Neurocognitive Functioning and Impulsivity in Veterans With Bipolar Spectrum Disorders:

Suicide Attempters Versus Nonattempters

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Abstract

Objective: Veteran status and bipolar disorder (BD) are two substantial risk factors for suicide. Models of suicide implicate neurocognition and impulsivity in suicidal behavior. We aim to examine neurocognitive dysfunction and impulsivity correlates of suicide in veterans with BD.

Methods: We included 29 veterans with a *DSM-5* bipolar spectrum disorder with a suicide attempt history (BD/SA+), 33 veterans with bipolar spectrum disorder without a suicide attempt history (BD/SA-), and 22 healthy control veterans (HC) recruited between January 2021 and July 2023. Participants were administered the MATRICS Consensus Cognitive Battery; Barratt Impulsivity Scale; Urgency, Premeditation, Perseverance, Sensation Seeking, Positive Urgency Impulsive Behavior Scale; and Impulsive/Premeditated Aggression Scale.

Results: BD/SA+ performed worse on working memory than BD/SA–; mean difference (MD [95% CI], –5.74 [–10.65 to –0.82], $P = .034$) and HC (–10.31 [–15.77 to –4.85], $P < .001$). BD/SA+ also performed worse on verbal learning than BD/SA– (MD [95% CI], –4.49 [–8.41 to –0.57], $P = .038$) and HC (–5.52 [–9.87 to –1.16], $P = .038$). Differences between BD/SA+ and BD/SA– in working memory remained significant when adjusting for depressive ($P = .037$) and manic ($P = .024$) symptoms, but verbal learning was no longer significantly different when adjusted for depression. BD/SA+ also had higher scores than BD/SA– on impulsive (MD [95% CI], 3.68 [0.64 to 6.73], $P = .018$) and premeditated (5.80 [1.51 to 10.10], $P = .013$) aggression. Across the BD groups, poorer working memory was associated with greater premeditated aggression ($r = –0.321$, $P = .013$) while poorer verbal learning was associated with greater impulsive ($r = –0.297$, $P = .021$) and premeditated ($r = –0.372$, $P = .003$) aggression.

Conclusion: Results suggest that in veterans with BD, poorer working memory is associated with suicide attempt independent of depression, while verbal learning impairments associated with suicide attempt may be influenced by depression. Neurocognitive dysfunction may underlie aggression to drive suicidal behavior. Findings support the role of neurocognition in models of suicide in BD and can inform risk detection and intervention.

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Suicide is a leading cause of death and a major public health concern, with over 49,000 people in the US dying by suicide in 2022.[1] The majority of individuals who attempt suicide have psychiatric disorders,[2–4] and bipolar disorder (BD) in particular is associated with one of the highest rates of suicide,[5,6] at 20–30 times that of the general population.[7,8] Military veterans are also at elevated suicide risk, with the age-adjusted suicide rate being 72% higher than nonveteran US adults in 2021.[9] Among veterans with any mental health disorder, those with BD have the highest suicide rate,[9] yet very few studies have investigated mechanisms underlying suicide behavior in this population.

Models of suicide posit that neurocognitive deficits contribute to negative appraisal and difficulty problem-solving during distress, leading to feeling trapped, hopelessness, and the desire to escape by suicide.[10,11] Neurocognitive impairments may be particularly relevant for suicide risk in BD, given the deficits in memory, executive functioning, and attention/processing speed in this disorder,[12–14] even during

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Clinical Points

- Veterans with bipolar disorder (BD) are at substantially elevated risk for suicide, yet specific cognitive correlates of suicide risk remain unclear.
- Working memory and verbal learning impairments may be considered when assessing suicide risk in this population.
- Findings suggest that treatments that target cognitive functioning, emotion regulation, and problem-solving could potentially mitigate against suicide in BD.

euthymia.[12–16] Although cognitive impairments have been implicated in suicide attempts across psychiatric diagnoses,[17–20] neuropsychological studies of suicide attempt in BD are sparse, with mixed results. Some studies reported that BD patients with a history of suicide attempt performed worse than BD nonattempters on a measure of decision-making, impulsivity, and risk taking[21] and on an immediate memory task,[22] while others found no difference between these groups on attention, executive functioning, memory, social cognition, processing speed, and decision-making.[21,23,24]

Neurocognitive impairments may underlie the impulsive and aggressive traits that are observed in BD[25–27] and associated with suicide risk.[28–31] Impulsivity refers to a tendency for rapid, unplanned reactions with little regard for consequences,[32] while aggression involves proneness toward acts of physical or verbal attacks, anger, and hostility.[33,34] Impulsivity has been conceptualized to include domains of motor, attentional, and nonplanning impulsivity[35] or domains of positive and negative urgency (ie, acting rashly when experiencing strong positive or negative emotions, respectively), lack of premeditation, lack of perseveration, and sensation seeking.[36] Evidence suggests that suicide attempts in BD are associated with greater impulsivity,[37,38] particularly positive and negative urgency.[38–40] Aggressive acts can be predominantly impulsive or predominantly premeditated.[33] Impulsive aggression is a loss of behavioral control during agitated mood when responding to a provocation,[33] while premeditated aggression involves planned aggression while not in an agitated state.[33] Understanding how impulsivity in BD may manifest in aggressive behavior can inform mechanisms of suicide risk; however, a distinction between impulsive and premediated aggression has rarely been used to study suicide in BD. In two studies of BD, one found that impulsive aggression was associated with greater suicidality,[41] while the other found that premeditated aggression, but not impulsive aggression, was associated with suicide attempt history.[38]

Despite the potential role of neurocognition and impulsivity in the elevated suicide rate in veterans with BD, the literature in this area is limited. The goal of this study was to examine neurocognitive functioning, impulsive traits, and aggression in veterans with BD with and without a history of a suicide attempt. We hypothesized that veterans with BD and a suicide attempt history would perform worse in neurocognitive domains that have been implicated in suicide, including executive functioning, memory, and social cognition. We also hypothesized that they would have greater impulsivity, particularly negative and positive urgency, and more impulsive aggression. We further predicted that worse neurocognitive functioning would be associated with greater impulsivity and impulsive aggression.

METHODS

Participants

Participants were US veterans recruited from the James J. Peters Veterans Affairs Medical Center (JJPVA) in Bronx, New York, between January 2021 and July 2023. Participants were recruited as part of a neuroimaging study examining the relationship of impulsivity and its underlying brain mechanisms to suicide in veterans with BD. All study procedures were approved by the Institutional Review Board (IRB), and all participants provided written informed consent prior to study procedures. General inclusion criteria were veteran status, age 18–65 years, and English language proficiency. Exclusion criteria were head injury with loss of consciousness >30 minutes, any significant neurological/medical disorders that could contribute to cognitive deficits and interfere with study procedures, any contraindication for neuroimaging (eg, metal in body), or any current severe substance use disorder. See Supplementary Figure 1 for a flowchart of sample selection.

Patients were recruited through flyers, community outreach, and JJPVA inpatient and outpatient clinician referrals. Given that BD pathology exists across bipolar spectrum and schizophrenia spectrum disorders, patients included those that met *DSM-5* criteria for bipolar spectrum disorder including schizoaffective disorder–bipolar type according to the Structured Clinical Interview for *DSM-5* Research Version (SCID-5-RV).[42] Patients were grouped into those with a lifetime history of a suicide attempt (BD/SA+) and those with no lifetime suicide attempt (BD/SA–) based on the Columbia-Suicide Severity Rating Scale (C-SSRS),[43] a gold standard assessment of suicidal ideation and behavior. A suicide attempt history was a lifetime history of ≥1 actual suicide attempts, defined as self-directed potentially injurious behavior with any intent to die, consistent with standard definition.[44,45] Patients in the BD/SA– group did not have any history of aborted,

interrupted, or actual attempts. Patients with only aborted or interrupted attempts, but no actual attempts, were excluded from the current analysis.

Healthy controls (HC) were recruited through IRB-approved advertisements targeting veterans who were not currently suffering from symptoms of mental illness. HCs did not have any lifetime major mood or psychotic disorders, history of suicidal behaviors, lifetime substance use disorder that was greater than mild in severity, or any substance use disorder within the past 3 months.

Materials and Procedures

All participants were assessed by a licensed psychologist or a trained graduate-level clinician supervised by a licensed psychologist. Results of the SCID-5 and C-SSRS were discussed in meetings led by clinical psychologists (C.C.C., P.R.S.) to arrive at consensus diagnosis and suicide attempt status.

Neurocognitive performance was assessed using the MATRICS Consensus Cognitive Battery (MCCB)[46] which has been validated for use in BD.[47–50] The MCCB consists of 10 standardized tests of 7 cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem-solving, and social cognition.[46] We used age- and sex-adjusted *T* scores based on published norms.[51]

Impulsivity was measured using the Barratt Impulsiveness Scale (BIS-11)[35] and the Urgency, Premeditation, Perseverance, Sensation Seeking, Positive Urgency (UPPS-P) Impulsive Behavior Scale.[36] Total and subscale scores of the BIS-11 were calculated as the sum of items on each subscale. For the UPPS-P, scores were calculated as the mean of the item scores on each subscale. Impulsive and premeditated aggression over the past 6 months was assessed using the Impulsive/Premeditated Aggression Scale (IPAS).[33] Scores were calculated as the sum of the items on each subscale.[33]

Current mood symptoms were assessed using clinician-rated scales. Depressive symptoms were rated using the Hamilton Rating Scale for Depression (HAM-D),[52] while manic and associated psychotic symptoms were rated using the Clinician-Administered Rating Scale for Mania (CARS-M).[53]

Statistical Analysis

Descriptive statistics, χ^2 tests, and analysis of variance (ANOVA) were used to characterize and compare groups on demographic and clinical characteristics. Given the substantial clinical and biological overlap between schizophrenia and BD[54,55] that challenges their traditional nosological distinction, we analyzed schizoaffective disorder–bipolar type and BD together. Prevalence of psychosis history did not differ between BD/SA+ and BD/SA– (Table 1), and few participants were actively psychotic (see Results); therefore, we did not adjust for psychosis. Separate 1-way multivariate analysis of variance (MANOVA) was used to examine group differences in the 7 neurocognitive domain scores of the MCCB, the 5 subscales of the UPPS-P, the 3 subscales of the BIS-11, and the 2 subscales of the IPAS. Post hoc pairwise tests were corrected for multiple comparisons using the false discovery rate (FDR)[56] correction. Composite and total scores on each measure were analyzed separately using ANOVA to minimize multicollinearity.

Pearson correlations were used to examine the relationship of neurocognition with impulsivity and aggression. Missing data (<5%) were imputed using multivariate imputation with chained equations.[57] One HC had no data on any of the HAM-D items. Three HC had no data on any of the CARS-M items. Two HCs and 2 BD/SA+ had no data on any of the BIS-11 items. Three HC, 1 BD/SA–, and 2 BD/SA+ had no data on any of the UPPS-P items. Two HC and 2 BD/SA+ had no data on any of the IPAS items. Therefore, these data were not imputed, and pairwise deletion was used for the analyses. Alpha value was set at 0.05. Analyses were conducted in R[58] and SPSS.[59]

RESULTS

Participants

A total of 84 veterans were included: 22 HC, 33 BD/SA–, and 29 BD/SA+. Sample characteristics are presented in Table 1. Groups did not differ significantly in distributions of age, sex, race, or education. At the time of assessment, patients scored in the minimal to mild range on mood symptoms on average, and 8 patients were experiencing psychotic symptoms (6 in BD/SA– and 2 in BD/SA+). BD/SA+ reported more depression than BD/SA– and HC. Both patient groups had greater manic symptoms and were more likely to have a lifetime history of substance use disorder than HC. BD/SA– and BD/SA+ did not differ significantly on distributions of BD-I vs other bipolar spectrum disorder, antipsychotic, mood stabilizer, or antidepressant medication use, current mania, history of psychosis, or lifetime or current substance use disorder. The BD/SA+ group had an average of 4.1 suicide attempts in their lifetime, 25% of whom had their most recent attempt(s) within the past year.

Neurocognitive Functioning

The MANOVA on the MCCB domains revealed a significant overall effect of group; $F_{14,\ 150} = 2.16$, Wilks lambda = 0.693, $P = .012$. Univariate tests indicated that there were significant effects of group on processing speed, working memory, verbal learning, visual learning,

Table 1.

Sample Demographic and Clinical Characteristics

	HC (n = 22) n (%) or mean (SD)	BD/SA– (n = 33) n (%) or mean (SD)	BD/SA+ (n = 29) n (%) or mean (SD)	Statistics	Post hoc (LSD)
Demographic factors					
Age	44.4 (12.9)	40.1 (10.2)	45.2 (11.2)	$F_{2, 81} = 1.80$, $P = .172$	…
Sex, male	18 (81.8)	30 (90.9)	20 (69.0)	$X^2_2 = 4.84$, $P = .089$	…
Race				$X^2_4 = 3.24$, $P = .519$	…
Hispanic/Latinx	8 (36.4)	16 (48.5)	13 (44.8)		
Non-Hispanic White	6 (27.3)	10 (30.3)	5 (17.2)		
Other	8 (36.4)	7 (21.2)	11 (37.9)		
Education				$X^2_4 = 8.53$, $P = .074$	…
≤High school diploma	5 (22.7)	5 (15.2)	11 (37.9)		
Some college	4 (18.2)	15 (45.5)	8 (27.6)		
≥4-year degree	13 (59.1)	13 (39.4)	10 (34.5)		
Clinical factors					
Diagnosis	…			$X^2_1 = 2.66$, $P = .103$	…
BD-I		16 (48.5)	20 (69.0)		
BD-II, other BD, or SZA-BP		17 (51.5)	9 (31.0)		
Depression (HAM-D)[a]	2.33 (3.3)	4 (4.3)	7 (6.0)	$F_{2, 80} = 6.31$, $P = .003$	BD/SA+ > BD/SA–, HC
Mania (CARS-M)[b]	0.5 (1.0)	7.3 (8.3)	6.3 (6.3)	$F_{2, 77} = 6.61$, $P = .002$	BD/SA+, BD/SA– > HC
History of psychosis	…	13 (39.4)	12 (41.4)	$X^2_1 = 0.025$, $P = .874$	…
Antipsychotic medication	…	24 (72.7)	21 (72.4)	$X^2_1 = 0.001$, $P = .978$	…
Mood stabilizer medication	…	18 (54.5)	20 (69.0)	$X^2_1 = 1.35$, $P = .245$	…
Antidepressant medication	…	9 (27.3)	13 (44.8)	$X^2_1 = 2.08$, $P = .149$	…
Lifetime substance use disorder	3 (13.6)	21 (63.6)	21 (72.4)	$X^2_1 = 19.59$, $P < .001$	BD/SA+, BD/SA– > HC
Current (past 3 months) substance use disorder	…	4 (12.1)	6 (20.7)	$X^2_1 = 0.838$, $P = .360$	…

[a]1 HC missing HAM-D data.
[b]3 HC missing CARS-M data.
Abbreviations: BD-I = bipolar I disorder, BD-II = bipolar II disorder, BD/SA– = bipolar disorder with no history of suicide attempt, BD/SA+ = bipolar disorder with history of suicide attempt, CARS-M = Clinician-Administered Rating Scale for Mania, HAM-D = Hamilton Depression Rating Scale, HC = healthy controls, LSD = least significant difference, SZA-BP = schizoaffective disorder–bipolar type.

and reasoning and problem-solving (Table 2; Figure 1), while attention/vigilance was trend-level but did not reach statistical significance ($P = .056$). Post hoc pairwise comparisons with FDR correction indicated that for the composite score and domains of processing speed, visual learning, and reasoning and problem-solving, both BD/SA– and BD/SA+ performed worse than HC, with no difference between BD/SA– and BD/SA+. BD/SA+ trended toward lower composite score than BD/SA– but did not reach statistical significance ($P = .053$). For working memory, BD/SA+ performed worse than BD/SA–, mean difference (MD) [95% CI], –5.74 [–10.65 to –0.82], $P = .034$, Cohen $d = 0.59$ and HC (–10.31 [–15.77 to –4.85], $P < .001$, Cohen $d = 1.09$). Similarly for verbal learning, BD/SA+ performed worse than BD/SA– (MD [95% CI], –4.49 [–8.41 to –0.57], $P = .038$, Cohen $d = 0.55$) and HC (–5.52 [–9.87 to –1.16], $P = .038$, Cohen $d = 0.87$). HC and BD/SA– did not differ on working memory and verbal learning (Ps > .05).

Given that working memory and verbal learning were significantly different between BD/SA– and BD/SA+, we further investigated whether these differences were due to mood state. We conducted 1-way ANCOVAs covarying for depression and mania. For working memory, poorer performance in BD/SA+ than BD/SA– remained when controlling for both depression (MD [95% CI], –5.57 [–10.79 to –0.35], $P = .037$, Cohen $d = 0.56$) and mania (MD [95% CI], –5.79 [–10.80 to –0.77], $P = .024$, Cohen $d = 0.59$). For verbal learning, poorer performance in BD/SA+ than BD/SA– remained when controlling for mania (MD [95% CI], –4.64 [–8.80 to –0.47], $P = .030$, Cohen $d = 0.57$). However, ANCOVA-adjusted verbal learning group differences were no longer statistically significant when controlling for depression ($P = .115$).

Impulsivity and Aggression

The MANOVA on the BIS-11 subscales revealed a significant overall effect of group; $F_{6, 150} = 3.63$, Wilks lambda = .762, $P = .002$. Univariate tests indicated that there were significant effects of group on the attention, motor, and nonplanning subscales (Table 3). BD/SA– and BD/SA+ groups scored higher than HC on all 3 subscales; however, there was no significant difference between the patient groups on any of the subscales.

Table 2.

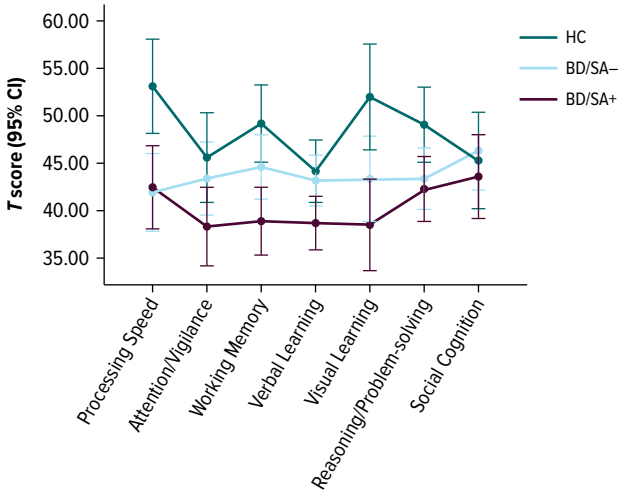
Between-Group Differences on Neurocognitive Performance on the MCCB[a]

	HC	BD/SA–	BD/SA+	Univariate *F* test	FDR-corrected post hoc
Processing Speed	52.91 (10.77)	41.73 (13.09)	42.28 (10.95)	$F_{2, 81} = 6.98$, $P = .002$	**SA– < HC, *P* < .003** **SA+ < HC, *P* = .003** SA+ vs SA–, $P = .856$
Attention/Vigilance	45.36 (11.36)	43.17 (12.3)	38.1 (9.29)	$F_{2, 81} = 2.98$, $P = .056$	…
Working Memory[b]	49 (9.61)	44.42 (10.04)	38.69 (9.4)	$F_{2, 81} = 7.23$, $P = .001$	SA– vs HC, $P = .091$ **SA+ < HC, *P* < .001** **SA+ < SA–, *P* = .034**
Verbal Learning[c]	44 (6.35)	42.97 (9.49)	38.48 (6.34)	$F_{2, 81} = 3.95$, $P = .024$	SA– vs HC, $P = .630$ **SA+ < HC, *P* = .038** **SA+ < SA–, *P* = .038**
Visual Learning	51.82 (11.38)	43.15 (11.99)	38.31 (15.18)	$F_{2, 81} = 6.77$, $P = .002$	**SA– < HC, *P* = .027** **SA+ < HC, *P* = .001** SA+ vs SA–, $P = .149$
Reasoning/Problem-solving	48.86 (10.35)	43.21 (8.91)	42.07 (9)	$F_{2, 81} = 3.68$, $P = .030$	**SA– < HC, *P* = .046** **SA+ < HC, *P* = .036** SA+ vs SA–, $P = .632$
Social Cognition	45.09 (11.36)	46.12 (12.50)	43.41 (11.67)	$F_{2, 81} = 0.401$, $P = .671$	…
Composite Score	46.54 (11.13)	39.21 (10.81)	33.69 (11.26)	$F_{2, 81} = 8.47$, $P < .001$	**SA– < HC, *P* = .027** **SA+ < HC, *P* < .001** SA+ vs SA–, $P = .053$

[a]Neurocognition scores are presented as *T* scores, and statistical results are shown without covarying for mood symptoms.
[b]Group difference between BD/SA+ and BD/SA– remained significant for working memory after controlling for depressive and manic symptoms.
[c]Group difference between BD/SA+ and BD/SA– remained significant when controlling for mania but was no longer significant after controlling for depressive symptoms.
Abbreviations: BD/SA– = bipolar disorder with no history of suicide attempt, BD/SA+ = bipolar disorder with history of suicide attempt, FDR = false discovery rate, HC = healthy controls, MCCB = MATRICS Consensus Cognitive Battery.

Figure 1.

Cognitive Performance on the MCCB Among Healthy Controls, Bipolar Disorder Without History of Suicide Attempt, and Bipolar Disorder With History of Suicide Attempt



Abbreviations: BD/SA– = bipolar disorder with no history of suicide attempt, BD/SA+ = bipolar disorder with history of suicide attempt, HC = healthy controls, MCCB = MATRICS Consensus Cognitive Battery.

BD/SA+ showed a trend toward higher inattention scores than BD/SA– but did not reach statistical significance ($P = .095$).

The MANOVA on the UPPS-P subscales revealed a significant overall effect of group; $F_{10, 144} = 2.03$, Wilks lambda = .768, $P = .034$. Univariate tests indicated significant effects of group on negative and positive urgency (Table 3). For negative urgency, BD/SA+ scored significantly higher than HC, with no significant difference between patient groups. BD/SA+ showed a trend toward higher scores than BD/SA– but did not reach statistical significance ($P = .068$). For positive urgency, both the BD/SA+ and BD/SA– groups scored significantly higher than HC, with no difference between the patient groups.

The MANOVA on the IPAS subscales revealed a significant overall effect of group; $F_{4,152} = 5.82$, Wilks lambda = .752, $P < .001$. Univariate tests indicated that there were significant effects of group on both the Impulsive Aggression and Premeditated Aggression subscales (Table 3). For the Impulsive Aggression subscale, BD/SA+ scored significantly higher than BD/SA– (MD [95% CI], 3.68 [0.64–6.73], $P = .018$, Cohen $d = 0.60$), and both patient groups scored significantly higher than HC. For the Premeditated Aggression subscale, BD/SA+ had higher scores

Table 3.
Between-Group Differences on Impulsive Traits and Aggression

	HC	BD/SA–	BD/SA+	Univariate *F* test	FDR-corrected post hoc
Impulsivity (BIS)[a]					
Attention	14.35 (4.52)	17.70 (5.47)	19.81 (4.13)	$F_{2, 77} = 7.39$, $P = .001$	**SA– > HC, *P* = .017** **SA+ > HC, *P* < .001** SA+ vs SA–, $P = .095$
Motor	20.50 (3.82)	24.36 (5.25)	24.67 (4.17)	$F_{2, 77} = 5.77$, $P = .005$	**SA– > HC, *P* = .006** **SA+ > HC, *P* = .006** SA+ vs SA–, $P = .799$
Nonplanning	21.00 (4.89)	24.94 (4.89)	26.81 (5.75)	$F_{2, 77} = 7.33$, $P = .001$	**SA– > HC, *P* = .014** **SA+ > HC, *P* < .001** SA+ vs SA–, $P = .168$
Total score	55.85 (10.49)	67.00 (13.65)	71.30 (9.88)	$F_{2, 77} = 10.33$, $P < .001$	**SA– > HC, *P* = .002** **SA+ > HC, *P* < .001** SA+ vs SA–, $P = .162$
Impulsivity (UPPS-P)[b]					
Negative urgency	1.94 (0.64)	2.28 (0.68)	2.64 (0.66)	$F_{2, 76} = 6.46$, $P = .003$	SA– vs HC, $P = .070$ **SA+ > HC, *P* = .002** SA+ vs SA–, $P = .068$
(Lack of) premeditation	1.77 (0.51)	2.07 (0.61)	2.07 (0.5)	$F_{2, 76} = 2.23$, $P = .114$	...
(Lack of) perseveration	1.82 (0.39)	2 (0.63)	1.98 (0.52)	$F_{2, 76} = 0.734$, $P = .484$	...
Sensation seeking	2.62 (0.76)	2.78 (0.7)	2.65 (0.75)	$F_{2, 76} = 0.386$, $P = .681$	...
Positive urgency	1.58 (0.48)	2.16 (0.72)	2.31 (0.81)	$F_{2, 76} = 6.66$, $P = .002$	**SA– > HC, *P* = .008** **SA+ > HC, *P* = .002** SA+ vs SA–, $P = .408$
Total score	1.94 (0.10)	2.27 (0.08)	2.35 (0.09)	$F_{2, 76} = 5.24$, $P = .007$	**SA– > HC, *P* = .012** **SA+ > HC, *P* = .008** SA+ vs SA–, $P = .498$
Aggression (IPAS)[c]					
Impulsive aggression	17.95 (5.2)	22.24 (6.95)	25.93 (4.87)	$F_{2, 77} = 10.54$, $P < .001$	**SA– > HC, *P* = .018** **SA+ > HC, *P* < .001** **SA+ > SA–, *P* = .018**
Premeditated aggression	27.7 (6.46)	28.61 (8.91)	34.41 (8.73)	$F_{2, 77} = 4.96$, $P = .009$	SA– vs HC, $P = .701$ **SA+ > HC, *P* = .013** **SA+ > SA–, *P* = .013**
Total score	45.65 (2.67)	50.85 (2.08)	60.33 (2.29)	$F_{2, 77} = 9.44$, $P < .001$	SA– vs HC, $P = .128$ **SA+ > HC, *P* < .001** **SA+ > SA–, *P* = .003**

[a]2 HC and 2 BD/SA+ missing BIS data.
[b]2 HC, 1 BD/SA–, and 2 BD/SA+ missing UPPS-P data.
[c]2 HC and 2 BD/SA– missing IPAS data.
Abbreviations: BD/SA– = bipolar disorder with no history of suicide attempt, BD/SA+ = bipolar disorder with history of suicide attempt, BIS-11 = Barratt Impulsiveness Scale, FDR = false discovery rate, HC = healthy control, IPAS = Impulsive/Premeditated Aggression Scale, UPPS-P = Urgency, Premeditation, Perseverance, Sensation Seeking, Positive Urgency Impulsive Behavior Scale.

compared to BD/SA– (MD [95% CI], 5.80 [1.51–10.10], $P = .013$, Cohen $d = 0.66$) and HC, with no difference between HC and BD/SA–.

Relationship of Neurocognition with Impulsive and Premeditated Aggression

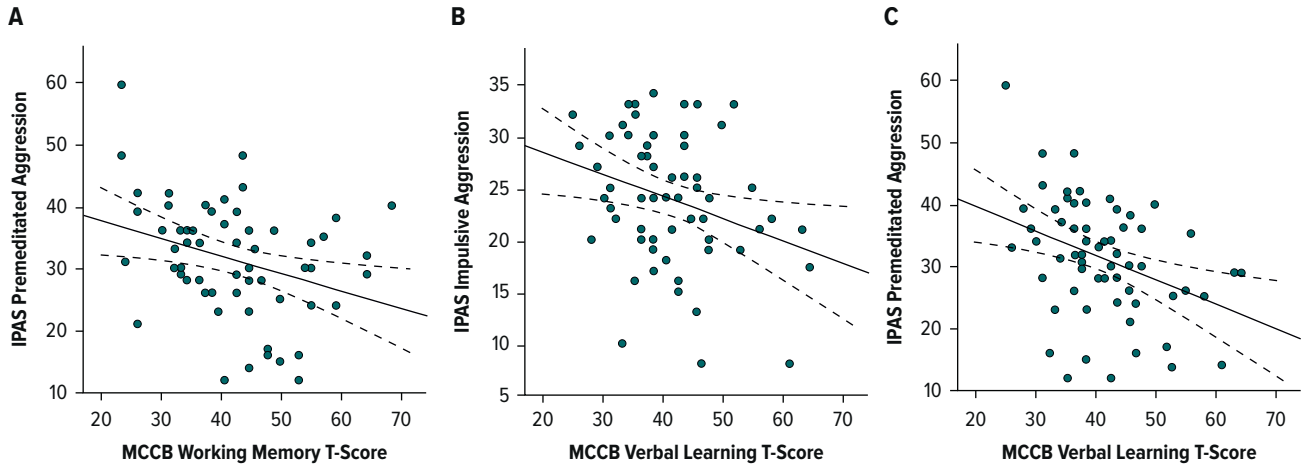
We examined whether the observed group differences between BD/SA+ and BD/SA– in working memory and verbal learning were related to the observed group differences in impulsive and premeditated aggression. In the patient groups combined, poorer working memory performance was associated with higher premeditated aggression ($r = –0.321$, $P = .013$; Figure 2A). In addition, poorer verbal learning performance was associated higher impulsive aggression ($r = –0.297$, $P = .021$; Figure 2B) and higher premeditated aggression ($r = –0.372$, $P = .003$; Figure 2C).

DISCUSSION

Bipolar disorder and military veteran status are two strong risk factors for suicide, but, to our knowledge, this is the first study of neuropsychological and impulsivity correlates of suicide attempts in veterans with BD. Consistent with models of suicide and empirical studies,[19,60] we found that impaired working memory was associated with suicide attempt, even after adjusting for depression. Working memory is critical for complex cognitive functioning[61]; therefore, impairments may lead to difficulty problem-solving, feelings of entrapment and defeat, and ultimately a desire to escape by suicide.[11,62] In contrast, verbal learning was no longer associated with suicide attempt after adjusting for depression, suggesting that depression may underlie verbal learning impairments associated with suicidal behavior. This finding aligns with

Figure 2.

Correlation Between MCCB Domains and Impulsive-Premeditated Aggression Scale Subscales in the Bipolar Patient Groups Combined[a]



[a]Left panel (A) shows correlation between working memory and premeditated aggression, center panel (B) shows correlation between verbal learning and impulsive aggression, and right panel (C) shows correlation between verbal learning and premeditated aggression.
Abbreviations: IPAS = Impulsive-Premeditated Aggression Scale, MCCB = MATRICS Consensus Cognitive Battery.

prior work showing that depression can exacerbate verbal learning impairments in BD (see Kurtz and Gerraty[15]) and extends the implications of impaired verbal learning to suicide in this population. Brain abnormalities in prefrontal and temporal regions that are found in BD[63,64] and that underlie working memory and verbal learning may be associated with suicide behavior, as shown in veterans with major depression.[65]

Our cognitive findings are inconsistent with some studies that did not find neurocognitive differences between BD suicide attempters and nonattempters,[23,24] possibly due to differences in sample and methods. Hasse-Sousa et al[23] used neuropsychological tests adapted for their Brazilian sample, which differs from the present study on versions of cognitive assessments used and sample characteristics. Their paper also did not specify how suicide behavior was assessed, and thus our studies potentially differ in definition or assessment of suicide behavior. Gilbert et al[24] did not find group differences in verbal learning. However, their groups were matched on depression; therefore, our finding that group differences in verbal learning was no longer significant when controlling for depression is consistent with their null result. Importantly, neither studies were in veterans, a predominantly male group with unique experiences and comorbidities that elevate their suicide risk.[66]

We found only trend-level differences between BD/SA+ and BD/SA– on impulsivity while the more robust findings were in aggression. BD/SA+ was higher in impulsive aggression than both BD/SA– and HC, with BD/SA– higher than HC. Consistent with the literature,[38,41,67] this finding suggests that impulsive aggression is increased in BD and that among BD, those with the greatest impulsive aggression may be at highest suicide risk. However, this was not specific to impulsive aggression, as BD/SA+ also exhibited greater premeditated aggression than BD/SA–. Results suggest that facets of aggression, or aggression with impulsivity (ie, impulsive aggression), may be more closely associated with suicidal behavior than impulsivity alone. Previous works show that in suicide attempters, impulsivity and aggression are correlated[68,69] and that impulsive aggression is increased compared to nonattempters.[29,70,71] Taken together, our results and existing work highlight the importance of the combination of impulsivity *and* aggression for risk when comparing BD attempters vs nonattempters.[68,69] The correlation between cognitive performance and aggression is consistent with suicide models that suggest neurocognitive dysfunction may prohibit adequate problem-solving to reduce distress, making aggression the dominant response.[72]

There were limitations to this study. The sample included a range of bipolar spectrum disorders including schizoaffective disorder–bipolar type, which likely introduced heterogeneity. Given that our findings were more robust in impulsive and premeditated aggression than impulsivity alone, our limited assessment of aggression did not allow for a more comprehensive examination of the role of aggression in risk for suicide attempt. Incorporating behavioral tasks of impulsivity and aggression in future work will be important. The study's sample size was small, which reduced the power to detect weaker effects and

precluded the ability to perform diagnostic subgroup or moderator analysis. The small sample may not be representative, limiting in generalizability to the larger population of veterans with BD. The use of a cross-sectional design does not allow modeling of directional effects; future studies employing a longitudinal design with larger sample sizes could potentially elucidate causal mechanisms underlying suicide attempts. Larger investigations could also address potential confounds such as military deployment status, trauma, sociodemographic factors, and level of social integration that were not included in the current study.

In conclusion, we found that neurocognitive impairments and greater impulsive and premeditated aggression were associated with suicide attempt in veterans with BD. Theories of suicide indicate that a key determinant of suicide attempt is "capacity," which can be acquired by habituation to fear-inducting situations and knowledge of lethal means.[62,73,74] Given that military experiences can contribute to suicide capacity, our results highlight the importance of understanding and mitigating potentially modifiable risk factors in this population, such as cognitive impairment and aggression. Our findings could guide neurobiological models of suicide and inform targets for pharmacologic or cognitive interventions. Interventions such as cognitive remediation, emotion regulation, and problem-solving therapies may help to improve problem-solving skills and downstream effects on aggression and suicidal thoughts and behavior.

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The Journal of Clinical Psychiatry

Supplementary Material

Article Title: Neurocognitive Functioning and Impulsivity in Veterans With Bipolar Spectrum Disorders: Suicide Attempters Versus Nonattempters

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

1. **Figure 1** Flowchart of Sample Selection

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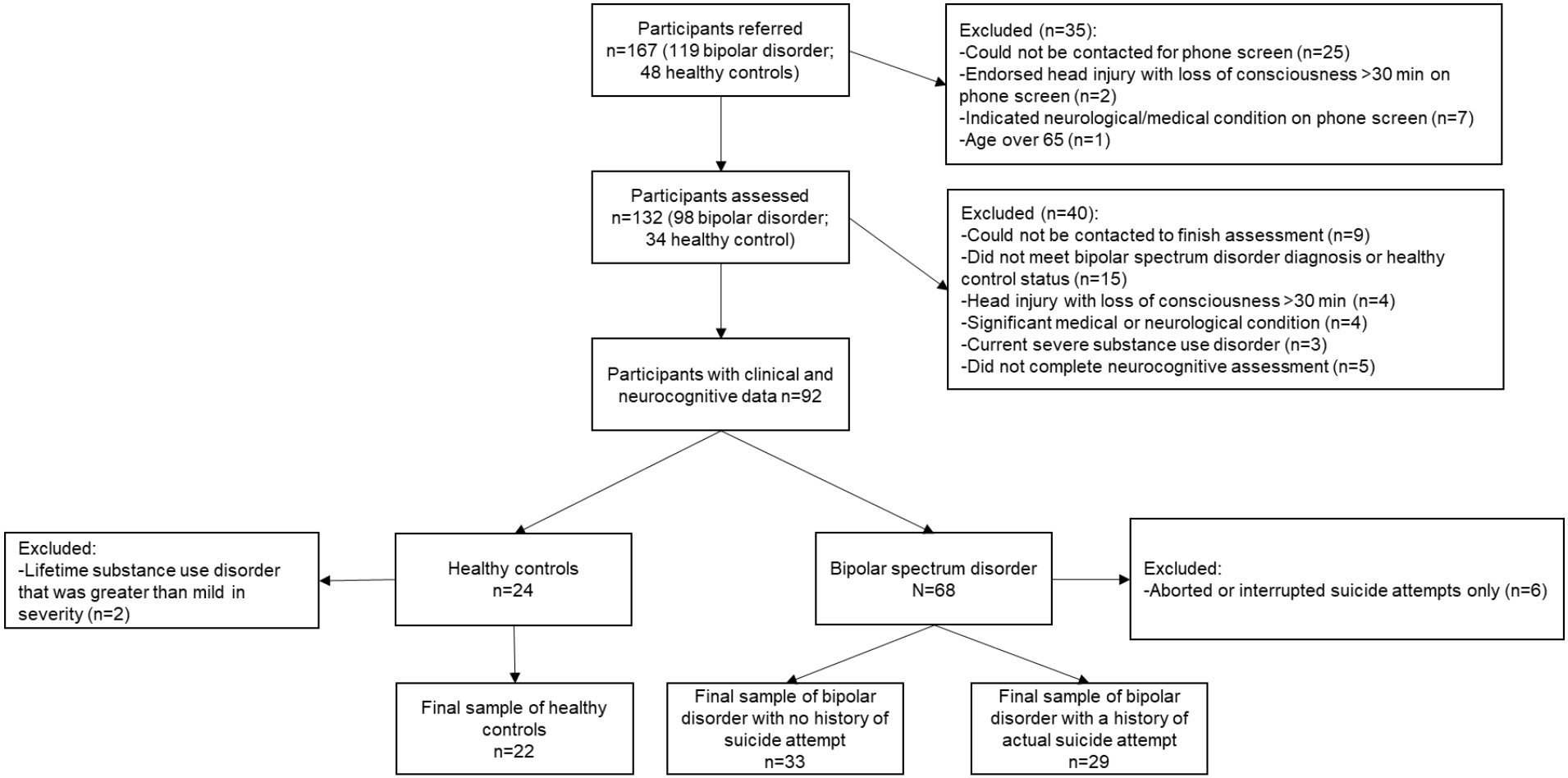

Supplementary Figure 1. Flowchart of sample selection