Risk-Sensitive Decision-Making and Self-Harm in Youth Bipolar Disorder

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Abstract

Background: Youth with bipolar disorder (BD) are at high risk for suicide and have high rates of self-harm, which includes both suicide attempts and non-suicidal self-injury. Greater risk-taking has been associated with suicide attempts in youth with major depression, although there are no studies examining the relationship between risk-related decision-making and self-harm in youth with BD. We aimed to examine the association of suicide risk with risk-sensitive decision-making in a controlled sample of youth with BD.

Methods: Eighty-one youth with BD (based on *DSM-IV* criteria; 52 youth with a history of self-harm [BD_{SH+}]; 29 without a history of self-harm [BD_{SH-}]) and 82 age- and sex-matched control youth aged 13–20 years were recruited between 2012 and 2020. Decision-making and risk-taking performance were assessed via the Cambridge Gambling Task within the Cambridge Neuropsychological Test Automated Battery (CANTAB). General linear models were used to examine differences between groups with control for age, sex, and IQ.

Results: There was a significant difference in the overall proportion of points bet ($F_{2,157}=3.87$, $P=.02$, $\eta^2=0.23$) such that BD_{SH-} youth performed better than both BD_{SH+} ($P=.02$) and control youth ($P=.04$). Mean latency was significant ($F_{3,156}=4.12$, $P=.017$, $\eta^2=0.03$), with BD_{SH-} youth deliberating longer than controls ($P=.03$). Risk-taking significantly differed between groups ($F_{2,157}=3.83$, $P=.02$, $\eta^2=0.23$), with BD_{SH-} youth showing greater self-control compared to BD_{SH+} ($P=.01$) and control youth ($P=.01$).

Conclusions: BD_{SH-} youth had greater self-control and lower risk-taking. We speculate this finding may be reflective of a compensatory process among BD_{SH-} youth serving a protective role in suicide risk. Future longitudinal studies are needed to examine the temporal association of neurocognition and self-harm among youth with BD.

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Suicide is the second leading cause of mortality among youth.[1] Currently, suicide risk assessment relies on an interview with the clinician and patient or family, and there is a major gap in knowledge regarding effective suicide risk prediction and prevention strategies. One group of youth at particularly high risk for suicide are youth with bipolar disorder (BD). These youth have high rates of non-suicidal self-injury (NSSI) and suicide attempts and have an even higher suicide risk than youth with major depressive disorder (MDD).[2,3] Longitudinal cohort studies of youth have demonstrated that history of suicide attempt and history of NSSI impart equal risk for future suicide attempts.[4,5] Therefore, here we examine the broader concept of self-harm, which encompasses suicide attempt and/or NSSI. Self-harm is one of the biggest risk factors for suicide, yet the mechanisms underlying risk for self-harm and progression to suicide remain poorly understood.

While suicide risk is multifactorial, one construct that is especially relevant to understanding suicide risk in adolescents with BD is reward dysfunction, specifically risk-sensitive decision-making. Risky decision-making has been associated with suicide attempts among adults[6,7]; however, studies among youth are few and show inconsistent evidence for this association.[8–12] Reward processing is involved in value-based decision-making and is particularly relevant in suicide risk.[13] Given that mania is unique to BD and is related to reward-driven behavior, including health-risk behavior, it is hypothesized that reward-related differences in BD contribute to suicide risk. Yet, variability in this population is expected, and some youth with BD will be more or less prone to risk-taking. In turn, those youth with a greater propensity for risk-taking are more likely to also engage in self-harm behaviors. Therefore, we need to further understand risk-sensitive decision-making in youth with BD to elucidate specific differences involved in suicide risk. Furthermore, both BD and the developmental epoch of adolescence are characterized by increased reward-seeking and risk-taking.[14–16] This fact is relevant to understanding

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Clinical Points

- Youth with bipolar disorder and no history of self-harm placed smaller bets overall and deliberated longer on their choices compared to youth with a history of self-harm and control youth.
- The findings from this study help clinicians understand the neurobiological phenotype of youth with bipolar disorder at risk for suicide, which in turn may help inform prevention strategies.

suicide risk, as neurocognitive dysfunction in domains involving cognitive control and value-based decision-making are associated with increased risk for suicide.[17,18] While risk-sensitive decision-making is associated with suicidality among adolescents in general, this association is especially important for youth with BD given their significant propensity for impaired risk-sensitive decision-making alongside their pronounced risk for suicidality.

Task-related behavioral risk-taking is associated with suicide risk in youth, adults, and the elderly.[19–21] The Iowa Gambling Task (IGT)[22] and the Cambridge Gambling Task (CGT)[23] are similar neurocognitive tests that have been used to examine risk-taking and decision-making in relation to suicide risk. A study of depressed adults with BD found no difference on IGT performance between suicide attempters and non–suicide attempters.[24] Young adults with a history of suicide attempts had impaired rational decision–making on the CGT.[25] There have been only 4 studies examining risk-taking and decision-making in relation to self-harm in youth,[9–12] and no studies specifically examining this topic in youth with BD. Youth with a history of a suicide attempt are more likely to take bigger risks and have impaired decision-making,[11,12] although the evidence is mixed with 2 prior studies reporting no difference on IGT performance in youth with history of a suicide attempt.[9,10] Aligning with clinical and neurocognitive findings, neuroimaging research examining suicide risk has shown both structural and functional alterations in reward-related brain regions among youth with BD.[26–31]

Self-harm is a strong predictor of future and more severe self-harm.[4,5] It is well-established that youth with BD have neurocognitive impairments across many domains, including decision-making and risk-taking, regardless of self-harm history.[32,33] Self-harm risk in youth has also been associated with deficits in these neurocognitive domains.[13] Despite this, there are no studies to date examining the relationship between risk-related decision-making and self-harm in youth with BD. Furthermore, given that self-harm often has onset in adolescence, these behaviors increase during this developmental era, and given that suicide in adolescence leads to many years of life lost, studying the neuropsychological underpinnings of self-harm during adolescence is critical to informing risk assessment strategies. This study, therefore, aims to elucidate the association of risk-sensitive decision-making with self-harm in youth with BD via the CGT, as this task assesses domains known to be highly relevant to suicide. We hypothesized that those with self-harm will take greater risks and make poorer decisions compared to psychiatric and non-psychiatric control groups without any history of self-harm. In addition, we hypothesized that the severity of self-harm would increase with poorer decision-making.

METHODS

Participants and Clinical Characteristics

Youth with BD were recruited from a tertiary subspecialty clinic, and control youth were recruited from the community via advertisement. This study represents a secondary analysis with a sample based on two separate neurocognitive study protocols. As such, participants were grouped post hoc based on operationalized definitions for NSSI and suicide attempt(s). Both study protocols were approved by the local research ethics board. All participants and their parents provided informed consent prior to completing any study procedures. All participants were between 13 and 20 years old, with no recent substance dependence in the past 3 months. Control youth were not included if they had any history of major mood disorder or any first- or second-degree family history of BD or psychotic disorders. Groups were matched by age (BD: 17.41 ± 1.91 years, control: 17.08 ± 1.67 years; $t = -1.18$, $P = .24$) and sex (BD: 53 females, control: 45 females; $\chi^2 = 1.89$, $P = .17$).

All participants and their parent(s)/guardian(s) were interviewed to screen for psychiatric disorders by a trained interviewer using the Kiddie Schedule for Affective Disorders–Present and Lifetime version (K-SADS-PL).[34] History of mood episodes was obtained via interview using the Mania Rating Scale (MRS)[35] and Depression Rating Scale (DRS),[36] yielding mood scores for current (worst week in the past month) and most severe lifetime episode. Youth with BD met diagnostic criteria for BD-I, BD-II, or BD not otherwise specified, operationalized according to the Course and Outcome of Bipolar Youth (COBY) study.[37] This sample was recruited from October 2012 through January 2020. For consistency, all diagnoses were based on *DSM-IV* criteria. A licensed child-adolescent psychiatrist confirmed all psychiatric diagnoses. Additional clinical methods are described in Supplementary Appendix 1.

Self-Harm

History of self-harm was collected via interview using the Longitudinal Interval Follow-up Evaluation (LIFE)[41] Self-Injurious/Suicidal Behavior Scale. Information on medical threat, intent, and method was collected for each self-harm behavior, and suicide attempt was operationalized as any behavior with a

score of 3 or greater on both medical threat ("Mild") and level of stated intent ("Definite but still ambivalent"). The anchors with descriptions for each intent and medical threat score on the LIFE Self-Injurious/Suicidal Behavior Scale can be found in Supplementary Table 1. All other self-damaging behaviors with a score of less than 3 on intent and/or medical threat were categorized as NSSI. Self-harm included any lifetime history of suicide attempt and/or NSSI.

Neurocognitive Assessment

Neurocognition was assessed via the Cambridge Neuropsychological Test Automated Battery (CANTAB eclipse version 2.0; Cambridge Cognition, Ltd.; 2005), a computerized battery of subtests. The Cambridge Gambling Task (originally named "Cambridge Gamble Task"), akin to the Iowa Gambling Task, probes decision-making and risk-taking. Participants are presented with 10 colored boxes (some red and some blue) at the top of the screen, and the participant has to guess which box contains the yellow token (Supplementary Figure 1). Participants choose which color box they believe the token to be under by touching the color they think it is under; then the participants choose how much they would like to bet by touching the stake box as the bets are displayed in ascending order. This task yields 5 outcome measures: (1) *risk-taking* represents the proportion of points gambled on trials in which they had chosen the more likely outcome, for which a lower score represents greater self-control; (2) *quality of decision-making* represents the proportion of trials in which the participant gambled on the more likely outcome, for which a higher score is better; (3) *deliberation time* represents the mean latency from the presentation of the colored boxes to the participants choice of which color box to bet on, for which a lower score is better; (4) *overall proportion bet* represents the mean proportion of points gambled on each trial (includes trials for which they bet on the less likely outcome and equally likely outcome), and lower scores indicate greater self-control; and (5) *delay aversion* represents the tendency to bet larger amounts when the possible bet amounts are presented in descending order than they bet when the amounts are presenting in ascending order, for which a higher score indicates more delay aversion. With respect to quality control of the CANTAB data, although we did not have access to review the trial-level output, the summary variables included in the analyses were tested for normality and outliers. Unfortunately, we were not able to perform this quality control on the trial-level output variables. IQ was assessed using the Welscher Abbreviated Scale of Intelligence (WASI-II), matrix reasoning and vocabulary subtests.[42]

Statistical Analysis

Demographic and clinical characteristics were compared between BD youth with a history of self-harm (BD_{SH+}), BD youth with no history of self-harm (BD_{SH-}), and control youth via χ^2 tests for categorical variables and Student *t* test for dimensional variables.

General linear models were used to examine differences between groups on deliberation time and delay aversion using SPSS (IBM SPSS Statistics, Version 27). The remaining neurocognitive outcome variables (overall proportion bet, risk-taking, and quality of decision-making) are reported as β-distributed proportions and as such were examined using quasi-binomial logistic regressions in R 4.2.2.[43] All analyses controlled for age, sex, and IQ. False discovery rate (FDR) was used to correct for multiple comparisons among the 5 tests.[44] Post hoc tests were performed for any significant neurocognitive outcome variables using FDR to correct for multiple comparisons.

Sensitivity analyses were conducted to individually examine the effect of medication (current second-generation antipsychotic use, current lithium use), mood symptoms (current DRS score, current MRS score), and comorbid ADHD on the CGT performance among youth with BD. A series of sensitivity analyses were performed with each variable of interest added individually into the main model alongside the original covariates (age, sex, and IQ). We opted to examine current second-generation antipsychotic and lithium use, as these were the most common medications (> 40% of the BD group). Given the higher rates of BD-I in the BD_{SH-} group, a sensitivity analyses was performed comparing BD_{SH+} and BD_{SH-} in BD-I participants only to examine the effect of BD subtype. In addition, a sensitivity analysis was conducted to concurrently examine the effect of current lithium use, current DRS score, and current MRS score alongside the original covariates (age, sex, and IQ) on CGT performance among youth with BD.

Finally, youth with BD and history of a suicide attempt (and/or NSSI; BD_{SA}) were compared to youth with BD and a history of NSSI (BD_{NSSI}) to examine the effect of NSSI versus co-occurring suicide attempt on CGT performance. Sensitivity analyses were performed examining these 3 groups (BD_{SA}, BD_{NSSI}, and BD_{SH-}) to examine the effect of medication (current second-generation antipsychotic use, current lithium use), mood symptoms (current DRS score, current MRS score), and comorbid ADHD on the CGT performance. A series of sensitivity analyses examining each of the 5 CGT outcome variables using the same analytic approach as the primary analyses between the BD groups individually covaried for each of the aforementioned variables in addition to age, sex, and IQ. In all sensitivity analyses, false discovery FDR was used to correct for multiple comparisons among the 5 tests.[44] Post hoc tests were performed for any significant neurocognitive outcome variables using FDR to correct for multiple comparisons.

RESULTS

A total of 163 youth completed the neurocognitive assessment (52 BD_{SH+}, 29 BD_{SH-}, and 82 controls). The

Table 1.

Demographic and Clinical Characteristics[a]

Variable	Controls (n = 82)	BD_{SH-} (n = 29)	BD_{SH+} (n = 52)	Statistic	*P* Value	Effect Size
Demographics						
Age, y[b]	17.08 ± 1.67	17.71 ± 1.88	17.24 ± 1.92	1.72	.18	0.01
SES[c]	4.45 ± 0.89	4.69 ± 0.47	4.12 ± 1.02	7.46	**.02**[d]	0.05
Sex, female, n (%)	45 (55)	12 (41)	41 (79)	12.79	**.002**[d,e]	0.28
Race, White, n (%)	50 (61)	26 (90)	38 (73)	8.74	**.01**	0.23
Intact family, n (%)	55 (67)	22 (76)	31 (60)	3.00	.23	0.14
Tanner Stage[40,c]	4.20 ± 0.68	4.24 ± 0.64	4.59 ± 0.73	14.68	**.001**[e]	0.06
CGAS score[38]						
Most severe past episode	…	43.14 ± 8.29	42.48 ± 9.05	0.32	.75	0.08
Highest past year[a]	90.29 ± 4.49	72.50 ± 11.92	68.04 ± 9.86	144.12	**<.001**[e,f]	0.59
Past month[a]	89.95 ± 4.72	65.83 ± 11.50	63.24 ± 11.79	184.38	**<.001**[e,f]	0.62
Clinical characteristics						
BD diagnosis				11.30	**<.01**	0.37
BD-I, n (%)	…	16 (55)	10 (19)			
BD-II, n (%)	…	5 (17)	20 (38)			
BD-NOS, n (%)	…	8 (28)	22 (42)			
Age at onset, y	…	15.36 ± 2.97	15.09 ± 2.21	0.44	.66	0.11
Lifetime psychosis, n (%)	…	13 (45)	11 (21)	5.00	.03	0.25
Lifetime suicide attempts, n (%)	…	0	17 (33)	…	…	…
Lifetime self-injurious behavior, n (%)	…	0	48 (92)	…	…	…
Lifetime suicidal ideation, n (%)	…	13 (45)	41 (79)	9.70	**.002**	0.35
Legal history, n (%)	…	6 (21)	12 (23)	0.06	.80	0.03
Lifetime physical abuse, n (%)	…	2 (9)	3 (6)	0.16	.69	0.05
Lifetime sexual abuse, n (%)	…	0	3 (6)	1.47	.23	0.15
Lifetime any abuse (physical and/or sexual), n (%)	…	2 (8)	5 (10)	0.11	.74	0.04
Lifetime psychiatric hospitalization, n (%)	…	13 (45)	19 (37)	0.54	.58	0.08
Current depression score	…	12.66 ± 9.77	18.58 ± 10.56	−2.48	**.02**	0.58
Lifetime depression score[c]	…	26.24 ± 12.63	34.19 ± 9.07	−2.99	**<.01**	0.76
Current mania score[c]	…	5.69 ± 8.28	13.02 ± 12.30	−3.19	**<.01**	0.66
Lifetime mania score	…	31.00 ± 10.20	31.96 ± 9.20	−0.43	.67	0.10
IQ	110.2 ± 11.9	108.7 ± 11.7	106.4 ± 14.5	1.43	.24	0.02
Lifetime comorbid diagnoses						
ADHD, n (%)	…	13 (45)	24 (46)	0.01	.91	0.01
Oppositional defiant disorder, n (%)	…	5 (17)	17 (33)	2.25	.13	0.17
Conduct disorder, n (%)	…	0	1 (2)	0.57	.45	0.08
Any anxiety disorder, n (%)	…	18 (62)	49 (94)	13.47	**<.001**	0.41
Number of anxiety disorders	…	1.52 ± 1.62	2.40 ± 1.46	−2.52	**.01**	0.59
Substance use disorder, n (%)	…	6 (21)	11 (21)	0.04	.84	0.03
Nicotine use (yes/no),[c] n (%)	…	10 (34)	17 (33)	0.03	.87	0.02
Family psychiatric history,[39] **n (%)**						
Mania/hypomania	…	18 (62)	19 (37)	4.89	**.03**	0.25
Depression	…	20 (69)	43 (83)	2.03	.15	0.16
Suicide attempt	…	9 (31)	17 (33)	<0.01	1.00	<0.01
Anxiety	…	19 (66)	31 (60)	0.27	.60	0.06
ADHD	…	16 (55)	16 (31)	4.64	**.03**	0.24
Substance use disorder	…	6 (21)	15 (29)	0.65	.42	0.09

(continued)

Table 1 (continued).

Variable	Controls (n = 82)	BD_{SH-} (n = 29)	BD_{SH+} (n = 52)	Statistic	*P* Value	Effect Size
Lifetime medications, n (%)						
SGA	...	23 (79)	40 (77)	0.06	.80	0.03
Lithium	...	13 (45)	9 (17)	7.10	**<.01**	0.30
SSRI antidepressants	...	10 (34)	27 (52)	2.28	.13	0.17
Non-SSRI antidepressants	...	5 (17)	12 (23)	0.38	.54	0.07
Stimulants	...	6 (21)	11 (21)	<0.01	0.96	0.01
Lamotrigine	...	5 (17)	9 (17)	<0.01	0.99	<0.01
Divalproex	...	3 (10)	3 (6)	0.57	0.45	0.08
Any medication	...	26 (90)	46 (88)	0.03	0.87	0.02
Current medications, n (%)						
SGA	...	17 (59)	28 (54)	0.17	0.68	0.05
Lithium	...	7 (24)	5 (10)	3.11	0.08	0.20
SSRI antidepressants	...	2 (7)	5 (10)	0.17	0.68	0.05
Non-SSRI antidepressants	...	0	1 (2)	0.57	0.45	0.08
Stimulants	...	1 (3)	2 (4)	<0.01	0.93	0.01
Lamotrigine	...	5 (17)	5 (10)	1.00	0.32	0.11
Divalproex	...	0	0	...	...	...
Any medication	...	22 (76)	33 (63)	1.31	0.25	0.13

[a]Test statistic represents *F*, *t*, or χ^2. Effect sizes are Cramer *V*, η^2, or Cohen *d*. Values are reported as mean ± SD unless otherwise indicated. Boldface indicates statistical significance. Depression score based on Depression Rating Scale and mania score based on Mania Rating Scale.
[b]Kruskal-Wallis test reported.
[c]Homogeneity of variance violated, Welsh test reported.
[d]Post hoc pairwise comparisons significant BD_{SH+} vs BD_{SH-}.
[e]Post hoc pairwise comparisons significant BD_{SH+} vs controls.
[f]Post hoc pairwise comparisons significant BD_{SH-} vs controls.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, BD = bipolar disorder, BD_{SH-} = youth with bipolar disorder and no history of self-harm, BD_{SH+} = youth with bipolar disorder and a history of self-harm, CGAS = Children's Global Assessment Scale, NOS = not otherwise specified, SES = socioeconomic status, SGA = second-generation antipsychotic, SSRI = selective serotonin reuptake inhibitor.

demographic characteristics of the 3 study groups and clinical characteristics of the BD groups are reported in Table 1. There were more females in the BD_{SH+} group compared to BD_{SH-} and control groups.

Compared to BD_{SH-}, BD_{SH+} youth had higher rates of suicidal ideation ($P < .01$), more severe lifetime depression ($P < .01$) and higher current depression symptom scores ($P = .02$), more severe current mania symptoms ($P < .01$), and higher rates of anxiety disorders ($P < .001$). In contrast, BD_{SH-} youth had greater rates of family history of BD ($P = .03$) and ADHD ($P = .03$) and higher lifetime lithium use ($P < .01$) compared to BD_{SH+} youth. There was no difference between groups in terms of family history of suicide attempts.

Control youth had the following lifetime psychiatric diagnoses: 7 (9%) had any anxiety disorder, 7 (9%) had ADHD, and 1 (1%) had a lifetime substance use disorder. There were no control youth with a history of self-harm or currently taking psychotropic medication.

Cambridge Gambling Task

CGT scores for each group are reported in Table 2. Full regression tables are reported in Supplementary Table 2. There was a significant difference in overall proportion of points bet (Figure 1A; $F_{2,157} = 3.87$, $P_{FDR} = .04$, $\eta^2 = 0.23$), such that BD_{SH-} youth performed better than both BD_{SH+} ($P_{FDR} = .02$) and control youth ($P_{FDR} = .02$). Deliberation time was also significant (Figure 1B; $F_{3,156} = 4.12$, $P_{FDR} = .04$, $\eta^2 = 0.03$), with BD_{SH-} youth deliberating longer than controls ($P_{FDR} = .03$). There were no significant differences between BD_{SH+} youth and BD_{SH-} youth or controls on deliberation time. Risk-taking was significantly different between groups (Figure 1C; $F_{2,157} = 3.83$, $P_{FDR} = .04$, $\eta^2 = 0.23$), with BD_{SH-} youth showing greater self-control compared to both BD_{SH+} ($P_{FDR} = .01$) and control youth ($P_{FDR} = .01$). There was no significant difference between groups on the quality of decision-making or delay aversion.

Sensitivity Analyses

In a series of analyses of covariance (ANCOVAs) controlling for current depression symptoms and current mania symptoms individually, all results from the primary analyses remained significant after correction for multiple comparisons. After control for current second-generation antipsychotic use, risk-taking and overall proportion bet remained significant. None of the primary results remained significant after control for current lithium use. Risk-

Table 2.

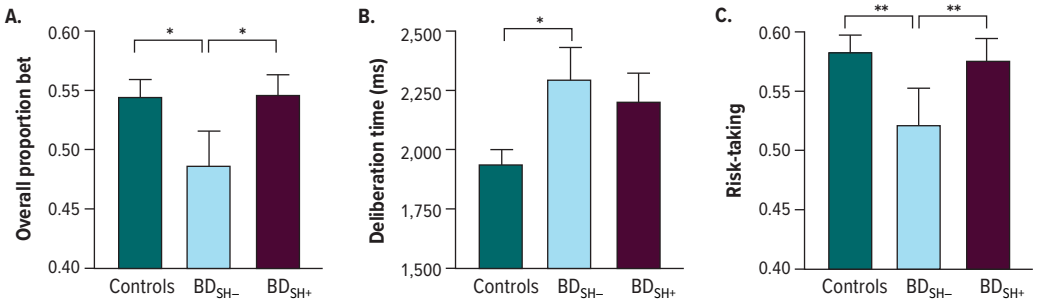
Cambridge Gambling Task[a]

Variable	Controls (n = 82)	BD_{SH-} (n = 29)	BD_{SH+} (n = 52)	Statistic	Uncorrected *P* Value	FDR-Corrected *P* Value	Effect Size
Overall proportion bet	0.55 ± 0.13	0.49 ± 0.15	0.55 ± 0.13	3.87	**.02**	**.040**	0.05
Risk-taking	0.58 ± 0.12	0.52 ± 0.17	0.57 ± 0.13	3.83	**.02**	**.040**	0.06
Deliberation time	3.27 ± 0.13	3.34 ± 0.13	3.32 ± 0.15	4.20	**.017**	**.040**	0.05
Delay aversion	0.28 ± 0.23	0.26 ± 0.25	0.39 ± 0.23	2.33	.10	.13	0.03
Quality of decision-making	0.94 ± 0.09	0.94 ± 0.08	0.92 ± 0.11	0.44	.64	.56	<0.01

[a]Values are shown as mean ± SD unless otherwise noted. Boldface indicates statistical significance. Effect size is reported as η^2.
Abbreviations: BD_{SH-} = youth with bipolar disorder and no history of self-harm, BD_{SH+} = youth with bipolar disorder and a history of self-harm, FDR = false discovery rate.

Figure 1.

Cambridge Gambling Task Outcomes for (A) Overall Proportion Bet, (B) Deliberation Time, and (C) Risk-Taking[a]



[a]For overall proportion bet (A), youth with bipolar disorder and no history of self-harm (BD_{SH-}) bet fewer points compared to both youth with bipolar disorder and a history of self-harm (BD_{SH+}) and controls. For deliberation time (B), BD_{SH-} youth deliberated longer compared to control youth. For risk-taking (C), BD_{SH-} youth bet fewer points on trials for which they had chosen the more likely outcome compared to both BD_{SH+} youth and controls.
*P < .05, **P < .01

taking and overall proportion bet remained significant after control for current ADHD. In sensitivity analyses concurrently controlling for current lithium use, current DRS score, and current MRS score among youth with BD, overall proportion bet and risk-taking remained significant.

Sensitivity analyses focused on BD-I subtype, as there were lower rates of this subtype within the group with self-harm. Findings were similar to those for the full BD sample: overall proportion bet and risk-taking were significantly different between BD_{SH+} and BD_{SH-} youth after correction for multiple comparisons within the BD-I subgroup, whereas deliberation time was not.

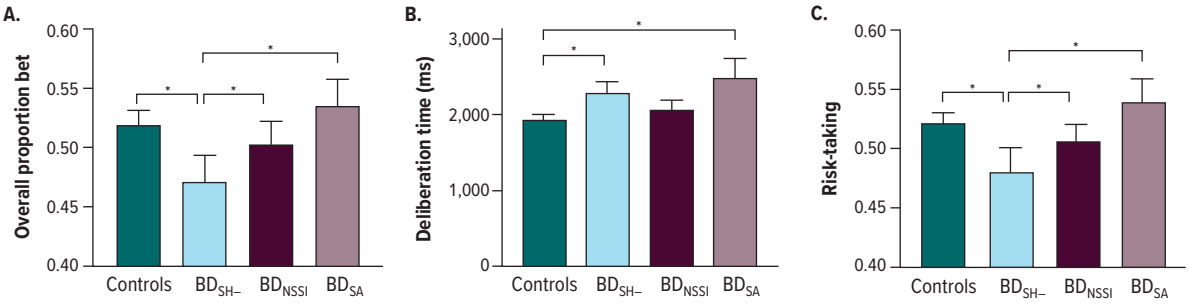
Within the BD group, there were 17 youth with a history of a suicide attempt (13 of whom also reported a history of NSSI), 35 youth with a history of NSSI only (no suicide attempt), and 29 youth without a history of either NSSI or suicide attempt. In analyses comparing these 4 groups, risk-taking and deliberation time remained significant; however, results did not remain significant after correction for multiple comparisons (see Table 3). Although the omnibus test for the overall proportion bet showed a significant trend (P < .080), FDR-corrected post hoc comparisons showed differences between groups. Post hoc analyses for overall proportion bet (Figure 2A) and risk-taking (Figure 2C) followed a pattern similar to that of the primary 3-group contrast, with BD_{SH-} youth betting fewer points compared to youth with BD and a history of NSSI, youth with BD and a history of suicide attempt, and control youth. For deliberation time (Figure 2B), youth with a history of suicide attempt and BD_{SH-} youth deliberated significantly longer than control youth; there were no other significant pairwise comparisons. Overall proportion bet and risk-taking remained significant in sensitivity analyses comparing the 3 BD groups (those with a history of suicide attempt[s], NSSI, or none) with control for medications, mood status, and comorbid ADHD.

DISCUSSION

The current study extends the sparse literature regarding neurocognitive phenotypes associated with self-harm among youth with BD, by focusing on a gambling task that assays risk-sensitive decision-making (CGT). BD_{SH-} youth differed from BD_{SH+} youth and

Figure 2.

Sensitivity Analyses Examining Suicide Attempt and Cambridge Gambling Task Outcomes for (A) Overall Proportion Bet, (B) Deliberation Time, and (C) Risk-Taking[a]



[a]For overall proportion bet (A), youth with bipolar disorder and no History of self-harm BD$_{SH-}$ bet fewer points compared to youth with bipolar disorder and a history of non-suicidal self-injurious behavior (BD$_{NSSI}$), youth with bipolar disorder and a history of suicide attempt (BD$_{SA}$), and controls. For deliberation time (B), BD$_{SH-}$ and BD$_{SA}$ youth deliberated longer compared to control youth. For risk-taking (C), BD$_{SH-}$ youth bet fewer points on trials for which they had chosen the more likely outcome compared to BD$_{NSSI}$, BD$_{SA}$, and control youth.
*P < .05.

Table 3.

Sensitivity Analyses

Variable	Controls (n = 82)	BD$_{SH-}$ (n = 29)	BD$_{NSSI}$ (n = 35)	BD$_{SA}$ (n = 17)	Statistic	Uncorrected *P* Value	FDR-Corrected *P* Value	Effect Size
Overall proportion bet	0.55 ± 0.13	0.49 ± 0.15	0.53 ± 0.13	0.57 ± 0.11	3.17	.08	.13	0.05
Risk-taking	0.58 ± 0.12	0.52 ± 0.17	0.56 ± 0.13	0.61 ± 0.12	4.00	**.047**	.12	0.05
Deliberation time	3.27 ± 0.13	3.34 ± 0.13	3.30 ± 0.14	3.37 ± 0.17	3.88	**.010**	.05	0.07
Delay aversion	0.28 ± 0.23	0.26 ± 0.25	0.42 ± 0.20	0.33 ± 0.28	1.86	.14	.18	0.04
Quality of decision-making	0.94 ± 0.09	0.94 ± 0.08	0.94 ± 0.10	0.87 ± 0.12	0.01	.91	.91	0.03

[a]Values are shown as mean ± SD unless otherwise noted. Boldface indicates statistical significance. Effect size is reported as η^2. Post hoc pairwise comparisons showed controls differed from BD$_{SH-}$ on deliberation time (P = .045), with no other differences between groups. There were no significant differences between groups in pairwise post hoc tests on overall proportion bet or risk-taking.
Abbreviations: BD$_{NSSI}$ = youth with bipolar disorder and a history of non-suicidal self-injury, BD$_{SA}$ = youth with bipolar disorder and a history of a suicide attempt, BD$_{SH-}$ = youth with bipolar disorder and no history of self-harm, FDR = false discovery rate.

from control youth on their performance of decision-making and risk-taking. We speculate this may be reflective of a compensatory process among BD$_{SH-}$ youth. There are life consequences to impulsivity, and there are individual differences in the extent to which individuals are able to integrate prior contingencies and outcomes (ie, they are able to protect themselves against negative consequences via less risky decision-making), serving a protective role mitigating suicide risk.[45]

We found that youth differed on the overall proportion of points bet across all trials, with lower scores indicating greater self-control. This outcome measure is hypothesized to assess youth's risk-sensitive decision-making. Specifically, BD$_{SH-}$ youth bet fewer points, indicating greater self-control compared to BD$_{SH+}$ youth and compared to control youth. We also found a significant difference between groups on deliberation time, with lower scores representing better decision-making, as there is no additional information presented over time. Post hoc tests showed BD$_{SH-}$ youth deliberated longer than control youth, whereas there were no significant differences in BD$_{SH+}$ youth. Lastly, we found a significant difference between groups on risk-taking, which is the average proportion of current points bet when odds were in the youth's favor. BD$_{SH-}$ youth had lower scores, representing greater self-control, compared to both BD$_{SH+}$ and control youth.

While the finding that BD$_{SH+}$ youth make more risky decisions compared to BD$_{SH-}$ youth was anticipated, we did not anticipate that BD$_{SH-}$ youth would make less risky decisions compared to control youth. It remains unclear whether this finding represents a conscious or unconscious process in cognitive control during the task. This finding may represent a learned adaptive response to aversive experiences that requires the recognition of a risk having been taken, the recognition of the consequences of that risk, and the ability to modify future approaches to similar circumstances.[46] While the similar lack of significant difference between BD$_{SH+}$ and control groups was unexpected, it is important to note that there are no prior youth BD studies on this topic that include a control group. Interestingly, we found a similar pattern of findings in our prior study such that BD$_{SH-}$ youth had

altered resting-state functional connectivity compared to both BD_{SH+} youth and healthy controls in regions relating to emotion processing and regulation.[26] Task-based functional magnetic resonance imaging (fMRI) studies examining risk-sensitive decision-making would allow us to gain valuable information on whether these youth without a history of self-harm have altered activation in regions relating to behavioral inhibition. Additional studies with larger sample sizes are needed to adequately examine these subtle phenotypic differences in risk-taking and self-harm.

In sensitivity analyses, we divided the self-harm group into youth with a history of a suicide attempt versus with those with NSSI only and found a pattern of results similar to that of our primary analyses. Interestingly, youth with a history of a suicide attempt were more likely to place greater bets and had lower self-control on measures of risk-taking and overall proportion bet compared to youth with a history of NSSI only. These signals require future larger studies with better power to assess these subgroup analyses. With respect to deliberation time, youth with a history of a suicide attempt deliberated significantly longer than control youth, whereas there was no significant difference between youth with history of NSSI and control youth. This finding may relate to a planning tendency in youth with history of suicide attempt versus those with only history of NSSI. Furthermore, this finding may relate to a specific type of suicide attempt, and future studies with larger samples are needed to compare deliberation time in youth with impulsive suicide attempts versus those with planned suicide attempts. Suicide attempt impulsivity has not been found to be associated with lethality in youth; however, in adults, impulsive attempts are associated with lower lethality.[47]

A study of depressed adults with BD found no difference on the IGT between those with versus without a prior suicide attempt.[24] In contrast to the current study, a prior study found young adults with a history of suicide attempt had lower quality of decision-making on the CGT compared to those without a history of suicide attempt.[25] There are only 4 studies to date examining risk-taking and decision-making in youth. Only one study reported on the CGT and, similar to the current study, found that youth with a suicide attempt history were more likely to take larger risks compared to psychiatric controls.[12] On the IGT, youth with a history of a suicide attempt have shown impaired decision-making; specifically, these youth were not able to learn advantageous strategies as the healthy controls were able to.[11] In contrast to the current findings, youth with a history of suicide attempt were previously found to be more likely to make low-risk decisions on the IGT compared to youth without a history of suicide attempt and healthy controls,[9] and another study found no differences between youth with a history of suicide attempt and controls on risk-taking and decision-making as measured by the IGT.[10] Importantly, the IGT begins with ambiguous uncertainty of the outcomes (ie, participants do not know which decks are high versus low risk); however, as the task progresses, participants are expected to learn from experience and gain information on which decks are high versus low risk. Whereas the CGT is a decision-making task in which decisions are made under known risk (that is, the participant has all of the information available to them at the time they place their bet), and there is no learning aspect involved in the task.

To our knowledge, this study is the only one assessing the relationship between risk-related decision-making and self-harm in a sample of youth with BD. Aligning with the current findings, adults with BD-I and a history of a suicide attempt displayed poorer decision-making on the IGT, and poorer decision-making was associated with greater number of suicide attempts.[48] Other studies among adults with BD have found no differences between groups in terms of suicidality.[49,50]

As expected, there were multiple clinical differences between youth with BD with and without a history of self-harm. Importantly, lifetime lithium use was more common among BD_{SH-} youth as compared to BD_{SH+} youth. Lithium is recognized as having antisuicidal properties, although its effect on self-harm more broadly is less clear.[51] While the current study is cross-sectional and observational, euthymic adults with BD treated with lithium had better decision-making on the IGT compared to patients not treated with lithium.[52] Lithium has also been shown to reduce aggressive impulsivity in animal models.[53] We speculate that lithium use in the current sample may contribute in part to the better performance of BD_{SH-} youth in making non-risky decisions.[52,54,55] Present findings add to the literature linking lithium with reduced impulsivity/risk-taking. Future studies with larger samples are needed to adequately control for current lithium use in primary analyses. BD_{SH+} youth had higher rates of suicidal ideation, more severe depression and mania symptom scores, and higher rates of anxiety disorders compared to BD_{SH-} youth. Furthermore, BD_{SH+} youth were more likely to be female. The overall more severe illness phenotype in BD_{SH+} youth may be associated with impairments in inhibitory processes relevant to risk-taking; however, future studies with larger samples are needed to examine the association of various clinical factors in relation to neurocognition and self-harm.

The current findings highlight the importance not only of a psychiatric control group but also of a psychiatrically healthy control group. The current study examined 3 groups and had both BD_{SH-} youth, serving as psychiatric controls, and youth without major psychiatric illness, serving as healthy controls. Although our findings are in line with previous studies, had we compared only within BD, we would not have observed that BD youth with a history of self-harm are similar

to control youth and, in fact, that BD youth without a history of self-harm differed from both of these groups.[12]

The findings in this study are constrained by several limitations. First, the cross-sectional design of the study limits our ability to infer causality in the relationship between self-harm and neurocognitive performance. The current study examined self-harm at any point among youth with BD; however, it would be interesting to examine neurocognitive performance soon after a self-harm behavior or immediately prior to self-harm. The recency of self-harm behaviors has previously been associated with poorer decision-making skills in youth, whereas youth who self-harmed longer than 1 month ago did not differ in decision-making abilities from controls.[10] The sample size is another important limitation of the current study; in particular the BD group without a history of self-harm was small (n = 29) in relation to the other two groups. Despite sensitivity analyses controlling for mood status, current medications, history of a suicide attempt, and comorbid ADHD, the current study was nonetheless underpowered to adequately control for all sources of heterogeneity simultaneously. Last, the results of this study should be interpreted cautiously given that these neurocognitive measures involve subject choice. Future studies with larger samples sizes and prospective designs with repeated measures are needed to further elucidate the relationship between self-harm and risk-sensitive decision-making among youth with BD.

In conclusion, the findings of the current study show BD_{SH+} youth were more likely, in comparison to BD_{SH-} youth, to take greater risks and make poor decisions. Given that youth with BD are at high risk for suicide, a greater understanding of the underlying neurobiology involved in this risk is crucial to inform individualized prevention strategies. There is an urgent need to understand who is at risk for suicide to target these youth specifically. The results of this study provide preliminary evidence of decision-making deficits associated with self-harm among youth with BD and suggest that improvement in decision-making skills may be beneficial for these youth.

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Supplementary Material

Article Title: Risk-Sensitive Decision-Making and Self-Harm in Youth Bipolar Disorder

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

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Supplementary Materials

Appendix 1:

The following disorders are included in anxiety disorders: generalized anxiety disorder, separation anxiety disorder, agoraphobia, and anxiety disorder not otherwise specified. Eating disorders included anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified. Functioning was assessed using the Children's Global Assessment Scale (CGAS) for current (past month), highest past year, and lifetime most severe episode.[38] CGAS scores are rated from 0-100, with higher scores reflecting better functioning. Physical and sexual abuse history was obtained from a medical history parent-report containing items querying physical and sexual abuse and from the post-traumatic stress disorder screener within the K-SADS-PL.[34] Legal history includes any police contact or arrests. Family psychiatric history was obtained using the Family History Screen interview for all first- and second-degree relatives to ascertain family psychiatric history.[39] The Pubertal Developmental Scale self-report was used to collect pubertal status and reported as Tanner stage (1-5).[40]

Supplementary Table 1. Measurement scale for level of intent and the medical threat of suicidal behaviors.

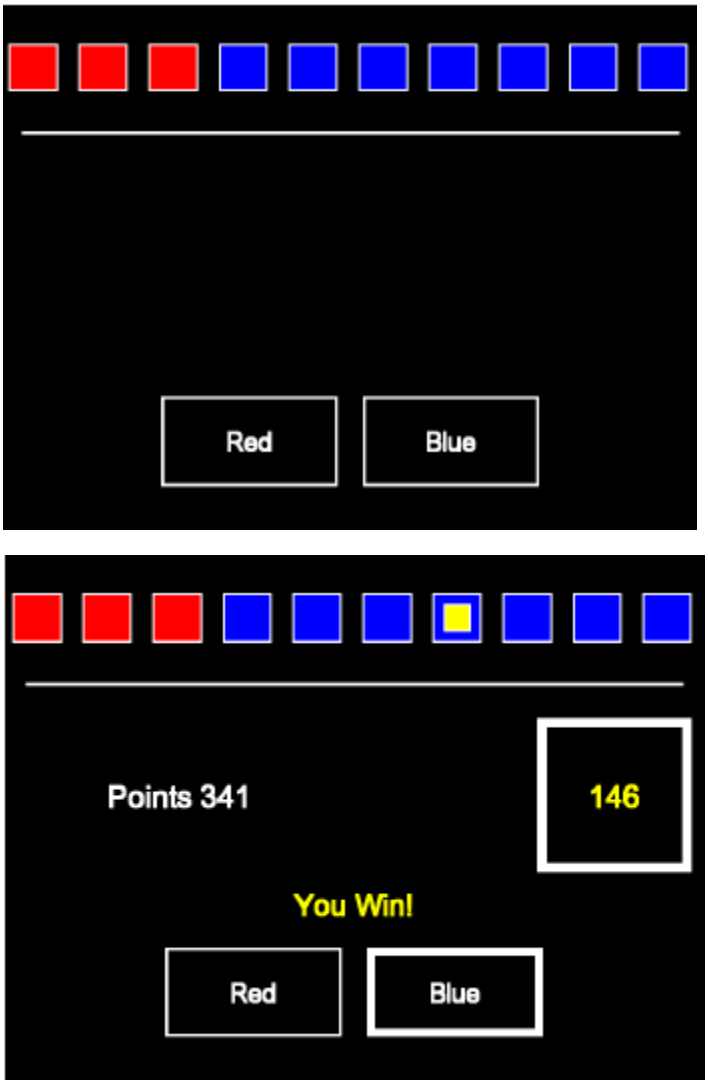
Intent	
0	No information
1	Obviously no intent
2	Only minimal intent
3	Definite but still ambivalent
4	Serious
5	Very serious
6	Extreme (e.g., careful planning and every expectation of death)
Medical Threat	
0	No information
1	No danger (e.g. no effect – held pills in hand)
2	Minimal (e.g. scratch on wrist)
3	Mild (e.g. took ten aspirins – mild gastritis)
4	Moderate (e.g. took ten secobarbital sodium – briefly unconscious)
5	Severe (e.g. cut throat)
6	Extreme (e.g. respiratory arrest or prolonged coma)
7	Death

Supplementary Table 2. Parameter Estimates for Covariates

	B	**Standard Error**	***t***	***p*-value**
Overall Proportion Bet				
Intercept	-0.60	1.22	-0.49	0.62
Age	<0.01	0.02	0.16	0.87
IQ	0.01	0.01	0.98	0.33
Sex	0.63	0.71	0.88	0.38
BD_{SH+}	0.05	0.09	0.53	0.59
BD_{SH-}	-0.28	0.11	-2.50	0.01
Controls[a]				
Risk-taking				
Intercept	-0.61	1.28	-0.48	0.63
Age	<0.01	0.02	0.16	0.88
IQ	0.01	0.01	1.12	0.26
Sex	0.71	0.74	0.96	0.34
BD_{SH+}	0.03	0.10	0.26	0.80
BD_{SH-}	-0.31	0.12	-2.63	0.01
Controls[a]				
Deliberation Time				
Intercept	3.95	0.31	12.76	<0.001
Age	<-0.01	<0.01	-0.80	0.43
IQ	<-0.01	<0.01	-2.04	0.04
Sex	-0.33	0.18	-1.81	0.07
BD_{SH+}	0.05	0.02	1.95	0.05
BD_{SH-}	0.08	0.03	2.63	0.01
Controls[a]				

	B	**Standard Error**	***t***	***p*-value**
Delay Aversion				
Intercept	0.92	0.54	1.70	0.09
Age	-0.02	0.01	-1.81	0.07
IQ	<-0.01	<0.01	-0.90	0.37
Sex	-0.14	0.32	-0.43	0.67
BD_{SH+}	0.09	0.04	2.10	0.04
BD_{SH-}	<0.01	0.05	0.166	0.88
Controls[a]				
Quality of Decision-making				
Intercept	4.39	3.55	1.24	0.22
Age	<0.01	0.07	0.13	0.90
IQ	-0.02	0.03	-0.57	0.57
Sex	-3.35	1.99	-1.68	0.09
BD_{SH+}	-0.20	0.28	-0.70	0.48
BD_{SH-}	<0.01	0.35	-0.02	0.98
Controls[a]				

Note: BD_{SH-} = Youth with bipolar disorder and no history of self-harm; BD_{SH+} = Youth with bipolar disorder and a history of self-harm; Beta values are unstandardized. [a]The control group was used as the reference category.



Supplementary Figure 1. Cambridge Gambling Task. Depiction of the Cambridge Gambling Task set up within the Cambridge Neuropsychological Test Automated Battery (CANTAB).

34. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997;36(7):980-988.

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