with Friends	0.17	0.33
School/Work	0.13	0.23
Recreation	0.16	0.21
Satisfaction	0.20	0.33

Poor psychosocial functioning: Adolescent Longitudinal Interval Follow-Up Evaluation (A-LIFE) Psychosocial Functioning Schedule (PSF) scores 3–5.

Table 5

Logistic Regression Analyses of Predictors of Poor Psychosocial Functioning in Symptomatically Euthymic Participants at Most Recent Follow-Up.

	Family		Friends		Work		Recreation		Satisfaction	
	Wald X^2	OR (95% CI)	Wald$_X2$	OR (95%CI)	Wald$_X2$	OR (95%CI)	Wald X^2	OR (95%CI)	Wald X^2	OR (95%CI)
Age Onset Bipolar Disorder	14.29 **	1.18 (1.08–1.28)	6.09 *	1.11 (1.02–1.21)	10.08 *	1.19 (1.07–1.32)	2.23	1.08 (0.98–1.19)	6.06 *	1.11 (1.02–1.21)
BD Subtype	0.08	0.99 (0.79–1.24)	1.60	1.16 (0.92–1.44)	0.70	0.91 (0.72–1.14)	0.04	1.03 (0.80–1.32)	1.20	0.88 (0.71–1.10)
Lifetime Physical/Sexual Abuse	0.62	0.68 (0.27–1.76)	0.09	1.17 (0.42–3.24)	0.06	0.57 (0.29–2.60)	0.39	1.51 (0.41–5.58)	3.16	0.42 (0.16–1.09)
1st Degree Relative with Hypo/Mania	0.05	1.02 (0.88–1.17)	0.2	1.05 (0.91–1.21)	0.59	0.92 (0.74–1.14)	0.62	0.91 (0.71–1.16)	0.35	1.05 (0.90–1.21)
1st Degree Relative with Sub Abuse	2.08	1.11 (0.96–1.29)	2.99	1.13 (0.98–1.30)	0.24	1.04 (0.89–1.21)	0.60	0.98 (0.81–1.18)	0.87	1.07 (0.93–1.23)
1st Degree Relative with Sub Dependence	1.22	1.09 (0.94–1.26)	1.15	1.08 (0.94–1.25)	0.03	0.99 (0.82–1.12)	0.01	0.99 (0.82–1.20)	0.10	1.01 (0.87–1.18)
2nd Degree Relative with Hypo/Mania	0.90	1.02 (0.88–1.19)	2.49	1.13 (0.97–1.32)	1.41	1.10 (0.94–1.29)	0.49	1.06 (0.90–1.26)	1.52	1.20 (0.95–1.28)
2nd Degree Relative with Sub Abuse	1.01	1.09 (0.92–1.30)	3.73	1.20 (0.10–1.45)	2.41	1.15 (0.97–1.37)	0.70	1.08 (0.90–1.30)	0.33	1.05 (0.89–1.25)
2nd Degree Relative with Sub Dependence	0.31	1.05 (0.89–1.21)	1.99	1.12 (0.96–1.32)	0.90	1.09 (0.92–1.28)	0.19	1.01 (0.83–1.23)	0.01	1.01 (0.85–1.19)
Disability	8.26 *	0.19 (0.06–0.58)	3.57	0.40 (0.15–1.04)	12.28 **	0.16 (0.06–0.45)	5.34 *	0.31 (0.11–8.84)	5.60 *	0.31 (0.12–0.82)
WASI IQ	1.67	1.01 (0.99–1.03)	0.52	1.01 (0.99–1.02)	1.51	1.01 (0.99–1.03)	0.76	0.99 (0.97–1.01)	0.03	1.00 (0.99–1.02)
SES Scores	9.29 *	1.03 (1.01–1.06)	4.23	1.02 (1.00–1.05)	1.37	1.02 (0.99–1.04)	0.08	1.00 (0.97–1.02)	2.74	1.02 (1.00–1.04)
SES Total	8.36 *	1.03 (1.01–1.06)	3.23	1.27 (0.98–1.63)	2.27	1.25 (0.94–1.67)	0.11	1.05 (0.78–1.41)	3.23	1.27 (0.98–1.63)

Poor psychosocial functioning: Adolescent Longitudinal Interval Follow-Up Evaluation (A-LIFE) Psychosocial Functioning Schedule (PSF) scores 3–5.

BD Subtype: Diagnosis of bipolar I, bipolar II, or bipolar spectrum not otherwise specified, per DSM-IV criteria.

Sub: Any Substance or Alcohol Use, excludes Nicotine

ADHD: Attention Deficit Hyperactivity Disorder Diagnosis

DBD: Disruptive Behavior Disorder Diagnosis (encompasses Oppositional Defiant Disorder [ODD] and Conduct Disorder [CD])

Disability: Receiving any form of local/state/federal compensation for physical/psychological disability status

WASI IQ: Intelligence Quotient evaluated by the Weschler Abbreviated Scale of Intelligence Vocabulary and Matrix Reasoning subtests.

SES: Socio-Economic Status, Scores: Raw Scores, Total: Hollingshead Classes 1–1V

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p < 0.05;

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p < 0.01