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Mild traumatic brain injury burden moderates the relationship between cognitive functioning and suicidality in Iraq/Afghanistan-era Veterans

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Abstract

Objective: Suicidal ideation (SI) is highly prevalent in Iraq/Afghanistan-era Veterans with a history of mild traumatic brain injury (mTBI), and multiple mTBIs impart even greater risk for poorer neuropsychological functioning and suicidality. However, little is known about the cognitive mechanisms that may confer increased risk of suicidality in this population. Thus, we examined relationships between neuropsychological functioning and suicidality and specifically whether lifetime mTBI burden would moderate relationships between cognitive functioning and suicidal ideation.

Method: Iraq/Afghanistan-era Veterans with a history of mTBI seeking outpatient services (N=282) completed a clinical neuropsychological assessment and psychiatric and postconcussive symptom questionnaires.

Results: Individuals who endorsed SI reported more severe PTSD, depression, and postconcussive symptoms and exhibited significantly worse memory performance compared to those who denied SI. Furthermore, mTBI burden interacted with both attention/processing speed and memory, such that poorer performance in these domains was associated with greater likelihood of SI in individuals with a history of three or more mTBIs. The pattern of results remained consistent when controlling for PTSD, depression, and postconcussive symptoms.

Conclusions: Slowed processing speed and/or memory difficulties may make it challenging to access and utilize past experiences to solve current problems and imagine future outcomes, leading

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to increases in hopelessness and SI in Veterans with three or more mTBIs. Results have the potential to better inform treatment decisions for Veterans with history of multiple mTBIs.

Keywords

suicidal ideation; neuropsychology; cognition; memory; Operation Iraqi Freedom; Operation Enduring Freedom

Introduction

Prevention of suicide is a public health priority, and there has been a recent increase in attention and concern regarding suicidality in Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) service members and veterans in particular; there is some evidence showing they are at increased risk relative to the general population (e.g., Kang et al., 2015). In an effort to improve veteran suicide prevention, the Department of Veterans Affairs (VA) conducted the largest analysis of veteran suicide rates in United States history, which revealed that an average of 20 veterans per day died from suicide in 2014 (Office of Suicide Prevention, 2016). Thus, it is essential to identify risk factors associated with suicidality in order to improve prevention and intervention approaches for vulnerable veteran populations.

It is well established that psychiatric conditions, particularly depression and posttraumatic stress disorder (PTSD), are prevalent in veterans and are associated with increased risk of suicidal behaviors and suicide completion (Jakupcak et al., 2009; Pietrzak et al., 2010; Pompili et al., 2013; Tanielian & Jaycox, 2008). In fact, research has shown that veterans with psychiatric disorders who utilized Veterans Healthcare Administration (VHA) demonstrated elevated rates of suicide relative to veterans without psychiatric disorders and the general population (e.g., Connor et al., 2013; Ilgen et al., 2010; Kang & Bullman, 2008). However, veterans also commonly experience other concerning conditions that contribute to elevated risk of suicidality, including traumatic brain injury (TBI). Numerous studies across community and military samples have demonstrated that history of TBI confers increased risk of suicidality, including suicidal ideation (SI; Mackelprang et al., 2014; Simpson & Tate, 2002), attempt (Silver, Kramer, Greenwald, & Weissman, 2001; Simpson & Tate, 2002), and completion (Bahraini, Simpson, Brenner, Hoffberg, & Schneider, 2013; Brenner, Ignacio, & Blow, 2011; Fazel, Wolf, Pillas, Lichtenstein, & Langstrom, 2014; Teasdale & Engberg 2001).

Approximately 20% OIF/OEF/OND veterans have experienced a TBI (Tanielian & Jaycox, 2008), with the overwhelming majority (more than 80%) of TBIs experienced falling in the mild range of severity (Defense and Veterans Brain Injury Center, 2017). Psychiatric conditions such as PTSD and depression commonly co-occur in veterans with a history of mild TBI (mTBI) and this comorbidity has been associated with more severe psychiatric and postconcussive symptoms and poorer functioning than mTBI alone (Belanger, Kretzmer, Vanderploeg, & French, 2010; Hoge et al., 2008; Lippa et al., 2015). There has been some debate about whether history of TBI confers additional risk of suicidality above and beyond presence of comorbid psychiatric conditions and symptom severity. This debate appears to

be driven by mixed findings across studies, as several studies have reported that history of TBI, including mTBI, was independently associated with or increased suicide risk when accounting for comorbid mental health conditions (e.g., Brenner et al., 2011; Silver et al., 2001; Simpson & Tate, 2005), whereas others found that TBI did not have an independent influence or increase risk relative to psychiatric conditions alone (e.g., Barnes, Walter, & Chard, 2012; Brenner, Betthausen et al., 2011; Finley et al., 2015).

Some of the discrepant findings across studies may be due to heterogeneity in TBI severity included in the study samples, with many including the full range of TBI severities, whereas others focused specifically on mTBI. Even within the mTBI literature, studies have frequently collapsed across individuals who experienced fewer versus greater lifetime mTBIs. Accumulating evidence indicates that individuals with a history of multiple mTBIs experience poorer outcomes relative to those with 1–2 mTBIs, including worse psychiatric, cognitive, and functional outcomes (Dams-O'Connor et al., 2013; Dretsch, Silverberg, & Iverson, 2015; Iverson, Gaetz, Lovell, & Collins, 2004; Spira, Lathan, Bleiberg, & Tsao, 2014). Thus, a consideration of lifetime mTBI burden may be important when examining suicidality in military and veteran populations and could clarify inconsistent results across studies. In fact, Wisco et al., (2014) showed that a history of multiple TBIs was more strongly associated with SI than history of a single TBI. Similarly, Bryan & Clemans (2013) found that number of TBIs experienced was associated with increased suicide risk and this relationship remained even when accounting for severity of depression, PTSD, and postconcussive symptoms.

Individuals with a history of multiple mTBIs may be at greater risk for suicidality because of the cognitive dysfunction that has been observed across several domains, including attention, processing speed, memory, and executive functioning (e.g., Belanger, Spiegel, & Vanderploeg, 2010; Cancelliere et al., 2014; Iverson, Echemendia, LaMarre, Brooks, & Gaetz, 2012; Iverson et al., 2004; Spira et al., 2014). Furthermore, greater severity of comorbid psychiatric and postconcussive symptoms has been shown to exacerbate neuropsychological dysfunction in these individuals (e.g., Cancelliere et al., 2014). Across numerous non-TBI focused studies, poorer cognitive functioning has been associated with suicidality, particularly in psychiatric populations (e.g., Keilp et al., 2001, 2013, 2014; Pu, Setoyama, & Noda, 2017; Richard-Devantoy, Berlim, & Jollant, 2014, 2015). In terms of TBI samples specifically, there appear to be only two studies conducted thus far examining relationships between neuropsychological functioning and suicidality and included veterans with primarily moderate to severe TBIs. Brenner and colleagues (2015) found that those with a history of both TBI and suicide attempt (SA) were impaired on a test of decision making relative to individuals with TBI history only, SA history only, and those without a TBI or SA. Similarly, Homaifar et al. (2012) showed that individuals with both TBI and SA were more perseverative on a test of executive function compared to those with a history of TBI but no previous SA.

Although these two studies suggest associations between cognitive difficulties and suicidality in veterans with a history of TBI, more research is warranted to better characterize the cognitive mechanisms that may confer increased suicide risk, particularly in individuals with mTBI. Studies examining cognitive risk factors for suicidality (both

ideation and attempt) in other populations have typically focused on executive functioning, predominantly measures of decision making and impulsivity (e.g., Bredemeier & Miller, 2015; Burton, Vella, Weller, & Twamley, 2011; Jollant et al., 2005; Richard-Devantoy et al., 2012). The focus on executive dysfunction is consistent with empirical and theoretical work suggesting that impairments in executive functioning make it difficult to regulate emotions, generate and implement problem solving/coping strategies, inhibit suicidal thoughts and impulsive behaviors, etc. (e.g., Bredemeier & Miller, 2015). However, poorer functioning in other cognitive domains may also play a role in risk of suicide. Other studies of suicidality have suggested that lower-level processes such as impaired processing speed may contribute to executive function difficulties (e.g., Keilp et al., 2014). In addition, there is some evidence that memory problems may increase risk for suicidal behaviors, such that individuals have difficulty accessing and using past experiences to solve current problems and imagine future outcomes, leading to increased hopelessness (Richard-Devantoy et al., 2015).

Therefore, the present study aimed to examine relationships between several domains of cognitive functioning and SI in OEF/OIF/OND veterans with a history of mTBI. SI was of particular interest given that it is common in this population (e.g., Pietrzak et al., 2010; Wisco et al., 2014) and is a well-established risk factor for suicide attempts and completion (e.g., Brown, Beck, Steer, & Grisham, 2000; Mann et al., 2008). We expected that worse performance on cognitive measures, particularly executive function tasks, would be associated with greater risk of suicidal ideation. Furthermore, based on the literature showing that a history of multiple mTBIs is associated with poorer neuropsychological functioning and increased risk for suicidality, we also explored the hypothesis that lifetime mTBI burden would moderate relationships between cognitive functioning and SI. Finally, given that psychiatric symptoms are typically the strongest predictors of suicide risk, we examined whether observed relationships would remain when accounting for psychiatric distress.

Method

Procedure

Veterans with a history of TBI who were seeking clinical services for cognitive complaints at the VA San Diego Healthcare System (VASDHS) completed a comprehensive clinical neuropsychological assessment. Prior to neuropsychological testing, clinical neuropsychologists or advanced doctoral trainees conducted a semi-structured interview to gather details regarding TBI injury characteristics (event history, presence and length of loss of consciousness [LOC] or posttraumatic amnesia [PTA], postconcussive symptoms, etc.), mental health symptoms/diagnoses, and demographic information. Following the clinical interview, neuropsychological measures were administered to assess various cognitive domains including attention, processing speed, executive functioning, and learning and memory.

Retrospective chart reviews were subsequently conducted by experienced research assistants who gathered data from the comprehensive clinical neuropsychological assessments, TBI interviews, and from VA medical records. The VA/Department of Defense (2016) guidelines were used to determine TBI severity classification based on the longest duration of LOC or

PTA reported during the clinical interview. Veterans who had a history of only mild TBI, defined as LOC < 30 minutes and PTA < 24 hours, were included in present analyses; those who sustained a moderate or severe TBI were excluded. When discrepancies were apparent between reported LOC and PTA, the greatest reported LOC or PTA was used to determine severity of injury. All procedures were approved by the VASDHS Institutional Review Board.

Participants

OEF/OIF/OND veterans with a history of mTBI were included in the present study if they were between the ages of 18 and 55, had a standard score of 70 or above on the Wide Range Achievement Test-4 (WRAT-4) Reading subtest, performed within expectations on performance validity measures (see Measures section for details), and completed self-report measures of depression and PTSD symptoms. Based on these inclusion criteria, a total of 282 participants were available for analyses. On average, veterans were 33 years old ($SD = 8.41$) and completed 13 years of formal education ($SD = 1.72$). The sample was predominantly male (93%), Caucasian (63%), and non-Hispanic (69%). Based on self-reported details gathered during the clinical interview along with those available in their medical charts, 59% of the sample experienced LOC and 38% experienced PTA for the worst TBI reported. Data regarding lifetime TBI burden were missing for six participants. The median number of lifetime TBIs was 2.00 ($M = 2.42$, $SD = 1.84$, range = 1–13). This variable was highly skewed with several notable outliers; thus, it was dichotomized (history of 1–2 vs. 3 or more mTBIs) based previous research that used this variable to group individuals and demonstrated that those with 3 or more mTBIs have poorer recovery and worse outcomes (e.g., Belanger et al., 2010; Dretsch et al., 2015; Guskiewicz et al., 2003, 2007; Iverson et al., 2004, 2012; Kerr et al., 2018; Spira et al, 2014). 65% of the sample ($n = 180$) reported experiencing 1–2 TBIs ($M = 1.42$, median = 1.0), whereas 35% ($n = 96$) reported experiencing 3 or more lifetime TBIs ($M = 4.30$, median = 3.0). In terms of mechanism of mTBIs, 64% reported a history of a blast-related TBI. According to medical records, 76% of the sample had a diagnosis of PTSD and 54% had a diagnosis of a depressive disorder.

Measures

Depression and suicidal ideation.—The Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) is a 21-item self-report measure that was used to assess depression symptoms in the past two weeks. Item 9 assesses for suicidal thoughts or wishes and was used to create a dichotomous variable indicating whether or not participants endorsed SI. Participants who endorsed “I don’t have any thoughts of killing myself” were placed in the SI- group ($n = 232$). Those who chose “I have thoughts of killing myself, but I would not carry them out” ($n = 49$) or “I would like to kill myself” ($n = 1$) were placed in the SI+ group ($n = 50$). No participants selected “I would like to kill myself if I had the chance.” This method is consistent with previous studies that used a similar item on a depression measure to create a dichotomous variable indicating the presence or absence of SI in OEF/OIF/OND veteran populations (e.g., Haller et. al, 2015; Hellmuth et al, 2012; Pietrzak et al, 2010). When calculating BDI-II total scores for analyses, item 9 was omitted.

PTSD and postconcussive symptoms.—The PTSD Checklist–Civilian Version (PCL-C; Weathers, Litz, Herman, Huska, & Keane, 1993) is a 17-item self-report measure used to assess PTSD symptoms in the past month. The Neurobehavioral Symptom Inventory (NSI; Cicerone & Kalmar, 1995) is a 22-item self-report measure in which participants rated how much they were disturbed by postconcussive symptoms in the past month. A subset of participants ($n = 57$) did not complete this measure, leaving $n = 225$ available for follow-up analyses using the NSI.

Neuropsychological measures.—The majority of participants received a core set of standard neuropsychological tests that were used in analyses, though the available data for each cognitive domain measured varied slightly due to the clinical nature of the visit (e.g., reason for referral, patient fatigue, time constraints). The WRAT-4 Reading subtest (Wilkinson & Robertson, 2006) standard score was used as a measure of premorbid intellectual functioning. Scaled scores on Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan & Kramer, 2001) Trail Making visual scanning, letter sequencing, and number sequencing subtests were used to assess attention/processing speed. Learning was measured using the California Verbal Learning Memory Test - Second Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000) trials 1–5 learning T-score and the Rey-Osterrieth Complex Figure (ROCF; Meyers & Meyers, 1995) copy trial T-score. Memory was assessed using the CVLT-II long delay free recall z-score and ROCF retention trial T-score. Executive functioning performance was measured using the Wisconsin Card Sorting Test-64 Card Version (WCST-64; Kongs, Thompson, Iverson & Heaton, 2000) perseverative responses T-score, D-KEFS Verbal Fluency switching subtest scaled score, and D-KEFS Trail Making number-letter switching subtest scaled score. Neuropsychological measures were z-scored and averaged by domain to create composite scores. In order to facilitate ease of interpretation of the significant interactions, cognitive composite scores were inverted such that higher scores indicated greater cognitive impairment. Participants were excluded based on suboptimal performance on the Test of Memory Malingering (TOMM; Tombaugh, 1996) or the CVLT-II forced choice condition. Standard cutoffs were used to define suboptimal performance: raw scores below 45 on trial 2 or the retention trial of the TOMM or below 15 on the CVLT-II forced choice condition.

Statistical Analyses

All statistical analyses were conducted in IBM SPSS Statistics, Version 23 (IBM Corp., Armonk, NY). Participants were first divided into two groups based on responses to item 9 (suicidal thoughts or wishes) on the BDI-II as described above: SI endorsers (SI+; $n = 50$) and non-endorsers (SI-; $n = 232$). Chi-square tests and independent t-tests were used to compare groups on demographic variables (age, years of education, gender, race, ethnicity), injury variables (presence of LOC and PTA for worst injury reported, history of blast-related mTBI, lifetime mTBI burden), and symptom measures (PTSD, depression, postconcussive symptoms). Independent samples t-tests were also used to examine group differences on neuropsychological measures of premorbid intellectual functioning, attention/processing speed, learning, memory, and executive functioning. For the neuropsychological measures that were significant in t-test analyses, follow-up logistic regressions examined whether performance on those measures uniquely predicted SI above and beyond PTSD, depression,

and postconcussive symptoms. Each symptom measure was entered into separate regression models to avoid multicollinearity given their significant intercorrelations. Including symptom measures in the same model would lead to suppression and obscure interpretation of the coefficients for each measure (see Cohen, Cohen, West, & Aiken, 2003).

Next, logistic regressions were used to examine whether there were interactive effects between neuropsychological composite scores and mTBI burden (1–2 vs. 3 or more mTBIs) on risk for SI. Composites for each cognitive domain were explored in separate regressions in which the cognitive composite score, TBI burden dichotomous variable, and their interaction were entered. For any significant interactions, additional logistic regression analyses were conducted to determine whether interactions predicted SI above and beyond PTSD, depression, and postconcussive symptoms. Analyses tested whether interactions between cognitive composites and symptom measures should also be included as covariates in these follow-up models. None of the cognitive composite by symptom measure interactions were significant predictors of SI (all p 's $>.12$) and including these interactions in the models of interest did not improve model fit or alter results. Thus, they were not included as covariates in final models reported for parsimony. Logistic regressions employed bootstrapping with 1000 samples in order to provide estimates robust to violations of assumptions given slight skew in the symptom scores.

Results

There were no differences on demographic or injury variables between individuals who endorsed SI versus those who did not (all p 's $>.16$, see Table 1). In terms of symptom measures, the SI+ group endorsed more severe PTSD ($t(280) = 4.66, p <.001, d = 0.68$), depression, ($t(280) = 7.12, p <.001, d = 1.14$), and postconcussive symptoms ($t(223) = 5.54, p <.001, d = 1.05$). In terms of cognitive measures, the SI+ group exhibited significantly worse memory performance relative to the SI- group ($t(268) = -2.73, p = .007, d = 0.43$). There were no group differences in premorbid intellectual functioning ($p = .290$) or in other cognitive domains ($ps >.40$). Worse memory performance remained a significant predictor of SI when controlling for PTSD symptoms ($B = .42, OR = 1.52; 95\% CI = [1.02, 2.27]; p = .039$), depression symptoms ($B = .44, OR = 1.55; 95\% CI = [1.02, 2.35]; p = .033$), and postconcussive symptoms ($B = .62, OR = 1.85; 95\% CI = [1.11, 3.07]; p = .020$; see Table 2)¹.

In the logistic regression examining interactions between cognitive composites and mTBI burden on SI, the interaction between attention/processing speed and mTBI burden predicted SI ($OR = 2.17, 95\% CI = [1.05, 4.46], p = .028$; see Table 3). Probing the interaction using the SPSS PROCESS macro (Hayes, 2012) indicated that there was no relationship between attention/processing performance and risk for SI in those with a history of 1–2 mTBIs ($B = -.23, SE = .24, OR = .80, p = .352$); however, poorer attention/processing speed was significantly associated with greater risk of SI in individuals who experienced 3 or more

¹Although entering all symptom questionnaires into the same model would obscure interpretation of the individual coefficients for the symptom measures and make it appear that PTSD symptoms were unrelated to SI, the coefficient for the memory composite can be interpreted in this context. Worse memory remained a significant predictor of SI ($B = .58, OR = 1.79; 95\% CI = [1.05, 3.04]; p = .031$) when PTSD, depression, and postconcussive symptoms were entered into the same model.

mTBIs ($B = .55$, $SE = .28$, $OR = 1.72$, $p = .048$). The interaction between the attention/processing speed composite and mTBI burden remained significant when controlling for PTSD symptoms ($OR = 2.39$, 95% $CI = [1.13, 5.05]$, $p = .020$), depression symptoms ($OR = 3.42$, 95% $CI = 1.50, 7.79]$, $p = .007$), and postconcussive symptoms ($OR = 3.59$, 95% $CI = [1.37, 9.41]$, $p = .009$) in separate regressions (see Table 3). The pattern of the interaction remained consistent across the three models that included symptom scores as covariates.

The interaction between memory performance and mTBI burden was also significantly associated with SI ($OR = 3.57$, 95% $CI = [1.32, 9.65]$, $p = .009$; see Table 3). Probing the interaction showed a similar pattern as the attention/processing speed composite. There was no relationship between memory performance and risk for SI in those with a history of 1–2 mTBIs ($B = .20$, $SE = .23$, $OR = 1.22$, $p = .377$); however, poorer memory performance was significantly associated with greater risk of SI in individuals who experienced 3 or more mTBIs ($B = 1.47$, $SE = .45$, $OR = 4.36$, $p = .001$). The interaction between the memory performance and mTBI burden remained significant when controlling for PTSD symptoms ($OR = 3.40$, 95% $CI = [1.22, 9.51]$, $p = .018$) and postconcussive symptoms ($OR = 3.16$, 95% $CI = [.98, 10.13]$, $p = .038$) but dropped below significance when accounting for depression symptoms ($OR = 2.48$, 95% $CI = [.90, 6.87]$, $p = .078$; see Table 3). For all three models including symptom measures as covariates, the pattern of the interaction remained consistent. Interactions with mTBI burden and other cognitive domains were not significant: learning ($B = .63$; $OR = 1.87$, 95% $CI = [.70, 4.98]$, $p = .168$) and executive function ($B = .61$; $OR = 1.84$, 95% $CI = [.82, 4.13]$, $p = .102$).

Discussion

The primary goal of the present study was to examine relationships between neuropsychological functioning and suicidality in OEF/OIF/OND veterans with a history of mTBI in order to better characterize the cognitive mechanisms that may confer increased risk of suicide in vulnerable individuals. In particular, we were interested in whether number of lifetime mTBIs would moderate relationships between cognitive functioning and SI, even when considering psychiatric symptom severity, an already well-established risk factor for suicide. Results indicated that memory dysfunction was associated with SI; however, this finding was qualified by an interaction between memory performance and mTBI burden. Specifically, in veterans with greater mTBI burden (three or more reported lifetime mTBIs), memory dysfunction was associated with greater risk of SI. Processing speed also interacted with lifetime mTBIs and demonstrated a similar pattern, such that veterans with a history of multiple mTBIs and poorer processing speed exhibited greater likelihood of suicidality. Observed relationships between cognitive functioning, mTBI burden, and SI remained significant when accounting for psychiatric distress and postconcussive symptoms.

To our knowledge, this is the first study to date that has examined cognitive functioning and SI within a sample of OEF/OIF/OND veterans with a history of mTBI. This is a particularly crucial area of research, given the frequency with which OEF/OIF/OND veterans experience mild TBI, cognitive symptoms, psychiatric distress, and SI (e.g., Tanielian & Jaycox, 2008; Wisco et al., 2014). These factors in combination appear to elevate risk of suicide attempts and completions, though very little is known about how these factors relate to each other and

the mechanisms through which they confer risk. Such research has the potential to inform intervention and prevention efforts in order to reduce rates of suicide in this population and potentially more broadly.

Although there has been very little research investigating relationships between neuropsychological functioning and suicide risk in individuals with a history of TBI of any severity, previous research in non-TBI samples has also implicated memory dysfunction in suicidality. For example, several studies showed that depressed individuals with a previous suicide attempt exhibited poorer performance on tests of verbal and visuospatial memory relative to depressed individuals without a previous attempt and healthy controls (Keilp et al., 2001, 2013, 2014). It has been proposed that memory dysfunction may confer risk for suicidality by making it challenging to retrieve relevant information from previous experiences to use when attempting to solve current problems (Richard-Devantoy et al., 2015). Additionally, such memory-related issues may make it difficult to envision the future and obtain long-term perspective on current stressors, leading to hopelessness (Richard-Devantoy et al., 2015), a factor strongly associated with suicidality (e.g., Brown et al., 2000; Simpson & Tate, 2007). Further evidence supporting this proposal comes from an imaging study that demonstrated overlapping brain regions, including the hippocampus, were involved in the construction and elaboration of both past and future events; thus, common processes appear to be engaged during memory retrieval and future-oriented thinking (Addis, Wong, & Schacter, 2007).

Numerous studies examining neuropsychological risk factors for suicidality in various populations have focused on impairments in higher-level cognitive functions such as executive functioning and memory; however, there has been limited research exploring whether deficits in more fundamental, lower-level processes, particularly information processing speed, may play a role. Prior research has demonstrated that processing speed is often slowed in individuals with a history of TBI, particularly those with comorbid mental health conditions, and contributes to the cognitive deficits that are often observed in these individuals, most notably executive dysfunction (e.g., Jurick et al., 2017; Madigan, DeLuca, Diamond, Tramontano, & Averill, 2000; Nelson, Yoash-Gantz, Pickett, & Campbell, 2009). In the present study, results indicated that, in addition to memory dysfunction, reduced processing speed was associated with greater risk of SI in individuals with a history of multiple mTBIs; however, these domains of cognitive functioning and suicidality were unrelated in those with a history of one or two mTBIs. Thus, these results indicate that future studies in this crucial area of research should consider the role of lifetime mTBI burden in this population and would benefit from examining both basic and higher-level cognitive functions.

Although no studies thus far have considered relationships between lifetime TBI burden and neuropsychological functioning in suicidality, numerous studies have shown that greater number of TBIs is associated with increased risk of SI (Bryan & Clemans, 2013; Wisco et al., 2014), more severe psychiatric and postconcussive symptoms (Dretsch et al., 2015; Iverson et al., 2004; Spira et al., 2014), and poorer overall functioning (Dams-O'Connor et al., 2013). In terms of cognitive outcomes, individuals with a history of 1–2 mTBIs appear to recover and return back to baseline functioning within three months, with no evidence of

enduring neuropsychological dysfunction (e.g., Iverson, Brooks, Lovell, & Collins, 2006). However, those with a history of multiple mTBIs frequently exhibit persisting cognitive impairments, including deficits in processing speed and memory, well past the acute stages of recovery (Belanger et al., 2010; Dams-O'Connor et al., 2013; Iverson et al., 2004, 2012).

In terms of the pathophysiological outcomes resulting from multiple mTBIs, research using various experimental models has demonstrated diffuse axonal injury and demyelination (Bailes, Dashnaw, Petraglia, & Turner, 2014; Fehily & Fitzgerald, 2017), as well as cumulative damage to hippocampal cells (Slemmer, Matser, De Zeeuw, & Weber, 2002). Given that myelin plays a key role in information processing speed and that hippocampal functioning is essential for memory performance, it is not surprising that observed pathophysiological changes in white matter and the hippocampus have been linked to motor and memory dysfunction following multiple mTBIs in both animal and human studies (Mouzon et al., 2012; Multani et al., 2016; Niogi et al., 2008). This line of research in conjunction with present findings informs our understanding of the potential neuropsychological mechanisms through which history of multiple TBIs confers increased risk of suicidality.

Although speculative, it seems reasonable to hypothesize that multiple mTBIs cause various brain changes including diffuse axonal damage, which in turn contribute to processing speed and memory dysfunction, as well as increases in distress; such problems may result in suicidal thoughts and behaviors that are difficult to regulate because of the cognitive impairment that is present. Future research would benefit from testing this causal hypothesis. In addition, future research should examine whether present results generalize to suicidal behaviors, specifically attempts, in individuals with a history of multiple mTBIs. Much of the previous research examining relationships between neuropsychological functioning and suicide attempts has implicated poorer executive functioning, particularly on tests of impulsivity and decision making, across various populations (Bredemeier & Miller, 2015; Burton et al., 2011; Jollant et al., 2005), including individuals with a history of moderate to severe TBI (Brenner et al., 2015; Homaifar et al., 2012). However, it has been proposed that distinct neuropsychological mechanisms may be involved in different aspects of suicidality (e.g., SI versus suicidal behaviors, high-lethality attempts versus low-lethality; Bredemeier & Miller, 2015; Burton et al., 2011; Keilp et al., 2013). This theory may explain why the present study did not find any relationships between tests of executive functioning and SI.

The present study has several limitations to consider. It was cross-sectional in nature, preventing the testing of causal hypotheses. In addition, the sample was predominantly male veterans; thus, it is unclear whether results will generalize to civilians and to women, as there is evidence of gender differences in suicide risk (e.g., Stack, 2000), including in those with a history of TBI (Oquendo et al., 2004; Wisco et al., 2014). Measures of inhibition or impulsivity were not included in the neuropsychological assessment; thus, it remains unclear whether difficulties in these particular types of executive functions would be associated with suicidal ideation in individuals with a history of mTBI. Finally, the present study was not able to explore other potential moderators of the relationship between cognitive impairment and SI (e.g., medications, sleep disturbance, pain); future research would benefit from examining whether other factors play a role in suicidality in this population. It is also

possible that modifiable factors such as medication usage and sleep dysfunction and/or certain personality traits like impulsivity and sensation seeking may put individuals at greater risk for sustaining multiple TBIs and poorer cognitive and emotional outcomes, thus making them more vulnerable to SI.

Despite the noted limitations, the present study has several strengths to highlight, including being one of the first studies to examine relationships among lifetime TBI burden, neuropsychological functioning in several domains, and suicidality in a sample of individuals with a history of mTBI. In addition, the present study utilized data from treatment-seeking veterans who participated in a neuropsychological assessment in the context of VA clinical services. Thus, the sample is likely representative of vulnerable veterans who may be at an increased risk of suicide, given that the research demonstrating elevated risk in OEF/OIF/OND veterans was conducted specifically in those who were receiving VA care (Connor et al., 2013; Ilgen et al., 2010; Kang & Bullman, 2008). Finally, present results showed that the interactions between TBI burden and memory/processing speed remained significant predictors of SI even when accounting for psychiatric and postconcussive symptom severity. Previous research has consistently demonstrated that psychiatric distress is one of the strongest predictors of suicidality (Brown et al., 2000; Jakupcak et al., 2009; Pietrzak et al., 2010; Zimmerman et al., 2015), including in active duty and veteran samples with a history of TBI (Brenner et al., 2011; Bryan & Clemans, 2013); however, our findings demonstrate that other non-emotional variables, specifically TBI-related and cognitive factors, together uniquely contribute to increased suicide risk, above and beyond psychiatric factors. As such, the present results may hold important treatment implications; cognitive training or interventions that simultaneously target both cognitive dysfunction and psychiatric distress may be most appropriate for this vulnerable group.

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Table 1. Descriptive and Group Differences on Demographic, Injury, Symptom, and Cognitive Measures for the Suicidal Ideation Endorsers (SI+) and Non-Endorsers (SI-).

	SI- group (n = 232)	SI+ group (n = 50)	t or χ^2	df	p
Demographics					
Age	32.50 (8.23)	34.32 (9.10)	1.39	280	.164
Education	13.23 (1.75)	13.02 (1.57)	-.79	280	.428
% Male	93.5	90.0	.78	1	.377
% Caucasian	61.6	68.0	.71	1	.399
% Hispanic	31.0	30.0	.02	1	.886
TBI Variables					
with LOC presence ^a	59.0	60.4	.03	1	.859
% with PTA presence ^a	39.0	31.3	.70	1	.404
% with blast history	63.2	66.0	.14	1	.709
% with 3 or more lifetime mTBIs	35.7	30.6	.46	1	.499
Symptom Measures					
PTSD (PCL-C)	51.70 (15.52)	61.50 (12.99)	4.66	280	.000*
Depression (BDI-II)	19.90 (10.09)	30.94 (9.22)	7.12	280	.000*
Postconcussive symptoms (NSI)	34.42 (13.45)	47.97 (12.46)	5.54	223	.000*
Cognitive Measures					
WRAT-4 Reading standard score	98.25 (10.15)	96.61 (8.21)	-1.06	277	.290
Attention/Processing Speed Composite	.00 (.84)	-.06 (.98)	-.47	275	.642
Learning Composite	.02 (.76)	-.07 (.79)	-.71	267	.476
Memory Composite	.06 (.83)	-.30 (.83)	-2.73	268	.007*
Executive Functioning Composite	.02 (.66)	-.07 (.69)	-.83	276	.408

* Notes: p <.05;

^a LOC and PTA presence for worst TBI reported.

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Abbreviations: SS = scaled scores; LOC = loss of consciousness; PTA = post-traumatic amnesia; TBI = traumatic brain injury; PTSD = posttraumatic stress disorder; BDI-II = Beck Depression Inventory-Second Edition; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian version; NSI = Neurobehavioral Symptom Inventory; WRAT-4 = Wide Range Achievement Test - Fourth Edition; Lower scores indicate worse performance for the cognitive measures.

Table 2. Results of Logistic Regressions Examining Memory and Symptom Measures Predicting Suicidal Ideation.

	R²	B	SE	OR [95% CI]	p
<i>Model 1</i> Memory composite	.119	.42	.21	1.52 [1.02, 2.27]	.039*
PTSD symptoms (PCL-C)		.04	.01	1.04 [1.02, 1.07]	.001*
<i>Model 2</i> Memory composite	.257	.44	.21	1.55 [1.02, 2.35]	.033*
Depression symptoms (BDI-II)		.10	.02	1.12 [1.07, 1.15]	.001*
<i>Model 3</i> Memory composite	.247	.62	.28	1.85 [1.11, 3.07]	.020*
Postconcussive symptoms (NSI)		.07	.02	1.08 [1.04, 1.11]	.001*

* Notes: $p < .05$; memory composite was coded such that higher scores reflected greater impairment; R^2 is Nagelkerke's method; Abbreviations: OR = odds ratio; CI = confidence interval; PTSD = posttraumatic stress disorder; PCL-C = PTSD Checklist Civilian Version; BDI-II = Beck Depression Inventory-Second Edition; NSI = Neurobehavioral Symptom Inventory.

Table 3.

Results of Logistic Regressions Examining Interactions Between Cognitive Composite Scores and mTBI Burden Predicting Suicidal Ideation.

	Attention/PS Composite					Memory Composite				
	R ²	B	SE	OR [95% CI]	p	R ²	B	SE	OR [95% CI]	p
<i>Model 1</i>	.031				.087					
Cognitive composite		-.23	.26	.80 [.49, 1.29]	.370		.20	.22	1.22 [.79, 1.90]	.360
mTBI burden		-.29	.37	.75 [.37, 1.50]	.410		-.47	.53	.63 [.28, 1.39]	.302
Cognitive composite x mTBI burden		.77	.41	2.17 [1.05, 4.46]	.028*		1.27	.60	3.57 [1.32, 9.65]	.009*
<i>Model 2</i>	.128				.156					
Cognitive composite		-.35	.29	.82 [.40, 1.68]	.618		.12	.23	1.13 [.72, 1.79]	.576
mTBI burden		-.20	.40	.70 [.43, 1.16]	.199		-.42	.51	.66 [.29, 1.48]	.340
Cognitive composite x mTBI burden		.87	.44	2.39 [1.13, 5.05]	.020*		1.22	.65	3.40 [1.22, 9.51]	.018*
PTSD symptoms (PCL-C)		.05	.01	1.05 [1.02, 1.07]	.001*		.04	.01	1.04 [1.02, 1.07]	.001*
<i>Model 3</i>	.279				.271					
Cognitive composite		-.54	.30	.58 [.34, 1.00]	.048*		.19	.24	1.21 [.74, 1.96]	.386
mTBI burden		-.37	.46	.69 [.32, 1.50]	.394		-.42	.53	.66 [.29, 1.51]	.376
Cognitive composite x mTBI burden		1.23	.55	3.42 [1.50, 7.79]	.007*		.91	.60	2.48 [.90, 6.87]	.078
Depression symptoms (BDI-II)		.12	.02	1.13 [1.08, 1.17]	.001*		.10	.02	1.10 [1.06, 1.15]	.001*
<i>Model 4</i>	.267				.284					
Cognitive composite		-.63	.39	.53 [.26, 1.09]	.082		.21	.37	1.23 [.66, 2.30]	.572
mTBI burden		-.18	.51	.83 [.35, 1.96]	.700		-.31	.58	.73 [.30, 1.81]	.525
Cognitive composite x mTBI burden		1.28	.58	3.59 [1.37, 9.41]	.009*		1.15	.67	3.16 [.98, 10.13]	.038*
Postconcussive symptoms (NSI)		.08	.02	1.09 [1.05, 1.12]	.001*		.08	.02	1.08 [1.04, 1.11]	.001*

* Notes: $p < .05$; mTBI burden is dichotomous; 1–2 vs. 3 or more mild traumatic brain injuries; neuropsychological measures were coded such that higher scores reflected greater impairment; R^2 is Nagelkerke's method; Abbreviations: OR = odds ratio; CI = confidence interval; PTSD = posttraumatic stress disorder; PCL-C = PTSD Checklist Civilian Version; BDI-II = Beck Depression Inventory-Second Edition; NSI = Neurobehavioral Symptom Inventory; PS = processing speed.