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CRITICAL REVIEW

Factors Associated with Mild Traumatic Brain Injury in Veterans and Military Personnel: A Systematic Review

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Abstract

A history of mild traumatic brain injury (mTBI) is common among military members who served in Operations Enduring Freedom, Iraqi Freedom, and New Dawn (OEF/OIF/OND). We completed a systematic review to describe the cognitive, mental health, physical health, functional, social, and cost consequences of mTBI in Veteran and military personnel. Of 2668 reviewed abstracts, the 31 included studies provided very low strength evidence for the questions of interest. Cognitive, physical, and mental health symptoms were commonly reported by Veterans/military members with a history of mTBI. On average, these symptoms were not significantly more common in those with a history of mTBI than in those without, although a lack of significant mean differences does not preclude the possibility that some individuals could experience substantial effects related to mTBI history. Evidence of potential risk or protective factors moderating mTBI outcomes was unclear. Although the overall strength of evidence is very low due to methodological limitations of included studies, our findings are consistent with civilian studies. Appropriate re-integration services are needed to address common comorbid conditions, such as treatment for post-traumatic stress disorder, substance use disorders, headaches, and other difficulties that Veterans and members of the military may experience after deployment regardless of mTBI history. (*JINS*, 2014, *20*, 249–261)

Keywords: Mild traumatic brain injury, Veteran, Military, Systematic review, Combat deployment, Cognitive functioning, Deployment related conditions

INTRODUCTION

History of traumatic brain injury (TBI) is common, especially among military members, and 12% to 23% of Operations Enduring Freedom, Iraqi Freedom, and New Dawn (OEF/OIF/OND) service members have experienced a TBI while deployed. Although various criteria are used to define TBI severity, the majority of documented TBI events among OEF/OIF/OND service members may be classified as mild in severity according to the definition used by the U.S. Departments of Veterans Affairs (VA) and Defense (DoD) (Hoge, Goldberg, & Castro, 2009).

While some researchers suggest most individuals recover within seven days (Belanger & Vanderploeg, 2005) to a month (Carroll et al., 2004) of a mild TBI (mTBI), others estimate that 10% to 20% of individuals continue to experience post-concussive symptoms (e.g., headaches, dizziness, balance problems) beyond this time frame (Ruff, 2005). This estimate may be higher among OEF/OIF/OND service members given the frequency of multiple TBI events, concomitant mental health conditions (e.g., depression and post-traumatic stress disorder [PTSD]), and other factors unique to combat deployments. As such, deployment-related mTBI is a significant issue for mental health and primary care providers seeing Veteran patients, particularly because patients may seek treatment for symptoms that persist many months after deployment, and treatment may be complicated by comorbid

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mental health or pain disorders (Wood, 2004). To examine complications of mTBI unique to this population, we conducted a systematic review of literature on mTBI consequences, potential risk and protective factors for mTBI outcomes, and costs among Veterans and members of the military.

METHODS

A detailed discussion of methods is available in the full length report online (O'Neil et al., 2012); we provide a brief overview of methods in this study.

Key Questions

The key questions were: (1) For Veteran/military populations, what is the prevalence of health problems (such as pain, seizure disorders, headaches, migraines, and vertigo), cognitive deficits, functional limitations (such as employment status, changes in marital status/family dynamics), and mental health symptoms (such as PTSD and depression) that develop or persist following mTBI? (2) What factors affect outcomes for Veteran/military patients with a history of mTBI? (2a) For Veteran/military populations with a history of mTBI, are there pre-injury (premorbid) risk/protective factors (e.g., pre-injury mental health factors, genetic factors, or prior concussions) that affect outcomes? (2b) For Veteran/military populations with a history of mTBI, are there post-injury risk/protective factors (e.g., PTSD) that affect outcomes? (3) What is the resource usage over time for Veteran/military patients with a history of mTBI?

Data Sources

We searched Medline, PsychINFO, and Cochrane Register of Controlled Trials (OVID) from database inception to October 3rd, 2012. We used a search strategy (see full length online report, O'Neil et al., 2012) adapted from the WHO Collaborating Center for Neurotrauma Prevention, Management and Rehabilitation Task Force and limited the search to Veteran/military population studies. We obtained additional articles from systematic reviews, reference lists of pertinent studies, reviews, editorials, and by consulting clinical and research experts.

Study Selection

We included studies reporting outcomes in Veterans or military personnel with a history of mTBI using a case definition consistent with VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury (see full length online report, O'Neil et al., 2012) which includes studies of patients meeting the commonly used American Congress of Rehabilitative Medicine (ACRM) definition of mTBI (Kay et al., 1993). The only exception to the VA/DoD criteria was that we did not exclude studies based on inclusion or exclusion of patients with positive imaging results since the vast majority of studies did not apply this exclusion criteria or did not report this information. We excluded studies with unclear definitions of mTBI or definitions not meeting VA/DoD criteria (see full length online report, O'Neil et al., 2012). We did not limit study eligibility based on number of mTBI incidents, mechanism of injury, or the presence of comorbid conditions.

Full-text articles of potentially relevant abstracts were dual reviewed and disagreements resolved through consensus. Eligible articles had English-language abstracts and provided data relevant to the key questions. Articles had to report health or cost outcomes for members of the U.S. armed forces or Veterans. Eligible study designs included systematic reviews; meta-analyses; randomized controlled trials; and cohort, case-control, cross-sectional, or case series studies, with a minimum of 30 mTBI cases.

Quality Assessment

We conducted dual assessment of the quality of included studies and resolved disagreements through consensus. We adapted an existing tool to assess the quality of observational studies and added topic specific domains (Wells et al., 2009). We did not provide summary scores of study quality, instead examining aspects of study design and methodology central to the clinical topic and questions of interest. We evaluated the overall strength of evidence for each key question as proposed by the GRADE Working Group (Guyatt et al., 2011). Based on study methodologic quality as well as precision and consistency of results across studies, the GRADE summary labels reflect confidence in the effect estimates for each outcome. For example, a "very low" strength of evidence label means that because of methodologic limitations of studies, imprecise results (i.e., those with a large confidence interval), inconsistent results across studies, and/or lack of data, any estimate of effect is very uncertain.

Data Extraction and Synthesis

We abstracted the following data for each included study: sample selection, population characteristics, subject eligibility and exclusion criteria, number of subjects, comparison(s), and outcome(s). Data were abstracted by one investigator and reviewed for accuracy by at least one additional investigator. We compiled a summary of findings for each outcome category and key question, and conducted a qualitative synthesis of findings. The heterogeneity of outcomes and study characteristics precluded meta-analysis.

RESULTS

We reviewed 2668 titles and abstracts from the electronic search, and identified an additional four studies from reviewing reference lists and conducting manual searches. After applying inclusion/exclusion criteria at the abstract level, 354 full-text articles were reviewed (Figure 1). Of the full-text articles, 323 did not meet inclusion criteria. We grouped the studies by outcome and key question. We identified 31 primary studies that addressed the key questions. Sixty studies otherwise very similar to the included studies were excluded because they selected participants using a definition of TBI falling outside of

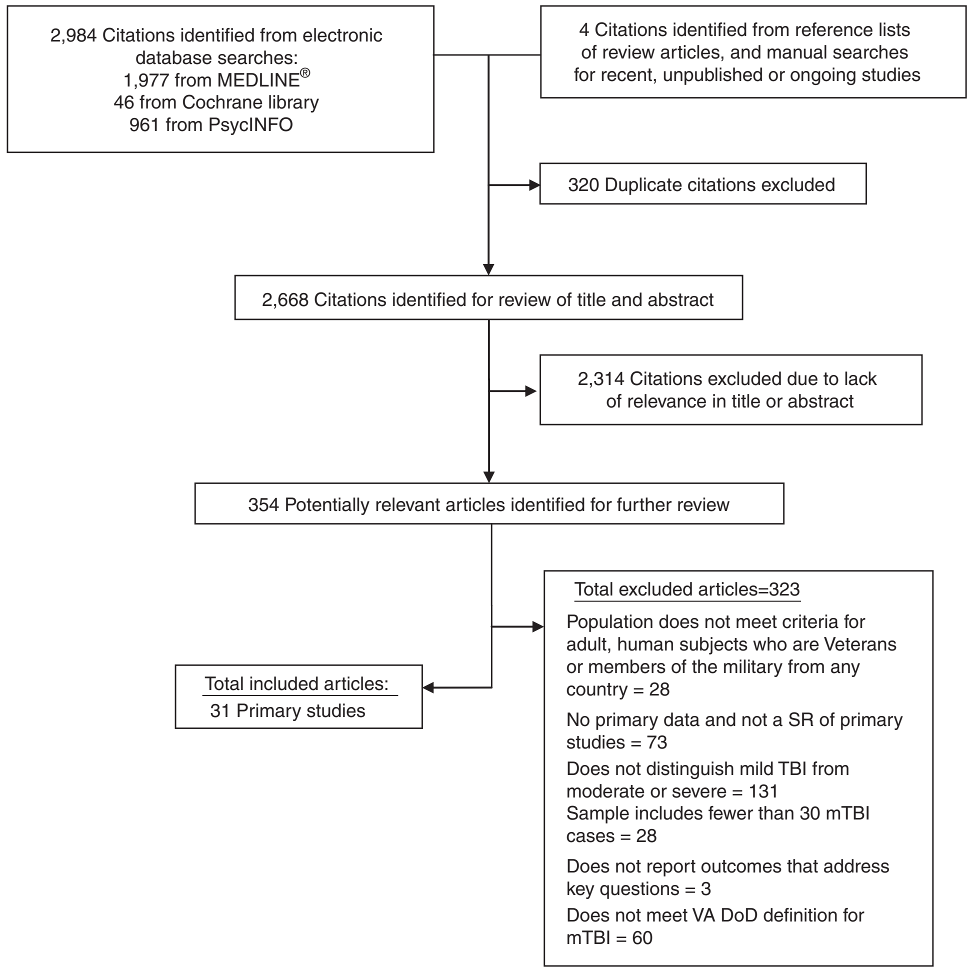

Fig. 1. Literature flow diagram. *Note.* This figure is reproduced with permission from the full, online report (O'Neil, et al., 2012).

the VA/DoD definition of mTBI. We reviewed this body of literature to determine whether the inclusion of these studies might increase the strength of evidence or change effect estimates for any of our outcomes of interest. These studies were similarly limited by methodologic concerns as the 31 included studies and their inclusion of participants with more or less severe TBI would have limited the generalizability of the findings without significantly changing the results for the outcomes examined in this review. Because the included studies most often analyzed group differences based on mean scores, the inclusion of data from those with more or less severe TBI could have biased the results. Therefore, we chose not to include these 60 studies so that our results would most accurately represent outcomes for Veterans and members of the military with a history mTBI meeting the specified criteria. Study characteristics including quality characteristics considered in this review are summarized in the full length report as are the complete results (O'Neil et al., 2012).

Overall, the included studies did not meet many important quality criteria specific to the key questions and clinical topic. Although individual study characteristics varied, all were limited by at least some of the following methodologic limitations: Studies did not use representative samples, blind outcome assessors to mTBI history, blind patients and assessors to study hypotheses, adjust for known confounders such as mental health conditions, use comparable controls, or have an adequate response rate. Although 31 studies met inclusion criteria, methodologic shortcomings in these observational studies, as well as diversity in outcomes and populations and inconsistent findings, provide only very low strength evidence for the key questions examined in this report (Guyatt et al., 2011). Therefore, findings are tentative and may change based on new, higher quality evidence.

In general, we found that, although Veterans/military members commonly reported cognitive, physical, and mental health symptoms following mTBI, there is very low strength evidence that, with few exceptions, deficits and symptoms are not significantly more common among Veterans with a history of mTBI than similar Veterans without a history of mTBI. Additionally, while individual studies investigated potential moderators of mTBI outcomes, no consistent patterns of potential risk or protective factors were identified. A summary of outcomes including p-values and effect size calculations from included studies reporting comparisons between those with and without a mTBI history are presented in Tables 1 and 2.

Table 1. Summary of evidence: Cognitive functioning outcomes for Veterans and Military Members with and without history of mTBI

Cognitive functioning domain	Citation	Sample characteristics	mTBI, control sample Size	Time since injury	Outcome measure	*p* Value	Effect size (95% CI)
Language Abilities and General Fund of Verbal Knowledge	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50,117	8.12 weeks (SD = 7.763)	RBANS Language	.73	−0.06 (−0.39–0.03)
	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	WAIS-III Information	NR	0.39 (−0.21–0.99)
					Wechsler Test of Adult Reading	NR	−0.07 (−.066–0.52)
	Nelson, Hoelzle, McGuire, et al., 2010	Excluded insufficient effort	28,31	327.0 weeks (SD = 425.6)	WAIS-III Information	NR	−0.02 (−0.53–0.49)
Visuospatial Abilities	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50,117	8.12 weeks (SD = .763)	RBANS Visuospatial/Constructional	.007	−0.46 (−0.79–−0.12)
	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	Rey Complex Figure Test: Figure Copy	NR	−0.27 (−0.87–0.32)
					WAIS-III Block Design	NR	0 (−0.59–0.59)
Memory	Coldren, Russell, Parish, et al., 2012	US Army Soldiers in Iraq	47,108	5 days	ANAM Code Substitution Delayed	.07	NR
				10 days	ANAM Code Substitution Delayed	.17	NR
				5 days	ANAM Matching to Sample	.47	NR
				10 days	ANAM Matching to Sample	.77	NR
	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50,117	8.12 weeks (SD = 7.763)	RBANS Language	.59	−0.09 (−0.43–0.24)
	Kelly, Coldren, Parish, et al., 2012	US Army Soldiers in Iraq	66,146	72 hours	ANAM Code Substitution Delayed	.04	NR
	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	CVLT-II Long Delay Free Recall	NR	−0.12 (−0.71–0.47)
					CVLT-II Trials 1-5	NR	−0.23 (−0.83–0.36)
					RCFT Delayed Recall	NR	0.15 (−0.44–0.75)
					RCFT Delayed Memory	.07	−0.31 (−0.90–0.29)
	Nelson, Hoelzle, McGuire, et al., 2010	Excluded insufficient effort	28,31	327.0 weeks (SD = 425.6)	CVLT-II Long Delay Free Recall	NR	−0.2 (−0.72–0.30)
					CVLT-II Trials 1-5	NR	−0.32 (−0.84–0.19)
Attention/ Concentration	Coldren, Russell, Parish, et al., 2012	US Army Soldiers in Iraq	47,108	5 days	ANAM Mathematical Processing	.29	NR
				10 days	ANAM Mathematical Processing	.51	NR
	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50,117	8.12 weeks (SD = 7.763)	RBANS Attention	.03	−0.39 (−0.73–0.06)
	Kelly, Coldren, Parish, et al., 2012	US Army Soldiers in Iraq	66,146	72 hours	ANAM Mathematical Processing	.03	NR
	Nelson, Hoelzle, McGuire, et al., 2010	Excluded insufficient effort	28,31	327.0 weeks (SD = 425.6)	WAIS-III Digit Span	NR	−0.06 (−0.58–0.45)
Processing Speed	Coldren, Russell, Parish, et al., 2012	US Army Soldiers in Iraq	47,108	5 days	ANAM Code Substitution	.03	NR
				10 days	ANAM Code Substitution	.14	NR
				5 days	ANAM Procedural Reaction Time	.13	NR
				10 days	ANAM Procedural Reaction Time	.2	NR

(Continued)

Table 1. Continued

Cognitive functioning domain	Citation	Sample characteristics	mTBI, control sample Size	Time since injury	Outcome measure	*p* Value	Effect size (95% CI)
				5 days	ANAM Simple Reaction Time	.97	NR
				10 days	ANAM Simple Reaction Time	.71	NR
	Kelly, Coldren, Parish, et al., 2012	US Army Soldiers in Iraq	66,146	72 hours	ANAM Code Substitution	.001	NR
	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	Stroop Color Word: Color Score	NR	0.09 (−0.50–0.68)
	Nelson, Hoelzle, McGuire, et al., 2010	Excluded insufficient effort	28,31	327.0 weeks (SD = 425.6)	Stroop Color Word: Color Score	NR	−0.16 (−0.67–0.35)
					Stroop Color Word: Word Score	NR	−0.26 (−0.77–0.25)
					Trail Making Test Part A	NR	−0.07 (−0.58–0.45)
					WAIS-III Digit Symbol Coding	NR	0.04 (−0.47–0.56)
	Swick, Honzel, Larsen, et al., 2012	Combat Veterans with PTSD	30, 43	3.8 years (SD = 1.5)	Go/No-go Reaction Time	> .70	NR
Executive Functioning	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	Controlled Oral Word Association	NR	−0.24 (−0.84–0.35)
					Stroop Color Word: Color-Word Score	NR	−0.19 (−0.78–0.41)
					Trail Making Test Part B	NR	−0.27 (−0.87–0.32)
	Nelson, Hoelzle, McGuire, et al., 2010	Excluded insufficient effort	28,31	327.0 weeks (SD = 425.6)	Controlled Oral Word Association	NR	0.01 (−0.50–0.52)
					Stroop Color Word: Color-Word Score	NR	−0.18 (−0.69–0.33)
					Trail Making Test Part	NR	−0.07 (−0.58–0.44)
Total/Composite Score	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50,117	8.12 weeks (SD = 7.763)	RBANS Total Score	.02	−0.39 (−0.72–−0.05)
	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	Overall Test Battery Mean	NR	−0.23 (−0.82–0.36)
	Nelson, Hoelzle, McGuire, et al., 2010	Excluded insufficient effort	28,31	327.0 weeks (SD = 425.6)	Overall Test Battery Mean	NR	−0.23 (−0.74–0.29)

Note. Complete data abstraction tables including information on additional population characteristics and subgroup comparisons are reported in the full online report (O'Neil, et al., 2012). We calculated effect size and confidence intervals when sufficient data was reported. RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; WAIS-III = Wechsler Adult Intelligence Scale—Third Edition; ANAM = Automated Neuropsychological Assessment Metrics.

Table 2. Summary of evidence: Physical health, mental health, functional, social, and service utilization outcomes for Veterans and Military Members with and without history of mTBI

Outcome domain	Citation	Sample characteristics	mTBI, control sample Size	Time since injury	Outcome measure	*p* Value	Effect size (95% CI)
Physical Health: Headache	Theeler & Erikson, 2009	US Army Soldiers with chronic headaches	33, 48	NR	Headache days/month after deployment	NR	0.18 (−0.26–0.62)
					Headache days/month during deployment	NR	0.49 (0.04–0.94)
Physical Health: Pain	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	Pain scale 1-10	.18	0.30 (NR)
Physical Health: Vestibular	Gottshall, Drake, Gray, et al., 2003	US active duty Marines and Navy personnel	53, 46	1 week	Dizziness Handicap Inventory	<.01	NR
				2 weeks	Dizziness Handicap Inventory	<.01	NR
				3 weeks	Dizziness Handicap Inventory	<.01	NR
				4 weeks	Dizziness Handicap Inventory	<.01	NR
				1 week	Dynamic Visual Acuity Test	<.01	NR
				4 weeks	Dynamic Visual Acuity Test	>.01	NR
Mental Health: PTSD	Cooper, Nelson, Armistead-Jehle, & Bowles, 2011	Active duty service members	179, 18	Range: 1 to >3 years	PCL-Military version	.03	0.81 (0.32–1.30)
	Gaylord, Cooper, Mercado, et al., 2008	Active duty service members with burn and blast injuries	31, 45	NR	PCL-Military score </ = 44	.04	0.58 (0.03–1.13)
	Theeler & Erikson, 2009	US Army Soldiers with chronic headaches	33, 48	NR	PCL: Civilian version	NR	−0.10 (−0.55–0.34)
	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	CAPS: B Re-experiencing subscale	.08	0.38 (−0.03–0.79)
					CAPS: Total score	.03	0.46 (0.05–0.88)
					PCL-Stressor specific version	.17	0.31 (−0.12-0.72)
Mental Health: Depression	Swick, Honzel, Larsen, et al., 2012	Combat Veterans with PTSD	30, 43	3.8 years (SD = 1.5)	Beck Depression Inventory-II	NR	−0.08 (−0.54–0.39)
	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	Beck Depression Inventory-II	.29	0.22 (−0.19–0.63)
					SCID-I Major Depressive Disorder	.14	0.15 (NR)
Mental Health: Substance Use	Nelson, Hoelzle, Doane, et al., 2012	Excluded Axis I disorders	18,28	177.2 weeks (SD = 85.5)	SCID-I Alcohol abuse/ dependence	NR	0.09 (NR)
	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	SCID-I Alcohol Problem	.37	0.10 (NR)
					SCID-I Drug Problem	.34	0.10 (NR)
Mental Health: Suicide	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	Suicidal ideation (single item)	.10	NR
Mental Health: Other	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	SCID-I Any Axis I disorder	.14	0.12 (NR)
	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50, 117	8.12 weeks (SD = 7.763)	Psychiatric diagnosis	.001	NR
Functional: Employment	Barnes, Walter, & Chard, 2012	Veterans with PTSD	46, 46	NR	Unemployment (single item)	.23	0.13 (NR)
Functional: Sleep	Coldren, Russell, Parish, et al., 2012	US Army Soldiers in Iraq	47, 108	72 hours	<4 hours sleep per night	.21	NR
					>2 hours sleep loss per night	.02	NR

(Continued)

Table 2. Continued

Outcome domain	Citation	Sample characteristics	mTBI, control sample Size	Time since injury	Outcome measure	*p* Value	Effect size (95% CI)
	Kelly, Coldren, Parish, et al., 2012	US Army Soldiers in Iraq	66, 146	72 hours	Hours sleep per night	.22	NR
					Hours of sleep lost per night	.001	NR
Social Outcomes	Barnes, Walter, & Chard, 2012	Veterans with PTSD	35, 35	NR	Lack of emotional support (single item)	.38	0.10 (NR)
					Marital status	.72	0.04 (NR)
Service Utilization	Coldren, Russell, Parish, et al., 2012	US Army Soldiers in Iraq	47, 108	72 hours	Current Counseling	.99	NR
					Current Mental Health Medication	.50	NR
	Kelly, Coldren, Parish, et al., 2012	US Army Soldiers in Iraq	66, 146	72 hours	Current Counseling	.46	NR
					Current Mental Health Medication	.99	NR
	Cooper, Mercado-Couch, Richfield, et al., 2010	US Service Members with burn injuries	50, 117	8.12 weeks (SD = 7.763)	Current Narcotic Pain Medication	.26	NR

Note. Complete data abstraction tables including information on additional population characteristics and subgroup comparisons are reported in the full online report (O'Neil et al., 2012). We calculated effect size and confidence intervals when sufficient data was reported. PTSD = Posttraumatic Stress Disorder; PCL = PTSD Checklist; CAPS = Clinician Administered PTSD Scale; SCID-I = Structured Clinical Interview for DSM-IV Axis I Disorders.

Cognitive Functioning Results

We found 17 studies reporting associations between cognitive outcomes and mTBI. The studies describing cognitive outcomes reported mean scores rather than proportions of individuals with impaired scores, making estimates of prevalence of cognitive impairment impossible. None of the included studies provided information on pre-morbid functioning such that change from baseline could be assessed at the intra-individual level.

Eight primary studies assessed language abilities and general fund of verbal knowledge (Belanger, Kretzmer, Vanderploeg, & French, 2010; Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009; Cooper, Chau, Armistead-Jehle, Vanderploeg, & Bowles, 2012; Cooper et al., 2010; Drag, Spencer, Walker, Pangilinan, & Bieliauskas, 2012; Gordon, Fitzpatrick, & Hilsabeck, 2011; Nelson et al., 2010, 2012) three of which compared outcomes with a non-TBI group from the same population, describing similar performance across groups (Cooper et al., 2010; Nelson et al., 2010, 2012). These three studies reported mean standardized scores not suggestive of clinically significant impairment. Six primary studies reported visuospatial outcomes (Cooper et al., 2010, 2012; Drag et al., 2012; Gordon et al., 2011; Nelson et al., 2012; Spencer, Drag, Walker, & Bieliauskas, 2010) and the two comparing mTBI with non-TBI participants described non-significant differences on two of three measures of visuospatial abilities (Cooper et al., 2010; Nelson et al., 2012). All mean standardized scores were not suggestive of clinically significant impairment. Eleven studies assessed memory (Belanger et al., 2009; Coldren, Russell, Parish, Dretsch, & Kelly, 2012; Cooper et al., 2010, 2012; Drag et al., 2012; Gordon et al., 2011; Kelly, Coldren, Parish, Dretsch, & Russell, 2012; Nelson et al., 2010, 2012; Schiehser et al., 2011; Spencer et al., 2010), five of which described similar results across mTBI and control groups in most cases (Coldren et al., 2012; Cooper et al., 2010; Kelly et al., 2012; Nelson et al., 2010, 2012). The notable exception was from two studies by the same group of authors and the same patient population which reported significant group differences on both 72-hr assessments, one of the two 5-day assessments, and neither of the 10-day assessments (Coldren et al., 2012; Kelly et al., 2012). Mean standardized scores were not suggestive of clinically significant impairment for memory functioning in all five studies (Belanger et al., 2009; Cooper et al., 2010; Drag et al., 2012; Nelson et al., 2010, 2012). Eight primary studies assessed attention and/or concentration (Coldren et al., 2012; Cooper et al., 2010, 2012; Drag et al., 2012; Kelly et al., 2012; Nelson et al., 2010, 2012; Spencer et al., 2010). In four studies that compared outcomes to non-mTBI controls, findings varied. The mTBI group performed similarly to a non-TBI comparison group on measures of attention in two studies (Nelson et al., 2010, 2012). In other studies, participants with a history of mTBI performed worse on two measures, but deficits noted at 72 hr diminished with time (Coldren et al., 2012; Cooper et al., 2010; Kelly et al., 2012). Mean scores on measures of attention and concentration were not suggestive of clinically significant impairment

(Nelson et al., 2010., 2012). We found nine primary studies that assessed processing speed (Belanger et al., 2009; Coldren et al., 2012; Drag et al., 2012; Gordon et al., 2011; Kelly et al., 2012; Nelson et al., 2010, 2012; Spencer et al., 2010; Swick, Honzel, Larsen, Ashley, & Justus, 2012), five of which compared outcomes to a non-TBI group (Coldren et al., 2012; Kelly et al., 2012; Nelson et al., 2010, 2012; Swick et al., 2012). In three of these studies, the mTBI group performed similarly to a non-TBI comparison group on multiple measures of processing speed (Nelson et al., 2010, 2012; Swick et al., 2012). By contrast, two studies conducted in the same patient population observed processing speed deficits soon after injury (72 hr and 5 days), although statistically significant differences were not detected upon longer term follow-up (10 days after injury) (Coldren et al., 2012; Kelly et al., 2012; Nelson et al., 2010). Of the seven primary studies that assessed executive functioning (Belanger et al., 2009; Drag et al., 2012; Gordon et al., 2011; Nelson et al., 2012; Schiehser et al., 2011; Spencer et al., 2010), two compared outcomes with a non-TBI control group (Nelson et al., 2010, 2012). In these studies, the mTBI group performed similarly to a non-TBI comparison group. Of the four studies reporting standardized scores, none of the mean scores were suggestive of clinically significant impairment for executive functioning.

Additional studies examined outcomes related to cognitive functioning, such as effort testing, composite scores, and self-reported cognitive complaints. One primary study assessed effort and motivation on cognitive tests, although this study did not report comparisons between those with and without a history of mTBI (Nelson et al., 2010). We found nine primary studies that assessed cognitive functioning across domains (Cooper et al., 2010, 2012; Gordon et al., 2011; Nelson et al., 2010, 2012; Ruff, Riechers, Wang, Piero, & Ruff, 2012; Ruff, Ruff, & Wang, 2008, 2009; Schiehser et al., 2011). Three studies examined outcomes compared with a non-TBI group (Cooper et al., 2010; Nelson et al., 2010, 2012). In two of these studies (Nelson et al., 2010, 2012), there were no significant differences between mTBI and non-mTBI participants, although one study (Cooper et al., 2010) reported significantly lower scores for mTBI participants. Of the two studies reporting standardized scores on assessments, none of the mean scores were suggestive of clinically significant impairment for cognitive functioning (Nelson et al., 2010, 2012). Seven primary studies examined self-reported cognitive complaints (e.g., self-reported blackouts, confusion, memory problems, and difficulties with decision-making), although none reported comparisons with a non-mTBI control group (Belanger et al., 2011; Benge, Pastorek, & Thornton, 2009; Cooper, Kennedy, et al., 2011; Drag et al., 2012; Kennedy, Cullen, Amador, Huey, & Leal, 2010; Nelson et al., 2012; Schiehser et al., 2011).

Physical Health Results

We found 17 studies reporting physical health outcomes for those with a history of mTBI. Self-reported physical symptoms are commonly experienced by Veterans with a history of mTBI, but the strength of evidence is very low. The most well researched physical health outcome was headaches, with 10 included studies reporting headache outcomes (Belanger et al., 2011; Benge et al., 2009; Cooper et al., 2012; Cooper, Kennedy, et al., 2011; Kennedy et al., 2010; Nelson et al., 2012; Patil et al., 2011; Ruff et al., 2008, 2009; Theeler & Erickson, 2009). One study without a comparison group reported prevalence of neurology referrals for headache in an mTBI population was 33.3% (Patil et al., 2011). Another study reported an average self-report headache score in the moderate range (Kennedy et al., 2010). Finally, one study reported average headache pain of 4.33 on a scale of 0–10 for Veterans with a history of mTBI (Ruff et al., 2008). All other prevalence estimates and comparisons with a non-mTBI population reported in the included studies were based on populations selected because they experienced headaches, potentially inflating estimates of headache prevalence compared with the general mTBI population.

Other reported physical health outcomes were sparse, with many outcomes assessed by single questions, and studies often not comparing outcomes to control participants without a history of mTBI. Only two studies documented outcomes related to pain (Barnes, Walter, & Chard, 2012; Lew et al., 2010) and only one compared pain with a non-mTBI population, describing statistically significant differences in median pain scores of 3.5/10 for the participants with a history of mTBI and 2.0/10 for those without a history of mTBI (Barnes et al., 2012). We found six primary studies reporting vestibular outcomes (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Gottshall, Drake, Gray, McDonald, & Hoffer, 2003; Kennedy et al., 2010; Nelson et al., 2012). Ranges of mean scores on vestibular questions ranged from mild–moderate symptom severity (Benge et al., 2009). One study compared vestibular symptoms in those with a history of mTBI with non-mTBI populations, reporting significantly more vestibular symptoms in mTBI groups up to 4 weeks following injury (Gottshall et al., 2003). We found five studies reporting vision-related outcomes (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Kennedy et al., 2010; Nelson et al., 2012). Ranges of mean scores on vision-related questions ranged from mild-moderate symptom severity (Benge et al., 2009). We found five primary studies reporting hearing-related outcomes (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Kennedy et al., 2010; Nelson et al., 2012). Average self-reported hearing difficulty and sensitivity to noise for those with a history of mTBI were in the moderate range (Benge et al., 2009). Five studies reported neurological outcomes (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Kennedy et al., 2010; Ruff et al., 2012) describing average self-reported numbness or tingling of mild-moderate severity (Benge et al., 2009). We found five primary studies reporting outcomes related to appetite and nausea (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Kennedy et al., 2010; Nelson et al., 2012). Average self-reported change in taste or smell, nausea, and loss of appetite ranged from mild to moderate in severity (Benge et al., 2009).

Mental Health Results

Twenty studies reported mental health outcomes for Veterans or members of the military with a history of mTBI. Mental health outcomes varied greatly in terms of methods of assessment, ranging from lengthy clinical interviews based on diagnostic criteria, to single-item, self-report screeners. The studies provide limited evidence that mental health concerns are common among Veterans and members of the military with a history of mTBI, although often are not significantly more common than among Veterans and members of the military without a history of mTBI.

There were 17 included studies that reported PTSD outcomes (Barnes et al., 2012; Belanger et al., 2010, 2009; Belanger et al., 2011; Benge et al., 2009; Cooper et al., 2012; Cooper, Nelson, Armistead-Jehle, & Bowles, 2011; Drag et al., 2012; Gaylord et al., 2008; Kennedy et al., 2010; Lew et al., 2010; Lippa, Pastorek, Benge, & Thornton, 2010; Patil et al., 2011; Ruff et al., 2012, 2008; Spencer et al., 2010; Theeler & Erickson, 2009). Mean scores on PTSD screening measures for those with a history of mTBI suggested clinically significant impairment. Similarly, one study reported that 45% of individuals with a history of mTBI obtained scores indicative of clinically significant impairment (Gaylord et al., 2008). Of the studies comparing PTSD in those with a history of mTBI to controls without a mTBI history, three reported non-significant differences between groups (Cooper, Nelson, et al., 2011; Gaylord et al., 2008; Theeler & Erickson, 2009) and one provided mixed results (Barnes et al., 2012). We found six primary studies reporting anxiety outcomes (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Drag et al., 2012; Kennedy et al., 2010; Spencer et al., 2010). Average self-reported anxiety symptoms were in the moderate–severe range in one study and in the clinically significant range in another (Benge et al., 2009; Spencer et al., 2010). Eight primary studies reporting depression outcomes (Barnes et al., 2012; Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Drag et al., 2012; Kennedy et al., 2010; Spencer et al., 2010; Swick et al., 2012) described average self-reported depression severity in the moderate range in one study (Benge et al., 2009), although average scores did not fall within the clinically significant range in another (Spencer et al., 2010). Of the two studies comparing depression symptoms for those with and without a history of mTBI (Barnes et al., 2012; Swick et al., 2012), neither reported significantly worse depression symptoms for mTBI participants. We found only two primary studies reporting substance use outcomes (Barnes et al., 2012; Nelson et al., 2012). One reported drug abuse/dependence in 9% of cases and another reported alcohol abuse/dependence in 28% (Barnes et al., 2012; Nelson et al., 2012). Both studies reported non-significant differences in prevalence compared with controls. Only one included study reported outcomes related to suicide (Barnes et al., 2012). This single study reported that the prevalence of suicidal ideation in this population was 25%, suicidal intent was 7%, and past suicide attempts was 4%, proportions that were not significantly different among controls without a history of mTBI.

We found six primary studies reporting other mental health outcomes (e.g., affective cluster scores, apathy, irritability, and frustration) (Barnes et al., 2012; Belanger et al., 2011; Benge et al., 2009; Cooper et al., 2010; Kennedy et al., 2010; Schiehser et al., 2011). The prevalence of Axis I disorder in mTBI populations was reported to be 50–78% in two studies, although these same studies had mixed results in terms of whether these estimates were significantly higher compared with controls without a history of mTBI (Barnes et al., 2012; Cooper et al., 2010). Self-reported irritability and frustration were both within the moderate to severe range in those with a history of mTBI in one study (Benge et al., 2009).

Functional/Social Outcome Results

We found 12 studies reporting functional/social outcomes. In two studies investigating employment status (Barnes et al., 2012; Toblin et al., 2012), one reported a rate of unemployment in the mTBI population of 20%, which was not significantly different than the rate in non-mTBI controls (Barnes et al., 2012). The other reported that odds of missing more than 2 days of work, difficulty carrying a heavy load in the past month, and difficulty performing physical training in the past month as indicators of employment outcomes were significantly increased compared with a non-mTBI group (Toblin et al., 2012). Ten studies reported sleep outcomes for Veterans and members of the military (Belanger et al., 2011; Benge et al., 2009; Coldren et al., 2012; Cooper, Kennedy, et al., 2011; Kelly et al., 2012; Kennedy et al., 2010; Lew et al., 2010; Patil et al., 2011; Ruff et al., 2008; Ruff, 2009). Of the two studies comparing participants with and without a history of mTBI, three of six sleep outcomes were significantly worse for those with a history of mTBI, and the others were approximately equivalent across groups (Coldren et al., 2012; Kelly et al., 2012). Only one study reported prevalence of sleep disturbance, estimated at 13% (less than 4 hr of sleep per night) and 23% (more than 2 hr sleep loss per night) for active duty military personnel within 10 days of injury (Coldren et al., 2012). Notably, self-reported sleep disturbance and fatigue ranged from approximately "mild" to "very severe" depending on the sub-population with a history of mTBI (e.g., those with and without PTSD), indicating clinically significant impaired sleep for at least some Veterans and members of the military with a history of mTBI (Belanger et al., 2011; Benge et al., 2009; Cooper, Kennedy, et al., 2011; Kennedy et al., 2010; Patil et al., 2011; Ruff et al., 2008; Ruff, 2009). Only one study reported social outcomes as indicated by lack of emotional support and marital status (Barnes et al., 2012). This study reported non-significant differences between mTBI and non-mTBI participants. The prevalence of lack of emotional support was reported to be 26% for Veterans with a history of mTBI.

Service Usage/Costs Results

We found seven studies that described service usage by Veterans with a history of mTBI, and no studies that reported costs associated with mTBI (Belanger et al., 2010; Coldren et al., 2012; Cooper et al., 2010; Gaylord et al., 2008; Kelly et al., 2012; Swick et al., 2012; Toblin et al., 2012). None of the studies comparing participants with a history of mTBI with those without a history of mTBI (Coldren et al., 2012; Cooper et al., 2010; Gaylord et al., 2008; Kelly et al., 2012) or to those with moderate/severe TBI history (Belanger et al., 2010) reported statistically significant differences on any service usage outcomes. One study reported that participants with a history of mTBI were prescribed an average of 18 medications, while participants without a history of mTBI were prescribed an average of five medications; no *p*-value was reported (Swick et al., 2012). Prevalence of current counseling by those with a history of mTBI was reported to be approximately 4–6%, and current mental health medication was 4–5% in two studies of the same population (Coldren et al., 2012; Kelly et al., 2012).

DISCUSSION

We found 31 studies examining the effects of mTBI history in Veteran and military populations. Several studies indicated that Veterans with a history of mTBI often report cognitive problems, but objective cognitive deficits did not differ consistently in studies that compared similar groups of deployed Veterans with and without mTBI history. We found similar results in studies of mental health outcomes, with non-significant differences across comparison groups. Physical symptoms were commonly reported by those with a history of mTBI, although a unique association with mTBI history was unclear. Studies of functional and social outcomes suggested that one fifth to one quarter of Veterans with a history of mTBI experienced unemployment, sleep disturbance, or lack of emotional support, although duration of symptoms and differences from those without mTBI history was not addressed in these studies. Finally, a variety of factors may affect the long-term resource needs of OEF/OIF/OND Veterans, including comorbid conditions and other consequences of deployment that may not be uniquely or solely related to having experienced an mTBI. The strength of evidence is very low due to inconsistent findings, methodologic shortcomings of many studies, and variation in outcomes considered and outcome measurement approaches. Therefore, conclusions drawn from this body of literature are uncertain and should be interpreted with caution.

Although the overall strength of evidence evaluating outcomes following mTBI in Veteran or military populations is very low (Guyatt et al., 2011), the findings are remarkably consistent with higher quality civilian literature (Carroll et al., 2004; Dikmen et al., 2009). Both bodies of research suggest that many health consequences resolve within the first few months following injury, often within hours or days, and suggest that, although objective cognitive impairment resolves quickly, subjective cognitive complaints may linger for years for some individuals who experience mTBI (Carroll et al., 2004; Dikmen et al., 2009). Specifically, reviews indicate that, although some impairment in memory and global cognitive functioning may be present for individuals with mTBI within a week of injury, these effects are no longer present after 7 days post-injury (Belanger & Vanderploeg, 2005), and most functional impairment resolves within a month for adults with a history of mTBI (Carroll et al., 2004). Even though the strength of evidence in civilian populations is higher, there is not enough information to identify how factors such as time since injury, mechanism of injury, service era, or number of mTBIs influence long-term outcomes. Additionally, the nature of war and attention to military-related mTBI has changed substantially in recent years, very likely influencing methods of selecting participants, defining mTBI, and measuring exposures and outcomes in newer versus older studies. However, our use of the contemporary VA/DoD definition of mTBI helps ensure that this review addresses concerns specific to the current generation of military members and Veterans who have sustained mTBI.

Despite the very low strength of evidence from this body of literature, implications for clinical care warrant consideration. Some symptoms that patients ascribe to mTBI history (e.g., non-specific, subjective cognitive complaints) may be related to comorbid mental or physical health concerns, or to other factors such as combat stress, readjustment to civilian life following deployment, or injury beliefs and perceptions. Difficulties related to post-deployment adjustment underscore the need to engage recently returned Veterans and members of the military quickly in efforts to identify physical and mental health problems and provide appropriate re-integration services. Patients should be encouraged to engage in treatment for these comorbid concerns with the best available treatments (e.g., evidence-based treatment of PTSD, substance use disorders, headaches, sleep disorders, and other post-deployment concerns). The current evidence base suggests that objective cognitive deficits are not common, particularly more than three months after injury. Therefore, should individuals with a history of mTBI experience ongoing cognitive deficits following first-line treatment for co-occurring symptoms and disorders such as PTSD, further evaluation—neuropsychological, neurological, and/or imaging—might be warranted.

The available literature consists of observational studies providing very low strength evidence (Guyatt et al., 2011). There was no evidence for some outcomes of interest such as cost. Inadequate accounting for time since injury and number of mTBI events limits the conclusions that can be drawn from many studies, and participants may be unable to accurately recall symptoms and timeframes so long after one (or more) mTBI events. Very few studies reported the prevalence of outcomes, instead reporting mean scores for the entire study group, limiting the ability to accurately describe the population and estimate service needs. Few studies reported their outcome selection and reporting rationale, and many relied on clinical datasets, which are generally not maintained for research purposes, making it impossible to know whether outcomes were chosen based on *a priori* hypotheses or significant findings. Although many of the included studies relied on well-validated measures commonly used with Veteran/military populations, many of the clinical outcomes relied solely on self-report, often single questionnaire items. Self-report data is often the only way to assess certain outcomes such as pain. However, a review of the civilian literature suggests that self-reported deficits are more likely to be reported by individuals with a history of mTBI compared with objective outcomes, and that mTBI evaluations associated with potential financial compensation are commonly associated with worse self-reported outcomes (Carroll et al., 2004). Because participants are rarely blinded to study hypotheses, self-reported outcomes should be interpreted with greater caution than objective findings evaluated by blinded outcome assessors.

Although a strength of this review was the use of clear criteria for defining mTBI, most studies did not assess or report imaging results, and those that did were inconsistent in their inclusion of participants with positive imaging results; therefore, we were not able to apply exclusion criteria based on positive imaging as is recommended by the VA/DoD criteria for mTBI. Additionally, because of our reliance on a stringent definition of mTBI, we excluded many studies that purported to study mTBI and may contribute to the TBI knowledge base, but did not meet the criteria for this report. Consequently, this report provides information on mTBI according to one definition and should not be viewed as all-encompassing. Findings from other systematic reviews on mTBI history in civilian populations should be considered for a more complete understanding of mTBI consequences.

Future primary research should clearly report criteria used to define mTBI, including assessment and reporting of imaging results. Additionally, future reviews should consider examination of differences in outcomes based on definitional criteria for mTBI, as it is possible that less stringent criteria could be associated with different results. Research investigating the possible effect of multiple mTBI events is needed, as many studies noted that individual Veterans often experienced more than one mTBI, although few examined this variable as a possible moderator of outcomes. Future research should take advantage of available VA and DoD data that includes time-since-injury information. Future studies should not only report mean scores for subgroups, but also report proportions of individuals with clinically significant impairment. For cognitive outcomes in particular, impairment is ideally determined not only by standardized scores within a certain range, but also by comparison to pre-injury functioning. Studies should report this intra-individual change as part of any cognitive findings so that accurate estimates of mTBI-related cognitive impairment are reported. Additionally, future studies should use objective and validated assessments, blinded outcome assessors, patient blinding to study hypotheses, and accounting for compensation factors whenever possible to reduce bias associated with outcome assessment. Future research should use commonly used outcome assessment tools to facilitate the combination of results across studies for meta-analytic purposes. There is a pressing need for large cohort studies of Veterans with and without mTBI history that prospectively collect data on all key risk and protective factors and outcomes of interest including variables such as service era. Such studies would be relatively costly but would result in higher-quality evidence on which more definitive conclusions could be based.

CONCLUSION

It is difficult to draw firm conclusions overall about the effects of mTBI history in Veteran and military populations, given the very low strength of evidence. The literature reviewed here is relatively consistent with findings from the more methodologically rigorous, prospective, longitudinal studies conducted in civilian populations. Both bodies of literature suggest that, although some adverse outcomes occur for a significant portion of individuals who have a history of mTBI, most objective results (e.g., objective cognitive test results), on average, are not significantly different from control participants, and deficits that are present shortly following injury most often resolve within hours to months. This literature on Veterans and members of the military provides very low strength evidence that many have physical and mental health symptoms, but it is not clear that those with a history of mTBI experience more or higher severity symptoms than those without a history of mTBI, suggesting that outcomes may be influenced by other deployment-related conditions such as PTSD. Included studies did not provide adequate data on percentages of patients with persistent symptoms, and a lack of significant mean differences does not preclude the possibility that some individuals could experience substantial, persistent effects related to mTBI history. The studies included in this report did not provide consistent evidence for potential moderators of mTBI outcomes. Overall, providers and researchers are cautioned that these results are very tentative due to the very low strength evidence of included studies.

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